सीएसआईआर-भारतीय समवेत औषध संस्थान, जम्मू - 180001

CSIR-Indian Institute of Integrative Medicine, Jammu - 180001

वार्षिक प्रतिवेदन 2024–25

ANNUAL REPORT 2024-25

CONTENTS

2024-2025

निदेशक की कलम

मुझे सीएसआईआर-भारतीय समवेत औषध संस्थान (सीएसआईआर-आईआईआईएम), जम्मू की वर्ष 2024-25 के लिए वार्षिक रिपोर्ट प्रस्तुत करते हुए गर्व की अनुभूति हो रही है। यह वर्ष केंद्रित वैज्ञानिक जांच, सार्थक उद्योग की विशेषता रही है जुड़ाव और निरंतर क्षमता-निर्माण, अनुसंधान में उत्कृष्टता को मूर्त सामाजिक प्रभाव में बदलने के हमारे संस्थान के मिशन को दर्शाता है।

वर्ष 2024-25 के दौरान, सीएसआईआर-आईआईआईएम ने भारत में 10 नए पेटेंट और विदेश में 21 पेटेंट दायर किए, जो नवाचार और बौद्धिक संपदा सृजन के प्रति हमारी प्रतिबद्धता को रेखांकित करता है। हमारे शोधकर्ताओं ने प्रतिष्ठित पत्रिकाओं में 164 वैज्ञानिक प्रकाशन प्रकाशित किए, जिनका औसत प्रभाव गुणांक 3.9 रहा। यह हमारे विज्ञान की गुणवत्ता, प्रासंगिकता और दृश्यता का सशक्त संकेतक है।

साझेदारी और संसाधन जुटाने के मोर्चे पर, संस्थान ने बाह्य वित्तपोषित परियोजनाओं (ईसीएफ) के अंतर्गत ₹7.4 करोड़ प्राप्त किए । नए ग्राहकों को जोड़ा और सात उद्योगों के साथ समझौता ज्ञापनों पर हस्ताक्षर किए, जिससे अनुवादक अनुसंधान और प्रौद्योगिकी परिनियोजन के लिए पाइपलाइन और अधिक सुदृढ़ हुई। शोध सहयोगों के माध्यम से हमें लगभग 50 लाख रुपये भी मिले, जो सीएसआईआर-आईआईआईएम की क्षमताओं में बढ़ते विश्वास को दर्शाता है।

राष्ट्रीय प्राथमिकताओं के अनुरूप कौशल विकास और नवाचार को सुदृढ़ करने के लिए हमने 15 से अधिक कौशल-विकास कार्यक्रम आयोजित किए, जिनसे 750 से अधिक प्रतिभागियों को व्यवहारिक प्रशिक्षण, क्षमता-निर्माण और अनुसंधान उन्मुख अनुभव का लाभ मिला। संस्थान ने वर्ष के दौरान 20 से अधिक कार्यक्रमों की मेजबानी की, शिक्षाविदों, उद्योग और सरकारी हितधारकों को एक साथ लाया गया। माननीय केंद्रीय मंत्री और सीएसआईआर के उपाध्यक्ष, डॉ. जितेंद्र सिंह की गरिमामयी उपस्थिति से हमें विशेष रूप से सम्मानित किया गया, जिनका प्रोत्साहन उत्कृष्टता की हमारी खोज को प्रेरित करता रहा है।

मैं वार्षिक रिपोर्ट के संपादक और संबंधित टीम को भी बधाई देना चाहूंगा हमारे अनुसंधान, नीतिगत पहलों, सामाजिक कार्यक्रमों और अन्य के पूर्ण स्पेक्ट्रम पर कब्जा करना वार्षिक रिपोर्ट 2024-25 में वैज्ञानिक गतिविधियाँ। यह व्यापक दस्तावेज हमारे हितधारकों के लिए एक मूल्यवान संदर्भ और हमारी टीमों के लिए प्रेरणा के स्रोत के रूप में काम करेगा।

ये उपलब्धियां हमारे वैज्ञानिकों, छात्रों, कर्मचारियों और साझेदारों के सामूहिक समर्पण का परिणाम हैं। भविष्य की और देखते हुए सीएसआईआर-आईआईआईएम प्रभावशाली अनुसंधान, रणनीतिक सहयोग और जिम्मेदार नवाचार के माध्यम से एकीकृत चिकित्सा को आगे बढ़ाना जारी रखेगा, जिसे राष्ट्रीय स्वास्थ्य,जैव-अर्थव्यवस्था , सामाजिक कल्याण और वैश्विक वैज्ञानिक नेतृत्व में योगदान सुनिश्चित हो सके।

डॉ. जबीर अहमद

From Director's Desk

It is with great pride that I present the Annual Report of CSIR–Indian Institute of Integrative Medicine (CSIR-IIIM), Jammu for the year 2024–25. This year has been characterized by focused scientific inquiry, meaningful industry engagement and sustained capacity-building, reflecting our institute's mission to translate excellence in research into tangible societal impact.

During 2024–25, CSIR-IIIM filed 10 new patents in India and 21 patents abroad, underscoring our commitment to innovation and intellectual property creation. Our researchers published 164 scientific publications in reputed journals, achieving an average impact factor of 3.9, a strong indicator of the quality, relevance and visibility of our science.

On the partnership and resource mobilization front, the institute secured ₹7.4 crore in Externally Funded Projects (ECF), added new clients and signed MoUs with seven industries, further strengthening the pipeline for translational research and technology deployment. We also received nearly ₹50 lakh through research collaborations, reflecting growing confidence in CSIR-IIIM's capabilities.

In alignment with national priorities in skill development and innovation, we organized more than 15 skill development programs, benefitting over 750 participants through hands-on training, capacity-building and research-oriented exposure. The institute hosted over 20 events during the year, bringing together academia, industry and government stakeholders. We were especially honored by the gracious presence of Hon'ble Union Minister and Vice President, CSIR, Dr. Jitendra Singh, whose encouragement continues to inspire our pursuit of excellence.

I would also like to congratulate the Editor of the Annual Report and the concerned team for capturing the full spectrum of our research, policy initiatives, societal programmes and other scientific pursuits in the Annual Report 2024–25. This comprehensive documentation will serve as a valuable reference for our stakeholders and a source of motivation for our teams.

These achievements are the result of the collective dedication of our scientists, students, staff and partners. As we look ahead, CSIR-IIIM will continue to advance integrative medicine through impactful research, strategic collaborations and responsible innovation, contributing to national health, bioeconomy, societal and global scientific leadership.

Dr. Zabeer Ahmed

RESEARCH ACTIVITIES

QAZI NAVEED AHMED

Dr. Qazi Naveed Ahmed (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

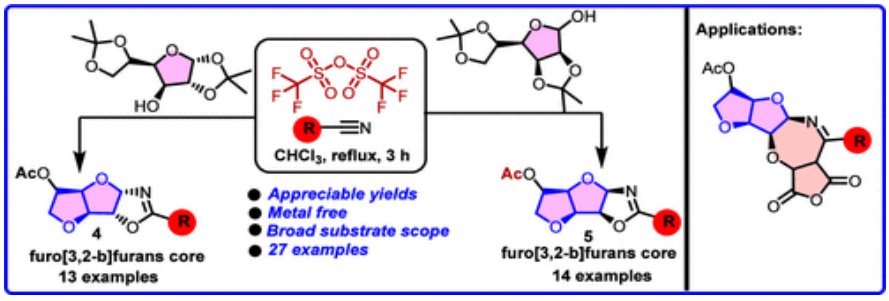
Publications:

Triflic Anhydride-Mediated Approach to Furo[3,2-*b*]furans from Diacetonide Protected Furanoses

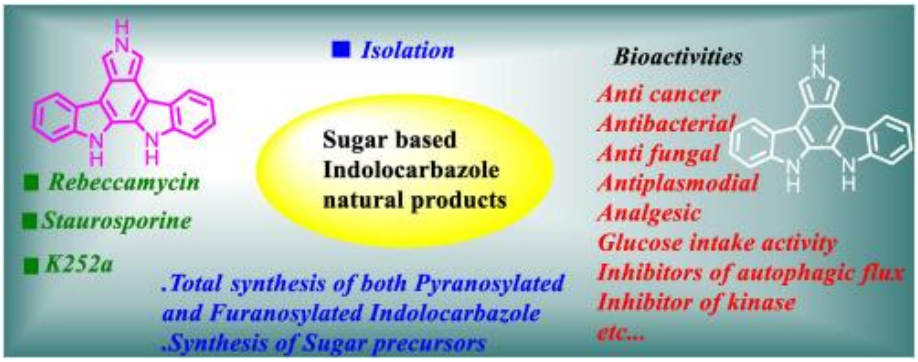
TA Dar, MY Bhat, N Sakander, QN Ahmed

The Journal of Organic Chemistry 89 (18), 13016-13025

Trifluoromethanesulfonic anhydride (Tf_2O) exhibits excellent reactivity as an electrophile, serving as a highly versatile reagent in diverse chemical transformations. Herein, we report an operationally simple, efficient, unique, and practical one-step strategy for synthesizing diverse valuable structures bearing furo[3,2-*b*]furans core leveraging Tf_2O's promoted reactivity of nitriles with diacetonide protected furanose. Furthermore, we demonstrate the potential of furo[3,2-*b*]furan as a precursor for complex structures through 1,3-dipolar cycloaddition.



[An account on pyranosylated and furanosylated indolocarbazole natural products]
N Sakander, F Hussain, QN Ahmed
Tetrahedron 162, 134116



The synthesis of biologically active indolocarbazole natural products has garnered significant attention due to their diverse pharmacological properties. This review provides a comprehensive overview of synthetic methodologies employed in the preparation of indolocarbazole derivatives, highlighting key strategies and recent advancements. Emphasis is placed on the isolation and synthesis of naturally occurring sugar based indolocarbazoles, such as rebeccamycin, staurosporine and K252a. Furthermore, the biological activities of these compounds and their potential applications in drug discovery are discussed. The present review aims to enhance understanding of sugar based indolocarbazole synthesis and inspire further research in this area.

[Synthesis of unsymmetric phosphorotrithioates by sequential coupling of 1, 1-dichloro-N, N-diethylphosphanamine with thiols and sulfenyl chloride]
F Hussain, S Mahajan, S Ahmed, QN Ahmed
Organic & Biomolecular Chemistry 22 (10), 2007-2011

Herein, we present the first, one-step, direct synthesis of unsymmetric phosphorotrithioates through a process involving sequential coupling of 1,1-dichloro-*N*,*N*-diethylphosphanamine with thiols and sulfenyl chloride. This method showcases excellent functional group tolerance, substrate compatibility, and mild reaction conditions, offering a streamlined approach for the challenging phosphorotrithioate synthesis. Additionally, the applicability of this method can be extended to the synthesis of mixed phosphoroselenodithioates.

[Unravelling the Spectrum: Recent Advances in the Synthesis of Phosphorous–Selenium Bonded Compounds]
F Hussain, N Sakander, S Mahajan, QN Ahmed

ChemistrySelect 9 (40), e202402367

The review highlights diverse methodologies from metal catalysis to photochemistry and electrochemical pathways providing insights into synthetic techniques that drive advancements in biochemistry and medicinal research.

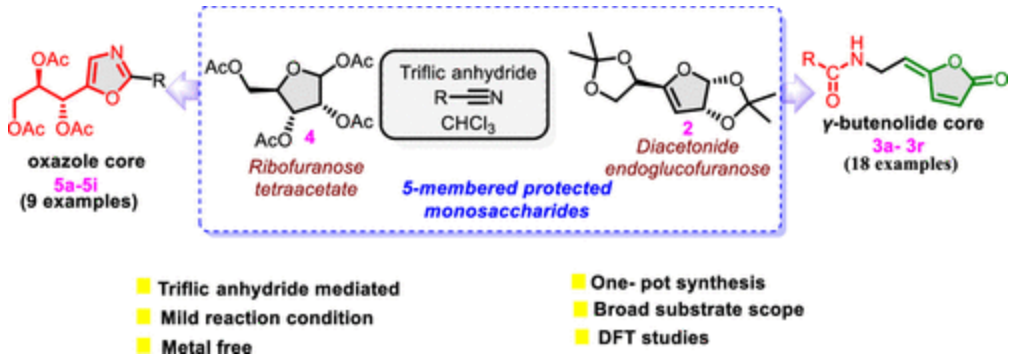
Abstract

The review delves into a rich tapestry of methodologies, spanning from the utilization of metals to the manipulation of light, and from electrochemical pathways to additive-free approaches. Its aim is to meticulously compile and elucidate these diverse pathways, providing comprehensive insights into the strategies and methodologies utilized for synthesizing these compounds. By undertaking this exploration, its goal is to shed light on the intricate techniques employed in this field, consequently driving notable progress across disciplines ranging from biochemistry to medicinal research.

Triflic Anhydride-Mediated Unprecedented Reactivities of Diacetonide Endoglucofuranose and Ribose Tetracetate: Direct Access to γ-Butenolides and Oxazoles

N Sakander, TA Dar, QN Ahmed

The Journal of Organic Chemistry 89 (18), 13308-13318



Herein, we present two unprecedented reactions for the synthesis of γ-butenolides and oxazoles, leveraging Tf_2O's promoted reactivity of nitriles with diacetonide endoglucofuranose and 1,2,3,5-tetra-*O*-acetyl-β-d-ribofuranose. This method is highly efficient and straightforward and employs a one-step,

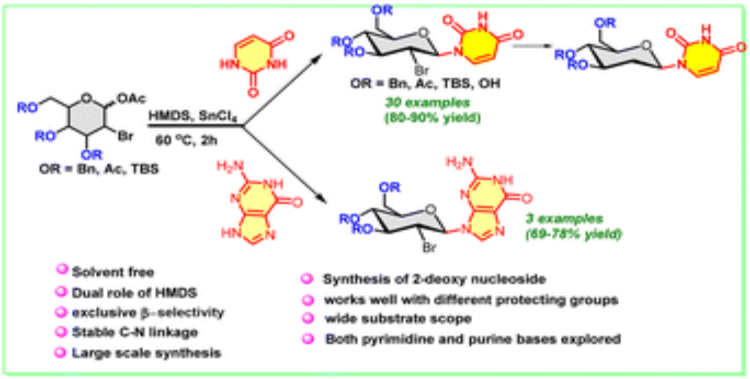
metal-free protocol. It is effective with both aromatic and aliphatic nitriles and demonstrates a broad substrate scope. Our approach provides a versatile and practical pathway for the synthesis of structurally diverse compounds, significantly expanding the utility of Tf_2O in synthetic chemistry.

Stereoselective synthesis of 2-deoxy-2-bromo-hexopyrano-β-nucleosides: solvent-free Lewis acid catalysis

N Sakander, QN Ahmed

Organic & Biomolecular Chemistry 23 (3), 579-588

An expedient solvent-free synthesis of 2-deoxy-2-bromo-hexopyrano-β-nucleosides stereo- and regioselectively from protected glycals and unactivated nucleobases using cheaper and easily available reagent systems has been developed. The synthesis is mediated by a Lewis acid and is solvent-free. The substrate scope of the reaction was analysed with ether, ester and silyl-protected glycals as donors and different pyrimidine and purine bases were taken into consideration. This method further finds application in the synthesis of 2-deoxynucleosides.

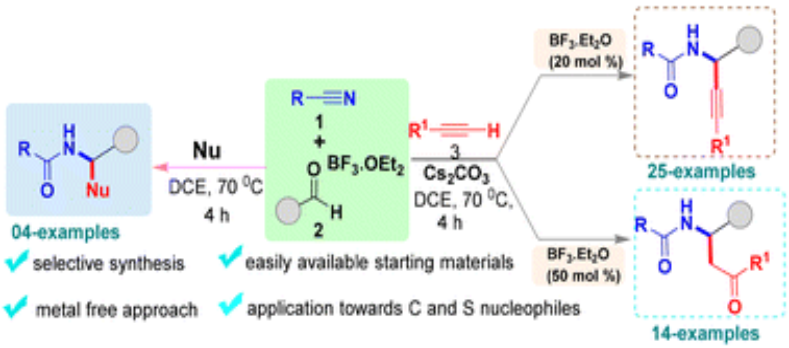


BF3· Et2O controlled selective synthesis of α-substituted propargylamides and β-(N-acylamino) ketones: application to carbon and sulphur nucleophiles

S Ahmed, JS Banday, QN Ahmed

Organic & biomolecular chemistry 23 (4), 803-808

This study presents a metal-free and selective synthesis of α-substituted propargylamides and β-(*N*-acylamino) ketones utilizing nitriles, aldehydes, and terminal alkynes, mediated by $BF_3{\cdot}Et_2O$. The unique reactivity of $BF_3{\cdot}Et_2O$, a potent Lewis acid, facilitates precise control over product formation. By adjusting the concentration of $BF_3{\cdot}Et_2O$, we can effectively manipulate reaction pathways and selectivity, ensuring the desired products are achieved with enhanced specificity. Notably, this method demonstrates remarkable tolerance to other nucleophiles, such as β-naphthol, indole, arenes and thiol, thereby enabling the synthesis of a diverse array of functionally significant compounds. This approach offers a valuable tool for advancing synthetic methodologies in organic chemistry.



BF 3· Et 2 O-promoted unconventional reactions of 2-oxoaldehyde: access to 4-amidooxazoles and β-keto amides/sulphonamides

AH Padder, B Ghora, F Hussain, MY Bhat, QN Ahmed

Organic & Biomolecular Chemistry 23 (8), 1809-1813

This study investigates the potential of boron trifluoride etherate ($BF_3 \cdot OEt_2$) to trigger unprecedented reactions of 2-oxoaldehydes with nitriles and amides/sulphonamides. In contrast to the mechanism in conventional reactions, the α-carbonyl group in 2-oxoaldehydes induces a cyclization pathway to be followed when reacting with nitriles, yielding 4-amidooxazoles. Additionally, reactions with weak nucleophiles produce β-keto amides/sulphonamides. $BF_3 \cdot OEt_2$ catalysis offers a novel, efficient, and operationally simple synthetic route to these valuable compounds, showcasing the versatility of boron Lewis acids in organic transformations.

Synthesis, application and regulatory consideration for the development of quinone-based drugs

N Sakander, A Ahmed, QN Ahmed

Quinone-Based Compounds in Drug Discovery, 271-282

Quinone-based compounds represent a broad spectrum of pharmaceutical applications, including anti-cancer, anti-malarial and anti-inflammatory treatments as the pharmaceutical industry continues to explore the therapeutic potential of quinones, as well as their use in humans Regulatory agencies play an important role in ensuring their safety and efficacy. This chapter provides an overview of regulatory considerations for quinone-based products, and highlights key aspects such as preclinical testing, clinical trials, and post-marketing evaluations. The development and approval of quinone-based drugs requires a comprehensive regulatory framework in order to ensure the safety and its effectiveness.

Total Synthesis of Natural Products and Medicinally Important Molecules from Glycals

N Sakander, QN Ahmed

Glycals and their Derivatives, 137-173

Glycals have been widely used as a versatile building block for the synthesis of C-glycosides and branched sugars and the total synthesis of natural products and biologically active molecules. The versatility of glycals is due to their easy availability and the presence of a ring oxygen connected to a double bond. The inherent chirality of glycals also makes them valuable

for the synthesis of various natural products and pharmaceuticals. This chapter provides a detailed overview of the progress made in synthesizing natural products and important molecules derived from glycals.

Copper (i)-catalyzed coupling of alkynyl glycosides: synthesis of buta-1, 3-diyne-linked disaccharides and dinucleosides

JS Banday, S Ahmed, QN Ahmed

Organic & Biomolecular Chemistry 23 (11), 2615-2619

Herein we report copper-catalyzed coupling of alkynyl glycosides facilitating the synthesis of buta-1,3-diyne-linked disaccharides. The reaction is characterized by mild conditions employing eco-friendly reagents, resulting in good yields of the desired products. This methodology exhibits significant functional group tolerance with broad substrate scope. Furthermore, we have successfully extended this approach to the synthesis of buta-1,3-diyne-linked dinucleosides.

Patents:

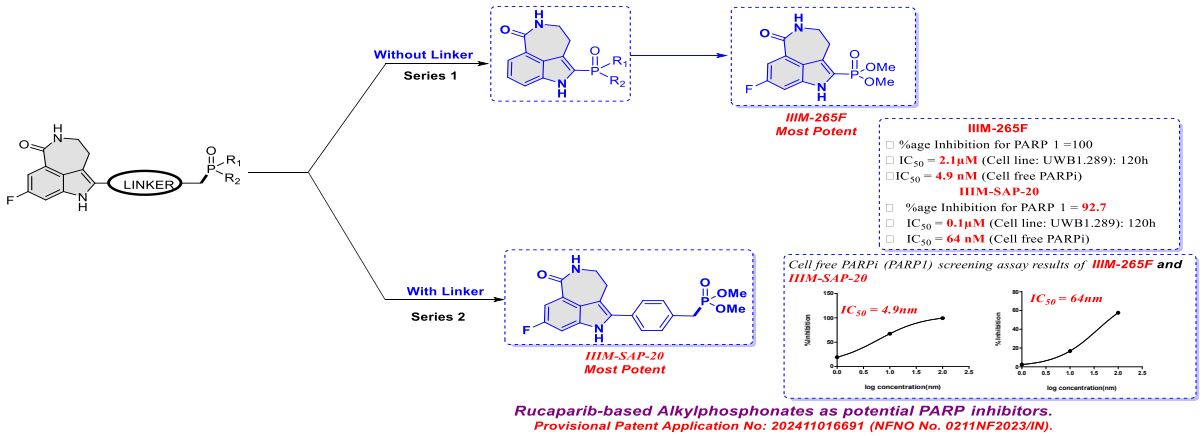
A process for the preparation of n4-hydroxycytidine and its derivatives

D MUKHERJEE, QN AHMED, A AHMED, JS BANDAY

US Patent App. 18/558,928

2. Scientific work done:

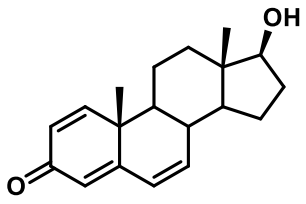
The research team is actively engaged in a series of experimental and analytical tasks. It is described as follows:



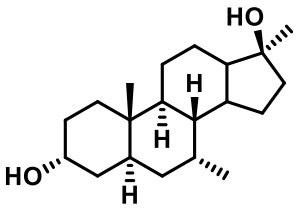
Poly (ADP-ribose) polymerase (PARP) inhibitors have emerged as an important class of targeted agents for cancers harboring defects in homologous recombination repair. In this study, a novel series of Rucaparib-based alkylphosphonates was designed and synthesized to enhance potency and PARP-trapping ability. Structural modifications were explored in two directions: Series 1 without linker units, in which the alkylphosphonate moiety was directly attached to the Rucaparib scaffold, and Series 2 containing flexible linkers to modulate binding interactions and pharmacokinetic properties. Both series yielded potent inhibitors, with IC50 values in the low nanomolar range against PARP1. Among these, IIIM-265F demonstrated exceptional potency (IC_{50} = 4.9 nM) and robust PARP1 trapping efficiency,

outperforming Rucaparib in comparable assays. Structure–activity relationship analysis revealed that alkylphosphonate substitution contributed to enhanced binding affinity, while linker incorporation modulated conformational flexibility and protein–ligand interactions. The lead compounds also maintained favorable biochemical selectivity profiles, suggesting reduced off-target effects. These findings underscore the potential of alkylphosphonate-functionalized Rucaparib derivatives as promising next-generation PARP inhibitors with applications in BRCA-mutant and homologous recombination-deficient cancers. The results pave the way for further optimization and preclinical evaluation of this chemotype in targeted oncology drug development.

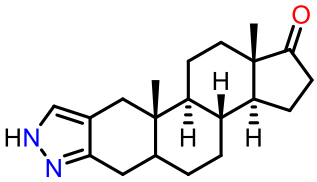
- In the project entitled **Synthesis of Reference Standards and *in-vitro* and *in-vivo* studies (PK studies) on the metabolites and long-term metabolites**, we have synthesized and dispatched 100 mg of the following compounds: 17 keto proatonozol, Bolasterone, ATD metabolite, GHRP1(2-7) to National dope testing Laboratory



ATD Metabolite



Bolasterone



17-Keto Prostanozol

- **Project Title: Strategic S-P Bond Forming Bio-orthogonal Functionalization Technique: A Systematic Analysis, Standardization and Site-Specific Coupling Strategy for Carrier Drugs Conjugates**

This project successfully developed a novel bioorthogonal strategy for S–P bond formation between phosphines and sulfonothioates under mild, additive-free conditions. Through the conversion of thiols to sulfonothioates, efficient coupling with phosphoramidite and phosphite compounds featuring sp^3 - carbons was demonstrated, offering broad substrate compatibility and excellent functional group tolerance. A standardized sequential coupling protocol was also established, enabling the one-pot synthesis of mixed unsymmetrical thiophosphonates, selenophosphonates, phosphorotrithioates, and phosphoroselenodithioates. Key achievements include the coupling of sulfonothioates with natural product derivatives and the successful replacement of sulfur with selenium within the phosphorothioate framework, extending the chemical diversity and utility of these scaffolds. Additionally, a cyclic sulfoxide-based coupling strategy was introduced, achieving clean formation of phosphorothioate derivatives without side products — a limitation encountered with acyclic sulfoxides and sterically hindered systems like lipoic acid. To broaden synthetic access, diverse designer P(III) reagents were screened, resulting in a general, versatile S/Se–P bondforming protocol applicable to alcohols, aromatics, heteroaromatics, and aliphatic substrates. These innovations collectively provide robust methodologies for site-specific conjugation, bioconjugation, drug development, and targeted therapeutics, with promising applications in antibody-drug conjugates (ADCs), prodrug systems, and next-generation biomolecular modifications.

PARVINDER PAL SINGH

Dr. Parvinder Pal Singh (Principal Scientist) with his Research Group

1. Publications/Patents

Publications:

- Negi A, Perveen S, Kour H, **Singh PP***, Sharma R. Keeping Up with the Q's: Mechanistic Insights and Validation of Quinoline and Quinazoline Scaffolds as Potent Drugs against Tuberculosis. *J. Med. Chem*. **2025** Jun 10. doi:https://10.1021/acs.jmedchem.4c02568PMID: 40493800.
- Akhter Z, Sharma S, Anand R, Samad M, Verma PK, **Singh PP***. Chemoselective benzylic Csp^3-H bond oxidation reactions catalyzed by the $Ag^{II}(bipy)_2S_2O_8$ complex. *Org Biomol Chem.***2025** May 28;23(21):5224-5233. doi: https://10.1039/d4ob02074j PMID: 40331291.
- Kaur S, Sharma K, Sharma A, Sandha KK, Ali SM, Ahmed R, Ramajayan P, **Singh PP**, Ahmed Z, Kumar A. Fluvoxamine maleate alleviates amyloid-beta load and neuroinflammation in 5XFAD mice to ameliorate Alzheimer disease pathology. *Front Immunol.***2024** Jul 29;15:1418422. doi: https://10.3389/fimmu.2024.1418422 PMID: 39136022
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- Cham PS, Singh A, Jamwal A, Singh R, Anand R, Manhas D, Sharma S, Singh VP, Nandi U, Singh SK, **Singh PP***. Discovery of Ring-Annulated Analogues of Cannabidiol as Potential Anticancer Agents: Synthesis and Biological Evaluation. *ACS. Med. Chem. Lett*. **2024,** Oct 17;15(11):1832-1842; doi: https://10.1021/acsmedchemlett.4c00233 PMID: 39563806.
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Patents:

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- Riyaz Ahmed, Gulshan Kumar, Sheena Mahajan, Praveen Verma, Pankaj Cham, Qazi Naveed Ahmed, D. Reddy, Ravi Shankar & Singh, **Parvinder Pal Singh*.** - process for the preparation of nafamostat, camostat and their derivatives. **Application PCT/IN2023/050123;US20250188022A1;JP2025505208A.**

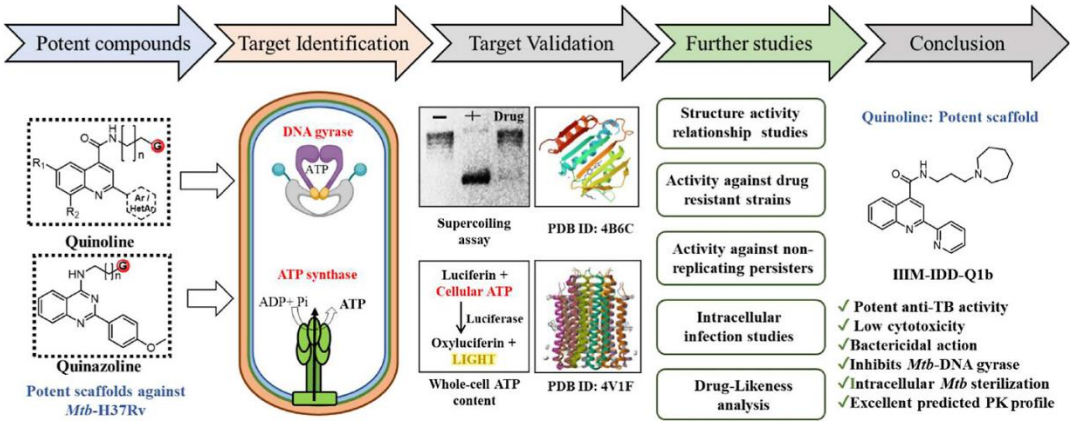
2. Scientific work done:

A brief description of research accomplishments attained during this reporting time:

1) **Keeping Up with the Q's: Mechanistic Insights and Validation of Quinoline and Quinazoline Scaffolds as Potent Drugs against Tuberculosis:** *J. Med. Chem*. **2025** Jun 10. doi:https://10.1021/acs.jmedchem.4c02568 PMID: 40493800

   The eternal battle against Tuberculosis necessitates the discovery of novel drugs. This study outlines identification of novel quinoline and quinazoline series through phenotypic screening of the ChemDiv library against Mtb-H37Rv. The potency, mode of inhibition, and structure–activity relationships around the confirmed actives are described. Both series disclosed potent anti-TB

activity against drug-sensitive and drug-resistant strains. The quinazoline series exhibited cytotoxicity toward eukaryotic cells, while the quinoline compounds were both active and noncytotoxic. Among the quinoline compounds, the most promising molecule, IIIM-IDD-Q1b, exhibited an IC90 of 9.7 µg/mL, with no observed cytotoxicity, resulting in a high safety index (>10). It demonstrated potent intracellular inhibition against Mtb as made evident by fluorescence imaging and CFU enumeration. Mode-of-action studies revealed that quinoline compounds target DNA gyrase, while quinazoline series target ATP synthase. Overall, both series demonstrate promising biological properties and a favorable pharmacokinetic profile. Further medicinal chemistry optimization could enhance and boost the anti-TB potency of the identified compounds. This work was done in collaboration with Dr. Rashmi's Group.

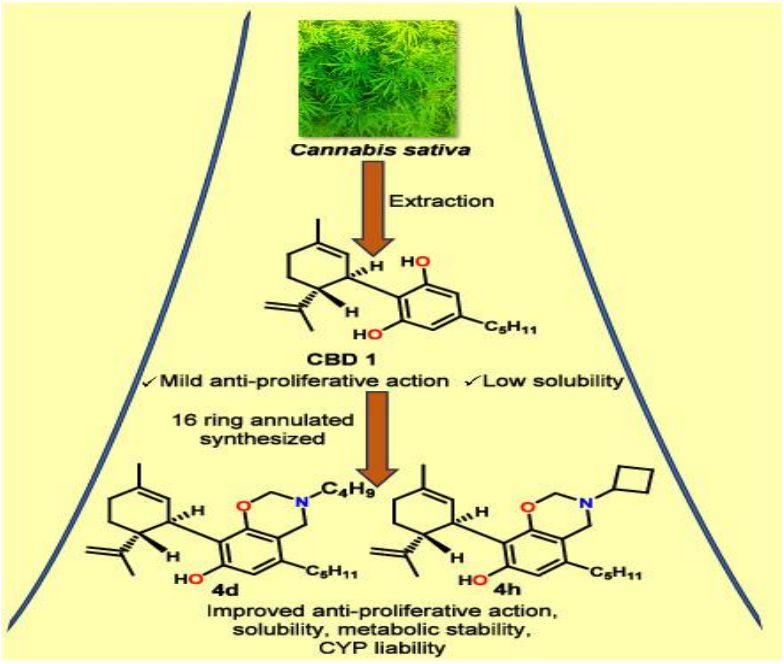


2) **Chemoselective benzylic Csp^3–H bond oxidation reactions catalyzed by the AgII(bipy)$_2$S$_2$O$_8$ complex:** *Org Biomol Chem.***2025** May 28;23(21):5224-5233

Herein, we present a silver-catalyzed method for the selective oxidation of benzylic Csp3 –H bonds with high chemo- and regioselectivity. This approach efficiently converts toluenes into aldehydes, benzylic methylenes into ketones, and benzylic alcohols into aldehydes. Notably, the reaction also proceeds under in situ generated catalytic conditions and is scalable. Control experiments further indicate that water serves as the oxygen source in the oxidized products.

3) **Discovery of Ring-Annulated Analogues of Cannabidiol as Potential Anticancer Agents: Synthesis and Biological Evaluation:** *ACS. Med. Chem. Lett*. **2024,** Oct 17;15(11):1832-1842;

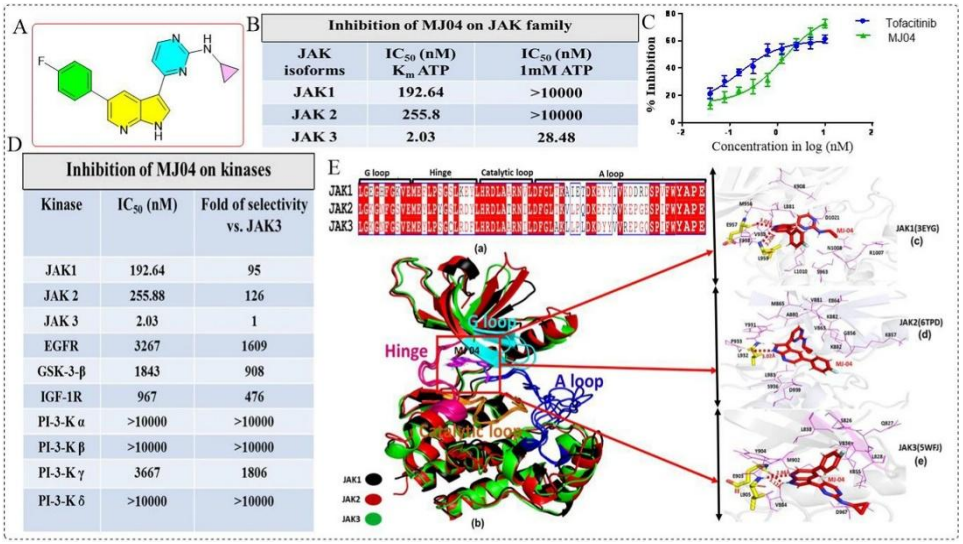
Cannabidiol (CBD) is a nonpsychoactive cannabinoid derived from *Cannabis sativa* and its potential therapeutic effects extend beyond its well-known antiepileptic properties. Exploring CBD and its analogues as anticancer agents has gained significant attention in recent years. In this study, a series of novel ring-annulated analogues of CBD with oxazinyl moiety were synthesized and evaluated for their antiproliferative effect. The analogues **4d** and **4h** demonstrate promising activity against breast and colorectal cancer. Furthermore, mechanistic insights revealed that the identified candidates arrest the G1 phase of the cell cycle and induce apoptosis via the mitochondrial pathway in breast cancer cell lines. Notably, CBD ring-annulated analogues **4d** or **4h** exhibit enhanced solubility, better metabolic stability, and lowered cytochrome P450 (CYP) inhibition liability compared to CBD. These multifaceted attributes highlight the potential of cannabinoid-based candidates for further preclinical development. This work was done in collaboration with Dr. Shashank's Group.



4) **Discovery of a novel and highly selective JAK3 inhibitor as a potent hair growth promoter:** *J Transl Med*. **2024** Apr 18;22(1):370.

JAK-STAT signalling pathway inhibitors have emerged as promising therapeutic agents for the treatment of hair loss. Among different JAK isoforms, JAK3 has become an ideal target for drug discovery because it only regulates a narrow spectrum of γc cytokines. Here, we report the discovery of MJ04, a novel and highly selective 3-pyrimidinylazaindole based JAK3 inhibitor, as a potential hair growth promoter with an IC_{50} of 2.03 nM. During in vivo efficacy assays, topical application of MJ04 on DHT-challenged AGA and athymic nude mice resulted in early onset of hair regrowth. Furthermore, MJ04 significantly promoted the growth of human hair follicles under ex-vivo conditions. MJ04 exhibited a reasonably good pharmacokinetic profile and demonstrated a favourable safety profile under in vivo and in vitro conditions. Taken together, we report MJ04 as a

highly potent and selective JAK3 inhibitor that exhibits overall properties suitable for topical drug development and advancement to human clinical trials.This work was done in collaboration with Dr. Jamal's Group.



B

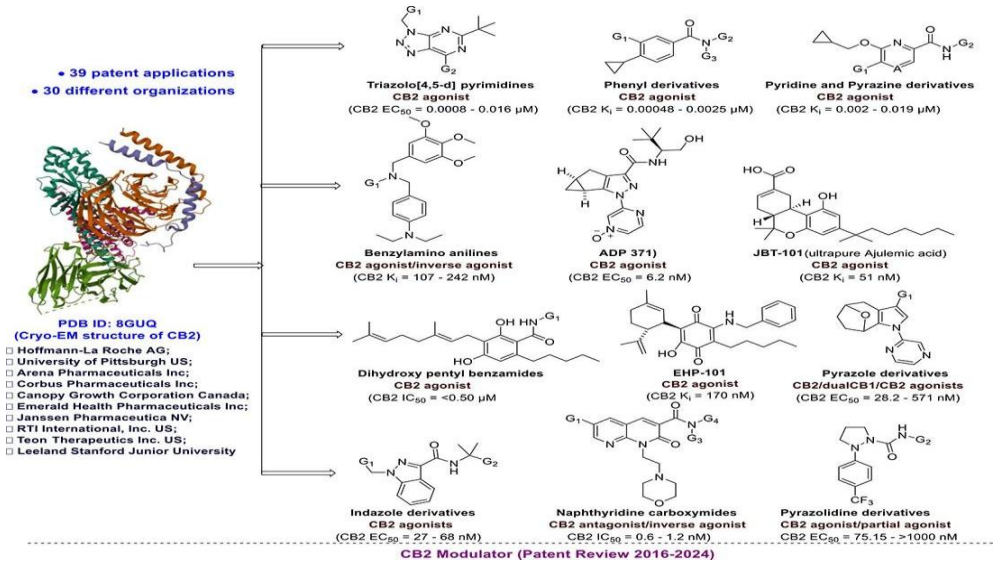
Inhibition of MJ04 on JAK family		
JAK isoforms	IC_{50} (nM) K_m ATP	IC_{50} (nM) 1mM ATP
JAK1	192.64	>10000
JAK 2	255.8	>10000
JAK 3	2.03	28.48

D

Inhibition of MJ04 on kinases		
Kinase	IC_{50} (nM)	Fold of selectivity vs. JAK3
JAK1	192.64	95
JAK 2	255.88	126
JAK 3	2.03	1
EGFR	3267	1609
GSK-3-β	1843	908
IGF-1R	967	476
PI-3-K α	>10000	>10000
PI-3-K β	>10000	>10000
PI-3-K γ	3667	1806
PI-3-K δ	>10000	>10000

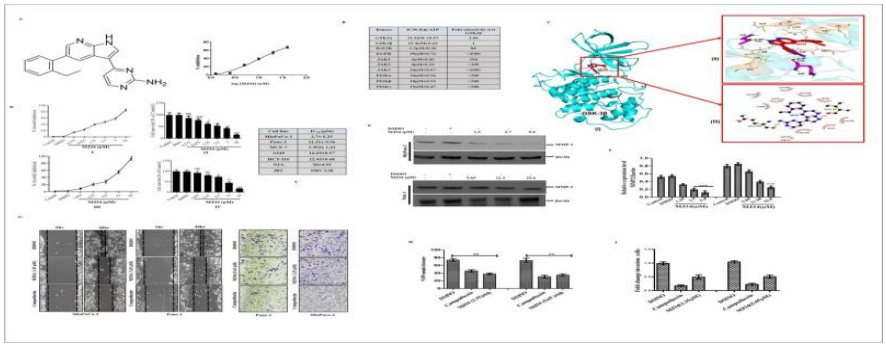
5) Cannabinoid receptor 2 (CB2) modulators: A patent review (2016–2024): *Bioorg Chem.***2024** Dec;153:107775.

Cannabinoid receptors CB1 and CB2 play critical roles in regulating numerous central and peripheral physiological activities. While efforts have been made to develop ligands for both CB1 and CB2 receptors, CB1 receptor ligands often have restricted use due to undesirable psychotropic side effects. Consequently, recent cannabis research has increasingly focused on CB2-specific ligands. Pharmacological agonists of CB2 receptors have shown potential in managing pain, inflammation, arthritis, neuroprotection, cancer, and other disorders. Despite several CB2 receptor ligands entering clinical trials, none have achieved market approval except natural cannabinoids and their derivatives, primarily due to insufficient CB2/CB1 receptor selectivity. However, new-generation ligands developed in recent years have demonstrated improved selectivity. This review covers patent literature on CB2 modulators from 2016 to 2024, highlighting the major advances in the field. During this period, the majority of research has concentrated on using CB2 modulators to alleviate inflammation and pain. Additionally, patents have explored CB2 modulators for a range of specific diseases, including: psychiatric and neuropsychiatric disorders, schizophrenia, multiple myeloma and osteoporosis, ocular inflammation and neuropathic Pain, cancer anorexia and weight loss, antioxidant and anti-aging agents, lymphocytopenia, hearing loss, Alzheimer's disease, cancer and non-malignant tumors. Notably, recent years have seen increased interest in CB2 antagonists/inverse agonists, with few candidates advancing to clinical studies. Significant progress has been made in the synthesis and modulation of selective CB2 agonists and antagonists, paving the way for future developments in CB2 modulators. This review provides insights and prospects for the continued evolution ofCB2-targeted therapies.



6) **Identification of a novel GSK3β inhibitor involved in abrogating KRas dependent pancreatic tumors in Wnt/beta-catenin and NF-kB dependent manner:** *Life Sci*. **2024** Aug 15;351:122840

Pancreatic cancer is an aggressive malignancy with a poor survival rate because it is difficult to diagnose the disease during its early stages. The currently available treatments, which include surgery, chemotherapy and radiation therapy, offer only limited survival benefit. Pharmacological interventions to inhibit Glycogen Synthase Kinase-3beta (GSK3β) activity is an important therapeutic strategy for the treatment of pancreatic cancer because GSK3β is one of the key factors involved in the onset, progression as well as in the acquisition of chemoresistance in pancreatic cancer. Here, we report the identification of MJ34 as a potent GSK3β inhibitor that significantly reduced growth and survival of human mutant KRas dependent pancreatic tumors. MJ34 mediated GSK3β inhibition was seen to induce apoptosis in a β-catenin dependent manner and downregulate NF-kB activity in MiaPaCa-2 cells thereby impeding cell survival and anti-apoptotic processes in these cells as well as in the xenograft model of pancreatic cancer. In vivo acute toxicity and in vitro cardiotoxicity studies indicate that MJ34 is well tolerated without any adverse effects. Taken together, we report the discovery of MJ34 as a potential drug candidate for the therapeutic treatment of mutant KRas-dependent human cancers through pharmacological inhibition of GSK3β.This work was done in collaboration with Dr. Jamal's Group.



RAVI SHANKAR

Dr. Ravi Shankar (Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Gulshan Kumar, Misbah Tabassum, Bhupesh K Sharma, Rajesh Kumar, Javeed Ahmad Tali, Davinder Singh, Ravindra K Rawal, Sanket K Shukla, **Ravi Shankar**, Design and Synthesis of C-8 spiro-isoxazoline analogues of 14-Deoxy-11, 12-didehydroandrographolide (14-DDA) for dual targeting of CDK4 and BCL2 mediated anticancer activity, Journal of Molecular structure, **2024**, 137072.
- Davinder Singh, Yashika Sharma, Divya Dheer, **Ravi Shankar**, Stimuli responsiveness of recent biomacromolecular systems (concept to market): A review, International Journal of Biological Macromolecules, **2024**, 129901.
- Bhupesh Kumar Sharma, Yashika Sharma, Manzoor Ahmed, Aarzoo Manzoor, Shaziya Choudhary, Ravindra K Rawal, **Ravi Shankar**. Design and synthesis of C-17 benzylidene derivatives of 14-deoxyandrographolide (14-DAG) and their TNF-α and IL-6 expression inhibitory activities. Journal of Molecular Structure, **2025**, 140770.

- Dolkar Rigzin, Gourav Paudwal, Davinder Singh, Chittaranjan Behera, Sumera Banoo Malik, Syed Mudassir Ali, Harjot Kaur Amit Nargotra, **Ravi Shankar**, Shashank K. Singh & Prem N. Gupta "Mechanistic Approach into 1, 2, 3-triazoles-based IIIM (S)-RS98 Mediated Apoptosis in Lung Cancer Cells." The AAPS Journal 27, no. 1 (**2025**): 35.

Patents:

- Gulshan kumar, Shazia Choudhary, Bhupesh Kumar Sharma, Alna Kuriyickal Martin, Yogesh sardana, Renuga Devi, Bokara Kiran Kumar, Manzoor Ahmed, Sanket Kumar Shukla, Qazi Naveed Ahmed, **Ravi Shankar**, Zabeer Ahmed, C-17 Benzimidazole, Benzothiazoles of 14-deoxy-11,12-didehydroandrographolide as a potential anti-viral agents and process for prepration, provisional patent, filed number :**0248NF2024**

2. Scientific work done:

- Design and Synthesis of C-8 spiro-isoxazoline analogues of 14-Deoxy-11, 12-didehydroandrographolide (14-DDA) for dual targeting of CDK4 and BCL2 mediated anticancer activity

14-Deoxy-11,12-didehydroandrographolide (14-DDA, 3), a secondary metabolite from *Andrographis paniculata* Nees, was modified to synthesise a new series of C-8 spiro-isoxazoline derivatives. Given the known anticancer potential of andrographolide derivatives, these compounds were evaluated against breast (MCF-7), lung (A549), pancreatic (MiaPaCa-2), and prostate (PC-3) cancer cell lines. Most derivatives showed greater activity than the parent molecules, with compound 4k being most potent in MCF-7 cells (IC_{50} = 3 μM). Mechanistic studies indicated that 4k induced ROS generation, reduced mitochondrial membrane potential, inhibited colony formation, and triggered apoptosis by downregulating BCl-2 and Cdk-4. These results highlight 4k as a promising anticancer lead with reduced in vitro toxicity.

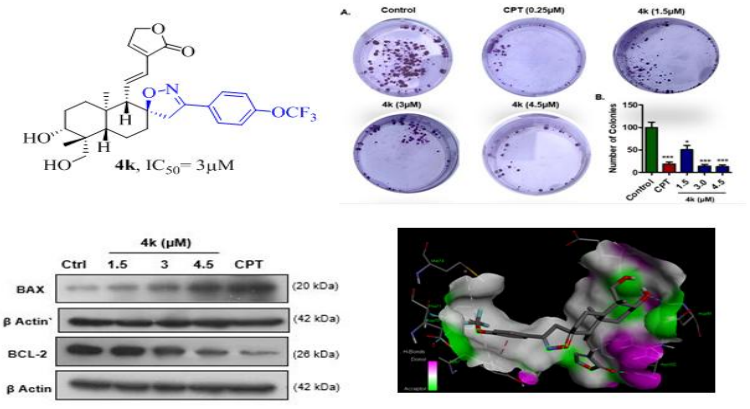


Figure 1: Synthesis of C-8-substituted spiroisoxazoline adducts of 14-DDA

- Design and Synthesis of C-17 benzylidene derivatives of 14-deoxyandrographolide (14-DAG) and their TNF-α and IL-6 expression inhibitory activities

  Benzylidene derivatives of 14-deoxyandrographolide (14-DAG) were synthesised in good to excellent yields and tested for anti-inflammatory activity. Most compounds were non-toxic and evaluated for nitric oxide (NO) inhibition in LPS-induced RAW 264.7 macrophages, with andrographolide as a reference. Compound 4e showed much stronger NO inhibition than andrographolide and was further tested for its effect on pro-inflammatory cytokines. It significantly reduced TNF-α levels (IC_{50} = 8.07 μM) compared to andrographolide (IC_{50} = 15.86 μM). Docking studies suggested strong hydrogen bonding and alkyl interactions of 4e with TNF-α. These results indicate 4e as a promising lead for developing new anti-inflammatory agents.

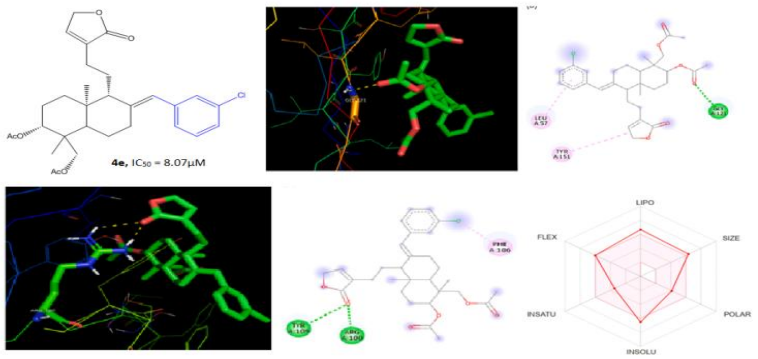


Figure 2: Synthesis of C-17 benzylidene derivatives of 14-deoxyandrographolide (14-DAG)

- C-17 Benzimidazole, Benzothiazoles of 14-deoxy-11,12-didehydroandrographolide as a potential anti-viral agents and process for prepration

  This work reports the design and synthesis of a novel compound, 3, 19-benzal-17-aldehyde-14-deoxy-11,12-didehydroandrographolide, with the C-17 position modified by a formyl or heteroaryl group to improve biological activity. The derivatives, prepared in good yield and purity, showed strong antiviral potential, especially those with a benzimidazole ring. Among them, IIIM(S)-RS-46 displayed potent activity against SARS-CoV-2, achieving 86% viral load reduction in animal models, highlighting its promise as a lead candidate for coronavirus therapy.

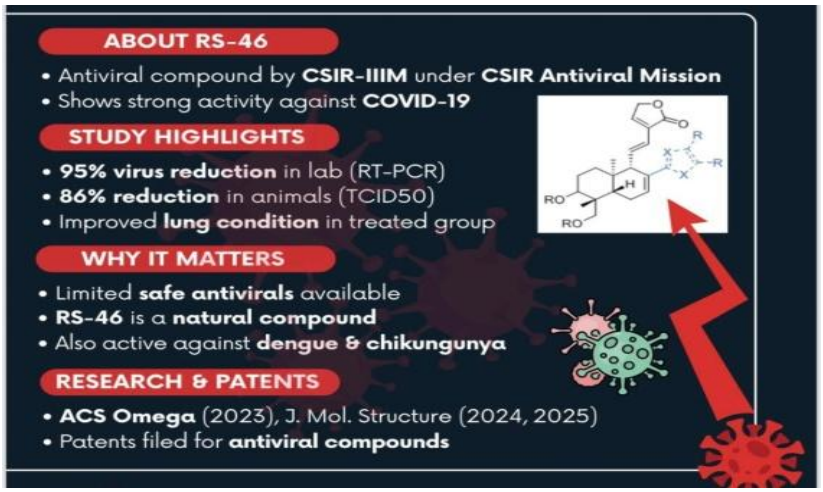


Figure 3: IIIM(S)RS-46 as potent inhibitor of SARS-CoV-2 (COVID-19)

- Mechanistic Approach into 1, 2, 3-triazoles-based IIIM (S)-RS98 Mediated Apoptosis in Lung Cancer Cells

  Lung cancer is the second most common cancer and the leading cause of cancer deaths worldwide, creating an urgent need for new treatments. 1,2,3-Triazole derivatives are emerging as promising anticancer agents. In this study, we tested our synthesised compound IIIM(S)-RS98 against various cancer cell lines and found it most effective against A549 lung cancer cells, with high selectivity over normal cells. IIIM(S)-RS98 induced apoptosis, increased ROS and nitric oxide, disrupted mitochondrial membrane potential, caused G1 cell cycle arrest, and reduced cell migration and colony formation. Mechanistic studies showed it suppressed the PI3K/p-Akt pathway, activated pro-apoptotic proteins, and triggered caspase-mediated apoptosis. Docking studies confirmed its strong binding to apoptotic target proteins, supporting its potential as a lead for lung cancer therapy.

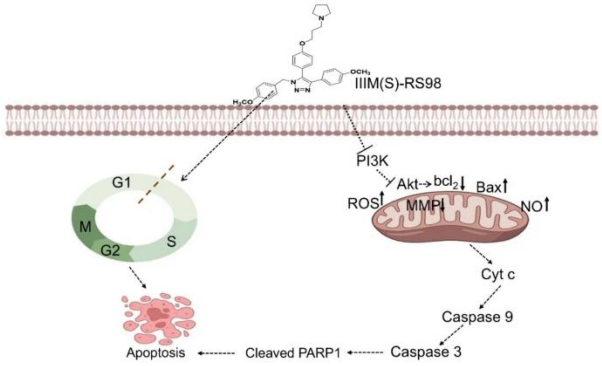


Figure 4: Mechanistic Pathway of (S)-RS98 1,2,3-Triazole–Induced Apoptosis in Lung Cancer Cells.

AMIT NARGOTRA

Dr. Amit Nargotra (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- MA Wani, P Kumari, A Nargotra. Machine learning framework coupled with CADD for predicting sphingosine kinase 1 inhibitors. Computers in Biology and Medicine (2025) 194, 110448
- H Kaur, M Gupta, Z Ahmed, A Nargotra. Psychoactive Plant Database: a phytochemical resource for neurological drug discovery. Frontiers in Pharmacology (2025) 16, 1569127
- R Dolkar, G Paudwal, D Singh, C Behera, SB Malik, SM Ali, H Kaur, A Nargotra, R Shankar, SK Singh, PN Gupta.Mechanistic Approach into 1, 2, 3-triazoles-based IIIM (S)-RS98 Mediated Apoptosis in Lung Cancer Cells. The AAPS Journal (2025) 27 (1), 35
- Manas Ranjan Barik, Harjot Kaur, Tanzeeba Amin, Harshita Tiwari, Gurleen Kour, Anindya Goswami, Zabeer Ahmed, Amit Nargotra. Network pharmacology and in vitro validation to elucidate the molecular mechanism of Boswellia serrata phytoconstituents on inflammation. Journal of Proteins and Proteomics (2024) 15 (3), 473-489
- Diksha Kumari, Harjot Kaur, Tashi Palmo, Amit Nargotra, Kuljit Singh. Exploring natural product library as potential target against sterol C-24 methyltransferase protein of Leishmania donovani. Natural Product Research (2024)
- Dixhya Rani, Diksha Kumari, Anil Bhushan, Vishwani Jamwal, Bashir Ahmad Lone, Gunjan Lakhanpal, Amit Nargotra, Kuljit Singh, Prasoon Gupta. Design, synthesis, and biological

evaluation of eugenol-isoxazoline hybrid derivatives as potential anti-leishmanial agents. Journal of Molecular Structure (2024) 1308, 138105

2. Scientific work done:

I. Classification & Prediction of Sphingosine Kinase 1 (SK1) Inhibitors

Sphingosine kinase 1 (SphK1) plays a pivotal role in cancer progression, metastasis, and chemotherapy resistance, making it a key target for therapeutic interventions in cancer, cardiovascular diseases, and inflammatory disorders. To explore potential inhibitors of SphK1, a comprehensive dataset of 655 molecules with reported IC_{50} values was curated from 32 peer-reviewed publications (2009–2024) and 2 patents. Chemical structures were drawn using ChemDraw and converted to SMILES format for machine learning (ML) model development. After removing duplicate entries, the dataset was refined to 535 unique molecules, enhancing the quality and reliability of the predictive models. A total of 200 molecular descriptors were computed using the RDKit module in Python, and the top 25 were selected via the Boruta feature selection method.

Machine learning models including Decision Trees (DT), Support Vector Machines (SVM), K-Nearest Neighbors (KNN), Random Forest (RF), Linear Regression (LR), and AdaBoost (ABDT) were trained on these selected descriptors. Among them, RF demonstrated the highest performance with an accuracy of 89.81%, specificity of 90%, and F1-score of 0.88, while ABDT followed closely with 87.94% accuracy and 88.34% recall. Statistical evaluation of all models employed metrics such as accuracy, precision, recall, F1-score, and Matthews correlation coefficient (MCC). For external validation, a dataset of 2,173 molecules from the Synthetic Library of Col Sir R.N. Chopra Repository at IIIM Jammu was screened, resulting in the identification of 187 potential SphK1 inhibitors.

Top-ranked hits were further subjected to molecular docking and 100 ns molecular dynamics (MD) simulations. Compounds IS01027, IS01265, and IS00998 remained stably bound within the sphingosine-binding pocket of SphK1, showing minimal RMSD fluctuations. MM/GBSA free energy calculations confirmed PF-543 as the most potent binder (–101.25 kcal/mol), followed by IS01265 (–94.52 kcal/mol), IS01027 (–85.53 kcal/mol), and IS00998 (–82.57 kcal/mol). The stability of these complexes was attributed to key hydrogen bonds, hydrophobic interactions, and π–π stacking. Additionally, all four ligands exhibited favorable drug-like properties, with IS00998 particularly noted for its high solubility and moderate oral bioavailability.

This integrated approach combining cheminformatics, machine learning, molecular docking, and molecular dynamics simulations provides a powerful framework for identifying and optimizing novel SphK1 inhibitors. The study has been published in *Computers in Biology and Medicine* under the title "Machine Learning Framework Coupled with CADD for Predicting Sphingosine Kinase 1 Inhibitors." The flowchart of the entire work is presented in figure 1.

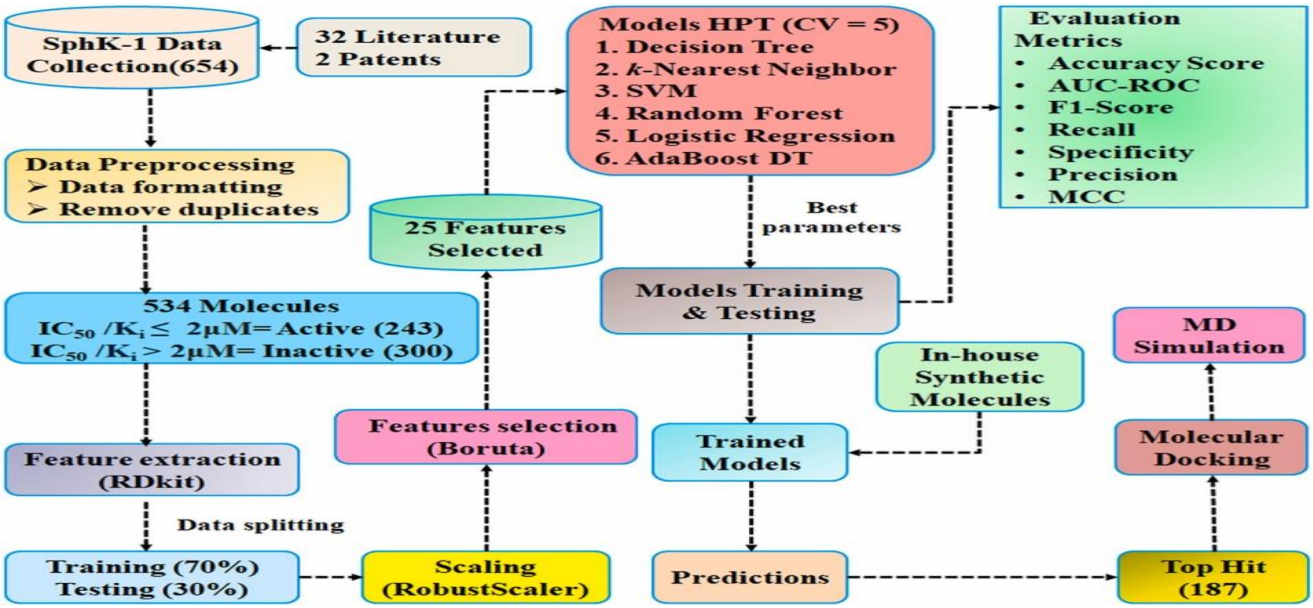


Figure 1: Flow chart for Classification & Prediction of Sphingosine Kinase 1 (SK1) Inhibitors.

II. Molecular docking study of *Tinospora cordifolia* compounds against covid-19 main protease (Mpro) target protein.

Molecular docking was conducted on the COVID-19 main protease (Mpro) (PDB ID: 6LU7, chain A) for understanding the mode of interactions. A total of 20 molecules were docked, and the docking results highlighted significant interactions between the main protease and the N3 inhibitor as well as the given set of test compounds. Among all, TC-34 showed the best binding (Figure 2). This study shows the potential of TC-34 and other top-ranking compounds as promising candidates for inhibiting COVID-19 main protease, paving the way for further experimental validation.

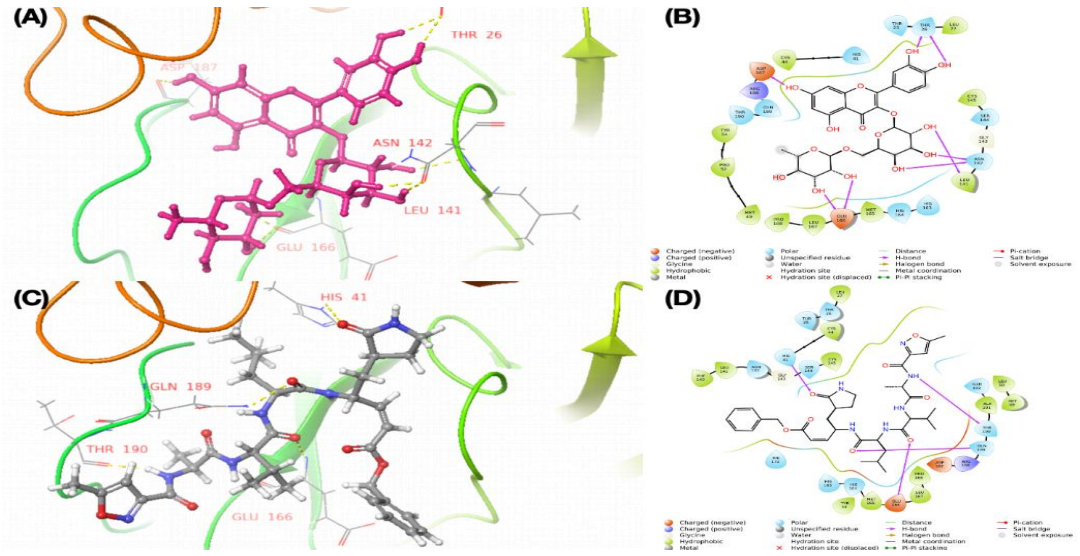


Figure 2. Compound TC-34: (A) 3D interaction and (B) 2D interaction diagrams showing hydrogen bond interactions with key residues Glu166, Asp187, Asn142, Leu141, and Thr26 (yellow dashed lines) within the active site of the

COVID-19 main protease. The N3 inhibitor: (C) 3D interaction and (D) 2D interaction diagrams highlight hydrogen bonding interactions with residues His41, Glu166, Gln189, and Thr190 in the active site of the same target protein.

The Psychoactive Plant Database (PPD) is a groundbreaking resource that bridges the gap between traditional medicine and modern drug discovery. By cataloging over 7,000 bioactive compounds from 124 medicinal plants, the database provides a comprehensive platform for exploring the therapeutic potential of psychoactive plants. The integration of ethnopharmacological knowledge, computational analyses, and detailed compound data makes it an invaluable tool for researchers targeting neurological and neurodegenerative diseases. Key features, such as ADMET profiling, molecular docking studies, and phytochemical classification, shows the therapeutic potential of plant-derived compounds. The PPD's emphasis on traditional knowledge ensures that valuable insights from Indigenous and ancient practices are preserved and used in modern research. By facilitating the discovery of novel neuroprotective agents, PPD paves the way for safer and more effective treatments for neurological disorders, addressing an urgent global need. A snapshot of the database

III. Development of Psychoactive Plant Database is given below as Figure 3.

This work is now published and the PPD database is copyrighted by CSIR-IIIM Jammu [Psychoactive Plant Database: a phytochemical resource for neurological drug discovery; https://doi.org/10.3389/fphar.2025.1569127.]

Figure 3. Home page of psychoactive plant database along with recent activities, plant gallery, statistical of database data, search engine and 124 plant list.

IV. In Silico to In Vitro Pipeline for TNF-α Inhibitors

This study focuses on targeting Tumor Necrosis Factor-alpha (TNF-α), a key pro-inflammatory cytokine implicated in systemic inflammation and various pathological conditions. Bridging computational modeling with experimental validation, the research aims to identify potent TNF-α inhibitors through an integrative approach. The in silico workflow included molecular docking to assess binding affinity and orientation, 100 ns molecular dynamics (MD) simulations to evaluate the stability of protein-ligand complexes, and MM/GBSA free energy calculations to quantify binding strengths. Based on computational outcomes, promising candidate molecules were selected for in vitro biological assays to ensure translational relevance and experimental validation of the predictions. The study involved comprehensive in silico analyses, including re-docking with co ligand, mutagenesis analysis, and detailed interaction profiling of shortlisted lead compounds. The workflow is given in figure 4.

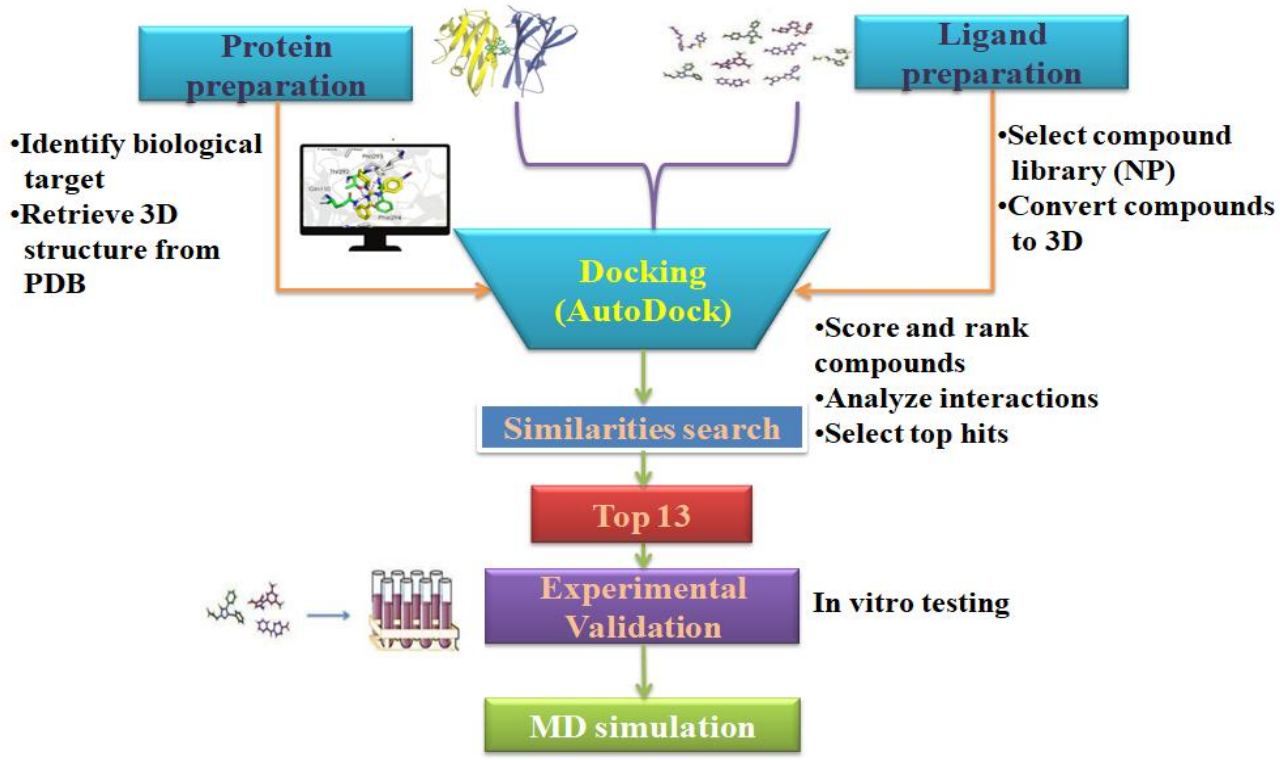


Figure 4. Flowchart for identification of potent TNF-α inhibitors from in-house compound library

V. Molecular docking study for PIK3CA target protein.

The present study aims to investigate the cytotoxic potential of institutional molecule based on 1,2,3 triazole [IIIM(S)-RS98] on multiple cancer cell lines in collaboration with Pharmacology Division. Molecular docking study of the test compound exhibited binding affinity of -9.9 kcal/mol for the PIK3CA target protein and identified as PIK3CA inhibitor. Notably, the compound demonstrated stable hydrogen interaction with apoptotic target protein PIK3CA and results were significant with respect to our biological results.

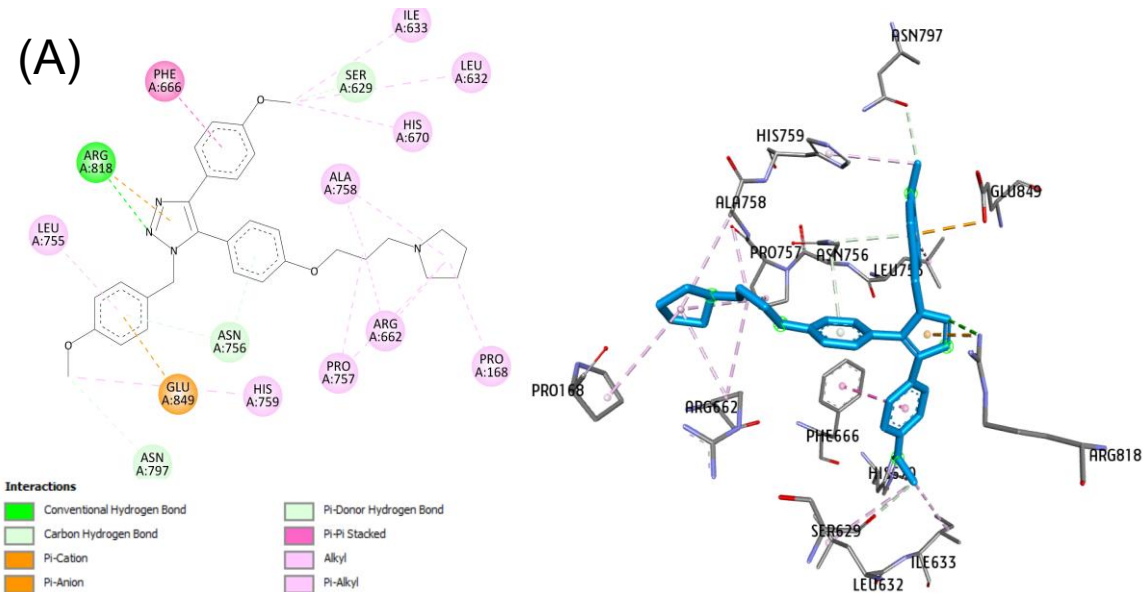


Figure 5. 2D and 3D interaction models of the compound with PIK3CA (A, B) target protein, displaying binding affinities of -9.9 kcal/mol. Various protein-ligand interactions are depicted using different color legends.

JASHA S. MOMO HMUNGSHEL ANAL

Dr. Jasha S. Momo Hmungshel Anal (Sr. Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Puneet Kumar, Kanhaiya Kumar, and **Jasha Momo H. Anal**. Isolation, Pharmacological Properties, Chemical Syntheses, and Biosynthesis of Isobavachalcone (IBC): A Historical Perspective for the Future Direction. *Mini-Reviews in Organic Chemistry* (2025).
- **Jasha Momo H. Anal**, Lobeno Mozhui, and Samuel Lalthazuala Rokhum. Unveiling the therapeutic potential of insect-derived natural products for drug discovery. *Future Journal of Pharmaceutical Sciences* 11, no. 1 (2025): 2.
- Kumar, Puneet, Sapna Saini, Anjali Gangwar, Rashmi Sharma, and **Jasha Momo H. Anal**. Antibacterial activity of structurally diverse natural prenylated isobavachalcone derivatives.*RSC Advances* 14, no. 45 (2024): 32771-32785.
- Choudhary, Rupali, Puneet Kumar, Sanket K. Shukla, Asha Bhagat, **Jasha Momo H. Anal**, Gurleen Kour, and Zabeer Ahmed. Synthesis and potential anti-inflammatory response of indole and amide

derivatives of ursolic acid in LPS-induced RAW 264.7 cells and systemic inflammation mice model: Insights into iNOS, COX2 and NF-κB. *Bioorganic Chemistry* 155 (2025): 108091.

- Shahi, Ashutosh, Rakshit Manhas, Srija Bhattacharya, Arti Rathore, Puneet Kumar, Jayanta Samanta, Manish Kumar Sharma, Avisek Mahapa, Prasoon Gupta, and **Jasha Momo H. Anal**. Synthesis and antibacterial potential of novel thymol derivatives against Methicillin-resistant *Staphylococcus aureus* and *P. aeruginosa* pathogenic bacteria. *Frontiers in Chemistry* 12 (2024): 1482852.
- Lone, Waseem Iqbal, Jagdish Chand, Puneet Kumar, Yashi Garg, Zabeer Ahmed, Debaraj Mukherjee, Anindya Goswami, and **Jasha Momo H. Anāl**. Discovery of colchicine aryne cycloadduct as a potent molecule for the abrogation of epithelial to mesenchymal transition via modulating cell cycle regulatory CDK-2 and CDK-4 kinases in breast cancer cells. *Bioorganic Chemistry* 150 (2024): 107581.
- Kumar, Puneet, Ruhi Singh, Deepak Sharma, Qazi Parvaiz Hassan, Boobalan Gopu, and **Jasha Momo H. Anal.** Design, synthesis, and biological evaluation of chalcone acetamide derivatives against triple negative breast cancer. *Bioorganic & Medicinal Chemistry Letters* 107 (2024): 129795.

2. Scientific work done:

I. Antibacterial activity of structurally diverse natural prenylated flavonoid derivatives

We synthesized a series of isobavachalcone (IBC) derivatives (IBC-2 to IBC-10) from *Psoralea corylifolia* and evaluated their antibacterial activity against Gram-positive and Gram-negative pathogens. **IBC**, **IBC-2**, and **IBC-3** showed potent bactericidal effects, with IBC-3 demonstrating broad-spectrum activity, minimal cytotoxicity, and a high selectivity index (>10). Mechanistic studies and SEM analysis indicated disruption of bacterial cell wall/membrane, while ADME-Tox profiling suggested good drug-likeness and oral bioavailability. Structure–activity relationship insights highlight key functional groups driving antibacterial potency, supporting their potential as leads for new antibiotic development.

II. Design, synthesis, and evaluation of indole- and amide-modified ursolic acid derivatives as anti-inflammatory agents: mechanistic insights from LPS-induced macrophages and systemic inflammation models

We isolated ursolic acid (UA) from *Lavandula angustifolia* marc and synthesized novel derivatives by introducing an indole ring at C-3 and an amide group at C-17 to overcome its poor solubility and bioavailability. Among them, UA-1 showed markedly enhanced anti-inflammatory activity, with a 7–8 fold lower IC_{50} for NO inhibition than UA, strong interactions with TNF-α and NF-κB, and significant suppression of pro-inflammatory cytokines and oxidative stress while upregulating IL-10. In vivo, UA-1 reduced systemic inflammation, tissue damage, and serum biochemical markers, while exhibiting improved solubility and favorable drug-like properties. These findings highlight UA-1 as a promising lead with superior therapeutic potential over native UA.

III. **Synthesis and evaluation of novel colchicine derivatives with selective antiproliferative activity against melanoma cells**

We synthesized novel colchicine derivatives via a multi-component reaction and evaluated their anticancer potential against lung, breast, and melanoma cell lines. Among them, compound 3g showed superior activity against melanoma, with a two-fold higher selectivity index than colchicine, inhibiting colony formation (62.5%) and cell migration (69%). In silico studies confirmed its strong binding interactions at the colchicine site on tubulin, supporting its mechanism of microtubule disruption. These results highlight compound 3g as a promising lead with improved efficacy and reduced toxicity compared to colchicine.

IV. **Isobavachalcone (IBC): Isolation, pharmacology, chemical synthesis, and biosynthesis—past achievements and future direction**

Isobavachalcone (IBC), a prenylated flavonoid from *Psoralea corylifolia*, exhibits diverse pharmacological activities including antibacterial, anti-inflammatory, anticancer, antiviral, neuroprotective, and bone-protective effects. This mini-review highlights its isolation, bioactivities, chemical synthesis, and biosynthesis, emphasizing structural features that make IBC a promising scaffold for future drug discovery and therapeutic applications.

V. **Exploring the therapeutic potential of insect-derived natural products in drug discovery**

Insect-derived natural products represent an underexplored reservoir of bioactive compounds with significant therapeutic potential, as illustrated by cantharidin from blister beetles leading to the FDA-approved drug Ycanth. Their structural diversity and historical use in traditional medicine highlight their promise for drug discovery, calling for greater global research efforts to harness these metabolites for addressing unmet medical needs and advancing human health.

YOGESH PANDHARINATH BHARITKAR

Dr. Yogesh P. Bharitkar (Sr. Scientist) with his Research Group

1. Publications/patents:

Publications:

S.No	Authors	Title of the Article	Year of Pubn	Name of Journal	Country	Vol No. Issue, Pages	DOI
1.	Chetan Paul Singh, Rohit Singh, Ghulam Mustafa, Ramajayan Pandian, Ravindra S. Phatake, **Yogesh P. Bharitkar***.	Discovery of structurally importantcycloartane-type triterpenes from *Dysoxylumbinectariferum* leaves and their anti-inflammatory activity	2024	Journal of Molecular Structure	Internati onal	1309, 138183	https://doi.org/10.1016/j.molstruc.2024.138183

2.	Diksha Kumari, Parampreet Kour, Chetan Paul Singh, Rinku Choudhary, Syed Mudassir Ali, Sagar Bhayye, **Yogesh P. Bharitkar,** *Kuljit Singh*	Anhydroparthenin as a dual-target inhibitor against Sterol C-24 methyltransferase and Sterol 14-α demethylase of Leishmania donovani: A comprehensive in vitro and in silico study	2024	International Journal of Biological Macromolecules	International		https://doi.org/10.1016/j.ijbiomac.2024.132034
3.	Aliya Tabassum, , Harshad B. Bhore, Jayanta Samanta, Anil Kumar Katare, Ravindra S. Phatake**Yogesh P. Bharitkar***	Diversity-oriented semi-synthesis of Alantolactone and Isoalantolactone hybrids employing azomethine ylide cycloaddition pathway	2025	Journal of Molecular Structure	International	1333, 141729.	https://doi.org/10.1016/j.molstruc.2025.141729
4.	Aliya Tabassum, Diksha Kumari, Harshad B Bhore, Tashi Palmo, Initha Venkatesan, Jayanta Samanta, Anil Kumar Katare, Kuljit Singh, **Yogesh P. Bharitkar***	Synthesis of novel spiroisoxazolidino hybrids of alantolactone and isoalantolactone via 1, 3 dipolar nitrone cycloaddition and its antimicrobial Evaluation	2025	Bioorganic Chemistry	International	154, 108087	https://doi.org/10.1016/j.bioorg.2024.108087
5.	Aliya Tabassum, Harshad B Bhore, Jayanta Samanta, Anil Kumar Katare, **Yogesh P. Bharitkar***	Discovery of two new tirucallane-type triterpenes anomers from *Toona ciliata*	2024	Natural Product Research	International		https://doi.org/10.1080/14786419.2024.2429115
6.	Chetan Paul Singh, Aliya Tabassum, Ravindra S. Phatake, **Yogesh P. Bharitkar***	Diversification of structurally significant cycloartane-type triterpenes: exploiting beddomeilactone	2025	Natural Product Research	International		https://doi.org/10.1080/14786419.2024.2429115
7.	Diljeet Kumar, Manzoor Ahmed, Nusrit Iqbal Andrabi, Chetan Paul Singh, Diksha Saroch, **Yogesh P Bharitkar**,	Anti-inflammatory and anti-oxidant potential of Dispiro-indanedione hybrid of parthenin via regulating Nrf2 and NF-κB/MAPK pathways	2025	European Journal of Pharmacology	International	996, 177547	https://doi.org/10.1016/j.ejphar.2025.177547

	Gurleen Kour, Sreedhar Madishetti, Asha Bhagat, Sanket K Shukla, Zabeer Ahmed						
8.	Clement Odunayo Ajiboye, Dorcas Olufunke Moronkola, Arfan Khalid, Akinbo Akinwumi Adesomoju, Sagar S Bhayye, **Yogesh P. Bharitkar**, Govind Yadav, Mahendra Kumar Verma	Isolation, characterization, HPLC quantification, in-vitro and in-silico evaluations of coumarins and coumarolignans from *Blighia unijugata* stem with their chemotaxonomic significance	2025	Biochemical Systematics and Ecology	International	120, 104950	https://doi.org/10.1016/j.bse.2024.104950
9	Jyoti Chandan, Suruchi Gupta, Zabeer Ahmed, Shashank Kumar Singh, Puneet Kumar, Rupali Choudhary, Sundeep Jaglan, **Yogesh Bharitkar**, Gurleen Kour, Ekta Nehra, Ravail Singh	Metabolite profiling and bioactivity of fungal endofauna from *Xiphinemanuragicum* in the rhizosphere of *Withaniasomnifera*	2025	Environmental Science and Pollution Research	International	32, 8448–8461	https://doi.org/10.1007/s11356-025-36228-3

2. Scientific work done:

The research group is engaged in discovery of novel natural products and synthesis of natural products hybrids for natural products driven drug discovery.

Discovery of Structurally Important Phytochemicals

1) Discovery of structurally important cycloartane-type triterpenes from *Dysoxylumbinectariferum*leaves

Dysoxylumbinectariferum (Cup-Calyx White Cedar) is a large tree from the Meliaceae family, known for its diverse natural products such as alkaloids, coumarins, steroids, and flavonoids. It has been a primary source for isolating the rohitukine scaffold, which has led to various clinical candidates. The leaves of D. *binectariferum*are particularly noted for their structurally interesting

triterpenoids, especially cycloartane-type triterpenes, which exhibit a wide range of pharmacological activities, including antitumor, anti-inflammatory, and anti-HIV effects. Recent studies have isolated 12 new cycloartane-type triterpenes (figure-1), with their chemical structures and stereochemistry determined through NMR and ESI-HRMS analysis, and their absolute configurations established using X-ray crystallography.

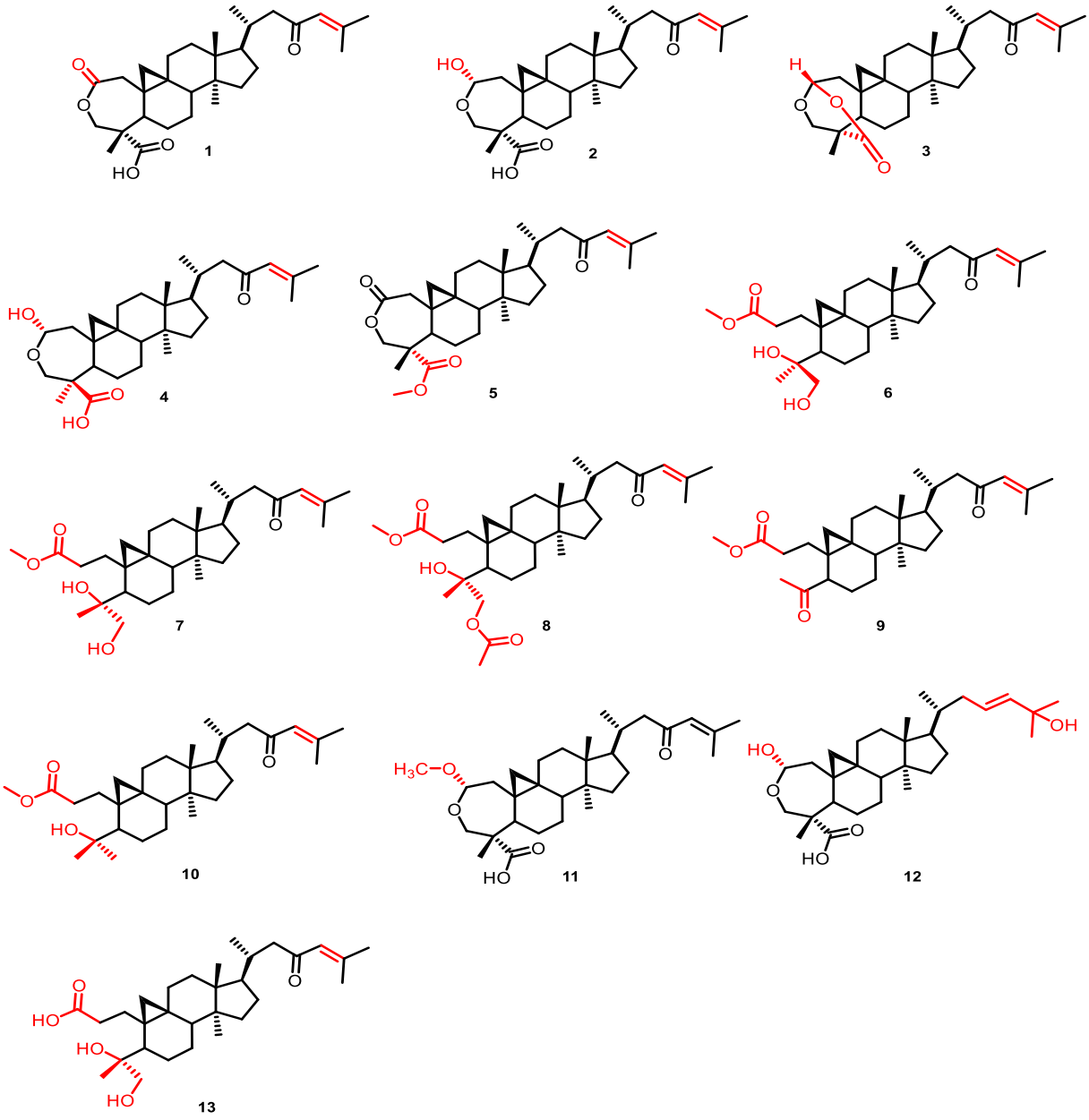


Figure 1: structures of isolatedcycloartane-type triterpenes (**1-13**) from *D. binectariferum*.

2) Discovery of two new tirucallane-type triterpenes anomers from *Toona ciliate*

The Toona genus belongs to the Meliaceae family and is primarily found in tropical and subtropical regions, particularly in Asia and Australia. The most notable species, Toona ciliata (also known as red cedar or Indian Mahogany), is prized for its reddish timber used in furniture,

cabinetry, and boat building. Its range extends from Afghanistan to Papua New Guinea and Australia. In traditional medicine, its bark and leaves are utilized to treat various ailments, including cardiovascular diseases, diabetes, and immune disorders. Toona ciliata is rich in bioactive compounds, including bioactive limonoids and triterpenoids, which contribute to its medicinal value. From chloroform extract we able to isolated two new tirucallane-type triterpene and which were characterized by ^{1}H, ^{13}C and 2D NMR analysis. However, ^{1}H, ^{13}C and HSQC NMR spectra indicated the presence of a mixture of two isomers.X-ray diffraction analysis authenticated the molecular structures of the compound. It further revealed that the isomers **1** and **2** were co-crystallized together in the crystal lattice with a ratio of approximately 67:33, as confirmed by X-ray crystal structure analysis (Figure-2).

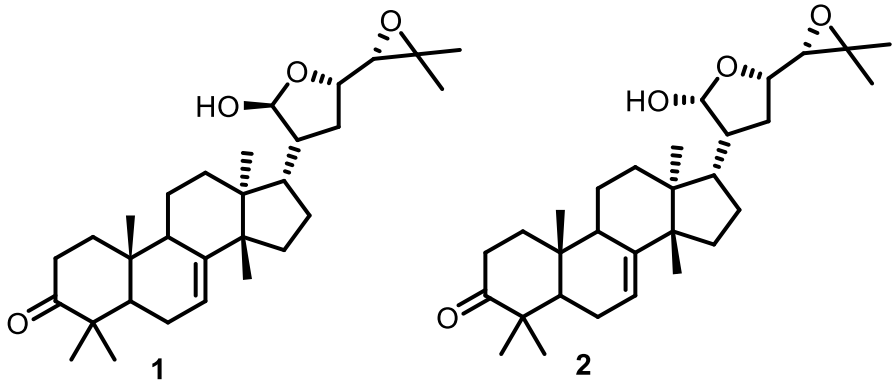
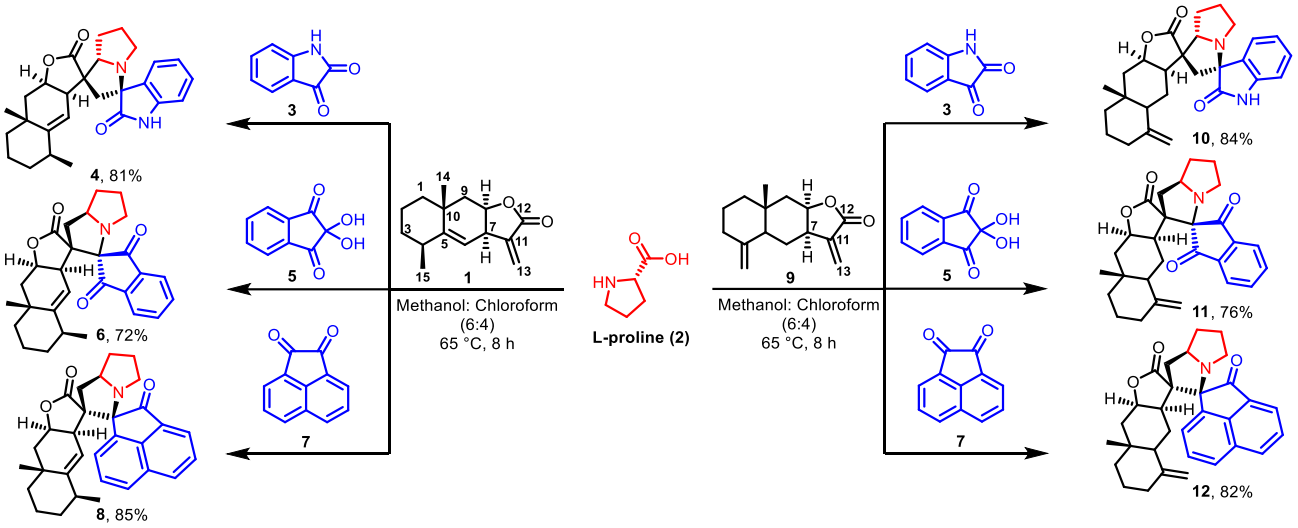


Figure 2. Compounds **1**–**2** isolated from *Toona ciliata* leaves

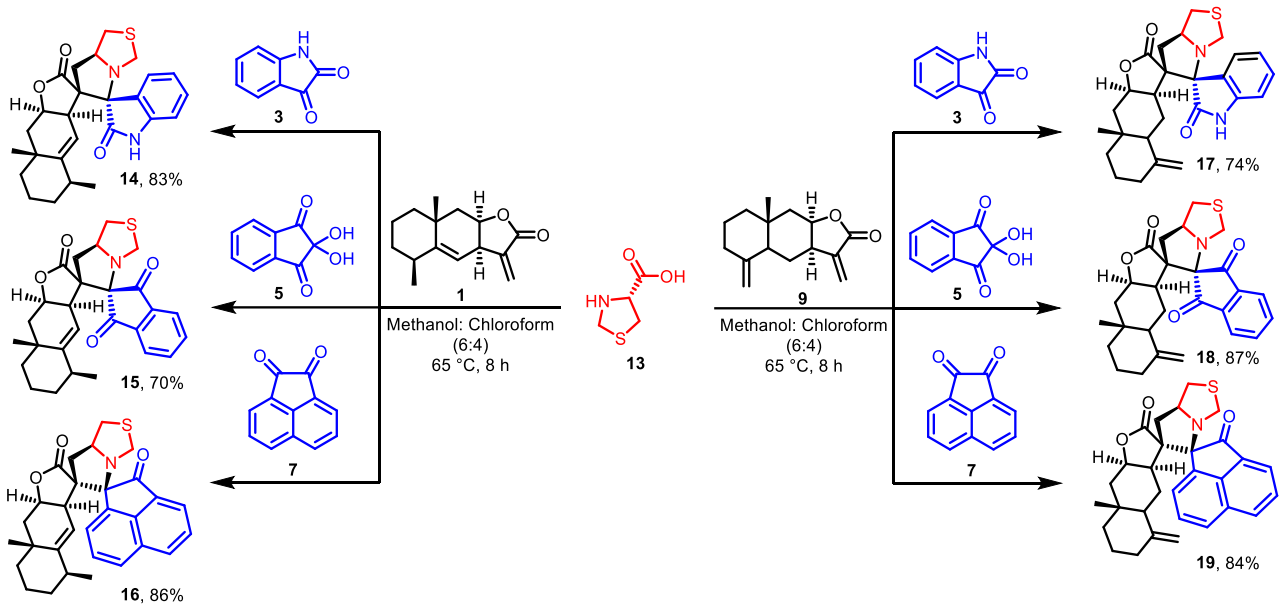
Synthesis of Natural Products Hybrids

1) Diversity-Oriented Semi-Synthesis of Alantolactone and Isoalantolactone Hybrids Employing Azomethine Ylide Cycloaddition Pathway

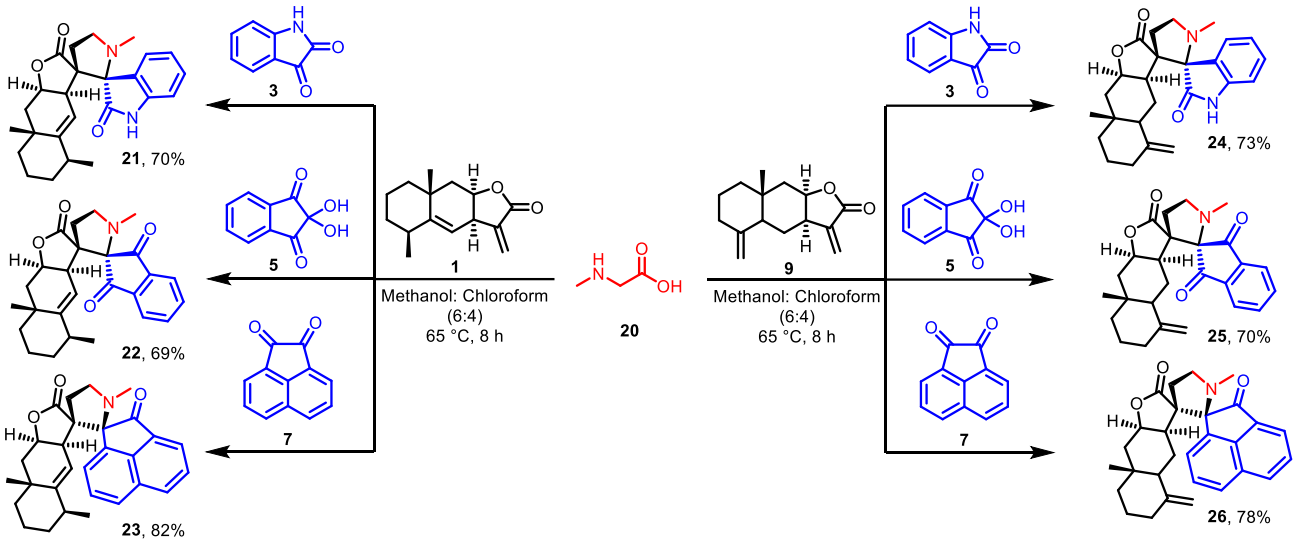
Alantolactone and isoalantolactone, sesquiterpene lactones from *Innularecemosa*, exhibit significant pharmacological effects, including anti-inflammatory, anticancer, and antimicrobial properties. This study focused on large-scale extraction and structural modification of these compounds through an azomethine ylide cycloaddition, leading to the creation of diverse novel hybrids such as dispiro-oxindolo and indanedione (Scheme 1-3). The synthesized compounds were characterized using various spectroscopic techniques, and in silico studies indicated their favorable drug-like properties, including ideal physicochemical traits and promising pharmacokinetics. This research demonstrates the potential of these modified derivatives in drug discovery, highlighting the utility of azomethine ylide cycloaddition for enhancing the diversity of natural products.



Scheme 1. Synthesis of dispiro-oxindolo/indanedione/acenaphthylen-2-one hybrids of alantolactone and iso-alantolactone using L-proline.



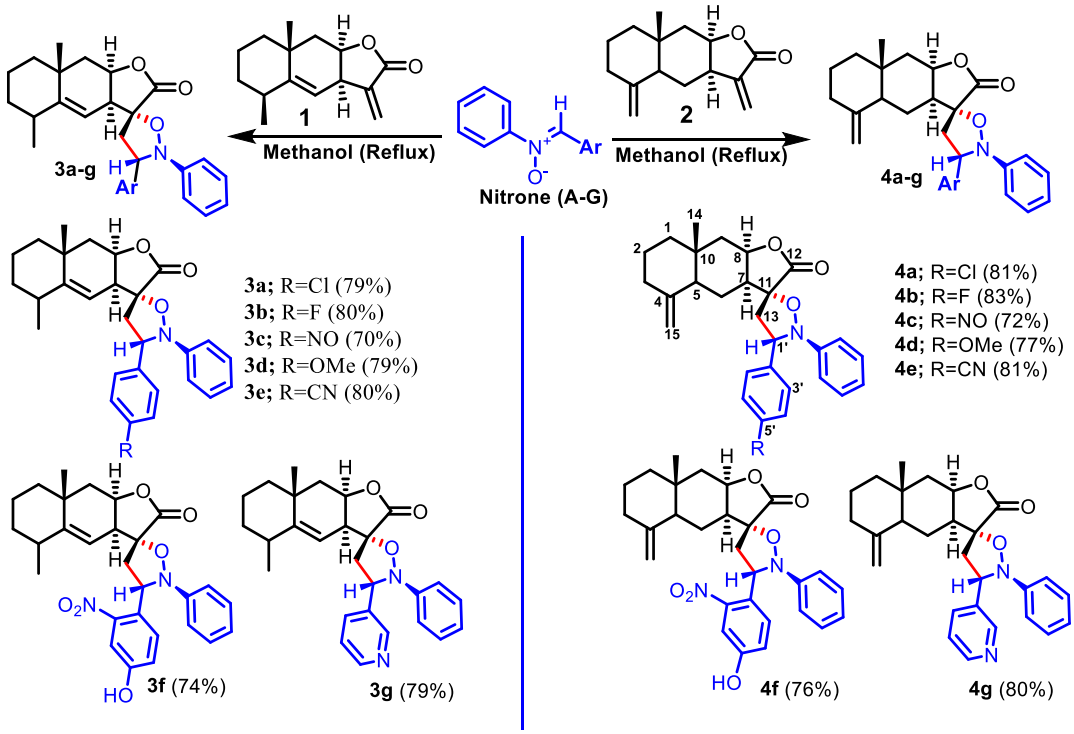
Scheme 2. Synthesis of dispiro-oxindolo/indanedione/acenaphthylen-2-one hybrids of alantolactone and iso-alantolactone using L-thiazolidine- 4- carboxylic acid (thioproline).



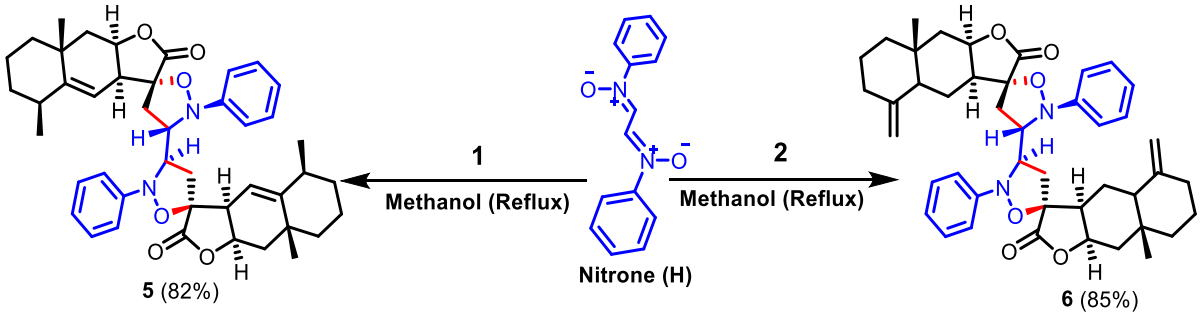
Scheme 3. Synthesis of dispiro-oxindolo/indanedione/ acenaphthylen-2-one hybrids of alantolactone and iso-alantolactone using sarcosine

2) Synthesis of Novel Spiro-isoxazolidino Hybrids of Alantolactone and Isoalantolactone*via* 1,3 Dipolar Nitrone Cycloaddition and its Antimicrobial Evaluation

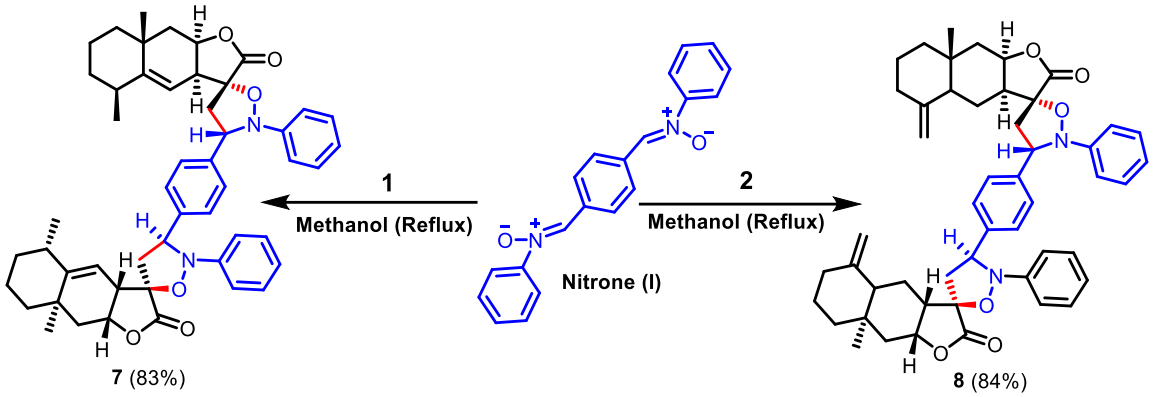
Alantolactone and isoalantolactone, two isomeric sesquiterpene lactones from Innularecemosa, were utilized to synthesize novel isoxazolidine hybrids through a two-step process involving nitrone synthesis and 1,3-dipolar cycloaddition (Scheme 4-6). The cycloadducts were characterized using advanced spectroscopic techniques, including HRMS and various NMR methods. The study also involved synthesizing a dinitrone for further cycloaddition, yielding products with high regio- and diastereoselectivity. The absolute configuration of the compounds was confirmed through 2D NMR and X-ray diffraction analysis. The antimicrobial activity of the synthesized compounds was tested against Gram-positive and Gram-negative pathogens, with compounds **3f** and **4f** showing promising activity against various Staphylococcus aureus strains at low concentrations. These compounds demonstrated bacteriostatic effects and caused significant cellular damage. Overall, the nitrone 1,3-dipolar cycloaddition method proved effective for creating spiroisoxazolidine hybrids, benefiting from the reactivity of the α,β-unsaturated bonds in alantolactone and isoalantolactone. The process yielded stable compounds without the need for chromatographic purification, resulting in excellent yields.



Scheme 4: Synthesis of spiro-isoxazolidino alantolactone and isoalantolactone hybrids



Scheme 5: Synthesis of di-spro di-isoxazolidino alantolactone and isoalantolactone hybrids using glyoxal dinitrone



Scheme 6: Synthesis of di-spiro di-isoxazolidino alantolactone and isoalantolactone hybrids using terephthalaldehyde di-nitrone

RAVINDRA S. PHATAKE

Dr. Ravindra Phatake (Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Synthesis and Anticancer Evaluation of Thia-Michael Addition Derivatives of Dehydrocostuslactone: *In Vitro* and *In Silico* Studies
  Anil Bhushan, Manzoor Ahmed, Salil Suresh, Rohit Singh, Dixhya Rani, Sanket K. Shukla, Zabeer Ahmed, Prasoon Gupta*, and **Ravindra S. Phatake***,*J. Mol. Struct.,* **2025**,*1342,* 142723.
- Anti-Cancer Potential of Dehydrozingerone's Phenoxy-Acetamide Derivatives: Discovery of a Potent Lead with Dual Anti-Proliferative and Anti-Metastatic Activities
  Chetan Kumar, Anshurekha Dash, Rohit Singh, Tanzeeba Amin, Salil Suresh, Anindya Goswami,*and**Ravindra S. Phatake***,*Bioorg. Chem.*, **2025**, *159*, 108413.
- Diversification of structurally significant cycloartane-type triterpenes: exploiting beddomeilactone
  Chetan Paul Singh, Aliya Tabassum, **Ravindra S Phatake***, Yogesh P Bharitkar*, *Nat Prod Res.,***2025**, doi.org/10.1080/14786419.2025.2477222.

- Diversity-oriented semi-synthesis of Alantolactone and Isoalantolactone hybrids employing azomethine ylide cycloaddition pathway
  Aliya Tabassum, Harshad B. Bhore, A. Mercy Abarna, Jayanta Samanta, Anil Kumar Katare, **Ravindra S. Phatake**, Yogesh P. Bharitkar*, *J. Mol. Struct*., **2025**,*1333*, 141729.

- Pharmaceutical applications of microbial biosurfactants
  Farina Sultan, Debraj Maji, **Ravindra S. Phatake**, Kanhaiya Kumar*, *Int. J. Pharm.,* **2025**, *661*, 125887.

- Discovery of structurally important cycloartane-type triterpenes from Dysoxylumbinectariferum leaves and their anti-inflammatory activity
  Chetan Paul Singh, Rohit Singh, Ghulam Mustafa, Ramajayan Pandian, **Ravindra S. Phatake**, Yogesh P Bharitkar*, *J. Mol. Struct*., **2024**,*1309*, 138183.

Book Chapters

- Is Structural Engineering of Quinone Offering New Research Directions for the Discovery of Anti-Cancer Drugs?
  Rohit Singh, Raniya Zubair, Salil Suresh and **Ravindra S. Phatake***
  Chapter-3, **2024**, Book- Quinone-based Compounds in Drug Discovery, by ELSEVIER INC

- Understanding Quinone Derivatives Antibacterial and Antimicrobial Activities Relies on the Structural Activity Relationship.
  Ujjawal Havelikar, Saranya S., Gowri K. Babu and **Ravindra S. Phatake***
  Chapter-4, **2024**, Book- Quinone-based Compounds in Drug Discovery, by ELSEVIER INC

- Pharmacological Diversity in Integrative Medicine: Exploring Sources and Approaches to Drug Discovery Utilizing Natural Products.
  Ritu Painuli, Biru Chauhan, Kanhaiya Kumar,Chetan Kumar*, and**Ravindra S. Phatake***
  Chapter 13,**2025**, Book- Secondary Metabolites and Drug Discoveries, by Wiley

- Assessing the Value of Allopathic Medicine in Non-Communicable Disease Management: Costs, Benefits, and Side Effects
  Ritu Painuli, Abhishek Kumar Gupta, Chetan Kumar*, and **Ravindra S. Phatake***
  Chapter 16,**2025**, Book- Secondary Metabolites and Drug Discoveries, by Wiley

- The Global Importance of Medicinal Plants in Healthcare and Traditional Medicine
  Ritu Painuli, Manoj Gautam, Dhanashree Shinde, Chetan Kumar*, and **Ravindra S. Phatake***
  Chapter 2,**2025**, Book- Importance of Medicinal Plants, by Wiley.

2. Scientific work done:

During April 2024–March 2025, Dr. Ravindra S. Phatake's research group at the NPMC Division made significant advances in the area of organic and medicinal chemistry, with a strong emphasis on the design, synthesis, and biological evaluation of bioactive small molecules inspired by natural products.

The work integrated synthetic organic chemistry, structure activity relationship (SAR) studies, and *in vitro*/*in silico* biological assessments to identify novel therapeutic leads.

A major thrust was directed toward natural product-inspired anticancer agent development. The group reported the synthesis of novel thia-Michael addition derivatives of dehydrocostuslactone, demonstrating promising anticancer activity validated through both *in vitro* cytotoxicity assays and computational docking studies. In a parallel effort, a library of phenoxy-acetamide derivatives of dehydrozingerone was prepared, leading to the discovery of a potent dual-acting lead with both anti-proliferative and anti-metastatic potential.

The group continued its expertise in terpenoids modification chemistry, with diversification of cycloartane-type triterpenes from *Dysoxylumbinectariferum* and semi-synthetic exploitation of rare lactone scaffolds such as beddomeilactone, alantolactone, and isoalantolactone. Diversity-oriented synthetic approaches, including azomethine ylide [3+2] cycloaddition pathways, enabled the generation of structurally complex hybrids with potential anti-inflammatory and anticancer activity.

In addition to synthetic programs, the group contributed to medicinal chemistry reviews and book chapters that highlight strategic molecular modifications of quinones, their SAR trends in antibacterial, antimicrobial, and anticancer contexts, and the pharmacological diversity of natural products in integrative medicine. These scholarly works provided a critical knowledge base for drug discovery from nature-derived scaffolds. Collaborative work extended into pharmaceutical biotechnology, particularly the application of microbial biosurfactants for drug delivery and pharmaceutical formulations, bridging green chemistry with medicinal applications.

Overall, the period marked a productive year of innovation at the interface of natural product chemistry and medicinal chemistry, with the research outputs advancing both fundamental synthetic methodologies and translational prospects for novel therapeutic agents.

YEDUKONDALU NALLI

Dr. Yedukondalu Nalli (Scientist) with Research Group

1. Publications/Patents:

Publications:

- (*3R*)-Obscurolide A: A New Obscurolide from *Streptomyces Chartreusis* SA-7 Isolated from Soil of The North Western Himalayas. Ravi S. Manhas, Neha Sharma, Safeya Begum, Yedukondalu Nalli, Asha Chaubey Natural Product Research, **2025**, https://doi.org/10.1080/14786419.2025.2.
- Two New Dibenzyl-*Γ*-Butyrolactone Lignans with Cytotoxic Activity from *HimalaiellaHeteromalla*, an Indian Himalayan Plant. Singh, B., Thappa, C., Komal, Laasya Priya, P., Begum, S., Yedukondalu Nalli & Gopu, B. Natural Product Research, **2025**, https://doi.org/10.1080/14786419.2025.2491122.
- Phytochemical Investigation of *Cannabis Sativa*: Isolation and Structure Determination of Spiro-Indans. Yedukondalu Nalli, Eleonora Boccia, Gianluigi Lauro, Giuseppe Bifulco, Gamidi Rama Krishna Journal of Molecular Structure, **2025**, https://doi.org/10.1016/j.molstruc.2025.141653.
- Canniprene B, A New Prenylated Dihydrostilbene with Cytotoxic Activities from The Leaves of *Cannabis Sativa*. Yedukondalu, N, Singh, B., Singh, A., Rana, S., Sharma, K., Viswakarma, P., Gopu, B. Natural Product Research, **2024**, 1-9.
- Canonical DDR Activation by EMT Inducing Agent 5-Fluorouracil is Modulated by A Cannabinoid Based Combinatorial Approach Via Inducing Autophagy and Suppression of Vimentin Expression.

Mir, K. B., Chakraborty, S., Amin, T., Kumar, A., War, A. R.; Yedukondalu Nalli, Kumar, R., Kumar, L. D., Ali, A.; Goswami, A. Biochemical Pharmacology **2024**, 223, 116126.

- Evaluation of Anti-Inflammatory and Immunosuppressant Potential of Isotelekin in Lipopolysaccharide (LPS) Stimulated Macrophage (RAW 264.7) and Sheep Red Blood Cells (SRBC) Sensitized Murine Models. Qasam, I., Nawaz, S., Kumari, H., Chauhan, N., Yedukondalu Nalli, Yadav, G. Advanced Biology **2025**, 9, 2400386.
- Neuroprotective Effects of Cannabispirenone A against NMDA-Induced Excitotoxicity in Differentiated N2a Cells. Thapa, S., Yedukondalu Nalli, Singh, A., Singh, S. K.; Ali, A. Oxidative Medicine and Cellular Longevity **2024**, https://doi.org/10.1155/2024/3530499.
- Bioassay-Guided Fractionations of *Cannabis Sativa* Extract and HPLC-Assisted Purifications of Anti-Proliferative Active Fractions Lead to The Isolation of 16 Known and One New Phytomolecule and Their In-Silico Analysis. Yedukondalu Nalli, Bharti, S., Amin, T., Singh, R., Behera, J., Bhayye, S. S., Bharitkar, Y. P., Goswami, A., Verma, M. K. Medicinal Chemistry Research **2024**, 33, 635-650.
- Divergent Synthesis of Fractionated *Cannabis Sativa* Extract Led to Multiple Cannabinoids C-&O-Glycosides with Anti-Proliferative/Anti-Metastatic Properties. Yedukondalu Nalli, Mir, K. B., Amin, T., Gannedi, V., Jameel, E., Goswami, A., Ali, A. Bioorganic chemistry **2024**, 143, 107030.

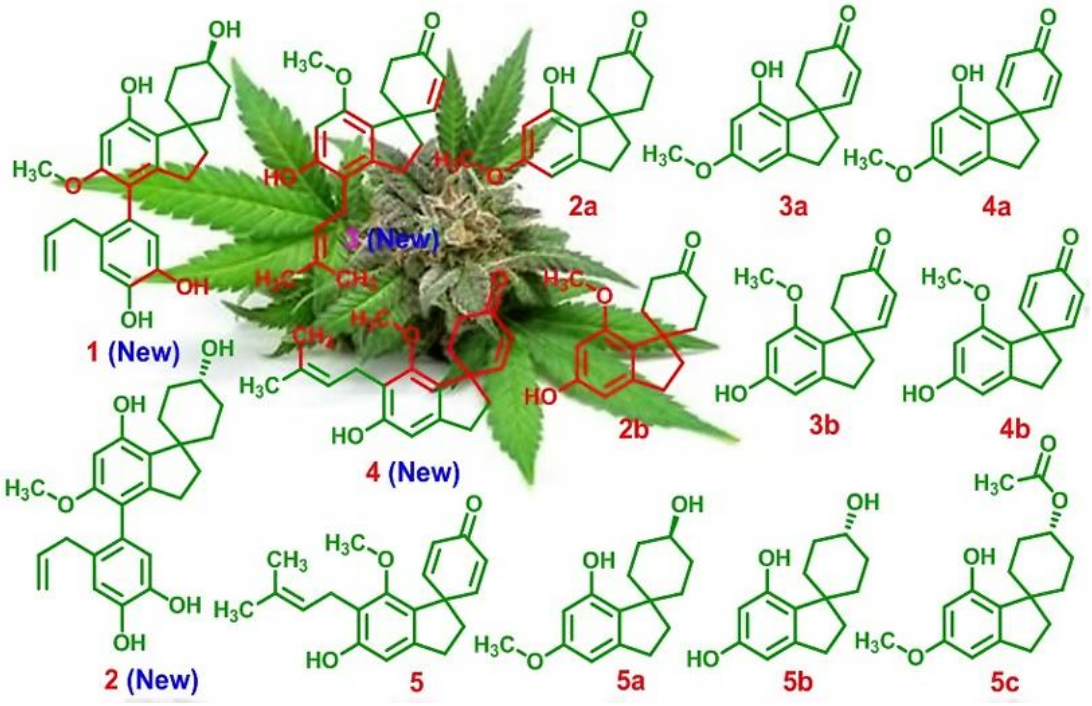
2. Scientific work done:

Dr. Nalli's group integrates ethnobotanical knowledge with cutting edge natural product chemistry to discover, characterize, and optimize bioactive molecules from plants, microorganisms, and marine invertebrates. Their work targets cancer, antimicrobial resistance, and neurodegenerative diseases through systematic chemical exploration and drug discovery innovation.

A major focus of their research work is the phytochemical and pharmacological investigation of *Cannabis sativa*. This has led to the discovery of structurally unique molecules such as four novel spiroindanes, cytotoxic stilbenes (Canniprene A and B), glycosylated cannabinoids, and *Cannabispirenone A*, a CB1 receptor modulator with neuroprotective activity. By pioneering an extract engineering strategy, Dr. Nalli's group has generated rare and novel cannabinoids with enhanced pharmacological profiles, including C- and O-glycosides that exhibit potent anti-invasive activity in breast and pancreatic cancer cells, and oxidized cannabinoids with strong anti-MRSA effects.

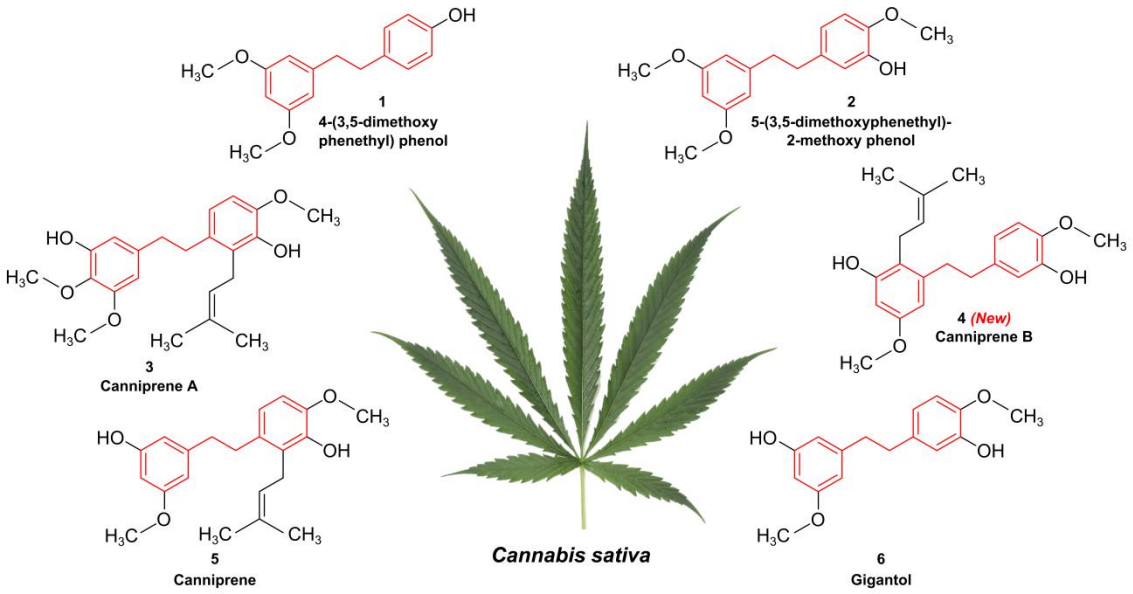
Key findings include:

- **Phytochemical Investigation of *Cannabis Sativa*: Isolation and Structure Determination of Spiro-Indans**



Four undescribed, *β*-, *α*-chevicospiranol (**1, 2**), 4-prenylspirenone B (**3**), and, 6-prenylspirenone B (**4**), along with ten known spiroindans were discovered in *Cannabis sativa*. The structures were determined through 1D, 2D NMR, HRMS, and quantum mechanical calculations. Compounds **1** and **2** have an unprecedented fused system of 3-hydroxychavicol with *β*- and *α*-cannabispiranol core, respectively, while **3** and **4** are prenylated spiroindan congeners. Detailed NMR data assignments of isomeric pairs **2a** – **2b, 3a** – **3b**, and **4a** – **4b**, corrected the misidentification of the previously reported spiroindane, prenylspirodinone (**5**). Besides, the crystal structures of **2a, 3a**, and **5a** were determined by SC-XRD experiments.

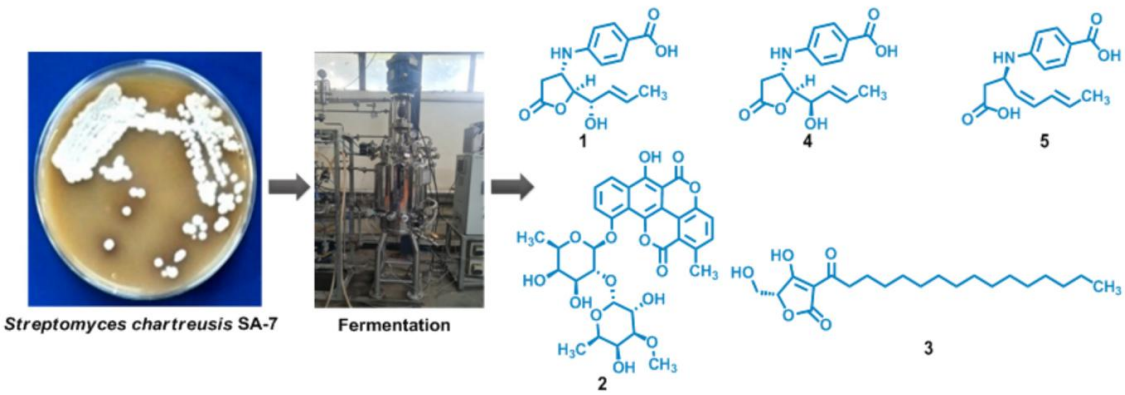
- **Canniprene B, a new prenylated dihydrostilbene with cytotoxic activities from the leaves of Cannabis sativa**



A new, canniprene B (**4**), along with five known (**1** – **3** and **5** – **6**) dihydrostilbenes were isolated from the leaves of *Cannabis sativa* collected at CSIR – IIIM, Jammu, India. Structures of all isolated compounds were elucidated by spectroscopic data analysis, including 1D and 2D NMR, and HR-ESI-MS. Canniprene B is a new prenylated dihydrostilbenes, a positional isomer of the known compound canniprene(**5**). The cytotoxic activities of these compounds (**1** – **6**) were evaluated using the SRB assay against a panel of five human cancer cell lines. Notably, canniprene B (**4**) exhibited varying levels of cytotoxicity with IC_{50} values ranging from 2.5 – 33.52 µM, demonstrating the most potent activity against pancreatic cancer cells.

Beyond *Cannabis*, the lab's systematic screening of bioresources has produced:

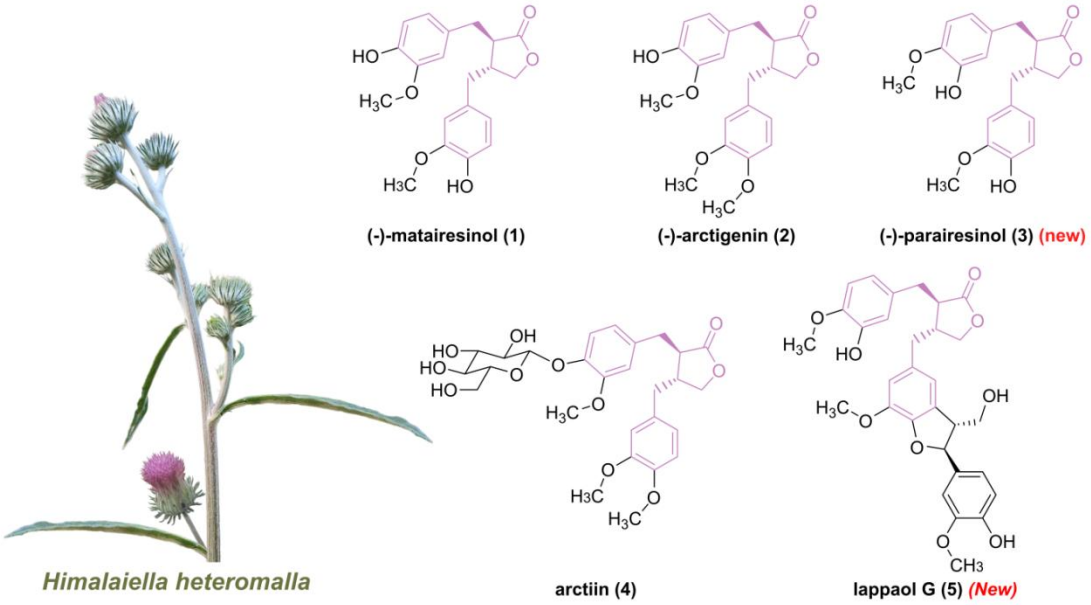
- **(3R)-obscurolide A, a new obscurolide from Streptomycessp. SA-7 isolated from soils of the North Western Himalayas.**



A new obscurolide, (3*R*)-obscurolide A (**5**) and four previously identified metabolites streptalbonin F (**1**), chartreusin (**2**), TAN 1364B (**3**) and streptalbonin G (**4**) were isolated from *Streptomyces chartreusis* SA-7, obtained from soil of the North Western Himalayas. The structure of new compound (3*R*)-obscurolide A (**5**) was elucidated by spectroscopic data analysis, including 1D and 2D NMR, and HR-

ESI-MS, while the known compounds (**1**–**4**) were identified by comparing their spectral data with the literature. Notably, chartreusin (**2**) is a wel-known antimicrobial agent with broad-spectrum activity, while the other compounds had been reported to display moderate antimicrobial effects against various test strains.

- **Two New Dibenzyl-Γ-Butyrolactone Lignans with Cytotoxic Activity from HimalaiellaHeteromalla, an Indian Himalayan Plant.**



Two new (-)-parairesinol (**3**), lappaol G (**5**), and three known (**1**, **2**, and **4**) dibenzyl-γ butyrolactone lignans were isolated from the Indian Himalayan herb *Himalaiellaheteromalla*. Their structures were characterized by NMR and mass data analysis. In vitro cytotoxic study revealed that arctiin (**4**) showed promising growth inhibition across seven human cancer cells, with potent activity against Mia-PaCa-2 cells. Notably, compounds **3** and **5** did not demonstrate significant cytotoxicity up to 80 μM concentrations.

Technical Expertise and Approach

Technically, Dr. Nalli's group deals in multidimensional NMR spectroscopy, high-resolution mass spectrometry, single-crystal X-ray diffraction, and advanced chromatographic methods (Flash, HPLC) for isolating complex natural products. They also employs semi-synthetic derivatization to enhance pharmacological potential. Their approach combines rigorous structural elucidation with bioassay-guided fractionation, ensuring that discoveries move efficiently from isolation to biological evaluation.
Through this integrated and multidisciplinary approach, Dr. Nalli's group has contributed significantly to the identification of novel molecular scaffolds with therapeutic promise, advancing both the scientific understanding of natural product chemistry and its application in addressing unmet medical needs.

SHEIKH TASDUQ ABDULLAH

Dr. Sheikh Tasduq Abdullah (Sr. Principal Scientist) with his Research Group

Research Interests

1. **Nonalcoholic fatty liver disease (NAFLD)**
   - To develop of small animal models of NAFLD model and to elucidate the longitudinal, tissue, and cell-specific sequence of events in the pathogenesis of NAFLD -induced chronic liver damage mimicking human conditions.
2. **Photo-Biology**
   - To decipher the Cellular, Molecular and Pathophysiological basis of in UVB -induced skin photodamage/photocarcinogenesis& Melanogenesis
3. **Drug Discovery**
   - To evaluate the therapeutic potential of natural compounds as therapeutic options and/or drug discovery approach in NAFLD, Photodamage and Skin Melanoma.

Recent publications

- Sajeeda, A., Rashid, H., Malik, T. A., Sharma, R. R., Bhat, A. M., Kumar, A., .&**Sheikh, T. A. (2024)**. Seabuckthorn pulp extract alleviates UV-B-induced skin photo-damage by significantly reducing oxidative stress-mediated endoplasmic reticulum stress and DNA Damage in human primary skin fibroblasts and Balb/c mice skin. **Environmental Science and Pollution Research,** 31(34), 46979-46993.
- Bhat, A. M., Bhat, I. A., Malik, M. A., Kaiser, P., Ramajayan, P., Rayees, S. R., ... **&Tasduq, S. A. (2025).** Inhibition of IKK complex by (2 methyl butyryl) Shikonin, a naturally occurring naphthoquinone, abrogates melanoma growth and progression via modulation of the IKK/NFκB/EMT signaling axis. International Immunopharmacology, 148, 114026..
- Umar, S. A., &Tasduq, S. A. (2025). Photophagy: Unveiling a Novel Cellular Mechanism in UVB-Induced Skin Aging and Resilience. International Journal of Dermatology.

Skin Biology:

The major research focus of our lab is skin photo-damage (Photo-carcinogenesis and Photo-aging), melanogenesis and melanoma. Solar UV radiation is known to elicit plenitude of events which culminates in skin photodamage. This lab studies major events responsible for initiating UVB induced photo-aging and skin cancer and the cellular, biochemical and molecular basis of UVB-induced photo-aging along with the identification of target based potent therapeutic agents. Melanogenesis, a highly complex process of melanin biosynthesis, is one of the most visible physiological responses of skin to UV exposure.

This lab also focuses on the mechanistic analysis of novel molecules that modulate melanogenesis for achieving therapeutically and cosmetically useful outcomes. A salient feature of UVB-irradiation is generation of reactive oxygen species (ROS) and simultaneous modulation of ER stress, autophagy and apoptosis. This lab is particularly interested in understanding the mechanistic basis for the UVB induced ROS generation, ER stress, autophagy and apoptosis in skin cells. The recent focus of our lab has been to understand the interplay of autophagy and DNA Damage Response in Ultraviolet-(B) –induced skin photodamage

Liver Biology:

In liver biology we wish to understand the pathophysiology/pathogenesis of Non-alcoholic fatty liver disease and develop therapeutic interventions using novel approaches.

Liver is the major player in the regulation of fat metabolism as it integrates endogenous and exogenous fatty acids. Any defect/perturbation in the liver fat metabolism potentially impacts the functioning of the liver. Prevalence of non-alcoholic fatty liver disease (NAFLD) has been on an inclined trajectory with the rise in obesity. Non alcoholic steatohepatitis (NASH), an advanced stage of NAFLD, has emerged as third most common cause of liver transplantation. NAFLD can progress to cirrhosis and liver failure in 3% to 15% cases and there have been emerging reports of a significant proportion of HCC cases in settings of NAFLD. Despite the high prevalence of NAFLD and its serious complications, the underling molecular events that implicate lipotoxicity remain poorly understood and need further investigation. Our research interest focuses on normal and diseased liver pathology. The research specifically focuses on metabolic and lipotoxic changes in the pathogenesis of NAFLD, the mechanism of action of various treatment options and response of In vivo model of disease to the treatment regimes

MUZAMIL AHMAD

Dr. Muzamil Ahmad (Principal Scientist) with his Research Group

1. Publication/Patents:

- **Research Article:**
  Dar NJ, Gull B, Hamid A, Ahmed Z, **Ahmad M**. Withaferin-A kills neuronal cells: An off-putting facet of Withaniasomnifera as a neuroprotectant. *Steroids*. 2025 Jul 20; 222:109662. doi: 10.1016/j.steroids.2025.109662. Online ahead of print. PMID: 40695418
- **Review Paper:**
  Muzaffer U, Gull B, Ahmed Z, **Ahmad M**. Neuropharmacological Interventions of Plant Origin for Parkinson's disease: A Comprehensive Appraisal. *Curr Neuropharmacol*. 2025 May 26. doi: 10.2174/1570159X23666250523112027. Online ahead of print. PMID: 40442916
- **Book Chapter:**
  Gul B, Faheem MM, Ahmed Z, **Ahmad M**. Andrographolide in neurological disorders: A detailed overview. In Dar NJ & Bhat SA (Eds.), 2025 *Small molecules in neurodegeneration* (1st ed., pp. 15). CRC Press. https://doi.org/10.1201/9781003520610

2. Scientific work done:

- **Treating Neuropathic Pain: Preclinical Studies Using Peptide Libraries Based On Conotoxins:** The project will entail the design and synthesis of peptide libraries incorporating non-protein amino acids and selenocysteine derived from native conotoxins and their purification and structural characterization using biophysical techniques. Neuropharmacological evaluation of the designed peptide libraries will be pursued using cellular models of neuropathic pain, using rodent spinal cord neurons, by quantification of relevant markers for chronic pain. Further on, the most potent conotoxin analogues will be assessed for pain-mitigating effects (biochemical as well as behavioural) after sciatic nerve ligation-induced neuropathic pain in rodents.

  Neuropathic pain is a significant issue for patients with conditions like cancer, diabetes, and arthritis, as well as those undergoing chemotherapy or spine surgery. It is often chronic, characterized by shooting or burning sensations, and results from nervous system dysfunction. Current treatments mainly provide only partial relief, but α-conotoxins from cone snails show promise as antagonists of nicotinic acetylcholine receptors (nAChRs). Inhibition of α9 α10 nAChRs can help alleviate neuropathology after nerve damage. α-conotoxins consist of 12–19 amino acids with a stable structure formed by two disulfide bonds and a conserved proline residue. However, their effectiveness in humans is limited by degradation by proteases. Improving their stability through modifications, such as diselenide bonds and alterations at specific positions, can enhance their antagonistic activity.

  This project aims to develop synthetic mimics of α-conotoxins (e.g., α4/7, α4/4, α4/3 subfamilies) that are resistant to proteolytic degradation to target nAChRs and alleviate chronic pain in cellular and animal models. It will involve designing and synthesizing peptide libraries with non-protein amino acids and purifying these compounds. Neuropharmacological evaluations will be conducted using rodent spinal cord neurons to measure chronic pain markers, followed by assessments of the most effective conotoxin analogues in relieving pain in rodent models of neuropathic pain.

- **Pre-clinical validation of Anti-Alzheimer activity of a classical Unani Formulation:** Alzheimer's disease (AD) is one of the major neurodegenerative disorders of old age affecting cognition. In India, 4 million people have some or other form of dementia. Despite the immense progress made in our understanding of Alzheimer's disease, developing a modality to check the disease progression has been majorly unsuccessful. Most of the established therapies are meant to afford functional benefit only and produce severe side effects on continued use. Thus, it becomes pressing to develop and implement newer treatments that delay the progression of the disease and are comparatively safe. In Unani Medicine, formulations containing medicinal are extensively used, particularly in the case of diseases that do not respond to therapies of modem medicine. Systematic scientific investigation of polyherbal formulations used in the Unani system of medicine offers great hope for use against diseases of the nervous system.
- **Role of PGE2-mediated inflammatory alterations in the deregulation of metastatic suppressors in glioblastoma:** Our studies focus on finding definitive molecular links that link the PGE2-mediated inflammatory landscape and deregulation of key metastatic suppressors in

glioblastoma. Our studies will help to understand glioblastoma disease progression better and unravel novel molecular targets for therapeutic intervention. We will systematically delineate the role of the inflammatory injunctions in the initiation and progression of glioblastoma; determine the potential association of inflammation with potential signaling mechanisms resulting in deregulation of major metastatic suppressors to regulate glioblastoma carcinogenesis.

- **Neuro- and mito- protective effects of small molecules in parkinson's disease:** The proposed studies aim to evaluate various small molecules of natural and synthetic origin aspotential as therapeutic agent for Parkinson's disease. By utilizing animal models and neuronal cell lines and focusing on neuroprotection, antioxidant and anti-inflammatory mechanisms, and mitochondrial health these studies will contribute to a deeper understanding of how *small molecules* can mitigate the progression of Parkinson's disease.

AJAY KUMAR

Dr. Ajay Kumar (Principal Scientist) with his Research Group

Research Interests

- Alzheimer's disease, Aging, Autophagy, NLRP3 inflammasome, Drug Transporters

1. Publications/Patents:

Publications:

- Kour D, Khajuria P, Sharma K, Sharma A, Sharma A, Ali SM, Wazir P, Ramajayan P, Sawant SD, Nandi U, Ahmed Z, Kumar A. Isobavachalcone ameliorates Alzheimer disease pathology by autophagy-mediated clearance of amyloid beta and inhibition of NLRP3 inflammasome in primary astrocytes and 5x-FAD mice. Front Pharmacol. 2025 Mar 20;16:1525364. doi: 10.3389/fphar.2025.1525364. PMID: 40183098; PMCID: PMC11965660.

- Kulkarni AS, Ramana SR, Nuthakki VK, Bhatt S, Jamwal A, Nandawadekar LD, Jotshi A, Kumar A, Nandi U, Bharate SB, Reddy DS. Silicon incorporated tacrine: design, synthesis, and evaluation of biological and pharmacokinetic parameters. RSC Med Chem. 2025 Mar 7. doi: 10.1039/d5md00019j. Epub ahead of print. PMID: 40177641; PMCID: PMC11959489.

- Sandha KK, Kaur S, Sharma K, Ali SM, Ramajayan P, Kumar A, Gupta PN. Autophagy inhibition alleviates tumor desmoplasia and improves the efficacy of locally and systemically

administered liposomal doxorubicin. J Control Release. 2025 Feb 10;378:1030-1044. doi: 10.1016/j.jconrel.2024.12.078. Epub 2025 Jan 3. PMID: 39746521.

- Choudhary S, Kumar V, Sharma K, Gour A, Sahrawat A, Jotshi A, Manhas D, Nandi U, Bharate SB, Ahmed Z, Kumar A. Crocetin Delays Brain and Body Aging by Increasing Cellular Energy Levels in Aged C57BL/6J Mice. ACS PharmacolTransl Sci. 2024 Sep 11;7(10):3017-3033. doi: 10.1021/acsptsci.4c00151. PMID: 39416964; PMCID: PMC11475333.

- Kaur, S., Sharma, K., Sharma, A., Sandha, K. K., Ali, S. M., Ahmed, R., Ramajayan, P., Singh, P. P., Ahmed, Z., & Kumar, A. (2024). Fluvoxamine maleate alleviates amyloid-beta load and neuroinflammation in 5XFAD mice to ameliorate Alzheimer disease pathology. Frontiers in Immunology, 15, 1418422. https://doi.org/10.3389/fimmu.2024.1418422

- Reddy CN, Nuthakki VK, Sharma A, Malik S, Tabassum M, Kumar R, Choudhary S, Iqbal F, Tufail Z, Mondhe DM, Kumar A, Bharate SB. Synthesis and Biological Evaluation of Colchicine─Aryl/Alkyl Amine Hybrids as Potential Noncytotoxic Cholinesterase Inhibitors: Identification of SBN-284 as a Dual Inhibitor of Cholinesterases and NLRP3 Inflammasome. ACS Chem Neurosci. 2024 Aug 7;15(15):2779-2794. doi: 10.1021/acschemneuro.4c00153. Epub 2024 Jul 26. PMID: 39056181..

- Manhas D, Dhiman S, Kour H, Kour D, Sharma K, Wazir P, Vij B, Kumar A, Sawant SD, Ahmed Z, Nandi U. ADME/PK Insights of Crocetin: A Molecule Having an Unusual Chemical Structure with Druglike Features. ACS Omega. 2024 May 2;9(19):21494-21509. doi: 10.1021/acsomega.4c02116. PMID: 38764638; PMCID: PMC11097163.

Patents

- Sonali Sandip Bharate, Vikas Kumar, Rohit Singh, Sarita Rani, Mehak Gupta, Ajay Kumar, Sandip Bibishan Bharate, Ram Vishwakarma Sustained release formulations of Crocus sativus. US Patent Number: US12023365B2, Date of Patent: Jul 02, 2024.

Clinical Development of CSIR-IIIM Leads

We have filed an IND application for Phase-1 clinical trials of IIIM-141 in November 2024. Apart from that, we are moving forward with 4 phytopharmaceutical leads, viz (IIIM-64, IIIM-160, IIIM-BECF-01, and IIIM-CSEF-01), against different disease conditions. In all these leads, the pre-clinical efficacy work has been done in my lab.

2. Scientific work done:

Alzheimer's disease is characterized by a complex pathophysiology involving the accumulation of amyloid-beta (Aβ) plaques and the formation of neurofibrillary tangles (NFTs) composed of TAU

protein in the brain. These intracellular and extracellular protein aggregates disrupt critical neuronal functions, such as neurotransmission and intracellular transport, ultimately leading to neuronal death.

Autophagy, a cellular clearance mechanism, plays a vital role in removing these harmful protein deposits. However, aging is associated with a decline in autophagy efficiency, which severely impairs this clearance process. Dr. Kumar's research group has demonstrated, using both cellular and transgenic mouse models, that pharmacological induction of autophagy can effectively clear these protein aggregates from the brain. His findings indicate that the removal of Aβ not only reduces neuroinflammation but also improves learning and memory in 5XFAD mice, a model of Alzheimer's disease.

In addition, Dr. Kumar's lab is exploring whether age-related declines in brain function can be reversed using small molecules to enhance the clearance of pathological protein aggregates. His research also highlights the connection between protein accumulation and the activation of the NLRP3 inflammasome, which triggers the release of IL-1β and fosters a pro-inflammatory microenvironment in the brain, further exacerbating neuronal damage. His work has revealed a strong correlation between autophagy impairment and NLRP3-mediated inflammation, underscoring the potential of simultaneously targeting both pathways for the development of novel Alzheimer's therapeutics.

Beyond his academic research, which has led to a significant number of publications during 2024-25, he has played a significant role in advancing phytopharmaceutical drug development at CSIR-IIIM. Notably, his work has led to the filing of an Investigational New Drug (IND) application with the CDSCO for a *Crocus sativus*-based phytopharmaceutical aimed at treating Alzheimer's disease in November 2024.

RASHMI SHARMA

Dr. Rashmi Sharma (Sr. Scientist) with her Research Group

1. Publications/Patents:

Publications:

Authors	Title	Journal
Anjali Negi, Summaya Perveen, Harpreet Kour, Parvinder Pal Singh, **Rashmi Sharma***	Keeping up with the Q's: Mechanistic Insights and Validation of Quinoline and Quinazoline scaffolds as potent drugs against Tuberculosis	*ACS Journal of Medicinal Chemistry* (2025)
Anjali Gangwar, Sapna Saini, and **Rashmi Sharma***	Galectins as Drivers of Host-Pathogen Dynamics in *Mycobacterium tuberculosis* Infection.	*ACS Infectious Diseases* (2025)
Sapna Saini, Sunny Pal, and **Rashmi Sharma***	Decoding the Role of Antimicrobial Peptides in the Fight against *Mycobacterium tuberculosis*	*ACS Infectious Diseases* (2025), 11, 2, 350–365
Summaya Perveen, Sunny Pal & **Rashmi Sharma***	Breaking the energy chain: importance of ATP synthase in *Mycobacterium tuberculosis* and its potential as a drug target.	*RSC Medicinal Chemistry* (2025), 16, 1476-1498
Sapna Saini, G. Lakshma Reddy, Anjali Gangwar, Harpreet Kour, Gajanan G. Nadre, Ramajayan	Discovery and Biological Evaluation of Nitrofuranyl-Pyrazolopyrimidine Hybrid Conjugates as Potent Antimicrobial Agents Targeting	*RSC Medicinal Chemistry*, (2025), 16, 1304-1328

Pandian, Sunny Pal, Utpal Nandi, **Rashmi Sharma***, and Sanghapal D. Sawant*	Staphylococcus aureus and Methicillin-resistant Staphylococcus aureus	
Puneet Kumar, Sapna Saini, Anjali Gangwar, **Rashmi Sharma***, and Jasha Momo H. Anal*	Antibacterial activity of structurally diverse natural prenylated isobavachalcone derivatives	*RSC advances*, (2024), 14 (45) 32771-32785

Patents:

- N-Substituted-2H-chromene-3-carboxamide derivatives as potent inhibitor of Mycobacterium tuberculosis and process for preparation thereof. Summaya Perveen, Anjali Negi, Atul Chopra, Zabeer Ahmed, **Rashmi Sharma**, Parvinder Pal Singh (File no. IN202411098131).
- Synthesis of "6-methyl-2-nitro-8-phenyl-5,6,7,8-tetrahydroimidazo[1,2-A] pyrimidin-6-ol" and "2-Benzyl-2-methyl-6-nitro-2,3-dihydroimidazo[2,1-B] oxazole" and their derivatives as anti-TB agents. Ria Gupta, Summaya Perveen, Anjali Negi, Zaheen Akhter, Atul Chopra, Muzamil Samad, Pankaj Singh Cham, Mahir Bharadwaj, **Rashmi Sharma**, Utpal Nandi, Zabeer Ahmed, Serge Mignani, Bernardes Genisson Vania, Parvinder Pal Singh (Patent filed).

2. Scientific work done:

2.1. Emergence of drug-resistant tuberculosis poses significant challenges to global TB drug discovery efforts, limiting treatment options and impeding efforts for TB eradication. To address this urgent need for novel and effective drugs, this study highlights 2*H*-chromene-3-carboxamides as a promising scaffold with anti TB activity. This scaffold showed potent activity against *Mtb*-H37Rv, Rifampicin-resistant strain, and a drug-resistant clinical isolate with the most potent hit exhibiting MIC of 4.5 µg/ml. Furthermore, it showed activity against dormant non-replicating persister cells. The most potent compounds, A7 and A8, exhibited synergistic and additive interaction with known anti-TB drugs and displayed time and concentration dependent bactericidal activity in the kill kinetic studies. Additionally, these compounds reduced *Mtb* growth by 2 $\log_{10}$ CFU/mL in an *ex vivo* infection model. Mechanistic studies revealed that 2*H*-chromene-3-carboxamides disrupt the bacterial respiratory chain, significantly altering the transcriptional profile of respiratory pathway genes. These compounds reduced intracellular ATP levels in various mycobacterial strains and inhibited ATP synthesis in an inverted membrane vesicle assay, with IC_{50} values ranging from 0.93 to 1.75 µg/ml. Importantly, they showed selectivity for mycobacterial ATP synthase over its mammalian mitochondrial counterpart, highlighting their potential as selective and host-safe anti-TB agents. In conclusion, the study revealed potent anti-mycobacterial activity of 2*H*-chromene-3-carboxamide derivatives exhibiting favourable anti-TB profiles and effectively inhibiting mycobacterial ATP synthase. With selective targeting and addressing heterogeneous *Mtb* population, this scaffold offers a potential breakthrough for future medicinal chemistry endeavours, advancing the fight against global health threat of drug-resistant tuberculosis.

2.2. Nitrofuran and pyrazolopyrimidine-based compounds possess a broad antimicrobial spectrum including Gram-positive and Gram-negative bacteria. In this present work, a series of conjugates of these scaffolds was synthesized and evaluated for antimicrobial activity against Staphylococcus aureus and methicillin-resistant S. aureus (MRSA). Many compounds showed MIC values of ≤2 μg ml−1, with compound 35 demonstrating excellent activity (MICs: 0.7 and 0.15 μg ml−1 against S. aureus and MRSA, respectively) and safety up to 50 μg ml−1 in HepG2 cells. Compound 35 also exhibited no hemolytic activity, biofilm eradication, and effectiveness against efflux-pump-overexpressing strains (NorA, TetK, MsrA) without resistance development. It showed synergistic effects with vancomycin (S. aureus) and rifampicin (MRSA). Mechanistic studies revealed that compound 35 exhibits good membrane-targeting abilities, as evidenced by DAPI/PI staining and scanning electron microscopy (SEM). In an intracellular model, it reduced bacterial load efficiently in both S. aureus and MRSA strains. With a strong in vitro profile, compound 35 demonstrated favorable oral pharmacokinetics at 30 mg kg−1 and potent in vivo anti-MRSA activity, highlighting its potential against antibiotic-resistant infections.

BILAL AHMAD BHAT

Dr. Bilal Ahmad Bhat (Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

S.No	Authors	Title of the Article	Year of Pubn	Name of Journal	Country	Vol No. Issue, Pages
1	Wani, M. M.; Bhat, B. A.	Micelle-driven organic synthesis: an update on the synthesis of heterocycles and natural products in aqueous medium over the last decade	2025	***RSc. Adv.***	UK	15, 25586
2	Teli, B.; Mubarak, M. M.; Ahmad, Z.; Bhat, B. A*	Trifluoroacetic acid-mediated synthesis of xanthene constructs and their extensive anti-tuberculosis evaluation	2024	***RSC. Med. Chem.***	UK	15, 1295
3	Lone, W. I.; Rashid, A.; Bhat, B. A*, Rashid S. *	Chemoselective Oxidation of Aromatic Aldehydes to Carboxylic Acids: Potassium tert-butoxide as an Anomalous Source of Oxygen	**2024**	***Chem.Comm***	UK	60, 6544

4	Rashid, A.; Lone, W. I.; Dogra, P.; Rashid S. *Bhat, B. A*,	HFIP-mediated C-3-alkylation of indoles and synthesis of indolo[2,3-**b**] quinolines& related natural products	**2024**	***Org. Biomol. Chem.***	UK	22, 3502
5	Rashid, S.; Hussain, A. Bhat, B. A* Mehta, G*	Incisive Analysis of Hydrogen-Bonded Architects in Polycyclitols: Observation of Some Interesting Self-Assembly Patterns	**2024**	***CrystEngComm***	UK	26, 1952
6	Teli, B.; Wani, M.; Jan, S.; Bhat, R. H.; Bhat, B. A*	Micelle-mediated Synthesis of Quinoxaline, 1,4-Benzoxazine and 1,4-Benzothiazine Scaffolds from Styrenes	**2024**	***Org. Biomol. Chem.***	UK	32, 6593
7	Rashid, S.; Lone, M. I.; Rashid, A.;. Bhat, B. A*	Inverse electron demand Diels-Alder reaction in total synthesis of bioactive natural products	**2024**	***Tetrahedron Chem.***	UK	100066

2. Scientific work done:

During the past few years our Group has shifted towards the sustainable organic synthesise. We have established some exciting strategies to access bioactive constructs using micellar catalysis in water. We are looking forward to apply these strategies in the synthesis of bioactive natural products and drug molecules.

VARUN PRATAP SINGH

Dr. Varun Pratap Singh (Sr. Technical Officer-III)

Research interests

- Peptides of natural origin
- Separation chemistry of peptides
- Structural elucidation of peptides
- Medicinal chemistry of peptides

1. Publications/Patents:

Publications:

- Neha Sharma, Devtulya Chander, Ravi S. Manhas, Varun P. Singhand Asha Chaubey; Genomics and metabolomics approach for deciphering the potential of *Micromonospora* sp. isolated from cold desert of NW Himalayas; *International Journal of Biological Macromolecules*, communicated

Book chapters:

- Varun Pratap Singh, Rohini Verma and Vandita Srivastava; Natural Product Drug Discovery – Progress & Prospect; RSC publishing, under communication.

2. Scientific work done:

1. **GAP-3153: Cyclic Peptides from Plants of Himalayan Region: Their Screening, Isolation and Characterization**

As PI of the project

Analysis, purification and identification of orbitides.

Based on the initial MS report and MS/MS studies, two orbitides were identified as FS-FR-F and FS-FR-G. The probable structure of these identified compounds are provided in **figure 1**.

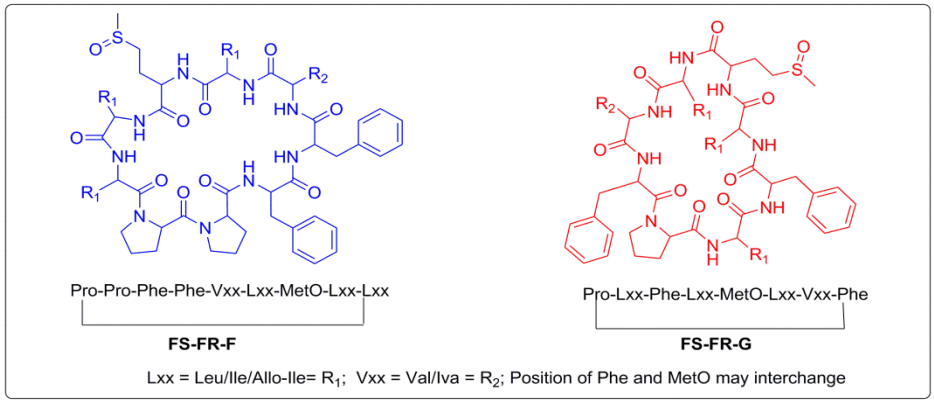


Figure-1: Probable structure of orbitides from *Linum usitatissimum* seeds (Commercial).

Exploring plants of Himalayan region for the search of cyclic peptides:

Various plants of the Himalayan region were explored for the production of cyclic peptides. The part majorly includes seeds, leaves, fruits etc. Similar strategy was followed to indentify cyclic peptides. The list of plants/ parts that are explored for the presence of putative cyclic peptides. These were subjected to mass spectrometry analysis. To our surprise, none of the mass value observed have shown presence of peptide in the MSMS studies except linseed seeds obtained from the Akhnoor region of Jammu. We were able to identifiy two cyclolinopeptidesi.e FS-AKH-3 and FS-AKH-5 (previously identified from commercial sample) as shown in **figure 2**. As these are present in miniscule quantity, further isolation and purification is underway.

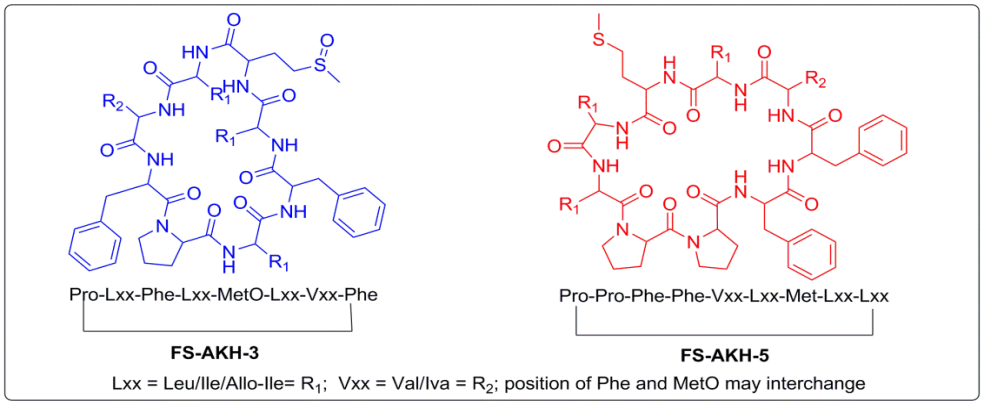


Figure 2: Cyclic peptides from *Linum usitatissimum*Seeds of Akhnoor region.

Cyclotides from Viola odorata

Cyclotides are one of the major class of cyclic peptides from plants comprising of 28-37 amino acid chain with 3 disulphide linkage i.ecycteine-cycteine knots (CCK motif). One of the known source is **Viola odorata.** The Initial Screening of viola odorata as done earlier has shown presence of cyclotides. The ethanol water extract was further chromatographed on RP-HPLC to obtain 10 fractions. Further, the MS analysis of one of the fraction revealed *m/z* values as 1440.07 as doubly charged, indicating a mass of 2880.1. Further analysis of the identified fraction is underway to establish the amino acid sequence of the cyclopeptides. Also, a protocol to examine the large peptides is to be established.

2. **Phytopharamaceutical mission**: **(GAP-3107) Development of *Boswellia serrata* Based Phytopharmaceutical Drug for Osteoarthritis**

Role: Co-PI in the project

The evaluation of the analytical results, outsourced data obtained from companies like Dabur Research Foundation, etc., compilation of the results, verifying the validation reports were carried out. We thoroughly examined the validation report for the analytical method for the enriched fraction to be used for further analysis. I also examined the stability report for the IIIM-BSEF-01enriched fraction and the formulated capsules against accelerated, intermediate and long term studies. I along with Dr. P P Singh Sir, evaluated the reports, reviewed the progress by regular meetings with Dabur Research Foundation.

3. **Metabolite identification of *Micromonospora Sp.* (Collaboration with Dr. Asha Chaubey)**

LCMS based metabolite screening

The metabolite identification using observed *m/z* values (monoisotopic mass) through the manual database mining approach was done using the natural products database libraries such as Dictionary of Natural Products (DNP), and Lotus for the presence of compounds of natural origin. The database mining gave multiple hits. Only those hits with ± 5 ppm error were considered for the structure probability. The probable compounds with respective m/z values are reported. Intrestingly, while closely observing TIC, multiple charged ions at Rt =2.2 min with *m/z* as 967.585 (+3 charged), 972.911 (+3 charged), 980.569 (+3 charged), 985.560 (+3 charged), and 739.419 (+4 charged) were observed. It corresponds to higher mass range such as 2902.755, 2918.733, 2941.707, 2856.68 and 2957.6 respectively. The database predicts these to be cyclic peptides of mass range of 2900 to 3000 Da. (**Table 1**)

Table 1: Higher molecular weight compound hits observed and analysed through DNP database.

S. No.	Retention time (Min)	Observed *m/z*	Deconvoluted *m/z*	Probable structure type
1	2.2	967.585 (+3 charged)	2902.755	Cyclic peptides
		972.911 (+3 charged)	2918.733	
		980.569 (+3 charged)	2941.707	
		985.560 (+3 charged)	2856.68	
		739.419 (+4 charged)	2957.6	

To confirm the metabolomic study and for further characterization, isolation of metabolites were carried out using RP-HPLC.

Isolation, purification and identification of metabolites

The microbial extract was isolated using RP-HPLC applying multiple purification steps to isolate and purify. Among multiple observed peaks in chromatogram, two compounds **1&2 (Figure 3)** were isolated in miniscule quantities with HPLC purity of >98% and 83% respectively. Both the compounds were subjected to mass based analysis for further identification. With the help of extensive MS and MSMS studies the compounds were identifies as Ferrioxamine E and Sinomontanine C (**Figure 3**)

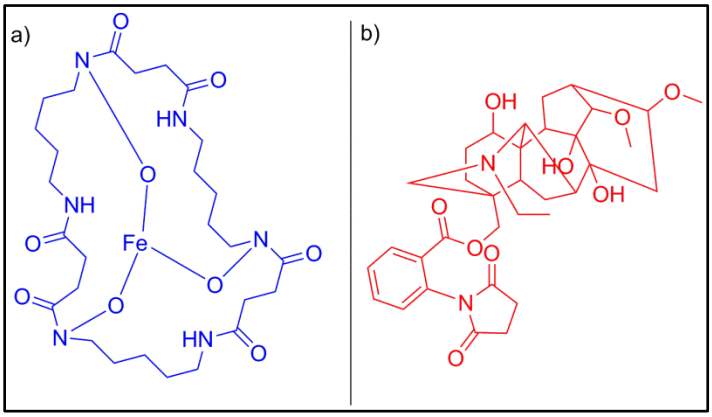


Figure 3: Chemical structure of a) Ferrioxamine E and b) Sinomontanine C

The draft for the chemistry part was written and it is under communication.

4. Identification of compounds from fungi *Trametes hirsita* (In collaboration with Dr. Sandeep Jaglan)

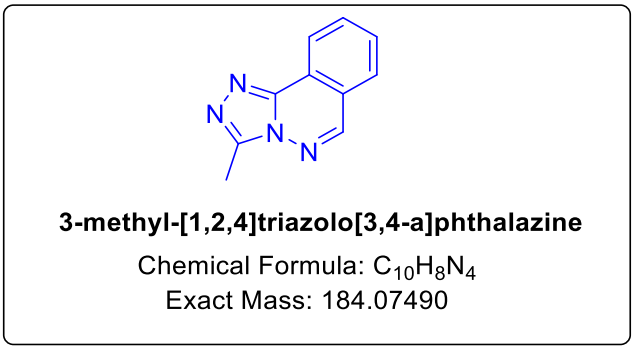


Figure 4: Structure of compound **3** (3-methyl-triazolo[3,4-a] phthalazine).

The isolated compounds were subjected to NMR and Mass spectroscopic analysis. Based on the 1D and 2D NMRs such as ^{1}H, ^{13}C, COSY, HMBC and HSQC, the compound **3** was characterized as 3-methyl-triazolo[3,4-a] phthalazine. The HRMS study showed *m/z* as $[M+H]^{+}$ 185.0831 (observed); 185.0822 (calculated). The HRMS along with the NMR studies confirmed the structure as 3-methyl-triazolo[3,4-a] phthalazine. (**Figure 4**)

5. Identification of compounds from fungus *Paecilomyceslilacimus* (In collaboration with Dr. Sandeep Jaglan)

The compound isolated from the fungus *Paecilomyceslilacimus* were studied for its structural elucidation. The HRMS study of compound **4** was found to be *m/z* = 278.1509 (278.1518 calculated). The extensive 1D and 2D NMRs studies along with MS studies revealed the structure of compound as butyl isobutyl phthalate. (**Figure 5**)

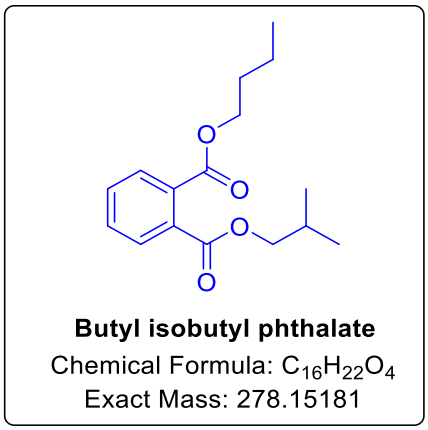


Figure 5: Structure of compound **4**

AVISEK MAHAPA

Dr. Avisek Mahapa (Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

S. No.	Authors	Title	Journal
1	Chowdhary R, Rathore A, Sarkar AR, Kumari J, Manhas R, Firdous S, **Mahapa A***, Rai R.	Antibacterial activity of 2-(4-aminopiperidin-4-yl) acetic acid (β3, 3-Pip) and Its peptide conjugated with lauric acid through the side chain against Methicillin-resistant *Staphylococcus aureus* (MRSA)	Microbial Pathogenesis (2025)
2	Firdous S, Sarkar AR, Manhas R, Chowdhary R, Rathore A, Kumari J, Rai R, **Mahapa A***.	Synthesis, Characterization, and Antimicrobial Activity of Urea-Containing α/β Hybrid Peptides against *Pseudomonas aeruginosa* and Methicillin-Resistant *Staphylococcus aureus*	ACS Omega (2025)

3	**Mahapa A***, Gautam S, Rathore A, Chatterji D	An HPLC-based Assay to Study the Activity of Cyclic Diadenosine Monophosphate (C-di-AMP) Synthase DisA from *Mycobacterium smegmatis*	Bioprotocol (2024)
4	Sarkar AR, Kumari J, Rathore A, Chowdhary R, Manhas R, Firdous S, **Mahapa A***, Rai R.	Antimicrobial activity of α/β hybrid peptides incorporating tBu-β3,3Ac6c against methicillin-resistant *Staphylococcus aureus*	The Journal of Antibiotics (2024)
5	Shahi A, Manhas R, Bhattacharya S, Rathore A, Kumar P, Samanta J, Sharma MK, **Mahapa A***, Gupta P, Anal JM.	Synthesis and antibacterial potential of novel thymol derivatives against methicillin-resistant *Staphylococcus aureus* and *P. aeruginosa* pathogenic bacteria	Frontiers in Chemistry (2024)

Patents:

S. No.	Inventors/Contributors	Title	Description	Year
1	Rubina Chowdhary, Aminur Rahman Sarkar, Rakshit Manhas, Arti Rathore, **Avisek Mahapa***, Zabeer Ahmed, Rajkishor Rai	Short β/γ-hybrid peptides as potent antimicrobial agents	The present invention relates to the process for the preparation of novel b/g hybrid peptides and their exploration as antibacterial agents.	2025

2. Scientific work done:

Synthesis and Antibacterial Evaluation of Trisindolines against Methicillin-resistant Staphylococcus aureus Targeting Cell Membrane

Methicillin-resistant *Staphylococcus aureus* (MRSA) poses a significant global health threat that requires novel antimicrobials to combat this WHO-designated priority pathogen. In this study, we designed, synthesized and evaluated a series of unexplored trisindoline derivatives against MRSA, including multidrug-resistant (MDR) clinical isolates. The Structure Activity Relationship (SAR) analysis of the trisindolines indicated the importance of strategic substitutions in the trisindoline core for their anti-staphylococcal efficacy. Biocompatibility studies revealed a high safety profile for the active compounds across various mammalian cell lines. Furthermore, the derivatives displayed rapid bactericidal action, anti-biofilm efficacy, intracellular MRSA killing and combinatorial effect with vancomycin. Mechanistic studies revealed that these compounds disrupt MRSA cell integrity by influencing several membrane-related pathways. Finally, in vivo assessments of a lead trisindoline in an MRSA-induced systemic infection model demonstrated a significant reduction of bacterial load.

Therefore, these trisindoline molecules may offer a promising therapeutic model for combating MRSA infections.

Cationic β-amino acid derivatives and peptides (synthesis, characterization, and antibacterial efficacy)

The present work describes the synthesis, characterization, and antibacterial efficacy of cationic β-amino acid derivatives and peptides, H_2N-$\beta^{3,3}$-Pip (LA)-PEA, **P1**; and H_2N-$\beta^{3,3}$-Pip (^{U}LA)-PEA, **P2;** H_2N-$\beta^{3,3}$-Pip (LA)-$\beta^{2,2}$-Ac_6c-PEA, **P3**; and H_2N- $\beta^{3,3}$-Pip (^{U}LA)- $\beta^{2,2}$-Ac_6c-PEA, **P4**. The compounds **P1-P4** were evaluated against the WHO priority multidrug-resistant (MDR) ESKAPE panel pathogens. **P2** and **P4** exhibited potent activity with MIC values ranging from 3.1 μM to 6.2 μM against MDR pathogens. Further, the kill-kinetics assay demonstrated that **P2** and **P4** eliminate MRSA in a concentration and time-dependent manner. **P2** and **P4** also showed the MRSA biofilm prevention and disruption of preformed biofilm. The SEM images and PI permeability assays confirmed the bacterial killing by **P2** and **P4** through membrane disruption, highlighting their strong bactericidal activity. Additionally, the very low hemolytic and cytotoxic activity of peptides indicate these compounds as promising candidates for further investigation. Subsequently, the compounds **P2** and **P4** showed synergistic effects with vancomycin. Altogether, the present study highlights the potential of short cationic β-amino acid derivatives and peptides conjugated with lauric acid through the side chain as novel antibacterial agents for combating antimicrobial resistance (AMR).

Short αβ cationic hybrid peptides (Synthesis, Characterization and biological evaluation)

The insertion of β-amino acids and replacement of the amide bond with a urea bond in antimicrobial peptide sequences are promising approaches to enhance the antibacterial activity and improve proteolytic stability. Herein, we describe the synthesis, characterization, and antibacterial activity of short αβ cationic hybrid peptides LA^{U}-Orn-$\beta^{3,3}Ac_6c$-PEA, **DY-01**; LA^{U}-Lys-$\beta^{3,3}Ac_6c$-PEA, **DY-02**; and LA^{U}-Arg-$\beta^{3,3}Ac_6c$-PEA, **DY-03** in which a C12 lipid chain is conjugated at the N terminus of peptide through urea bonds. Further, we evaluated all the peptides against both *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA) and their multidrug resistant (MDR) clinical isolates. All of the peptides exhibited significant bactericidal efficacy with minimal inhibitory concentration (MIC) values ranging from 2.5 to 6.25 μM (1.4 to 3.9 μg/mL) against *P. aeruginosa* and its MDR clinical isolates, whereas the MIC values ranging from 0.78 to 6.25 μM (0.45 to 3.9 μg/mL) against MRSA and MDR clinical isolates of *S. aureus*. To understand the potency and mechanism of action of **DY-01** to **DY-03**, time-kill kinetics, biofilm inhibition and disruption, synergistic interactions with standard antibiotics, swarming motility, scanning electron microscopy (SEM) analyses, and ex vivo infection assay were performed. The SEM images revealed that all of the peptides exert antibacterial activity through a membrane disruption mechanism. Additionally, negligible cytotoxicity was observed against mammalian cell lines RAW 264.7 and J774A.1, with mild hemolysis at higher concentrations. The comprehensive antimicrobial assessments of **DY-01** to **DY-03** against *P. aeruginosa* and MRSA highlight their potential for clinical applications in combating resistant microbial infections.

Short α/β hybrid peptides (Synthesis, characterization and biological evaluation)

The incorporation of β-amino acids into peptides is a promising approach to develop proteolytically stable therapeutic agents. Short α/β hybrid peptides containing tBu-$\beta^{3,3}Ac_6c$: H_2N-Lys-tBu-$\beta^{3,3}Ac_6c$-

PEA, P1; H_2N-Orn-tBu-$\beta^{3,3}Ac_6c$-PEA, P2; H_2N-Arg-tBu-$\beta^{3,3}Ac_6c$-PEA, P3; LA-Lys-tBu-$\beta^{3,3}Ac_6c$-PEA, P4; LA-Orn-tBu-$\beta^{3,3}Ac_6c$-PEA, P5; LA-Arg-tBu-$\beta^{3,3}Ac_6c$-PEA, P6; LA^u-Lys-tBu-$\beta^{3,3}Ac_6c$-PEA, P7; LA^u-Orn-tBu-$\beta^{3,3}Ac_6c$-PEA, P8; and LA^u-Arg-tBu-$\beta^{3,3}Ac_6c$-PEA, P9 were prepared. The antimicrobial efficacies of all the peptides were evaluated against ESKAPE pathogens, along with a small panel of multi-drug resistant (MDR) clinical isolates of *S. aureus*. Among all the peptides, P4, P6, and P7 showed significant efficacies against *P. aeruginosa*, *S. aureus*, and MRSA with an MIC value ranging from 6.25 to 12.5 μM. Further, in vitro, anti-staphylococcal assessment with their antimicrobial synergy of the peptides P4, P6, and P7 was carried out against MRSA, due to its better efficacy. The peptides P6 and P7 exhibited MRSA biofilm inhibition of 70% and 77%, respectively, at 4×MIC concentration. At its MIC concentration, about 19% hemolysis was observed for P4, P6, and P7.

FIRDOUS AHMAD MIR

Dr. Firdous Ahmad Mir (Sr. Scientist) with his research group

1. Publications/Patents:

Publications:

- Firdous Ahmad Mir, Padma Lay. A comprehensive review of the critically endangered medicinal plant *Sassuraecostus*. Volume 14, 2024, Indian journal of applied research.
- Firdoous Ahmad Mir, Mahruk Irshad. Himalayan Plants: A green gold for ayurveda, conservation, and future health care. Journal of Ayurvedic and Herbal Medicine (Accepted).

2. Scientific work done:

1. Exploration and Germplasm Collection of High-Value Medicinal Plants

A series of meticulously planned plant exploration missions were conducted in the high-altitude ecosystems of Jammu & Kashmir—particularly across Pir Panjal, Harmukh, and Sarbal Lake regions—ranging from 2500 to 4000 meters above sea level. These expeditions aimed to collect genetically diverse and viable populations of rare, endangered, and high-demand medicinal plant species vital to Indian systems of medicine and pharmaceutical industries.

Key species collected:

- *Podophyllum hexandrum* (Himalayan Mayapple)
- *Picrorhizakurroa* (Kutki)
- *Arnebiabenthamii* (Ratanjot)
- *Bergenia ciliata* (Pashanbheda)

- *Swertia chirayta* (Chirata)
- *Dioscorea deltoidea* (Wild Yam)
- *Rheum emodi* (Himalayan Rhubarb)
- Additional endemic species with ethnomedicinal significance

All collections were geo-referenced using handheld GPS devices and meticulously documented. Samples were transported under controlled conditions for further propagation and research. Special care was taken to avoid overharvesting, thus maintaining the ecological integrity of source populations.

Figure 1. Field collection of from alpine zones in the Harmukh foothills.

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2. Field Preparation and Establishment of Living Collections at Verinag Farm

The CSIR-IIIM Verinag Research Farm, situated at an elevation conducive to Himalayan plant adaptation, was transformed into a cultivation site. The originally sloped and rocky terrain was rehabilitated into structured conservation blocks through terracing, stone removal, and organic soil amendment.

Major achievements:

- Establishment of live collections for over 20 medicinal plant species
- Introduction and adaptation trials of high-altitude species to subtler farm conditions
- Soil health improvement using green manure and native composting techniques
- Standardized irrigation and shade systems mimicking wild microhabitats

The Verinag site now functions as a **regional hub for ex-situ conservation, QPM generation, and field validation of agro-techniques** for elite germplasm.

Figure 2. Terraced plots at Verinag under cultivation.

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3. QPM Generation under Mission Projects:

Under the ambit of National Missions like the **CSIR-Aroma Mission** and **Phytopharmaceutical Mission**, targeted efforts were directed towards the multiplication of elite planting material and development of agro-techniques for commercially and medicinally important species.

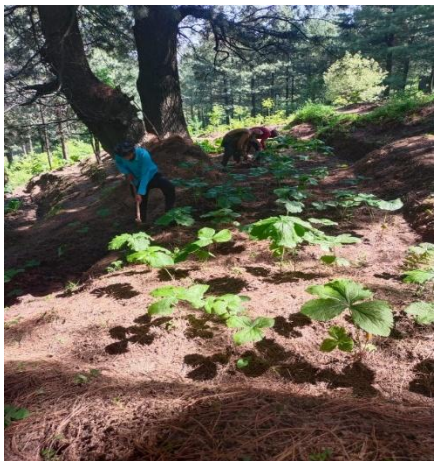
Species-Specific Outcomes:

- **Swertia chirayta**: High-elevation accessions were evaluated for survival, morphology, and phytochemical yield. Seed-based and in-vitro propagation modules were developed for mass multiplication.
- **Lavandula angustifolia** (Kashmir Lavender): Propagation using stem cuttings and root divisions enhanced the nursery's capacity to support ~10,000 saplings/year for farmer deployment.

Saussureacostus: Critical conservation status prompted development of rhizome propagation and seed viability assessment tools. Trials at Verinag show 90% establishment success.

These activities directly support the goal of ensuring **year-round availability of Quality Planting Material (QPM)** to farmers and industries.





4. Advanced R&D at the Plant Tissue Culture Division, CSIR-IIIM Srinagar

The Plant Tissue Culture (PTC) Division played a pivotal role in conserving and enhancing these species at a cellular level. By using advanced biotechnological interventions, we worked toward:

a. Development of In Vitro Conservation Protocols

- Axenic cultures initiated for *Swertia chirayta*, *Saussureacostus*, *Picrorhizakurroa*, and *Dioscorea deltoidea*.

b. In Vitro Secondary Metabolite Production

- Callus cultures established for:
    - **Podophyllotoxin** from *Podophyllum hexandrum*
    - **Shikonin** from *Arnebiabenthamii*
    - **Swertiamarin** from *Swertia chirayta*

c. Tissue Culture Technology Advancements

- Protocols under development include:
    - Somatic embryogenesis in *Bergenia ciliata*
    - Anther culture and protoplast isolation for future genomic studies

These protocols ensure **pathogen-free, uniform, and scalable production** of plants suitable for direct field transfer, research, and industry linkages.

Concluding Remarks and Future Vision

This multi-tiered strategy—spanning from field to lab—demonstrates a robust model for **integrated conservation, sustainable utilization, and technology-driven scalability** of endangered Himalayan botanicals. By combining traditional knowledge, cutting-edge biotechnology, and community-based models, the program envisions:

- Strengthening supply chains of prioritized medicinal plants
- Enhancing livelihoods through farmer-linked cultivation
- Conserving plant biodiversity for future generations
- Generating research-grade plant materials for academic and industry R&D.

RAJKISHOR RAI

Dr. Rajkishor Rai (Sr. Scientist) with his Research Group

1. Publications/Patents:

Publications:

- A. R. Sarkar, J. Kumari, A. Rathore, R. Chowdhary,R. Manhas, S. Firdous, A.Mahapa, **R. Rai.** Antimicrobial activity of α/β hybrid peptides incorporatingtBu-$\beta^{3,3}Ac_6c$ against methicillin-resistant Staphylococcus aureus. *Journal of Antibiotics***2024**, 77(12):794-801.
- H. A. Kantroo, M. M. Mubarak, R. Chowdhary, **R.Rai**, Z. Ahmad. Antifungal Efficacy of Ultrashort β-Peptides against *Candida* Species: Mechanistic Understanding and Therapeutic Implications**.** *ACS Infectious Diseases***2024**, 10(11):3736-3743.

- S. Firdous, A. R. Sarkar, R. Manhas, R. Chowdhary,A. Rathore, J. Kumari, **R. Rai,** A. Mahapa.Synthesis, Characterization, and Antimicrobial Activity of Urea-Containing α/β Hybrid Peptides against *Pseudomonas aeruginosa* andMethicillin-Resistant *Staphylococcus aureus.* *ACS Omega***2025**, 10(2):2102-2115.
- M.M.Mubarak, R. Chowdhary, J.U. Rahim, H. A. Kantroo, Z.A. Wani, A. Malik, S. Shah, I. Ahmad Baba, A. R. Sarkar, **R. Rai**, Z. Ahmad. Lauric acid conjugated ureido derivatives of 2-(4-aminopiperidin-4-yl) acetic acid ($\beta^{3,3}$-Pip): Overcoming resistance and outperforming standard antibacterials**.** *Eur. J. Med. Chem. Rep*. **2025**, 100260.

Patents:

- Short b/g-hybrid peptides as potent antimicrobial agents (0059NF2025).
  Inventors: Rubina Chowdhary, Aminur Rahman Sarkar, Rakshit. Manhas, Arti Rathore, Avisek Mahapa, Zabeer Ahmad, **Rajkishor Rai**.

2. Scientific work done:

➢ **Synthesis, characterization, and conformational studies of αβ hybrid peptides containing $\beta^{2,2}$-Ac_6c**

The following αβ hybrid peptides incorporating $\beta^{2,2}$-Ac_6c, Boc-$\beta^{2,2}$-Ac_6c-Leu-OMe, **HP1**; Boc-($\beta^{2,2}$-Ac_6c-Leu)$_2$-OMe, **HP2**; and Boc-($\beta^{2,2}$-Ac_6c-Leu)$_3$-OMe, **HP3** (**Figure 1**) were synthesized to investigate how various substituents influence the conformation of the peptide backbone. The synthesis of these specific peptides allows for a closer examination of the relationship between side chain characteristics and backbone conformational behavior.

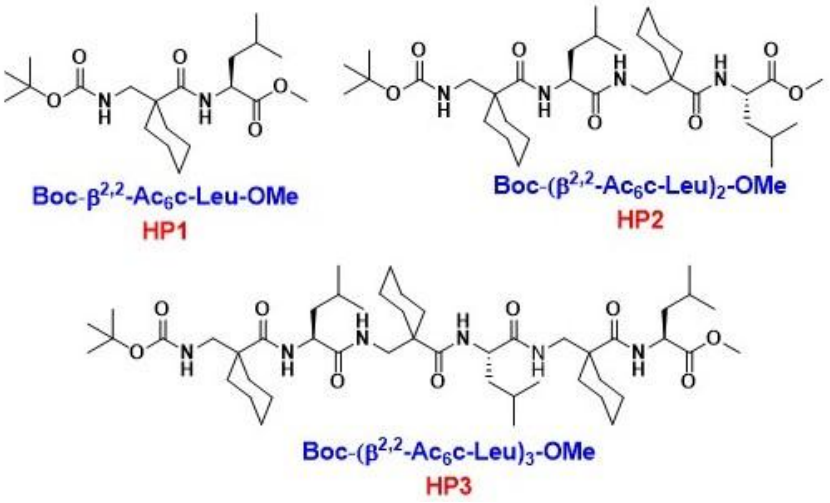


Figure1.Chemicalstructures of αβ hybrid peptides Boc-$\beta^{2,2}$-Ac_6c-Leu-OMe, **HP1**; Boc-($\beta^{2,2}$-Ac_6c-Leu)$_2$-OMe, **HP2**; and Boc-($\beta^{2,2}$-Ac_6c-Leu)$_3$-OMe, **HP3.**

All the peptides were synthesized in the solution phase, purified by HPLC, and characterized by NMR and mass spectroscopy. The NMR studies established that **HP1-HP3** adopt a helical C_{11}/C_9 conformation in solution and solid state.

➢ **Synthesis, characterization, and conformational studies of *αβ* hybrid peptides containing $\beta^{2,2}$-amino acid.**

The following β hybrid peptides incorporating $\beta^{2,2}$-Ac_6c, Boc-$\beta^{2,2}$-Ac_6c-Γ^4Phe-OMe, **HP4**; Boc-($\beta^{2,2}$-Ac_6c-Γ^4Phe)$_2$-OMe, **HP5**; Boc-($\beta^{2,2}$-Ac_6c-Γ^4Phe)$_3$-OMe, **HP6** and Boc-($\beta^{2,2}$-Ac_6c-Γ^4Phe)$_4$-OMe, **HP7** (Figure 2) were synthesized to investigate the backbone conformation.

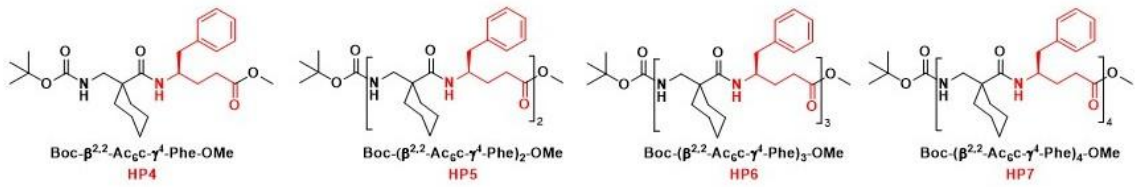


Figure 2. Chemical structures of Boc-$\beta^{2,2}$-Ac_6c-Γ^4Phe-OMe, **HP4**; Boc-($\beta^{2,2}$-Ac_6c-Γ^4Phe)$_2$-OMe, **HP5**; Boc-($\beta^{2,2}$-Ac_6c-Γ^4Phe)$_3$-OMe, **HP6** and Boc-($\beta^{2,2}$-Ac_6c-Γ^4Phe)$_4$-OMe, **HP7.**

The above peptides were synthesized in the solution phase, purified by HPLC, and characterized by NMR and mass. The detailed NMR experiments established that peptides **HP4-HP7**favor a C_{13}/C_{11} helical conformation.

- **Hybrid peptides incorporating *tBu*-ß^{3,3}Ac$_6$c as antimicrobial agents against Methicillin-resistant *Staphylococcus aureus***

Theshort α/β hybrid peptides containing *tBu*-ß^{3,3}Ac_6c, H_2N-Lys-*tBu*-ß^{3,3}Ac_6c-PEA, **P1**; H_2N-Orn-tBu-ß^{3,3}Ac_6c-PEA, **P2**;H_2N-Arg-*tBu*-ß^{3,3}Ac_6c-PEA, **P3**;LA-Lys-*tBu*-ß^{3,3}Ac_6c-PEA, **P4**; LA-Orn-tBu-ß^{3,3}Ac_6c-PEA, **P5**; LA-Arg-*tBu*-ß^{3,3}Ac_6c-PEA, **P6**; LA^u-Lys-*tBu*-ß^{3,3}Ac_6c-PEA, **P7**; LA^u-Orn-*tBu*-ß^{3,3}Ac_6c-PEA, **P8**; and LA^u-Arg-*tBu*-ß^{3,3}Ac_6c-PEA, **P9 (**Figure 3)were syntrhesized.

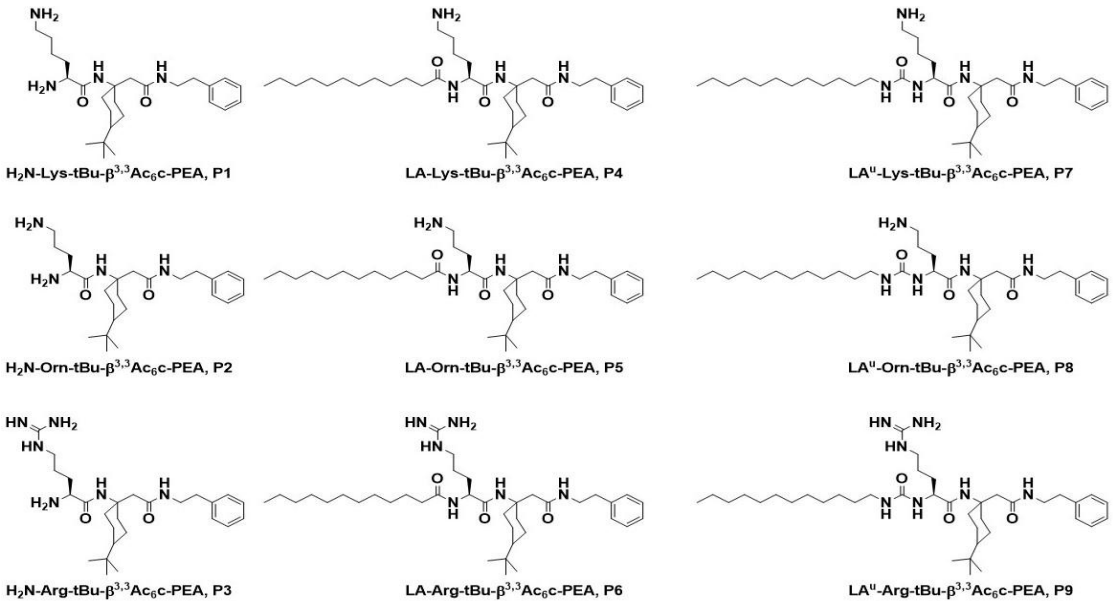


Figure 3: Chemical structure of α/ß hybrid peptides, H_2N-Lys-*tBu*-ß^{3,3}Ac_6c-PEA, **P1**; H_2N-Orn-tBu-ß^{3,3}Ac_6c-PEA, **P2**;H_2N-Arg-*tBu*-ß^{3,3}Ac_6c-PEA, **P3**;LA-Lys-*tBu*-ß^{3,3}Ac_6c-PEA, **P4**; LA-Orn-tBu-ß^{3,3}Ac_6c-PEA, **P5**; LA-

Arg-*tBu*-ß^{3,3}Ac$_6$c-PEA, **P6**; LA^u-Lys-*tBu*-ß^{3,3}Ac$_6$c-PEA, **P7**; LA^u-Orn-*tBu*-ß^{3,3}Ac$_6$c-PEA, **P8**; and LA^u-Arg-*tBu*-ß^{3,3}Ac$_6$c-PEA, **P9.**

The antimicrobial efficacies of all the peptides were systematically evaluated against a selection of ESKAPE pathogens, which are known for their clinical relevance and resistance profiles. Additionally, we included a curated panel of multi-drug resistant (MDR) clinical isolates, specifically of *Pseudomonas aeruginosa* and *Staphylococcus aureus*. Among all the peptides, **P4, P6**, and **P7** demonstrated significant antimicrobial activity against both *P. aeruginosa* and *S. aureus*, including the methicillin-resistant strain, *MRSA*. The Minimum Inhibitory Concentration (MIC) values for these peptides were notably effective, ranging from 6.25 to 12.5 μM, indicating their potential as candidates for further development in combating these resistant pathogens.

The in vitro evaluation of the antimicrobial effects and synergy of peptides **P4,P6**, and **P7** was conducted against Methicillin-Resistant *Staphylococcus aureus* (MRSA). The results demonstrated that peptides **P6** and **P7** were particularly effective, achieving significant biofilm inhibition rates of 70% and 77%, respectively, when tested at four times their Minimum Inhibitory Concentration (4×MIC). This indicates a promising ability of these peptides to disrupt bacterial communities that are often resistant to traditional antibiotics. Additionally, an evaluation of hemolytic activity revealed that at their respective Minimum Inhibitory Concentrations (MIC), peptides **P4**, **P6**, and **P7** exhibited approximately 19% hemolysis. This data provides crucial insights into the therapeutic potential of these peptides, highlighting their antimicrobial efficacy while also noting the importance of monitoring hemolytic effects to ensure safety in further applications.

- **Evaluation of hybrid peptides containing ß-and Γ-amino acids as anticancer agents.**

Peptides containing ß-and Γ-amino acids,Boc-ß^{2,2}-Ac$_6$c-Leu-OMe, **HP1,** Boc-(ß^{2,2}-Ac$_6$c-Leu)$_2$-OMe, **HP2**; Boc-(ß^{2,2}-Ac$_6$c-Leu-)$_3$-OMe, **HP3**; H-ß^{2,2}-Ac$_6$c-Leu-OMe, **HP4**; H-(ß^{2,2}-Ac$_6$c-Leu)$_2$-OMe, **HP5**; H-(ß^{2,2}-Ac$_6$c-Leu-)$_3$-OMe, **HP6**; Boc-ß^{2,2}-Ac$_6$c-ß^4-Phe-OMe, **HP**7; Boc-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_2$-OMe, **HP8**; Boc-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_3$-OMe, **HP9**; Boc-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_4$-OMe, **HP10**; H-ß^{2,2}-Ac$_6$c-Γ^4-Phe-OMe, **HP11**; H-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_2$-OMe, **HP12**; H-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_3$-OMe, **HP13**; and H-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_4$-OMe, **HP14** were synthesized, purified and characterized by mass and NMR spectroscopic techniques. The chemical structures are shown in Figure 4.

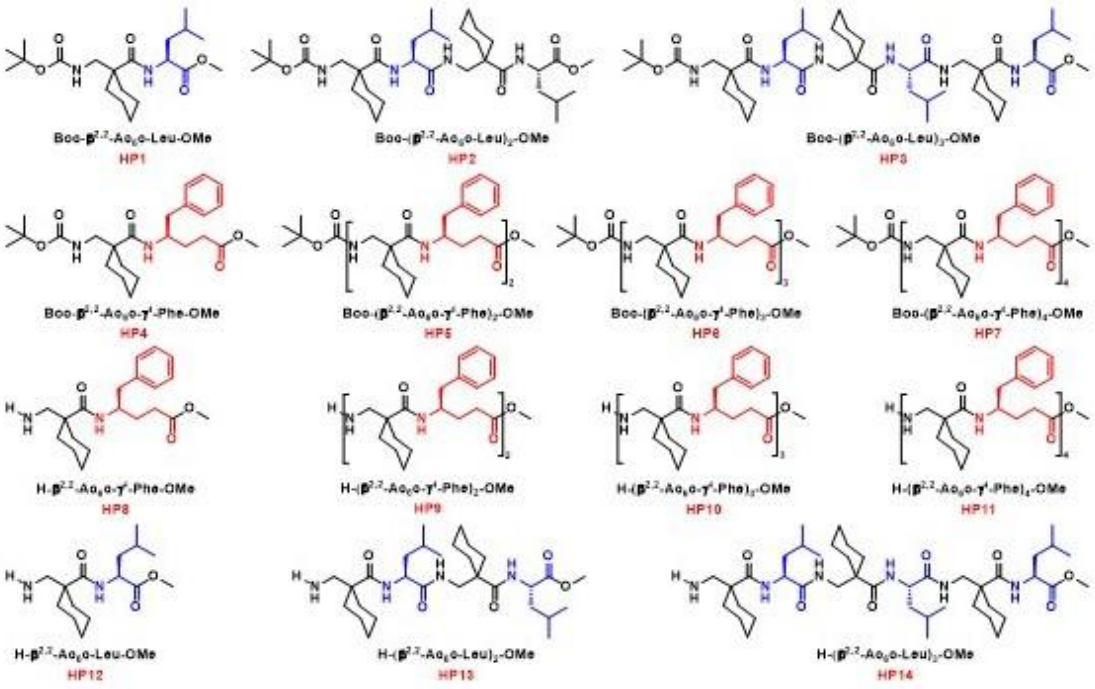


Figure 4. Chemical structures ofBoc-ß^{2,2}-Ac$_6$c-Leu-OMe, **HP1,** Boc-(ß^{2,2}-Ac$_6$c-Leu)$_2$-OMe, **HP2**; Boc-(ß^{2,2}-Ac$_6$c-Leu-)$_3$-OMe, **HP3**; H-ß^{2,2}-Ac$_6$c-Leu-OMe, **HP4**; H-(ß^{2,2}-Ac$_6$c-Leu)$_2$-OMe, **HP5**; H-(ß^{2,2}-Ac$_6$c-Leu-)$_3$-OMe, **HP6**; Boc-ß^{2,2}-Ac$_6$c-Γ^4-Phe-OMe, **HP**7 ; Boc-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_2$-OMe, **HP8**; Bocß^{2,2}-Ac$_6$c-Γ^4-Phe)$_3$-OMe, **HP9**; Boc-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_4$-OMe, **HP10**; H-ß^{2,2}-Ac$_6$c-Γ^4-Phe-OMe, **HP11**; H-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_2$-OMe, **HP12**; H-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_3$-OMe, **HP13**; and H-(ß^{2,2}-Ac$_6$c-Γ^4-Phe)$_4$-OMe, **HP14.**

All the peptides **HP1**-**HP14** were evaluated against various cancer lines, including HCT-116 (Colon cancer), MCF-7 (Breast cancer), and A549 (Lung Cancer). Among all, **HP 14** exhibited potent anticancer activity against the screened cell lines with an IC_{50} ranging from the lowest 3.3µM to the highest 5.6µM. The *in vitro and in vivo* studies with **HP14**demonstrated its therapeutic potential against colon cancer.

ANIL KUMAR KATARE

Er. Anil Kumar Katare (Sr. Principal Scientist) with his research group

1. Publications/Patents:

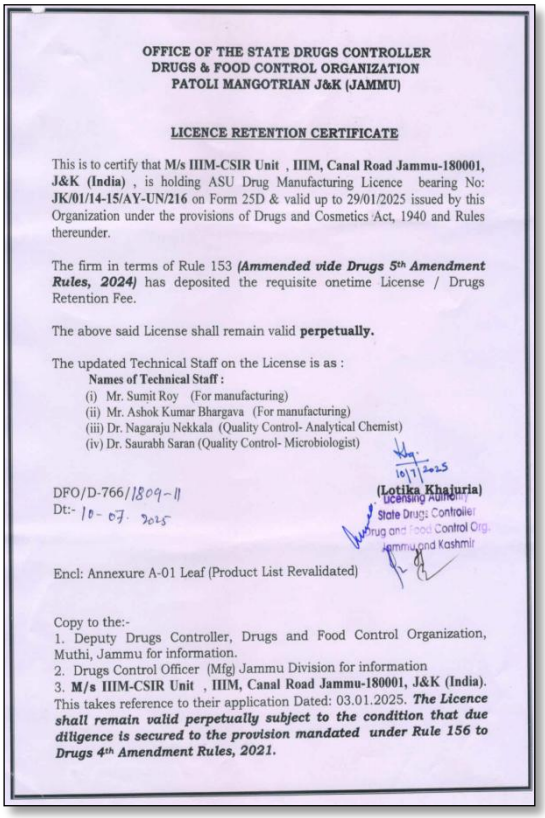
Publications:

- "Discovery of two new tirucallane-type triterpenes anomers from Toona ciliate," Aliya Tabassum, Harshad B. Bhore, Jayanta Samanta, Anil Kumar Katare, Yogesh P. Bharitkarhttps://doi.org/10.1080/14786419.2024.2429115.
- "Synthesis of novel spiroisoxazolidino hybrids of alantolactone and isoalantolactone *via* 1,3 dipolar nitrone cycloaddition and its antimicrobial valuation." Aliya Tabassum, Diksha Kumari, Harshad B. Bhore, Tashi Palmo, Initha Venkatesan, Jayanta Samanta, Anil Kumar Katare, Kuljit Singh, Yogesh P. Bharitkar, Bio-organic Chemistry 154 (2025) 108087. https://doi.org/10.1016/j.biorg.2024.108087.
- "Diversity-oriented semi-synthesis of Alantolactone and Isoalantolactone hybrids employing azomethine ylide cycloaddition pathway." Aliya Tabassum, HarshadB.Bhore, A.Mercy Abarna, Jayanta Samanta, Anil Kumar Katare, Ravindra S. Phatake, Yogesh P. Bharitkar**.**Journal of Molecular StructureVolume 1333, (2025), 141729. https://doi.org/10.1016/j.molstruc.2025.141729.

2. Scientific work done:

a. "cGMP pilot plant for extraction, formulation, and packaging of traditional (ISM) herbal medicinal formulations" is a state-of-the-art national facility for small and medium-scale manufacturers from north India and the state of J&K, in particular, to get their products manufactured under GMP/GLP conditions, besides its use for research in IIIM. CSIR-IIIM can help set up the rules and conditions for herbal products, which shall give strength to the regulatory authorities for coming up with regulatory guidelines for herbal/botanicals that have yet to be enforced in the country. **License renewed by the state regulatory authority (Drug & Food Control OrganizationJ&K Govt.) for the cGMP unit [license No: DFO/Drugs 766/5756-57 dated 19.01.2025] for the next tenure (05 years) from the due date. Licensed under Schedule-T to the D&C Act, 1940 (GMP Certified by state FDA) with the nomenclature "IIIM-CSIR unit (for manufacturing herbal drugs), Jammu." Renewal of the GMP license is applied, inspection of regulatory body done, and regular follow-up is taken.**

cGMP pilot plant



OFFICE OF THE STATE DRUGS CONTROLLER
DRUGS & FOOD CONTROL ORGANIZATION
PATOLI MANGOTRIAN J&K (JAMMU)

LICENCE RETENTION CERTIFICATE

This is to certify that **M/s IIIM-CSIR Unit , IIIM, Canal Road Jammu-180001, J&K (India)** , is holding ASU Drug Manufacturing Licence bearing No: **JK/01/14-15/AY-UN/216** on Form 25D & valid up to 29/01/2025 issued by this Organization under the provisions of Drugs and Cosmetics Act, 1940 and Rules thereunder.

The firm in terms of Rule 153 ***(Ammended vide Drugs 5th Amendment Rules, 2024)*** has deposited the requisite onetime License / Drugs Retention Fee.

The above said License shall remain valid **perpetually.**

The updated Technical Staff on the License is as :

Names of Technical Staff :

(i) Mr. Sumit Roy (For manufacturing)
(ii) Mr. Ashok Kumar Bhargava (For manufacturing)
(iii) Dr. Nagaraju Nekkala (Quality Control- Analytical Chemist)
(iv) Dr. Saurabh Saran (Quality Control- Microbiologist)

DFO/D-766/1809-11
Dt:- 10-07-2025

19/7/2025
(Lotika Khajuria)
Licensing Authority
State Drugs Controller
Drug and Food Control Org.
Jammu and Kashmir

Encl: Annexure A-01 Leaf (Product List Revalidated)

Copy to the:-
1. Deputy Drugs Controller, Drugs and Food Control Organization, Muthi, Jammu for information.
2. Drugs Control Officer (Mfg) Jammu Division for information
3. **M/s IIIM-CSIR Unit , IIIM, Canal Road Jammu-180001, J&K (India).**

This takes reference to their application Dated: 03.01.2025. ***The Licence shall remain valid perpetually subject to the condition that due diligence is secured to the provision mandated under Rule 156 to Drugs 4th Amendment Rules, 2021.***

License of cGMP pilot Plant (GMP)

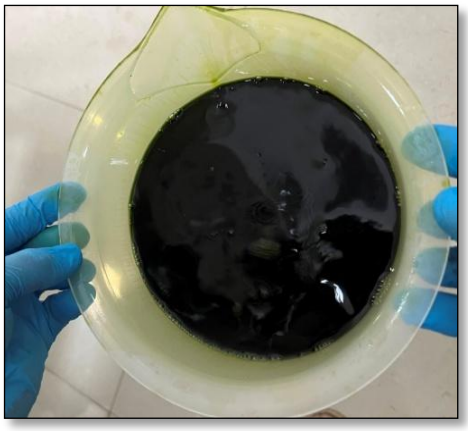
b. GMP extraction of *Phyllanthus amarus* for CSIR-CIMAP:

Phyllanthus amarus is a leafy herbal plant found in tropical regions in the Americas, Africa, India, China, Sri Lanka and South East Asia. Phyllanthus amarus is known as Bhumyamlaki/ Bhumi Amla. Phyllanthus amarus contains flavonoids (quercetin-3-0-glucoside and rutin), tannins (geraniin, amariin and gallocatechin) and alkaloids (phyllantine, quinolizidine type, securinine, norsecurinine, isobubbialine and epibubbialine). Phyllanthus amarus has been used in the traditional medicine of various cultures, including Amazonian tribes for the treatment of gallstones and kidney stones; in Ayurvedic medicine for bronchitis, anaemia, diabetes; and in Malay traditional medicine for diarrhoea, kidney ailments and gonorrhea. When it comes to the extraction of *Phyllanthus amarus* in compliance with Good Manufacturing Practices (GMP) for CIMAP, the general principles of GMP for herbal medicines applied.

Plant Material *Phyllanthus amarus*

Extraction Process

Extract Phyllanthus amarus



Enrich Fraction

CSIR-IIIM Jammu received the purchase order of Rs. 7.08 lakh and SOP received from the CSIR-Central Institute of Medicinal and Aromatic Plants (CIMAP), Lucknow (U.P.). The extraction work at the cGMP plant, as per the SOP has been successfully completed in compliance with Current Good Manufacturing Practice (cGMP) standards. The process involved the meticulous alcoholic extraction, filtration, distillation, wiped film evaporation and vacuum tray drying of extracts from medicinal plant *Phyllanthus amarus* (3 Batches x 25 Kg), under State-of-the-art equipment and controlled environmental

conditions, including centralized air-conditioning and epoxy flooring, were utilized to prevent contamination and maintain product integrity. The Extractive values of three batches were (1) 4.88% (2) 5.32% and (3) 8.8%, which was at par of the supplied SOP. The Suspend extract-A is distilled with water (extract/water ratio: 1:2) and partitioned with distilled ethyl acetate (Solvent B). The first wash of extract with the solvent ratio (1:2) and the second wash of extract with solvent ratio (1:2) were also carried out. A third wash of extract with solvent (distilled water) at a ratio (1:2) was carried out, then removal of the solvent in WFE under reduced pressure at 45°C to get extract B (enrich fraction: LiPa). The extractive value of the extract at the pilot scale achieved more than 5 %. The completed extracts have been handed over/transferred to CSIR-CIMAP, Lucknow.

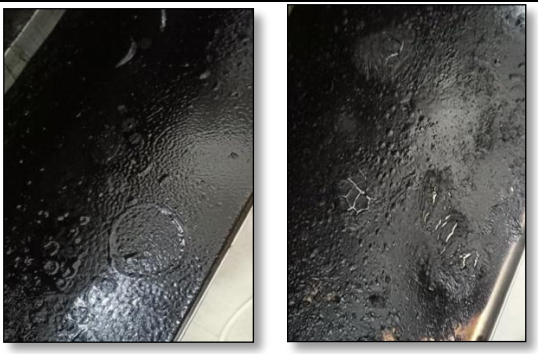
c. cGMP-compliant extraction, formulation and CMC Studies for *Dillenia indica* for NIPER, Guwahati:

Dillenia indica (commonly known as elephant apple) is a medicinal plant native to India, rich in bioactive compounds like betulinic acid, flavonoids, and tannins. Its extracts have shown potential in treating inflammation, diabetes, infections, and oxidative stress, making it a valuable candidate for pharmaceutical research. The strict adherence to cGMP standards ensures that the extraction process is reproducible, scalable, and compliant with regulatory requirements (e.g., Indian Pharmacopoeia, ICH guidelines). The extractive value aligns with typical yields for polar solvent-based extractions of such plants, but further characterization (e.g., HPLC, GC-MS) is needed to confirm the presence of target compounds. This is critical for NIPER, Guwahati, as the extracted bioactive compounds may be used in pre-clinical or clinical studies, requiring high standards of quality and documentation. **A purchase order worth ₹18 lakh was received from NIPER, Guwahati,** along with a Standard Operating Procedure (SOP) for the extraction of *Dillenia indica*. The SOP ensured compliance with Current Good Manufacturing Practice (cGMP) standards, which are critical for ensuring product quality, safety, and regulatory compliance in pharmaceutical manufacturing. The plant material *Dillenia indica*, was supplied by NIPER, Guwahati. The material was sent for Chemistry, Manufacturing, and Controls (CMC) analysis to verify its quality, identity, and compliance with pharmacopoeial standards. Extraction commenced only after receiving an approved CMC report, ensuring the raw material met the required specifications. The extraction process followed cGMP standards and involved, **Precise Extraction**: To isolate bioactive compounds from *Dillenia indica*, **Filtration**: To remove impurities and ensure clarity of the extract, **Distillation**: To concentrate the extract by removing solvents or unwanted volatile components, **Wiped Film Evaporation**: A high-efficiency technique to further purify and concentrate the extract under controlled conditions. **Vacuum Tray Drying**: To dry the extract, ensuring stability and preservation of bioactive compounds. Advanced equipment was used under controlled conditions to maintain product quality, purity, and compliance with regulatory requirements. The yield of the extract from the 23 kg batch was 15.13%, equivalent to approximately 3.48 kg of extract.

Plant Material *Dillenia indica*

Grinded Plant Material

Extraction *Dillenia indica*



Dried Extract

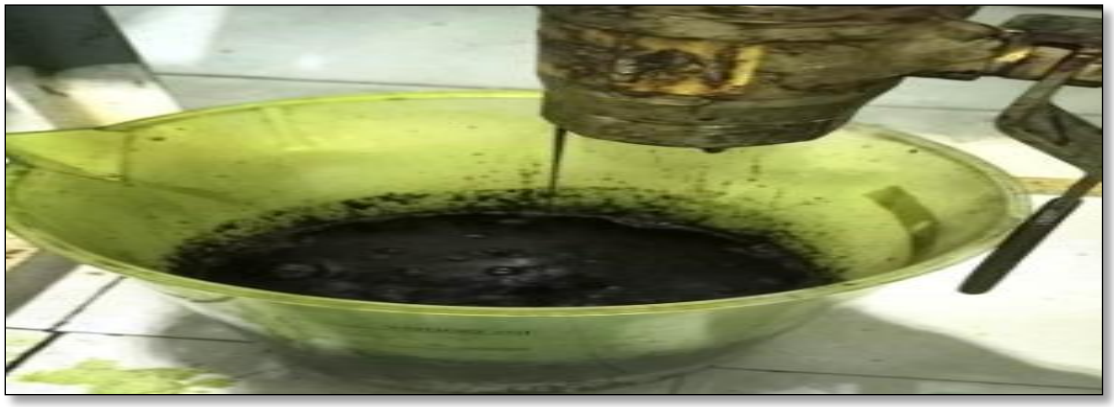
A sample of the extract has been submitted to the Natural Products and Medicinal Chemistry (NPMC) division for the isolation and characterization of bioactive compounds. CMC samples of the extract were deposited in the Quality Control/Quality Assurance (QC/QA) lab for further testing, with reports pending for downstream formulation processing. High-quality excipients, meeting pharmacopoeial standards, were procured from approved vendors. These excipients are ready for use in formulation development, ensuring the production of safe and effective pharmaceutical products as per NIPER's specifications.

d. Standardized extract development of *Cannabis sativa*:

The extraction of 25 kg (3 batches) of powdered leaves of *Cannabis sativa was*processedat normal temperature and pressure with a 1:8 solute-solvent ratio (plant material: alcohol). The leaves were taken into an extractor, and then distilled water was added to it. The mixture was kept on the stirrer for 5 h. The rpm was set to 500-600, and looping was done with the help of a pump for excellent mixing of solvent and solute. It was then filtered, and the residue was again topped up with solvent, and the mixture was kept stirring for 4 h. It was again filtered, and the extract was collected in a horizontal SS vessel. Again, fresh/recovered solvent was added, and the whole procedure was repeated a third time. The three extracts were pooled in a distillator. The extract was filtered and concentrated with the help of distillation. The extract was heated with the help of a boiler at 50-60°C for 2-3 hours. During heating, the volume of the extract was concentrated to 1/3 of its original volume. Then the distilled extract was processed for further concentration with the help of a wiped film evaporator.

Plant Material

Alcoholic Cold Extraction



Extract Cannabis sativa

e. IIIM-BioNEST Bio-incubation Centre and Quality Management & Instrumentation (QMI) Division of CSIR-Indian Institute of Integrative Medicine, Jammu jointly organized six-month high-end training program on operation of cGMP facility for phyto-pharmaceutical drugs manufacturing. The training program on "cGMP Phytopharmaceutical Drug Development" was inaugurated by Dr. Zabeer Ahmed, Director, CSIR-IIIM, Jammu at the conference hall of the institute which was attended by BOG members of IIIM-TBI, faculty members and research scholars of CSIR-IIIM. Head QMI Division, deliberated on the importance of phyto-pharmaceutical drugs in the coming time and how this six months elaborative training on cGMP will help the trainees in shaping their careers. Er. Anil K Katare, In-charge cGMP division, discussed about the course modules with the trainees. Ten numbers of students from AKS University Satna (M.P.) and three from Bahera University solan, (H.P.) were attended these six months training programme. The program included a series of lectures over the six-month training period. The program concluded on June 2024.

f. Four days hands on training program conducted for the students across the country on topic "**Hands on Training on cGMP Pilot Plant on Traditional Herbal Medicinal Plants**" was held from 20th to 22nd January 2025.

g. Work for CSIR-IIIM:

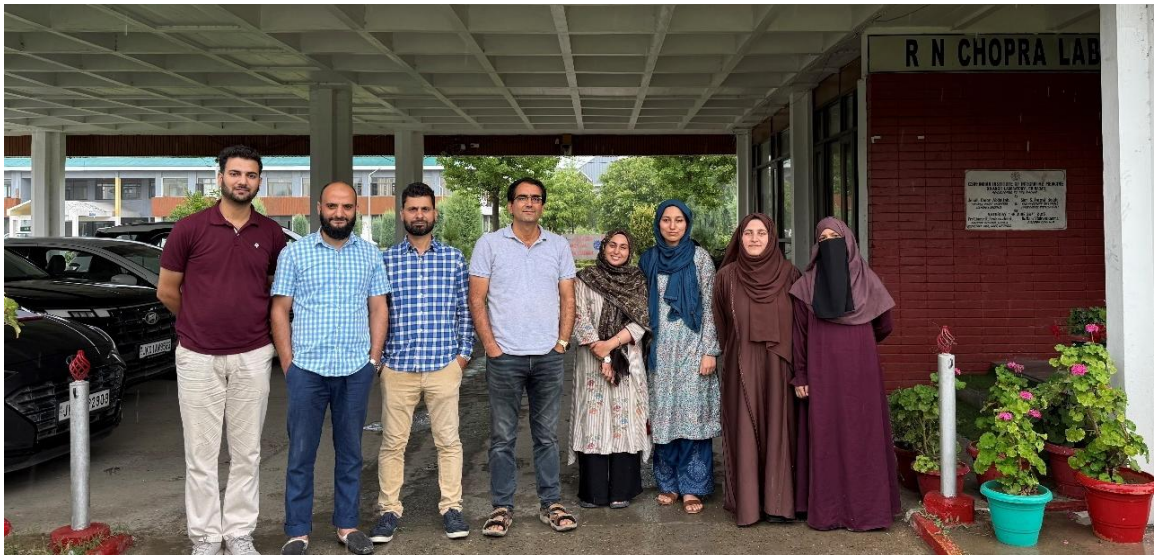
i. Finalized extract according to in-house specifications as outlined below:

- *Trillium govanianum*(1 Batche, Batch Size: 10kg)

ii. Formulation and Stability study:

- Developed a hard gelatin capsule formulation using Ayurvedic ingredients for M/s. Velanutrition Nutraceuticals Pvt. Ltd. **Batch Size:** Batch 1 (1000 Capsules): Dose limits 566mg.
- A stability study of the sustained-release capsules of *Dysoxylumbinectariferum* has been completed for 12 months.

SYED SAJAD HUSSAIN



Dr. Syed Sajad Hussain (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

2. Scientific work done:

- The enriched fraction of Andrographis paniculata was evaluated for its therapeutic efficacy in Sickle Cell Anaemia, wherein it significantly induced γ-globin expression in Berkeley transgenic mice, exhibited potent anti-sickling activity in ex vivo assays, and mitigated key pathophysiological manifestations associated with the disease.
- A Caenorhabditis elegans model system was established in the laboratory, encompassing standardised protocols for maintenance, controlled mating, pharmacological interventions, and cryopreservation. In addition, a transgenic strain relevant to Alzheimer's disease was introduced in the lab, providing a platform to evaluate the neuroprotective potential of candidate molecules and plant-derived extracts.
- In our lab, we established sphere formation in colon cancer cells, which is a robust in vitro model for colon CSC self-renewal. This phenotype is tightly regulated via Wnt/β-catenin, where we found GSK-3β inhibition sustains β-catenin activity, and EpCAM reinforces this activation signaling in presence of Cisplatin and LY24009. Conclusively, targeted inhibitors effectively disrupt sphere formation and CSC-associated signalling.
- The core histone genes of Crocus sativus have been successfully cloned into the desired vector (pHCE). Target histone sequences were amplified by PCR as part of the cloning process, which was then followed by restriction digestion and ligation into the plasmid. After cloning, the recombinant clones were transformed into E. coli BL21 (DE3) host strains and expressed under optimised culture conditions. SDS-PAGE analysis was used to confirm expression. The proteins were purified by affinity chromatography using Ni-NTA beads, utilising the His-tag that was incorporated into the histone gene construct.

NAGARAJU NEKKALA

Dr. Nagaraju Nekkala (Scientist) with his Research Group

1. Publications/Patents:

Publications:

- An effective method for developing cellulose-based polymer from spent lemongrass for use as packaging material
  Sonali Sharma, Ishfaq Nabi Najar, Anu Radha, **Nagaraju Nekkala**, Varsha Sharma, Vinod Kumar
  Biomass Conversion and Biorefinery
  https://doi.org/10.1007/s13399-025-06607-4

2. Scientific work done:

1. Operation and maintenance of Central Instrumentation Facility (CIF)

- Operation and maintenance of analytical instruments such as HPLC, GCMS/MS, LCMS/MS, FTIR, and CD Spectroscopy in the Central Instrumentation Facility.

Total number of samples analyzed from Apr-2024 to Mar-2025

Total number of samples analyzed in CIF		
S.No.	Analysis	Apr-2024 to Mar-2025
		No. of samples
1	MASS	8623
2	LCMS	207
3	GCMS	3409
4	HPLC	1490
5	FTIR	216
6	CDS	23
Total		13968

- Number of Students completed training during different sessions
  Between Jan-2024 to Jun-2024: 02

  Between Mar-2024 to Aug-2024: 02

  Between Jan-2025 to Mar-2025: 01

  Between Jan-2025 to Jun-2025: 02

2. Contribution to Aroma Mission (Phase-III)

- Method development for the qualitative and quantitative analysis of essential oils through GC-MS.
- Sample analysis through optimized methods.
- Identification and Quantification of major components.
- An approximate 1100 samples of essential oils such were analyzed by GCMS (Lavendor oil, lemon grass, oscimum, rose marry oil, Artemisia Annua oil and Monardra oil)

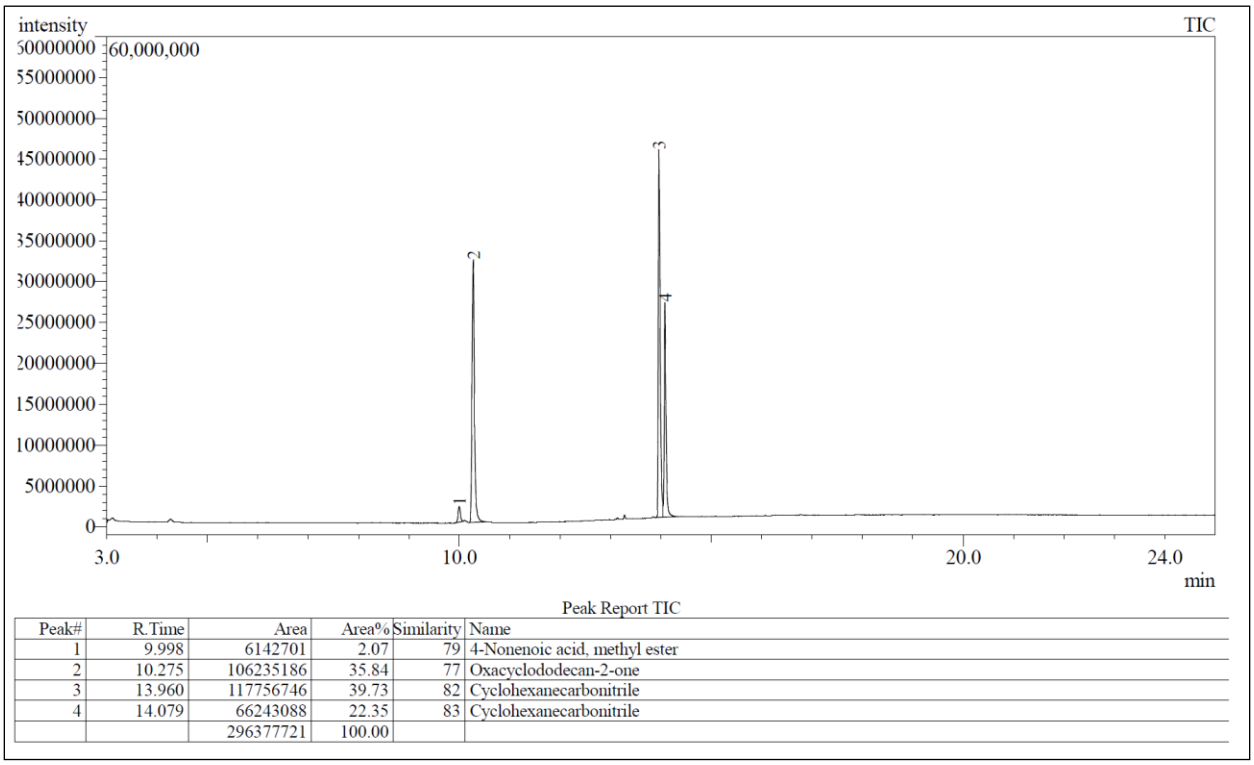
Essential oil	Major constituents identified and quantified through by area normalization method
Lavender oil	Linalool, Linalyl acetate
Artemisia Annua oil	Camphor, Eucalyptol, Artemisia ketone
Lemon grass oil	Citral, Neral, Geranyl acetate
Rosemary oil	Eucalyptol, α-pinene, Camphor
Ocimum oil	Linalool, Methyl Eugenol, Carvacrol

4.3 Contribution to Phyto pharma mission

- An approximate 8600 samples were analyzed by MASS spectrometry (Direct mass through LCMS) for the identification of masses of the compounds submitted from various labs. Samples submitted include natural, synthetic and semisynthetic.

3. New Chemo-Enzymatic Process for the Synthesis of Pregabalin

- We are working on the development of new chemoenzymatic process for the synthesis of pregabalin FTT-020510.
- Developed method for isomeric separation of ISBN (starting material of pregabalin) compounds by using GCMS.



Peak Report TIC

Peak#	R.Time	Area	Area%	Similarity	Name
1	9.998	6142701	2.07	79	4-Nonenoic acid, methyl ester
2	10.275	106235186	35.84	77	Oxacyclododecan-2-one
3	13.960	117756746	39.73	82	Cyclohexanecarbonitrile
4	14.079	66243088	22.35	83	Cyclohexanecarbonitrile
		296377721	100.00		

Figure 1: Isomeric seperation for ISBN by GCMS

4.5 Contribution to Drug Discovery Programme

HPLC and LC-MS developed methods for the quantification of drugs in the formulations and release studies for Doxorubin HCl, Resiquimod, Honokiol, and IIIM-019.

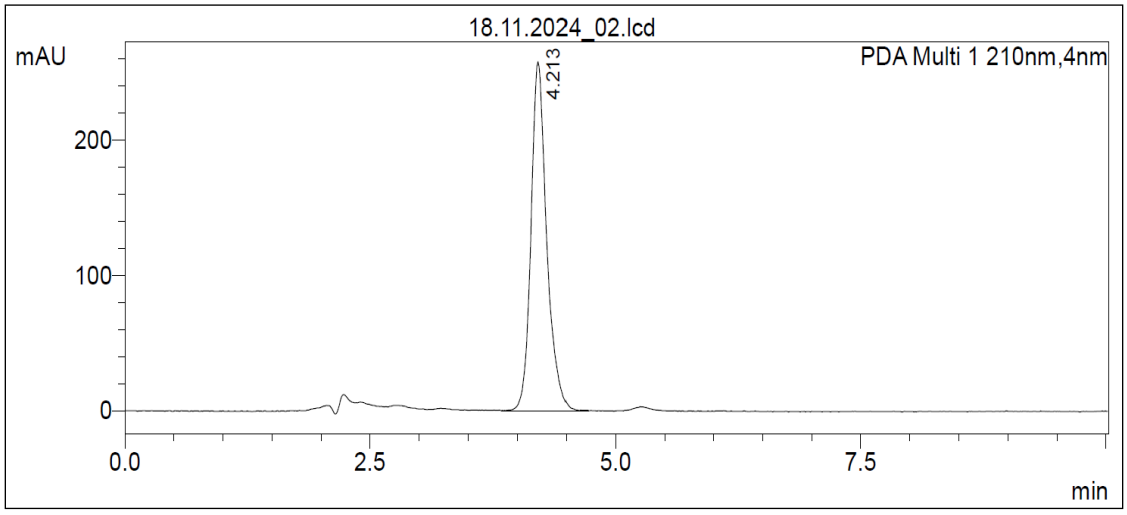


Figure 2: HPLC chromatogram of Doxorubicin

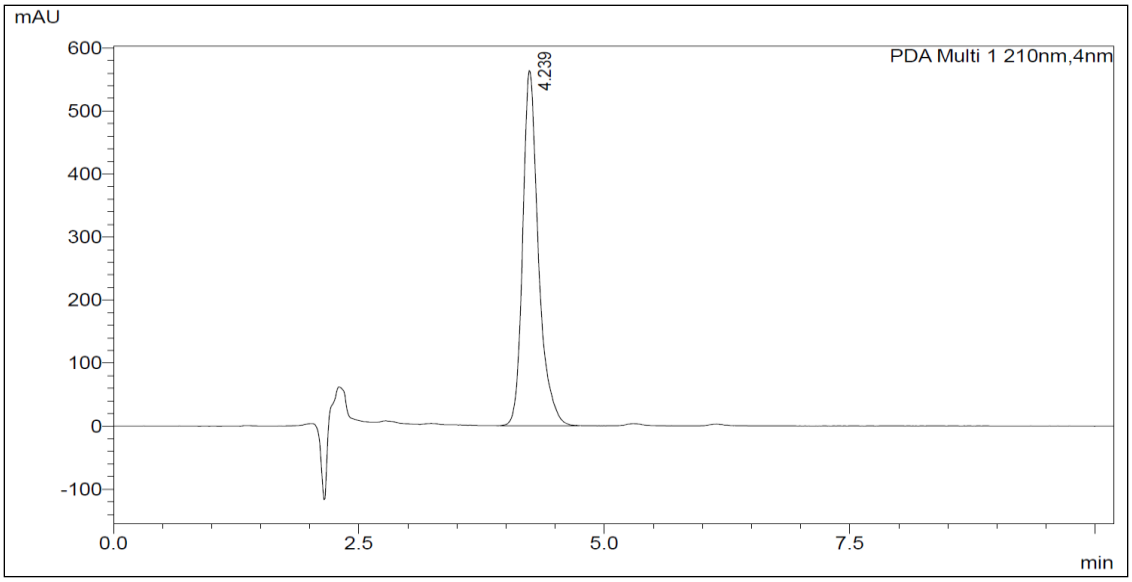


Figure 3: HPLC chromatogram of Honokiol

4.6 **Quantification of Diosgenin in Dioscorea plant**

- LCMS/MS MRM method was developed for the quantification of Diosgenin in the Dioscorea plant species

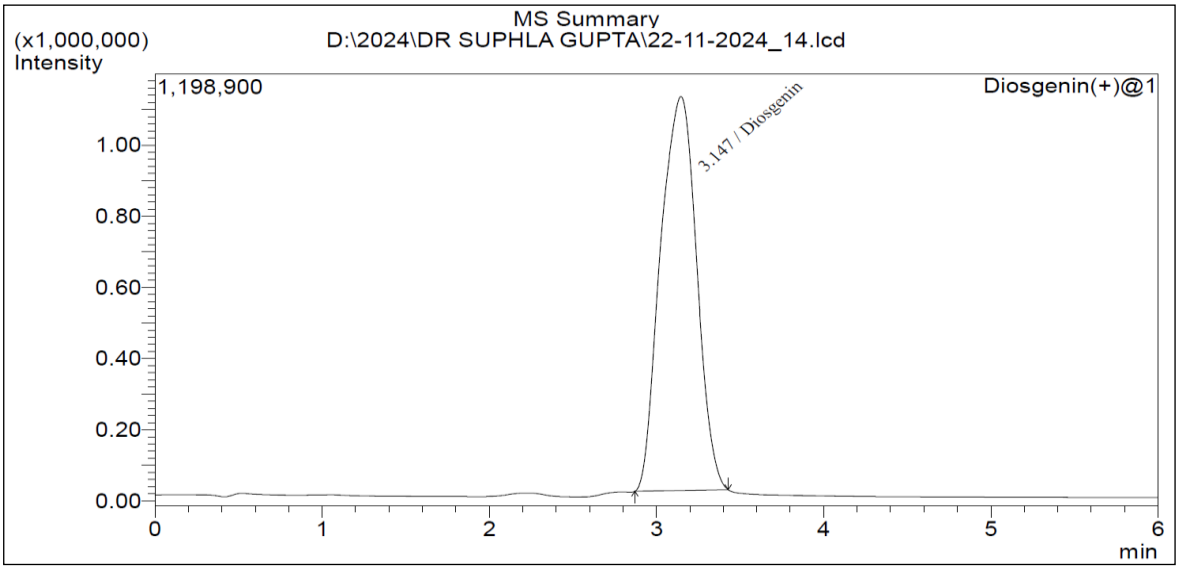


Figure 4: LCMS chromatogram of Diosgenin

4.7 **Quantification of Ectoine production by HPLC**

- An HPLC-PDA method was developed for the quantification of Ectoine production using novel isolated Halomonas sp. IIIM VA-6 at low salt concentration approach.

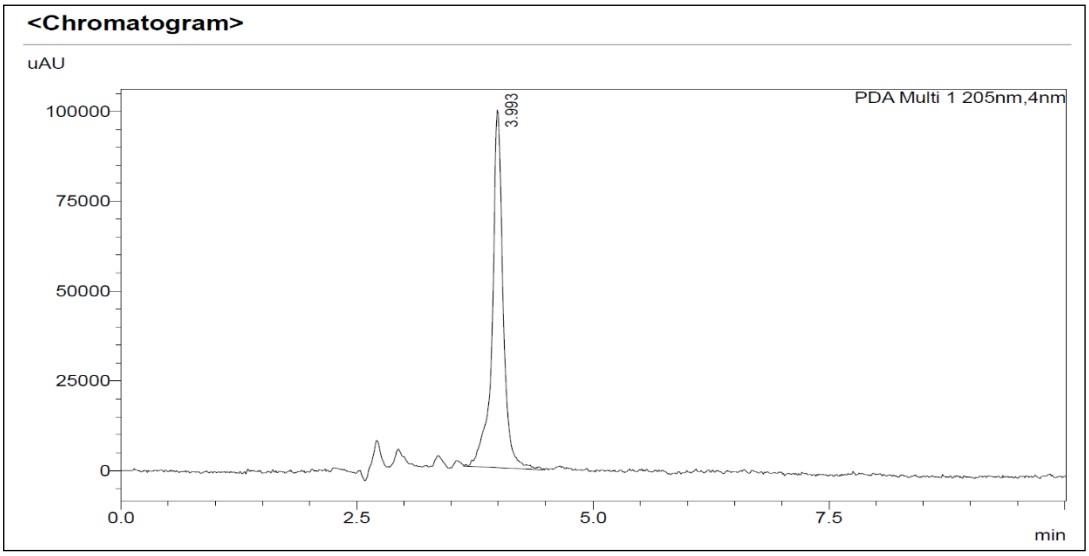


Figure 5: Ectoine standard chromatogram by HPLC

4.8 **Quantification of 3-Hydroxy butyric acid by LC-MS/MS**

- An efficient LC-MS/MS MRM method was developed for the quantification of 3-hydroxybutyric acid.
- Using the method, approximately 130 samples were quantified in the project entitled Process Development, Purification, Scale-up & Potential Applications of 3-Hydroxy butyric acid.

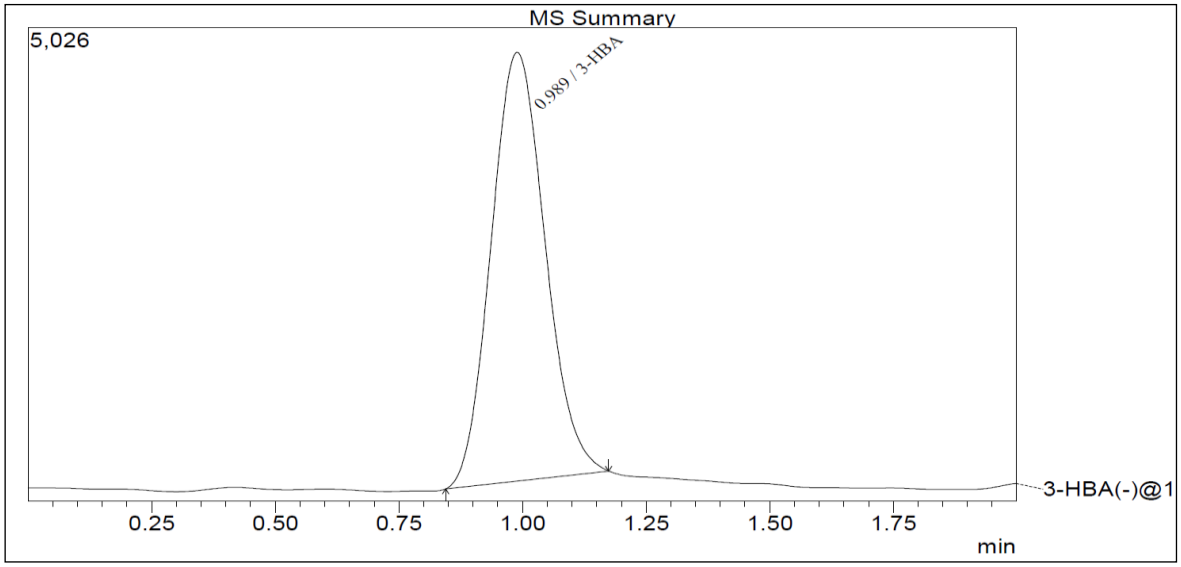


Figure 6: LCMS chromatogram of 3-Hydroxy butyric acid

4.9 **Individual quantification of some biochemical compounds in Rosa.L**

- Untargeted metabolome analysis in seven species of the genus Rosa. L through GCMS.
- Quantification of Ascorbic acid (Vitamin-C) in seven species of genus Rosa. L through HPLC.
- Quantification of ten phenolic and flavonoid compounds in seven species of genus Rosa. L through HPLC.

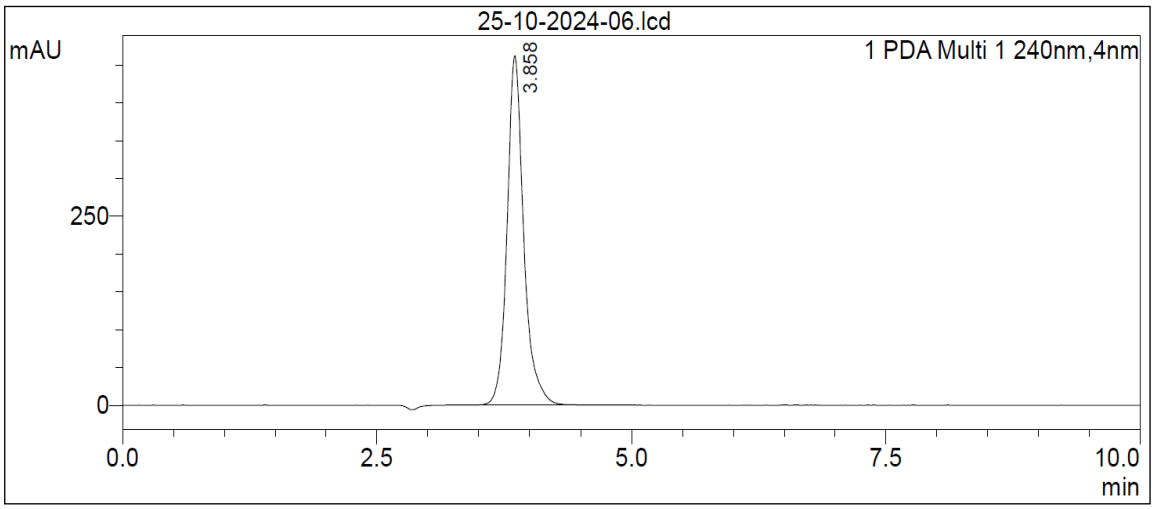


Figure 7: HPLC chromatogram of Vitamin-C (Ascorbic acid)

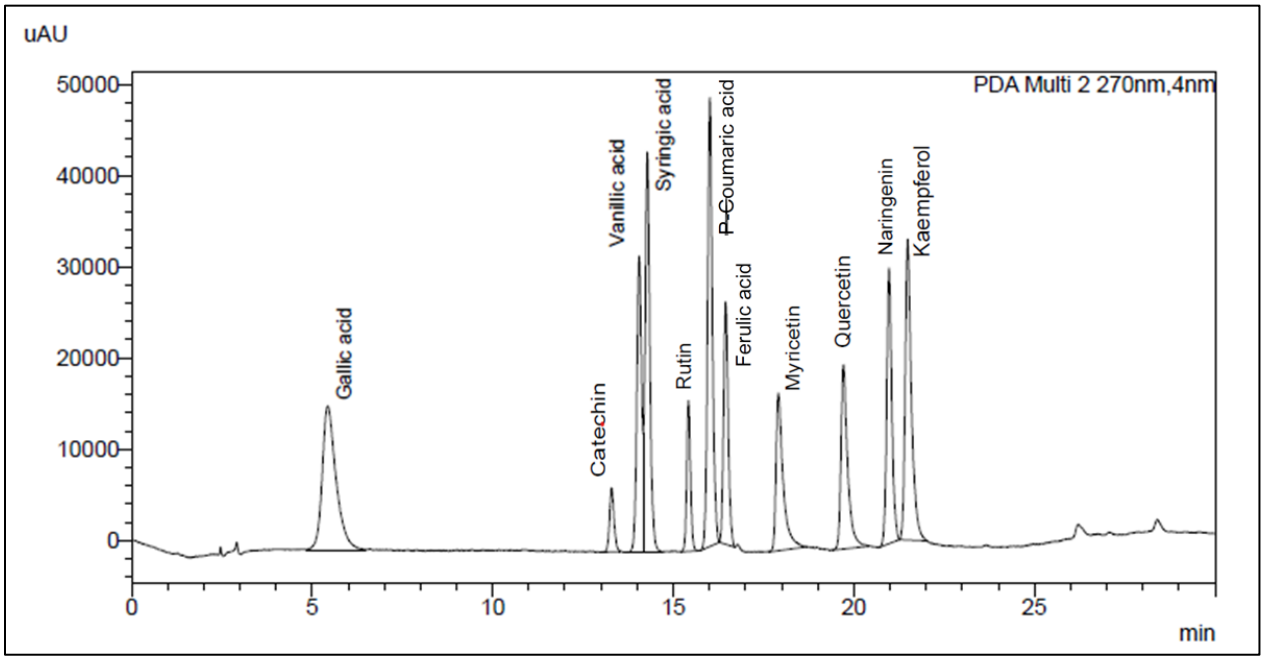


Figure 8: HPLC chromatogram of ten phenolic and flavonoid compounds

4.10 Quantification of Glucosinolate hydrolysis products in Brassicaceae family

- Standardized the GCMS method for identifying and quantifying glucosinolate hydrolysis products like nitriles, thiocyanates, isothiocyanates, etc. in Brassicaceae family.

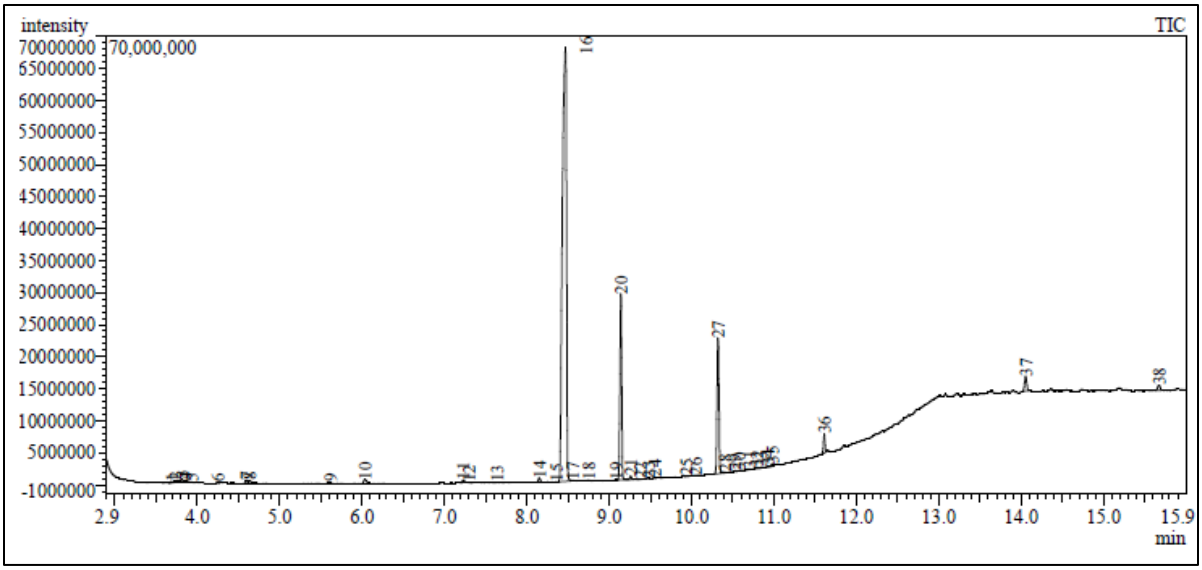


Figure 9:GCMS chromatogram of Glucosinolate hydrolysis products

SUMIT G. GANDHI

Dr. Sumit G. Gandhi (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

S.No	Authors	Title of the Article	Year of Publication	Name of Journal
1	Awzia Amin, Nancy Sharma, Phalisteen Sultan*, **Sumit G. Gandhi**, Kota Srinivas, Qazi Parvaiz Hassan & Zabeer Ahmed	In vitro propagation of *Bergenia stracheyi*: an alternative approach for higher production of valuable bioactive compounds	May 2024	**Vegetos** **IF:0.3**

2	Ishfaq Nabi Najar, Prayatna Sharma, Rohit Das, Sonia Tamang, Krishnendu Mondal, Nagendra Thakur, **Sumit G. Gandhi**, Vinod Kumar*	From waste management to circular economy: Leveraging thermophiles for sustainable growth and global resource optimization	May 2024	**Journal of Environmental Management** **IF: 8.0**
3	Jaspreet Kour, Tamanna Bhardwaj, Rekha Chouhan, Arun Dev Singh, **Sumit G. Gandhi***, Renu Bhardwaj*, Abdulaziz Abdullah Alsahli, Parvaiz Ahmad*	Phytomelatonin maintained chromium toxicity induced oxidative burst in *Brassica juncea* L. through improving antioxidant system and gene expression	May 2024	**Environmental Pollution** **IF: 7.6**
4	Tamanna Bhardwaj, Jaspreet Kour, Rekha Chouhan, Kamini Devi, Harpreet Singh, **Sumit G. Gandhi***, Puja Ohri, Renu Bhardwaj*, Abdulaziz Abdullah Alsahli, Parvaiz Ahmad	Integrated Transcriptomic and Physio-Molecular Studies Unveil the Melatonin and PGPR Induced Protection to Photosynthetic Attributes in *Brassica juncea* L. Under Cadmium toxicity	June 2024	**Journal of Hazardous Materials** **IF: 12.2**
5	Nancy Sharma, Vijay Lakshmi Jamwal, Sakshi Nagial, Manish Ranjan, Dharitri Rath* &**Sumit G. Gandhi***	Current status of diagnostic assays for emerging zoonotic viruses: Nipah and Hendra	June 2024	**Expert Review of Molecular Diagnostics** **IF: 3.9**
6	Shagun Verma, Nancy Singla, Siloni Singh Bhadwal, Rekha Chouhan, Subodh Kumar, **Sumit G.**	Exploring Multifaceted Roles of Nitroreductases in Bacterial, Animal and Plant	July 2024	**ChemistrySelect** **IF: 1.9**

	Gandhi, Satwinderjeet Kaur*	Biosystems and their Detection using Fluorescent Probes		
7	Neha Sharma, Rasdeep Kour, Shagun Verma, Vandana Sharma, Deepika Singh, **Sumit G. Gandhi**, Vaseem Raja*, Satwinderjeet Kaur*, Naveen Kumar, Khalid Mashay Al-Anazi, Mohammad Abul Farah	Growth inhibitory potential of quinone-rich fraction of *Plumbago zeylanica* L. Against MG-63 osteosarcoma cells via Bax/Bcl-2 modulation	August 2024	**Journal of King Saud University – Science** **IF: 3.7**
8	Sheikh Showkat Ahmad, Chandni Garg, Rasdeep Kour, Aashaq Hussain Bhat, Vaseem Raja, **Sumit G. Gandhi**, Farid S. Ataya, Dalia Fouad, Arunkumar Radhakrishnan and Satwinderjeet Kaur*	Metabolomic insights and bioactive efficacies of *Tragopogon dubius* root fractions: Antioxidant and antiproliferative assessments	August 2024	**Heliyon** **IF: 3.4**
9	Ishfaq Nabi Najar, Prayatna Sharma, Rohit Das, Krishnendu Mondal, Ashish Kumar Singh, Sonia Tamang, Palash Hazra, Nagendra Thakur, Rajendra Bhanwaria, **Sumit G Gandhi**, Vinod Kumar*	In search of poly-3-hydroxybutyrate (PHB): A comprehensive review unveiling applications and progress in fostering a sustainable bio-circular economy	August 2024	**Food and Bioproducts Processing** **IF: 3.5**
10	Tamanna Bhardwaj, Ruby Singh, Harpreet Singh, Rajendra Bhanwaria, **Sumit G. Gandhi***, Renu Bhardwaj*, Ajaz Ahmad, Parvaiz	*Pseudomonas* consortium improves soil health and alleviates cadmium (Cd) toxicity in *Brassica juncea* L. via biochemical and	September 2024	**Plant Stress** **IF: 6.8**

	Ahmad*	in silico approaches		
11	Rekha Chouhan, Nancy Sharma, Vijay L. Jamwal*, Sahaurti Sharma and **Sumit G. Gandhi***	Transcriptome Mining, Identification and *In silico* Characterization of Thaumatin-Like Protein Sequences from *Mentha Longifolia*	September 2024	**Current Biotechnology**
12	Kamini Devi, Sahaurti Sharma, Arun Dev Singh, Tamanna Bhardwaj, **Sumit G. Gandhi**, Puja Ohri, Renu Bhardwaj*, Abdulaziz Abdullah Alsahli, Parvaiz Ahmad*	Plant-derived Biochar and Salicylic Acid as Biostimulants for *Lycopersicon esculentum* Under Chromium Toxicity Conditions: Insights from Physiochemical Attributes, Antioxidants, and Relative Gene Expression	October 2024	**Journal of Environmental Chemical Engineering** **IF: 7.4**
13	Gagandeep Jaiswal, Rekha Rana, Praveen Kumar Nayak, Rekha Chouhan, **Sumit G. Gandhi**, Hitendra K. Patel & Prabhu B. Patil*	*Luteibactersahnii* sp. nov., A Novel Yellow-Colored Xanthomonadin Pigment Producing Probiotic Bacterium from Healthy Rice Seed Microbiome	October 2024	**Current Microbiology** **IF: 2.3**
14	Pooja Sharma*, Palak Bakshi, Rekha Chouhan, **Sumit G. Gandhi**, Rupinder Kaur, Ashutosh Sharma, Renu Bhardwaj*, Abdulaziz Abdullah Alsahli, Parvaiz Ahmad*	Combined application of earthworms and plant growth promoting rhizobacteria improve metal uptake, photosynthetic	November 2024	**Journal of Hazardous Materials** **IF: 12.2**

		efficiency and modulate secondary metabolites levels under chromium metal toxicity in *Brassica juncea* L		
15	Arun Dev Singh, Nancy Sharma, Kamini Devi, Jaspreet Kour, **Sumit G. Gandhi**, Renu Bhardwaj, Abdulaziz Abdullah Alsahli, Parvaiz Ahmad*	Efficacy of Salicylic acid (SA) in Modulating the Dynamics of Pesticide-Thiamethoxam-induced Stress responses in *Brassica juncea* L. Insights from Biochemical and Molecular Dissection	December 2024	**Environmental Pollution** **IF: 7.6**
16	A. A. Chowdhary, R. Chouhan, S. Mishra, D. Bagal, S. Rathore, A. Guleria, D. Singh, G. Sharma, **S. G. Gandhi***& V. Srivastava*	H2S and NO Mitigate Cadmium and Lead Toxicity in *Solanum lycopersicum* L.	January 2025	**Russian Journal of Plant Physiology** **IF: 1.1**
17	Raja Feroz Ahmad Haji*, Bashir Ahmad Dar, Sumit. G. Gandhi, Irshad Ahmad Rather &Vijeshwar Verma	Development of SCAR marker for authentication in germplasm conservation and SSR & inter-transcribed spacer genetic diversity analysis in medicinally important herb *Uraria picta*	February 2025	**Journal of Plant Biochemistry and Biotechnology** **IF: 1.6**

2. Scientific work done:

In vitro evaluation of *Cymbopogon khasianus X pendulus* and *Ocimum viride* essential oils and their o/w emulsions as antimicrobial agents against oral pathogens
Sahaurti Sharma, Ankit Patil, Yogesh Nimdeo and Sumit G. Gandhi*

The rising prevalence of oral infections and the limitations of conventional agents such as sodium hypochlorite—widely used in dentistry but associated with high toxicity and tissue irritation—necessitate the search for safer, natural alternatives. Essential oils, with their antimicrobial and biocompatible properties, hold strong promise in this regard. In this study, essential oils from *Cymbopogon khasianus X pendulus* (lemon grass) and *Ocimum viride*, along with their emulsified formulations, were evaluated against oral pathogens, *Streptococcus mutans* and *Enterococcus faecalis*. Zone of inhibition assays revealed concentration-dependent antimicrobial activity, with maximum efficacy at 2% concentration. Biofilm inhibition assays showed a marked reduction in *E. faecalis* biofilm formation, with 1.5% concentrations reducing optical density values to 0.49 (lemongrass) and 0.38 (*O. viride*), compared to 1.33 in positive controls. Time-dependent biofilm assays on artificial teeth further confirmed enhanced antimicrobial action with prolonged exposure, where 1.5% formulations reduced biofilm density to 0.004 (lemongrass) and 0.22 (O. viride) after 10 minutes of exposure to emulsions, in contrast to water controls (1.258–1.260).

Rheological characterization of emulsified formulations demonstrated favorable viscoelastic properties, with storage modulus (G′) consistently higher than loss modulus (G″), confirming structural stability and preventing phase separation. Viscosity profiling indicated shear-thinning behaviour, allowing ease of application while maintaining sufficient viscosity at rest to prevent runoff and enable sustained release of active compounds. Further, toxicity analysis revealed minimal brine shrimp mortality and low hemolytic activity at effective concentrations, establishing superior biocompatibility compared to sodium hypochlorite. Notably, emulsified oils exhibited improved stability and equal or greater antimicrobial activity than pure oils.

Collectively, these findings highlight *Cymbopogon khasianus X pendulus* and *Ocimum viride* essential oils, particularly in emulsion-based formulations, as potent, stable, and biocompatible natural agents with strong potential to replace sodium hypochlorite in oral healthcare products such as mouthwashes and dental irrigants.

Biotechnological applications of microbes associated with *Monarda citriodora*
Sakshi, Sofia Bhagat, Sahaurti Sharma, Siya Ram Meena and Sumit G. Gandhi*

*Monarda citriodora*Cerv. ex-Lag, commonly known as lemon beebalm, is a valuable aromatic plant belonging to the *Lamiaceae* family (mint family). The variety: IIIM (JMC-02, is particularly rich in commercially important secondary metabolites, possessing 62-70% thymol, 14-20% r-Terpinene, 12-20% p-Cymene, 2-6% Carvacrol and other aromatic compounds in minor quantities. The herb is native to the Southern United States of America and Northern Mexico. In India, the plant is cultivated in Jammu and Kashmir, Uttarakhand, Himachal Pradesh, Haryana, Punjab, Uttar Pradesh, Rajasthan, and

the North-East Region. Natural microbial diversity associated with plants plays important roles in their development and tolerance to abiotic and biotic stresses, as well as in the induction of secondary metabolites. Microbial isolates from the endophytic, exophytic, and rhizospheric niches of *M. citriodora* were evaluated for their biotechnological potential, including secondary metabolite production, enzyme activities, and plant growth-promoting traits. Among the isolates from different stages of growth of plant, a high proportion demonstrated protease activity, with 32/52 in January, 27/37 in February 31/42 in March, 27/35 in April, and 29/36 in May showing significant hydrolytic zones, confirming efficient protein degradation, further supported by fluorogenic substrate assays. Cellulase activity was also widespread, detected in 11/37 (January), 24/42 (March), 21/35 (April), and 10/36 (May) isolates, with DNS assays validating the release of reducing sugars. Phosphate solubilization was absent in January isolates but observed in 5/37 (February), 10/42 (March), 6/35 (April), and 7/36 (May), indicating gradual enrichment of functional strains. Several isolates also displayed antifungal activity against phytopathogens including *Fusarium oxysporum*, *Alternaria alternata, Botrytis cinerea, Aspergillus niger*, and *Colletotrichum gloeosporioides*, while auxin production screening identified MCAEX07 as the strongest IAA producer. These findings highlight *M. citriodora*-associated microbes as a rich source of industrially relevant enzymes and bioactive compounds with potential applications in agriculture and biotechnology. Future work will focus on optimizing protease activity across temperature and pH ranges, evaluating gibberellic acid production, and assessing overall plant growth-promoting potential.

Genomic And Phenotypic Characterization of Virulence in Uro-Pathogenic *Klebsiella sp.*: A Multi-Modal Integrated Analysis of Clinical Isolates

Sahaurti Sharma, Manish Ranjan, Zabeer Ahmed and Sumit G. Gandhi*

This study presents a comprehensive investigation of virulence and antimicrobial resistance (AMR) mechanisms in uro-pathogenic *Klebsiella sp.* using a multi-modal approach integrating genomic analysis with phenotypic characterization. Clinical isolates (UC-971, UC-318, KP-R) were compared with well-characterized reference strains (MTCC-4031) to explain the molecular basis of urinary tract infection (UTI) pathogenesis. Whole genome sequencing (WGS), combined with targeted in vitro assays, revealed important associations between specific genetic determinants and phenotypic traits linked to virulence and resistance. Four *K. pneumoniae* isolates (MTCC reference strain, UC-318, UC-971, and KP(R)) were comprehensively characterized through phenotypic, biochemical, antimicrobial, and genomic analyses. On Chromogenic Coliform Agar, colonies appeared blue to purple, while on *Klebsiella* Selective Agar, all strains except UC-318 developed purple colonies, confirming selective growth. Biochemical profiling revealed consistent nitrate reduction and variable sugar utilization (glucose, lactose, arabinose, sorbitol, sucrose, rhamnose), amino acid decarboxylation, and urease activity, reflecting strain-specific metabolic traits. Antibiotic susceptibility testing demonstrated extensive multidrug resistance, with isolates exhibiting elevated MIC values against β-lactams, aminoglycosides, tetracyclines, fluoroquinolones, chloramphenicol, and folic acid inhibitors, while colistin retained partial activity. Serum resistance assays confirmed the ability of all isolates to withstand complement-mediated killing, and motility assays verified their non-motile phenotype. Biofilm assays (Congo red binding and crystal violet quantification) demonstrated strong biofilm production, with UC-971 showing the highest accumulation.

Whole genome sequencing (WGS) provided molecular insights into resistance and virulence, revealing the presence of extended-spectrum β-lactamase (ESBL) and carbapenemase genes, multidrug efflux pumps, virulence-associated loci, capsule biosynthesis operons, and iron acquisition systems. Genomic analysis further correlated with phenotypic traits, confirming the genetic basis of antimicrobial resistance and biofilm formation in these isolates. Collectively, the integrated phenotypicand genomic characterization highlights the multidrug-resistant, biofilm-forming, and serum-resistant nature of these *K. pneumoniae* strains. This research provides fresh insight on mechanisms for adaptation in the urinary tract and reveals potential targets for anti-virulence and resistance-modifying therapies. The findings also contribute to a deeper understanding of patho-adaptation and the evolving challenge of antimicrobial resistance in UTIs.

MOHD JAMAL DAR

Dr. Mohd Jamal Dar (Sr. Principal Scientist) with his Research Group

Research Interests:

Cell Biology and Regenerative Medicine:

- The role of Wnt /beta-catenin signalling in cancer and stem cell biology
- The role of PI3K pathway in cancer and stem cell biology
- Understanding mechanism of hair regeneration

1. Publications/Patents:

Publications:

- Faruqui T, Akhtar A, Showket F, Dar MJ, Akhter Y Identification and Evaluation of IGF1R and Its Associated Proteins as Targets and Design of Novel Inhibitors for Cancer Therapy..J Cell Biochem. 2025 Mar;126(3):e70008. Impact Factor-4.48
- Dhawan B, Alam MS, Hamid H, Yadav A, Akhter G, Dar MJ, Alam O, S Y. Synthesis and biological evaluation of thiourea-tethered benzodiazepinones as anti-proliferative agents targeting JAK-3 kinase.NaunynSchmiedebergs Arch Pharmacol. 2025 Mar 3
- Md Mehedi Hossain [#], Arfan Khalid [#2], Zaheen Akhter [#], Sabra Parveen, Mir Owais Ayaz, Aadil Qadir Bhat, Neetu Badesra, Farheen Showket, Mohmmad Saleem Dar, Farhan Ahmed, Sumit Dhiman, Mukesh Kumar, Umed Singh, Razak Hussain [7], Pankaj Keshari [8], Ghulam Mustafa [2 3], Amit Nargorta [2 4], Neha Taneja, Somesh Gupta, Riyaz A Mir, Aravind Singh Kshatri, Utpal Nandi, Nooruddin Khan, P Ramajayan [2], Govind Yadav, Zabeer Ahmed, Parvinder Pal Singh, Mohd Jamal Dar. Discovery of a novel and highly selective JAK3 inhibitor as a potent hair growth promoter. Journal of Translational Medicine. 2024 Apr 18;22(1):370. Impact Factor-8.44

- Ayaz MO, Bhat AQ, Akhter Z, Badsera N, Hossain MM, Showket F, Parveen S, Dar MS, Tiwari H, Kumari N, Bhardwaj M, Hussain R, Sharma A, Kumar M, Singh U, Nargorta A, Kshatri AS, Nandi U, Monga SP, Ramajayan P, Singh PP, Dar MJ. Identification of a novel GSK3β inhibitor involved in abrogating KRas dependent pancreatic tumors in Wnt/beta-catenin and NF-kB dependent manner.Life Sci. 2024 Aug 15;351:122840. Impact Factor-6.7

Patents

- Functional triazines as anti-cancer agents and process for the preparation thereof- patent files recently. (Patent Application No. 202411053209)
- Rucaparib analogues as novel anti-cancer agents - and process for the preparation thereof- patent files recently. Qazi Naveed Ahmed, Ashiq Hussain Padder, Sajjad Ahmed, Zoya Shafeeq, Mohammad Yaqoob Bhat, Jagdish Chand, Mohammad Saleem Dar, Yashi Garg, Feroze Hussain, Anindya Goswami, Mohd Jamal Dar, Zabeer Ahmed. Patent Application No.202411016691. (Patent Application No.202411016691). (submitted).
- Novel tricyclic compounds as parp 1 & 2 inhibitors for breast and ovarian cancer treatment. Dumbala Srinivasa Reddy, Anindya Goswami, Mohd Hamal Dar, Sanket Shette, Yashi Garg, Dar Saleem, Amit Nargotra
- Sila-phthalainone analogues as parp 1 & 2 inhibitors for breast and ovarian cancer treatment. Dumbala Srinivasa Reddy, Anindya Goswami, Mohd Hamal Dar, Sanket Shette, Yashi Garg, Dar Saleem, Amit Nargotra. (submitted).

2. Scientific work done:

Identification of MJ34 as a novel GSK-3 beta selective inhibitor as a novel anti-cancer agent: Glycogen Synthase Kinase-3 beta (GSK3β) is considered one of the key factors involved in the onset, progression as well as in the acquisition of chemoresistance in pancreatic cancer. Therefore, pharmacological interventions to inhibit GSK3β activity is an important therapeutic strategy for the treatment of pancreatic cancer. We screened compound libraries and identified MJ34, a pyrimidinylazaindole based small molecule, as a potent and selective GSK3β inhibitor using in silico and cell free based assays. Furthermore, we explored the impact of identified lead, MJ34, using a battery of cell based assays and investigated its impact on Wnt/beta-catenin signaling, a downstream signaling pathway of GSK3β, in KRas mutant pancreatic cancer cells. We also carried out xenograft studies to investigate the effect of MJ34 on tumor growth in BALB/c athymic nude mice implanted with MiaPaCa-2 tumor. Pertinently, MJ34 was seen to induce apoptosis in a β-catenin and c-Myc dependent manner in both in vitro and in vivo conditions. Taken together, we report MJ34 as aGSK3β specific inhibitor that has the potential to be developed for the treatment of malignancies where GSK3β is dysregulated and in KRas mutant tumors that are resistant to chemotherapy MJ34 exhibits overall properties suitable for its drug development and advancement to human clinical trials. This work was published in Life Sci. 2024 Aug 15;351:122840. Impact Factor-6.7.doi: 10.1016/j.lfs.2024.122840. Epub 2024 Jun 13.

SREEDHAR MADISHETTI

Dr. Sreedhar Madishetti (Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Kumar, P., Dar, S.A., Manhas, O., Bhushan, A., Gupta, P., **Madishetti, S**. and Ahmed, Z., 2024. Anti-diabetic and anti-inflammatory activities of Marrubiin isolated from Marrubium vulgare: Indications of its interaction with PPAR γ. *Phytomedicine Plus*, *4*(4), p.100664.
- Kumar, D., Ahmed, M., Andrabi, N.I., Singh, C.P., Saroch, D., Bharitkar, Y.P., Kour, G., **Madishetti, S**., Bhagat, A., Shukla, S.K. and Ahmed, Z., 2025. Anti-inflammatory and anti-oxidant potential of Dispiro-indanedione hybrid of parthenin via regulating Nrf2 and NF-κB/MAPK pathways. *European Journal of Pharmacology*, p.177547

2. Scientific work done:

2.1 Bioassay-guided fractionation of *Cannabis sativa*: Identifying a bioactive sub-fraction with antioxidant and anti-inflammatory activities

Cannabis sativa preparations have long been explored for their therapeutic utility in multiple sclerosis, Parkinson's disease, Alzheimer's disease, cancer, cardiovascular diseases, rheumatoid arthritis, and Crohn's disease. *Cannabis* contains several chemical constituents like cannabinoids, terpenes, flavonoids, phenols etc. The major cannabinoids include tetrahydrocannabinol, cannabidiol, tetrahydrocannabivarin, cannabinol, cannabigerol, and cannabichromene.

The present study investigated the chemical composition, antioxidant, and anti-inflammatory activities of a sub-fraction, F3-14, identified through bioassay-guided fractionation of *C. sativa* leaf extract.

The leaves of *C. sativa* were extracted using 1:1 dichloromethane and methanol solution followed by partition column chromatography to isolate subfractions. The major compounds of the bioactive sub-fraction were characterized by NMR and mass spectral data. The antioxidant activity was assessed using a standardized 96-well plate format DPPH assay. The anti-inflammatory effects were evaluated using RAW 264.7 cells.

Bioassay-guided fractionation led to the identification of a bioactive sub-fraction F3-14. HPLC and TLC analysis revealed the presence of cannabitriol-C3, cannabitriol-C5, cannabiripsol, stearic acid, 12,15-octadecadienoic acid(z,z) and 10,12,15-octadecatrienoic acid(z,z,z) compounds within the sub-fraction (Fig 4.1.1). The EC_{50} of free radical scavenging activity was concentration and time-dependent (Fig. 4.1.2 and Table 1). At 10 µg/ml, F3-14 exhibited inhibition of LPS-induced release of nitric oxide (Fig. 4.1.3), TNF-α, IL-6, and IL-1β by 42.1%, 31.3%, 56.9%, and 76.9%, respectively (Fig. 4.1.4). This concentration was non-toxic in cell viability (MTT) assay (Fig. 4.1.5).

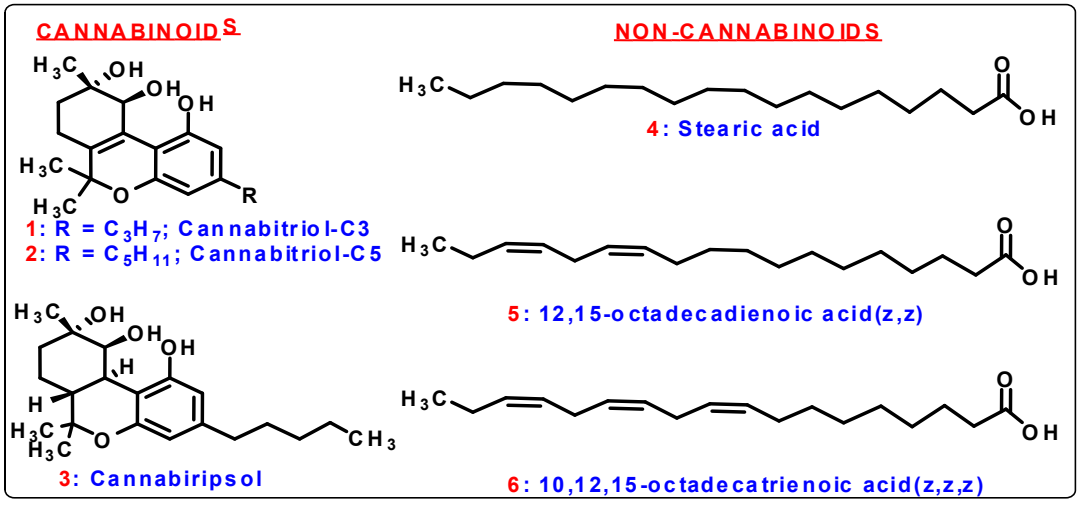


Figure 2.1.1 Structure of cannabinoid and non-cannabinoid compounds

Antioxidant Activity:

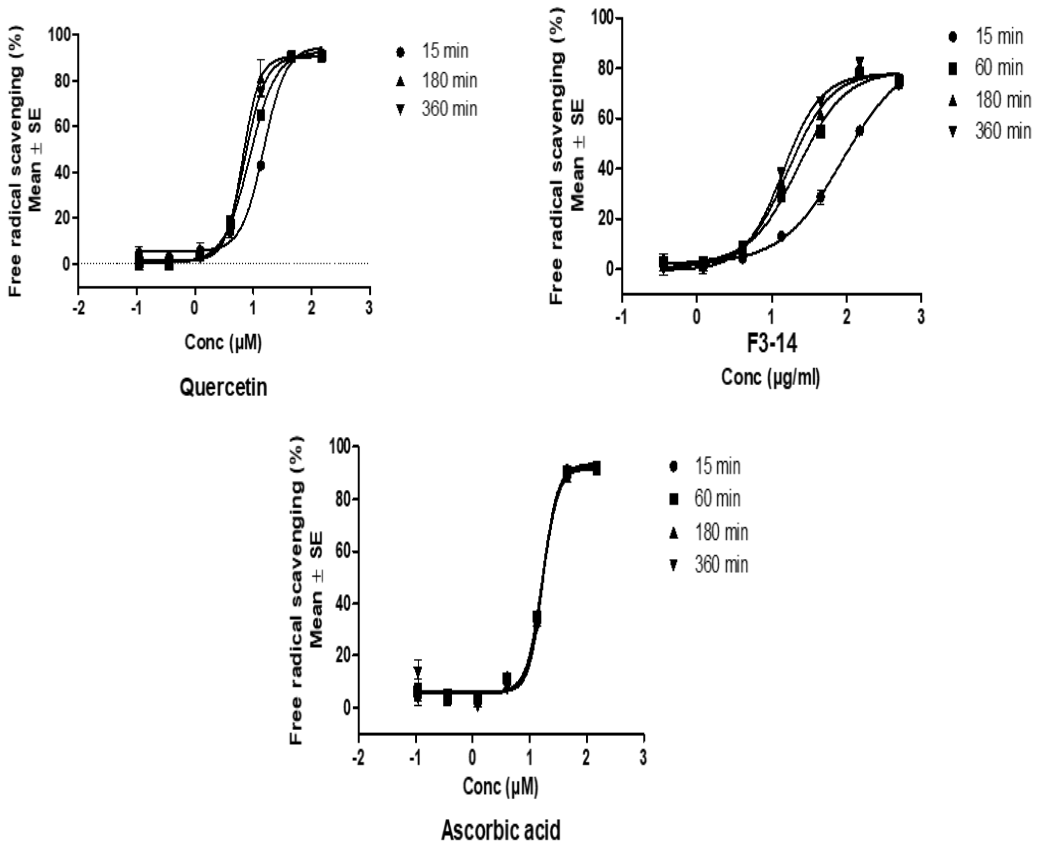


Figure 2.1.2 EC_{50} determination of *Cannabis sativa* subfraction (F3-14), ascorbic acid, and quercetin

Table 1:EC_{50} of *Cannabis sativa* subfraction (F3-14), ascorbic acid, and quercetin

	15min	**60 min**	**180 min**	**360 min**
F3-14 (µg/ml)	88.8	22.3	16.7	14.0
Ascorbic Acid (µM)	16.6	16.8	17.0	17.1
Quercetin (µM)	15.1	8.5	6.6	7.1

Anti- Inflammatory Activity:

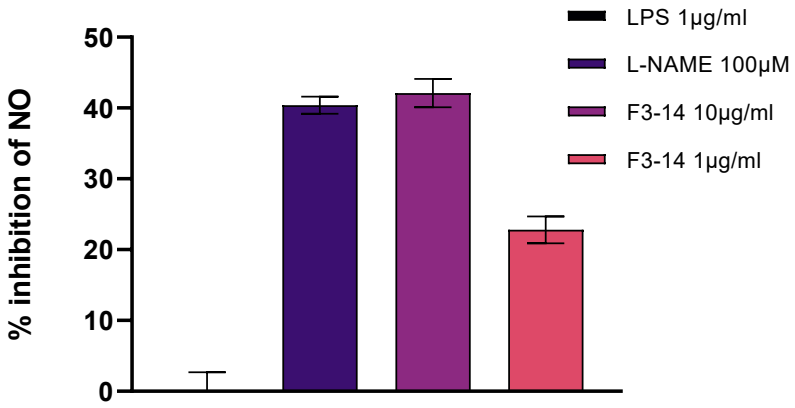


Figure 2.1.3 Effect of F3-14 on LPS-induced nitric oxide production

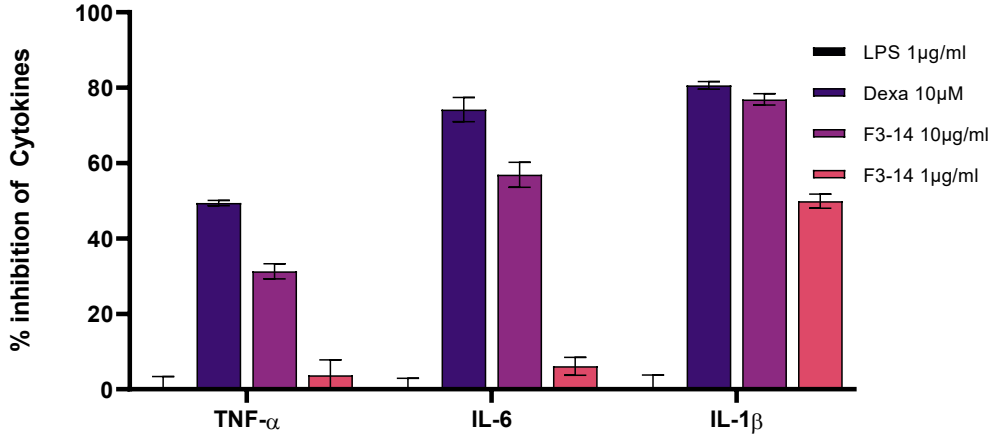


Figure 2.1.4 Effect of F3-14 on LPS-induced cytokine release

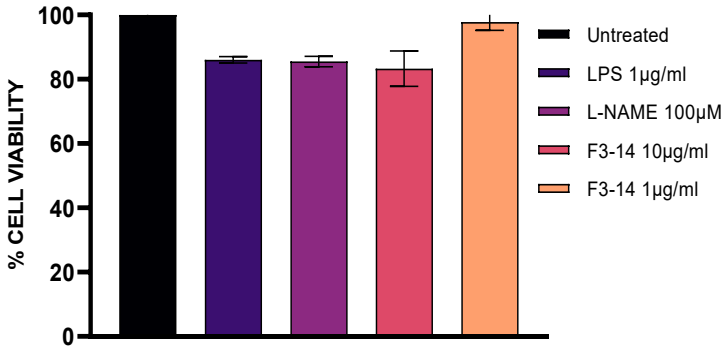


Figure 2.1.5 Effect of F3-14 on cell viability

The sub-fraction F3-14, confirmed to contain cannabinoids and fatty acids, demonstrated potent anti-inflammatory and antioxidant activities. The chemical composition or individual compounds identified can be explored for beneficial effects in chronic disease conditions with exacerbated oxidative stress and chronic inflammatory conditions such as neuropathic pain and rheumatoid arthritis etc. due to their dual antioxidant and anti-inflammatory properties.

2.2 Free radical scavenging potential of setomimycin: *in vitro* and in acute inflammatory mice models

Setomimycin, a rare 9,9′ bisanthraquinone antibiotic discovered in 1978, remains under-researched despite its long-standing existence. Limited studies have focused on its isolation and biological activity, with little exploration of its potential antioxidant and anti-inflammatory effectiveness.

This study aimed to evaluate the antioxidant potential of setomimycin using DPPH free radicals and determine its time and concentration-dependent EC_{50} in comparison to standard antioxidants like ascorbic acid and quercetin. Additionally, the study sought to investigate the effect of setomimycin on nitric oxide inhibition *in vitro* and *in vivo* models and its impact on inducible nitric oxide synthase (iNOS**).**

The EC_{50} for antioxidant activity was determined using a 96-well plate format DPPH free radical scavenging assay following different incubation time-periods. The effect of setomimycin on nitric oxide release was investigated in LPS-induced RAW 264.7 cells and systemic inflammatory mice model using Griess reagent. Further effect on the expression of iNOS level in LPS-induced RAW 264.7 cells was examined through western blot analysis.

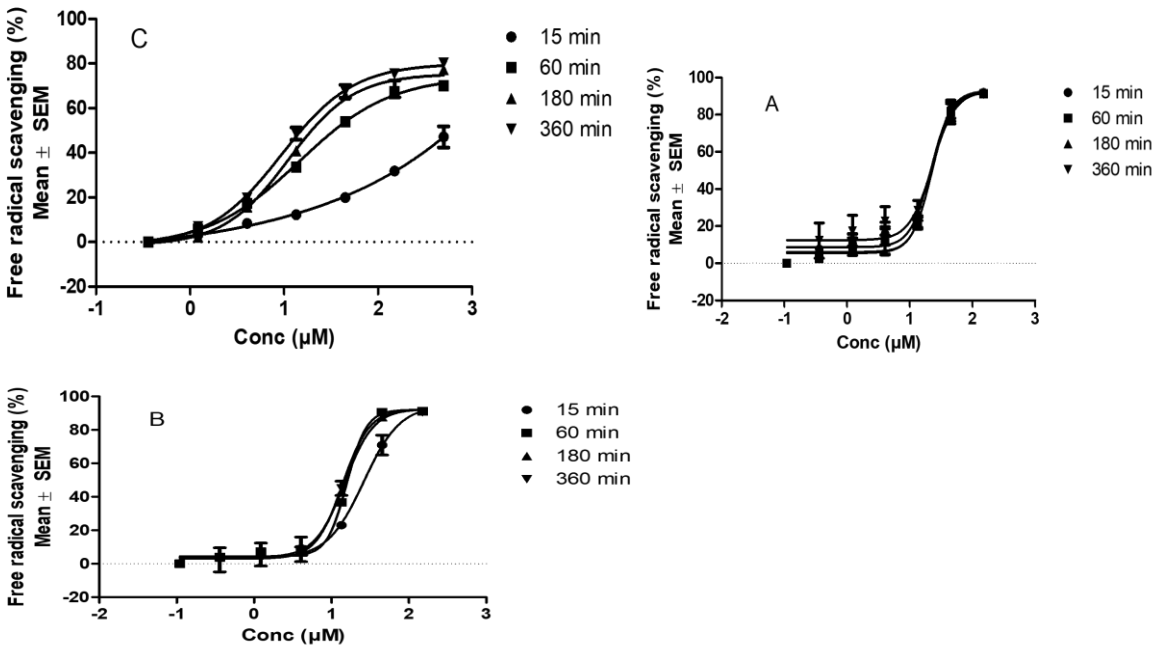


Figure 2.2.1 Determination of EC_{50} of free radical scavenging activity of ascorbic acid (A), quercetin (B) and setomimycin (C)

Table 2: DPPH free radical scavenging activity: EC_{50} (µM) determination

	15 min	60 min	180 min	360 min
Ascorbic acid	21.8	22.4	22.5	22.9
Quercetin	26.1	15.8	14.7	14.0
Setomimycin	ND	14.5	11.2	9.4

Setomimycin exhibited antioxidant properties by scavenging DPPH free radicals, with EC_{50} of 14.5 µM at 60 minutes and improving to 9.4 µM after 360 minutes of incubation period (Fig. 2.2.1 and Table 2). *In vitro* experiments revealed that setomimycin, at non-toxic concentrations ranging from 0.01 to 1 µM, inhibited LPS-induced nitric oxide release in a concentration-dependent manner (Fig. 2.2.2). Additionally, *in vivo* study showed that setomimycin administration at 30, 10, and 3 mg/kg reduced LPS-induced nitric oxide levels in serum by 48.9 ± 1.6 %, 23.6 ± 5.6 %, and 10.4 ± 4.9 %, respectively (Fig. 4.2.3). Western blot analysis demonstrated that setomimycin suppressed LPS-activated iNOS expression dose-dependently (Fig. 2.2.4).

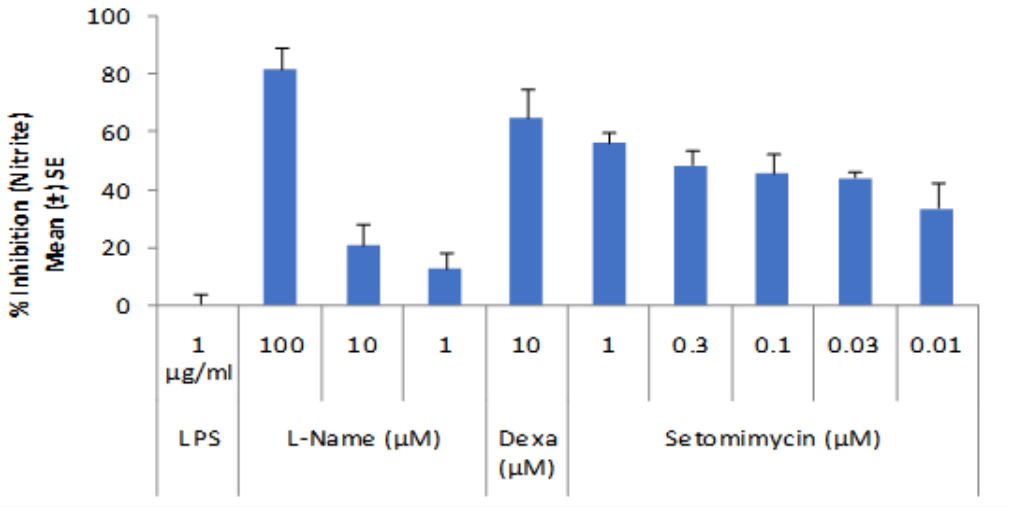


Figure 2.2.2 Effect of setomimycin on nitric oxide release from LPS-induced RAW 264.7 cells

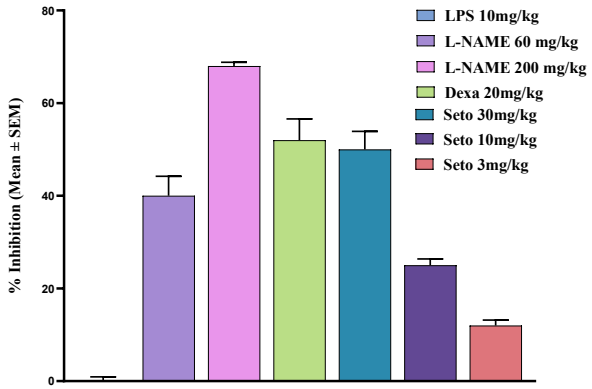


Figure 2.2.3 Effect of setomimycin on nitric oxide release in LPS-induced systemic inflammatory model (in vivo)

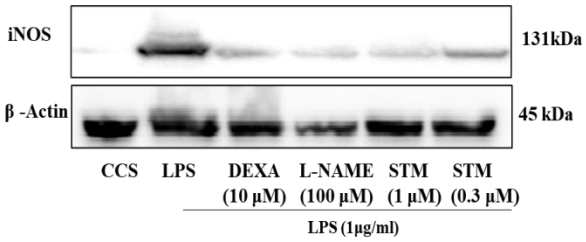


Figure 2.2.4 Effect of setomimycin on expression of iNOSin LPS-induced RAW 264.7 cells

The findings suggest that setomimycin exhibits delayed free radical scavenging activity similar to quercetin. Additionally, setomimycin effectively reduces LPS-induced nitric oxide release and iNOS expression.

2.3 Setomimycin attenuates diabetic neuropathic pain in mice

2.3.1 Effectiveness of setomimycin in alleviating mechanical hyperalgesia

Diabetic (NA+STZ-induced, mild hyperglycemic) mice exhibiting altered mechanical and thermal hyperalgesia served as a model of neuropathic pain. Over a 14-day treatment period, setomimycin's potential to provide analgesia in response to mechanical pressure and heat was evaluated. Gabapentin was the positive control used.

Untreated and NA-treated groups exhibited similar pain thresholds hence the later group has been shown in here further. The pain thresholds observed for STZ or NA+STZ groups were not statistically different compared to each other. Both the groups showed significantly lowered pain thresholds than untreated and NA-treated groups suggesting that induction of diabetes indeed resulted in altered pain behavior i.e. development of hyperalgesia condition. The pain threshold was recorded pre- and day 15-post STZ/NA+STZ treatment followed by treatment with test compound/drug from day 22 onwards, accommodating the development of physiological changes induced by diabetes to take place in the form of altered pain behavior**.** Gabapentin exhibited significant analgesia from the first dose onwards that remained throughout the treatment period and extended until 96 h treatment-free period also. Setomimycin showed dose-dependent analgesia. At 10 mg/kg, the analgesia started after the first dose

and continued throughout the treatment period, but as the treatment was withdrawn, a reversal of analgesia occurred. At 3 mg/kg, significant analgesia was observed after the first dose and up to the sixth dose. At 1 mg/kg, significant analgesia was observed up to the fourth dose only. The reasons for this behavior need further exploration. For example, the compound stability in the formulation might be affecting the activity. Further, glimepiride treatment exhibited a reversal of pain suggesting blood glucose level correction resulted in reduction in the pain in diabetic conditions, to some extent (Fig. 2.3.1).

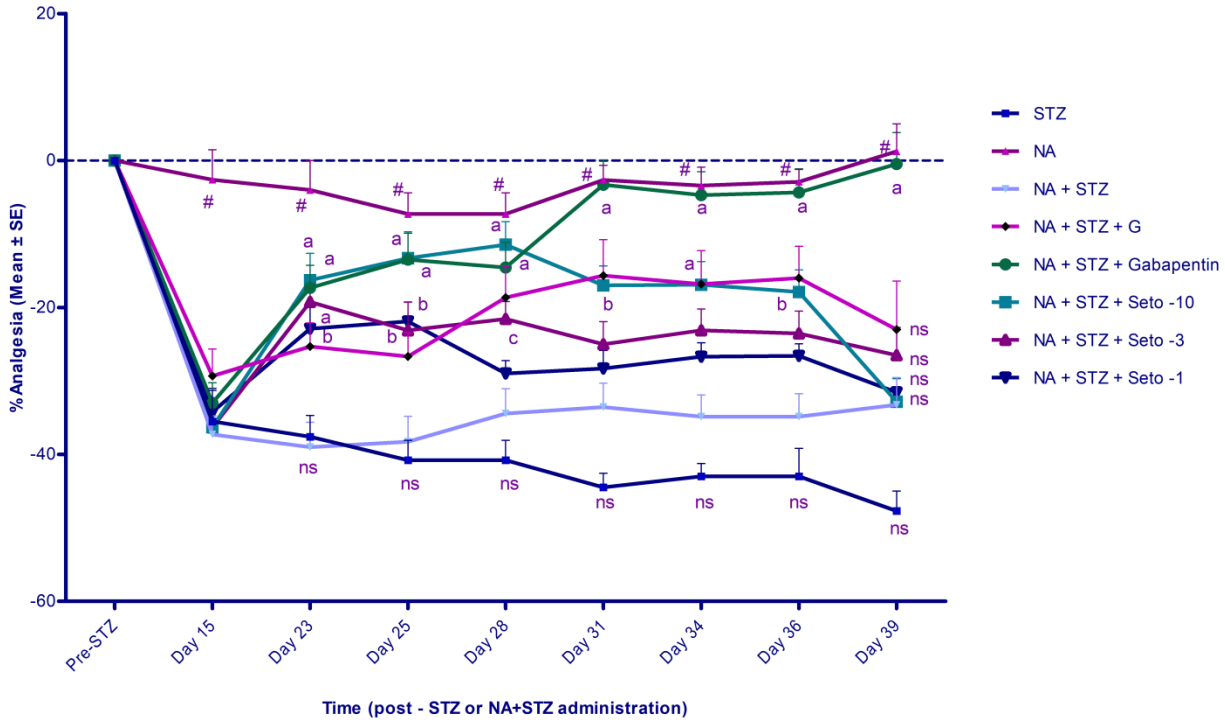


Figure 2.3.1 Effect of setomimycin on mechanical hyperlagesia in diabetic mice: Pain threshold measured using Randall-Selitto method. a - p< 0.001; b - p< 0.01; c - p< 0.05; # - p< 0.001; ns - not significant vs NA+STZ group; Two-way ANOVA with Bonferroni's post-hoc test. Values are mean ± SE, N = 9-10; on day 36 N = 4-7

2.3.2 Effectiveness of setomimycin in alleviating thermal hyperalgesia

Diabetic control (STZ/NA+STZ) groups exhibited significantly reduced hot plate latency compared to the vehicle-treated group. Gabapentin exhibited improved latency compared to diabetic mice groups. Setomimycin exhibited a dose-dependent improvement in latency. At 10 and 3 mg/kg, the latency measured was (16 ± 0.4 and 14.8 ± 0.3 s, respectively) significantly, longer, whereas at 1 mg/kg, it was insignificant compared to NA+STZ (T2DM like) mice group (Fig. 4.3.2).

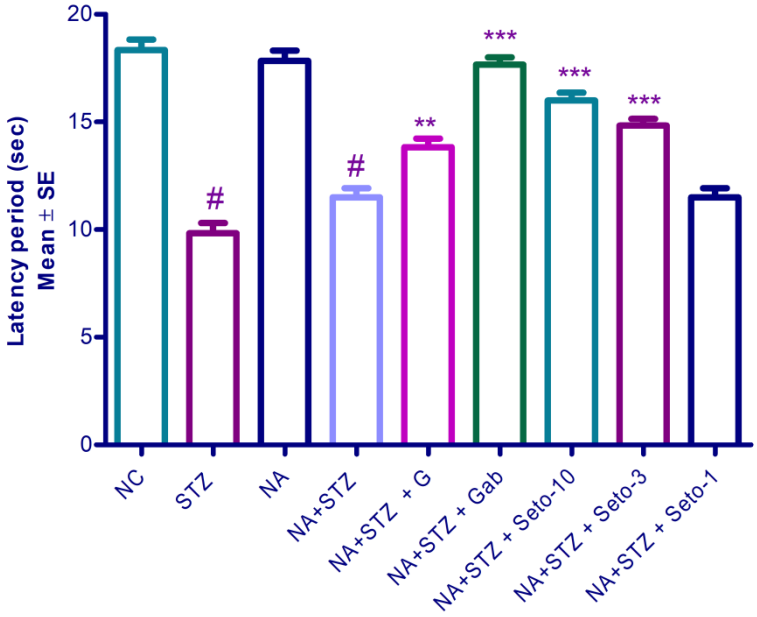


Figure 2.3.2 Effect of setomimycin on thermal hyperlagesia – Hot plate latency in diabetic mice: NC: Untreated; STZ: Streptozotocin; NA: Nicotinamide; G: Glimepiride; Gab: Gabapentin; Seto: Setomimycin; # $p < 0.05$ vs NC; ** / * $p < 0.05$ vs NA+STZ; One-way ANOVA with Bonferroni's multiple comparison test; Values are mean ± SE, N = 6

The findings confirm the effectiveness of setomimycin in alleviating diabetic neuropathic pain through its antioxidant and anti-inflammatory effects, although further studies are required to establish its stability in the formulation, cellular and molecular targets that it interacts with to exert its effects.

VP RAHUL

Dr. VP Rahul (Principal Scientist) with his Research Group

1. Publications/Patents:

2. Scientific work done:

Sustainable Intercropping of Lemongrass and Mustard: Improved Agro-technology for the Northern Region of India

The intercropping of lemongrass and mustard presents a sustainable and improved agro-technology solution for farmers in the northern region of India. Lemongrass is typically harvested during the months of September and October, after which it enters a slow-growth or dormancy period lasting until January–February.

During this fallow phase**, rapeseed and mustard (*Brassica spp*.),** which are among the most important edible oilseed crops of the Rabi season, can be cultivated successfully. In northern India, rapeseed and mustard thrive at mid-altitudes (below 1300 meters above mean sea level) and can be sown between the last week of September and the second week of October. With the adoption of improved production technologies, farmers can maximize the use of residual soil moisture, nutrients, and other inputs.

This intercropping strategy not only enhances the **efficient utilization of available resources**but also improves **land use efficiency** and provides **additional income** during the lean growth phase of lemongrass.

Field trials conducted in the **Jammu region** have shown promising results. The **Land Equivalent Ratio (LER)** was recorded at **1.85** for **1:1 row spacing** of lemongrass and mustard, and **1.5** for **2:1 row spacing**, indicating that intercropping significantly enhances productivity and profitability over monocropping.

The **genotype IIIM-LG 7** of lemongrass, when cultivated with balanced nutrient management, delivered higher yields and resulted in an **additional return of approximately Rs. 12,000 perhectare.** Importantly, **no allelopathic effects** were observed between lemongrass and mustard.

Pic- 1:1 row spacing of lemongrass and mustard

Pic-Vivid presentation of field Lemongrass and Mustard Intercropping

KULJIT SINGH

Dr. Kuljit Singh (Sr. Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Synthesis of novel spiroisoxazolidino hybrids of alantolactone and isoalantolactone via 1, 3 dipolar nitrone cycloaddition and its antimicrobial Evaluation. A Tabassum, D Kumari, HB Bhore, T Palmo, I Venkatesan, J Samanta, AK Katare, YP Bharitkar, **K Singh***. Bioorganic Chemistry 154 (**2025**) 108087
- Breaking the resistance: integrative approaches with novel therapeutics against *Klebsiella pneumoniae*. V Koul, A Sharma, D Kumari, V Jamwal, T Palmo, **K Singh***. Archives of Microbiology 207 (**2025**) 18
- Understanding the mechanisms of antimicrobial resistance and potential therapeutic approaches against the Gram-negative pathogen *Acinetobacter baumannii*. V Jamwal, T Palmo, **K Singh***. RSC Medicinal Chemistry 15 (**2024**) 3925.
- Repurposing FDA Approved Drugs against Sterol C-24 methyltransferase of *Leishmania donovani*: A Dual in silico and in vitro Approach. D Kumari, V Jamwal, A Singh, SK Singh, S Mujwar, MY Ansari, **K Singh***. Acta Tropica 258 (**2024**) 107338.
- Harnessing computational and experimental approaches to identify potent hits against *Leishmania donovani* sterol C-24 methyltransferase from ChemBridge library. D Kumari, T Palmo, S Mujwar, **K Singh***. Acta Tropica 260 (**2024**) 107473.

2. Scientific work done:

Our research group prime focus is to investigate novel strategies to give an impetus to the drug discovery pipeline against deadly bacterial and parasitic infections. Our group aims to identify potent scaffolds and validate novel therapeutic targets to bolster and diversify the chemical space accessible for drug discovery. We have developed various assays to decipher the mechanism of action of bioactive molecules using molecular biology and biochemical approaches. We employ high-throughput screening platforms to find new and effective hits against resistant bacterial species.

In the present current study, we utilized nitrone cycloaddition to synthesize novel spiro-isoxazolidino hybrids of alantolactone and isoalantolactone. This involved targeting the exocyclic α,β-unsaturated double bonds (dienes) of the compounds. The spiro motif serves as a highly attractive structural framework for drug discovery; thus, we aimed to introduce a new bioactive motif in alantolactone and isoalantolactone to reduce toxicity, increase specificity, and improve physicochemical properties. Following successful preparation, we tested the antimicrobial efficacy of the newly synthesized spiro-isoxazolidino hybrids against Gram-positive (*Staphylococcus aureus,*methicillin-resistant *S. aureus*, and *E. faecalis*) and Gram-negative (*A. baumannii*) bacterial strains. A preliminary whole-cell-based screening assay confirmed that two compounds (**3f** and **4f**) were active against *S. aureus* and MRSA strains. Furthermore, various *in vitro* assays, including MIC, MBC, time-kill kinetics, andscanning electron microscopy analysis, have confirmed that these two compounds have potential antimicrobial activities. The workflow of the present study is illustrated in **Fig. 1**.

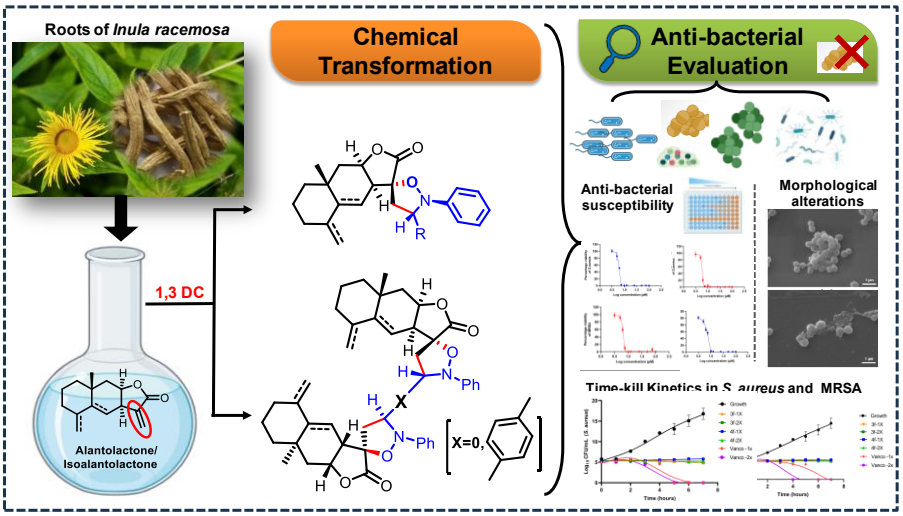


Fig.1: Schematic workflow of the study.

High-throughput screening (HTS) is a critical technique that can accelerate the process of drug discovery by evaluating millions of drug-like molecules using various automation tools and biological assays. In the present study, we have employed the HTS strategy to identify potent hits against *Leishmania donovani*sterol C-24 methyltransferase (LdSMT) from the in-house ChemBridge library. Firstly, a robust dataset was prepared with previously reported sterol C-24 methyltransferase inhibitors, belonging to diverse structural classes. Then, ligand-based virtual screening using similarity search was performed to screen the ChemBridge library having ~20,000 molecules. This computational approach

yielded 81 candidate compounds, which were selected for further molecular docking and biological evaluation. Anti-leishmanial assays revealed that out of 81 molecules, seven showed potential parasitic killing. Three molecules namely **IIIM-CB-14**, **IIIM-CB-29**, and **IIIM-CB-45** were the most potent ones with 50% inhibitory concentration (IC_{50}) of 5.76, 8.08, and 10.64 µg/mL, respectively. SEM analyses suggest that these potent hits cause considerable morphological alterations. ADME studies of the potent hit molecules indicate that all the hits have considerable drug-likeness properties. Further, molecular dynamics studies were also performed to check the stable confirmation of LdSMT protein with the top two hits (**IIIM-CB-14** and **IIIM-CB-45**). Thus, the present study harnesses computational and experimental approaches tounravel potent anti-leishmanial scaffolds. The complete workflow of the present study is illustrated in **Fig. 2**.

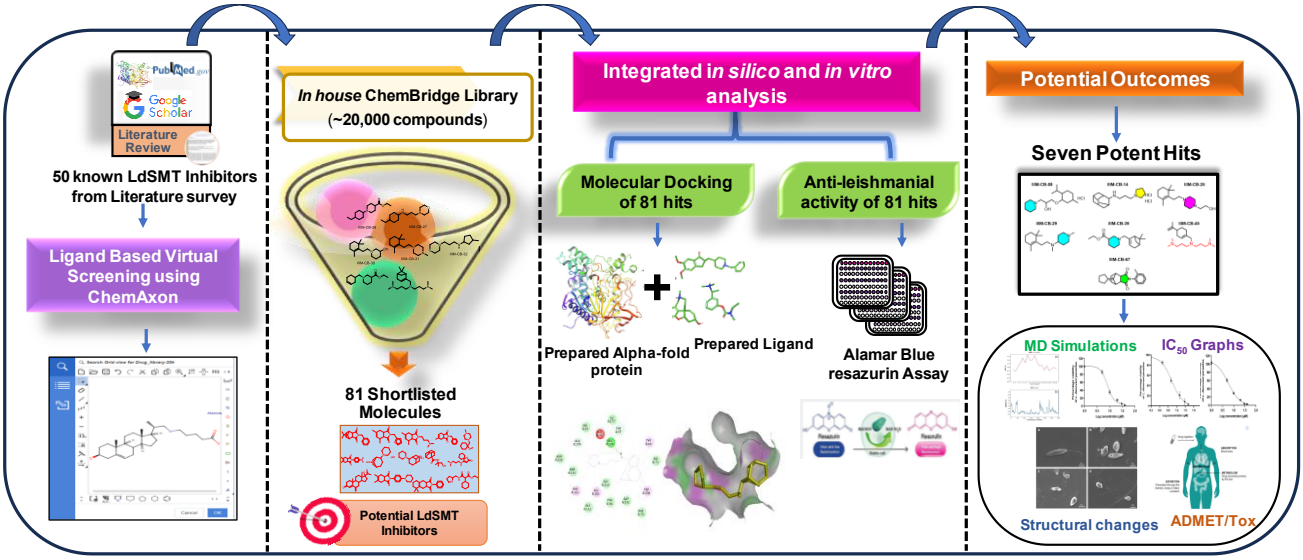


Fig. 2: Schematic workflow of the study.

VIKASH BABU

Dr. Vikash Babu (Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Kumari, Hema, Ananta Ganjoo, Haseena Shafeeq, Nargis Ayoub, **Vikash Babu**, and Zabeer Ahmed. "Microbial transformation of some phytochemicals into value-added products: A review." Fitoterapia (2024): 106149**.**
- Shafeeq, Haseena, Bashir Ahmad Lone, Ananta Ganjoo, Nargis Ayoub, Hema Kumari, Sumeet Gairola, Prasoon Gupta, **Vikash Babu**, and Zabeer Ahmed. "Biotransformation of Geraniol to Geranic Acid Using Fungus *Mucor irregularis* IIIMF4011." *ACS Omega* (2024). *9*(40), pp.41314-41320.
- Ganjoo, Ananta, and **Vikash Babu**. "Recombinant Amidases: Recent Insights and its Applications in the Production of Industrially Important Fine Chemicals." Molecular Biotechnology (2024): **67**, 910–924 (2025).
- Nargis Ayoub, Bashir Ahmad Lone, Haseena Shafeeq, Hema Kumari, Prasoon Gupta, Sumeet Gairola, **Vikash Babu** and Zabeer Ahmed. Biotransformation of limonene to limonene-1, 2-diol

using an isolated fungus *Lasiodiplodiapseudotheobromae* IIIMF4013 (2025). Biocatalysis and Biotransformation (1-9).

Patents:

- **Vikash Babu,** Prasoon Gupta, Govind Yadav, Sumeet Gairola, Hem Kumari, Ananta Ganjoo, Bashir Ahmad Lone, Deepika Singh, Ajay Prakash Gupta, Narendra Singh Chauhan, Haseena Shafeeq, Nitika Sharma. Process for the preparation of immunomodulatory fermented polyherbal formulation. **Filed (IN 202311070420)**
- Vikash Babu, Prasoon Gupta, Sumeet Gairola, Haseena Shafeeq, Bashir Ahmad Lone, Ananta Ganjoo, Nargis Ayoub Bhat, Amit Kumar, Zabeer Ahmed. Process for the Biotransformation of Geraniol to Geranic acid. **(IN 202311074007)**

2. Scientific work done:

2.1 Microbial Production of Co-enzyme Q10 (CoQ10)

An *Agrobacterium* sp. strain, designated as strain 51, was obtained from a recognized microbial culture repository and screened for Coenzyme Q10 (CoQ10) production. Preliminary identification was based on morphological characteristics, as illustrated in Figure 1. The presence of CoQ10 was confirmed through thin-layer chromatography (TLC) analysis. TLC plates were visualized under UV light and subsequently developed with anisaldehyde reagent. A distinct spot corresponding to CoQ10 was observed, which exhibited similar Rf value on comparison with standard CoQ10 spot, as shown in Figure 2.

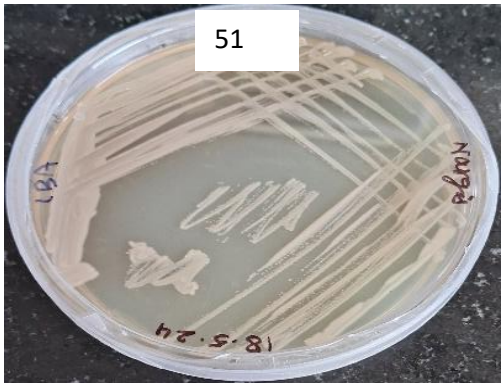


Fig. 1: Morphological appearance of *Agrobacterium* sp.

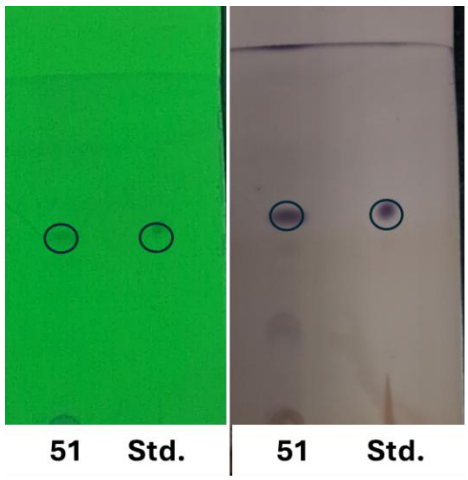


Fig. 2. Thin-layer chromatography (TLC) analysis of Coenzyme Q10 (CoQ10) produced by *Agrobacterium* sp. strain 51. Lane 1: extract from strain 51; Lane 2: CoQ10 standard.

Thereafter, confirmation of CoQ10 production in the extract of *Agrobacterium* sp. strain 51 through TLC analysis, the sample was subjected to mass spectrometric analysis to further validate the presence of CoQ10. The mass chromatogram revealed a prominent peak at m/z 862.70 in negative ionization mode, which corresponds to the molecular ion [M–H] ⁻ of Coenzyme Q10, thereby confirming its production by the strain. The corresponding mass chromatogram is presented in Figure 3.

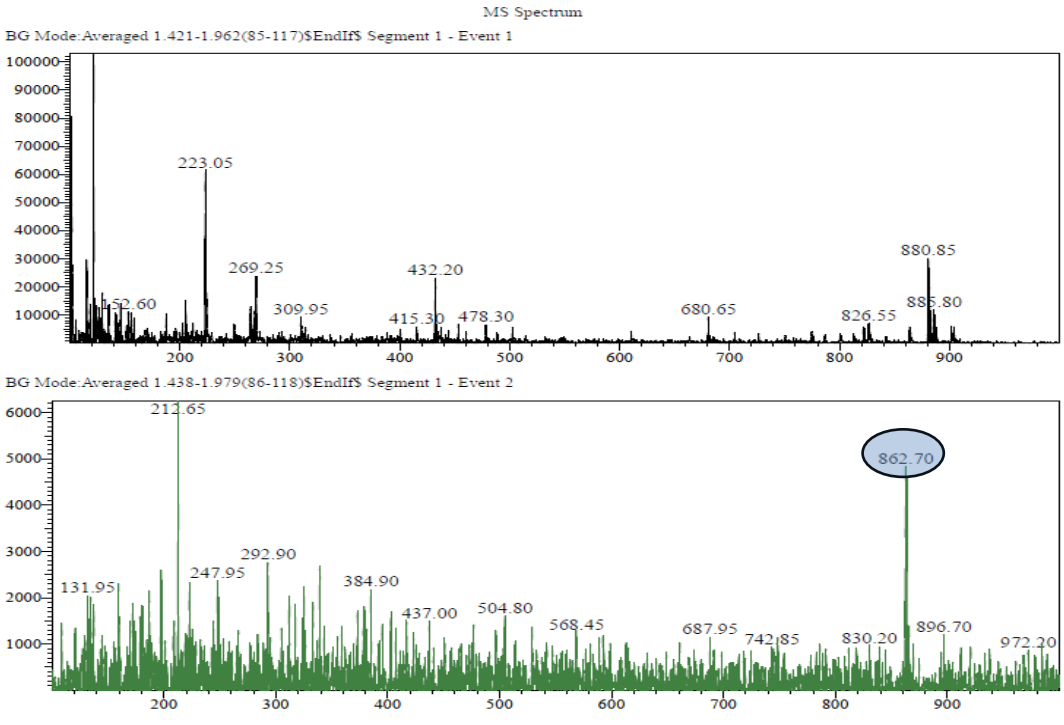


Fig.3: Mass spectra of crude extract of 51 showing a peak at 862.70

Purification of CoQ10 from microbial extract of selected strain

CoQ10 was isolated and purified from microbial extracts using column chromatography through a series of steps. First, microbial biomass is harvested by centrifugation, and extracted using solvents hexane:isopropanol (5:3) at 37°C for 20 minutes with agitation. The extract is concentrated under reduced pressure using a rotary evaporator. For purification, a silica gel column (100-200 mesh) is packed, and the crude extract is loaded after dissolving it in minimal volume of hexane. A gradient elution is then performed using increasing polarity solvent starting with hexane, followed by hexane:ethyl acetate (99:1to 90:10), and ending with ethyl acetate:hexane (90:10). Fractions are collected and monitored by thin-layer chromatography (TLC) (Fig. 4), and those containing CoQ10 (identified using UV detection) are pooled and concentrated again. The concentrated compound was analyzed by mass spectrometry and further characterized using NMR spectroscopy, including ^{1}H NMR (Fig. 4) and ^{13}C NMR (Fig. 5).

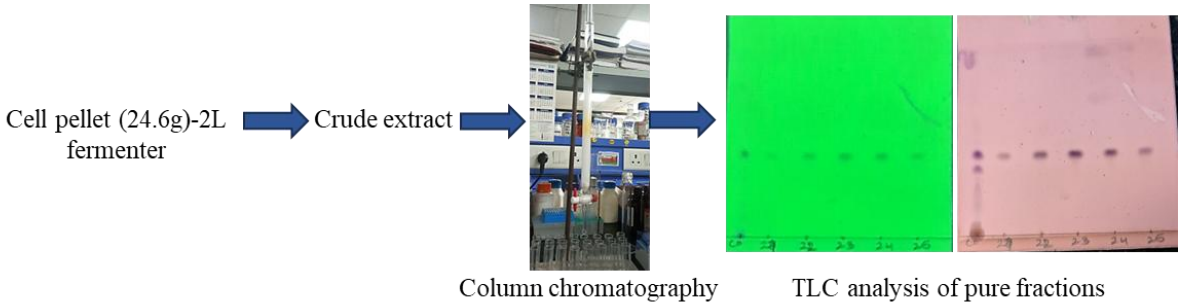


Fig. 4: Purification of Coenzyme Q10 (CoQ10) using column chromatography

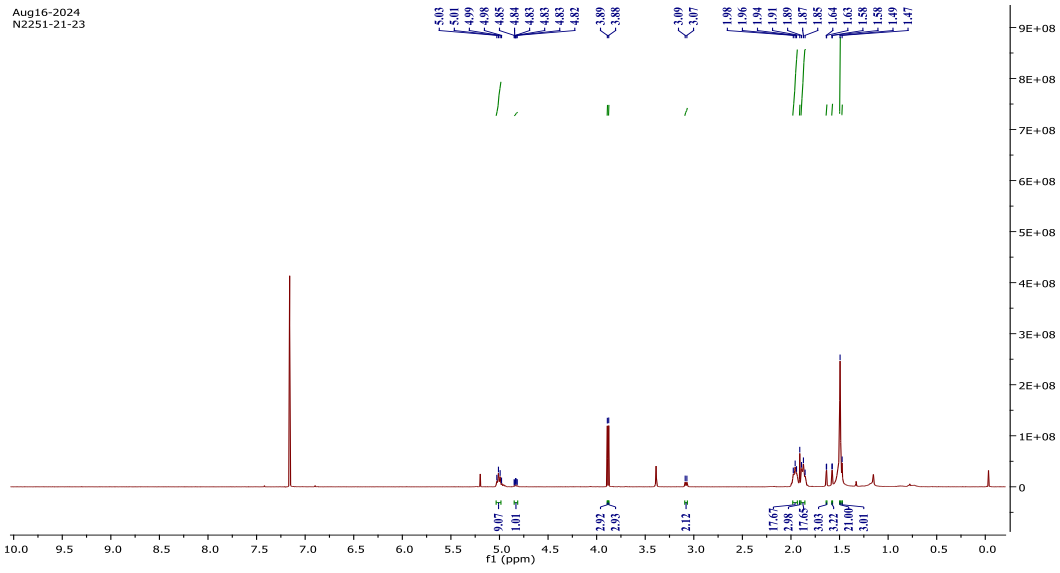


Fig.5: ^{1}H-NMR of Purified CoQ10

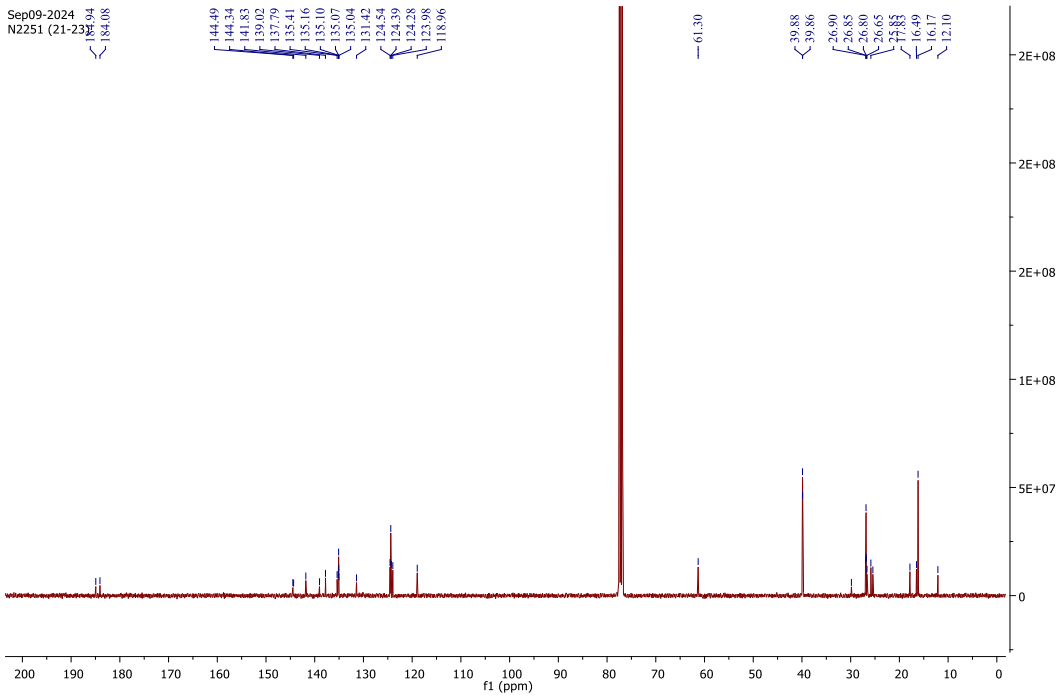


Fig.6: ^{13}C-NMR of Purified CoQ10

2.2 Biotransformation of Limonene to value-added compounds

The biotransformation of monoterpenes, viz. limonene, has been widely studied for the production of an array of molecules. Limonene is a compound found abundantly in nature, mainly in a number of plants and herbs. In addition, it is found in peels of citrus fruit, red pepper, chamomile, rosemary, ginger, and turmeric and is readily available in the market. Thus, this compound is a very suitable starting material for the production of terpenoids with a higher economic value. Limonene, being readily available and low-priced, is commonly used as a substrate to produce its value-added compounds such as limonene-1,2-diol, perillyl derivatives, α-terpineol, menthol, carvone, and carveol.

2.2.1 Biotransformation of limonene to Limonene-1,2-diol

Limonene-1,2-diol, a hydroxylated derivative of limonene, has been reported to inhibit tumor growth by modulating p21-dependent and TGF-β signaling pathways, inducing apoptosis, and arresting the G1 phase of the cell cycle. In this study, we developed an efficient microbial biotransformation process to produce limonene-1,2-diol from limonene, a readily available monoterpene. In this process, *Lasiodiplodiapseudotheobromae* IIIMF4013, an endophytic fungus isolated from the peel of a lemon, is used for the selective hydroxylation of limonene (Fig.7). After optimization of production parameters, the transformation achieved >99% conversion efficiency, which was consistently maintained during scale-up. Structural confirmation of the biotransformed product was performed using gas chromatography–mass spectrometry (GC–MS) along with detailed 1D and 2D nuclear magnetic resonance (NMR) analyses, confirming the production of limonene-1,2-diol.

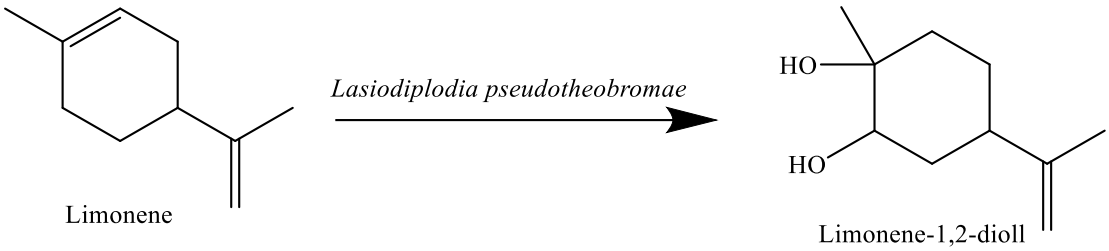


Fig.7: Biotransformation of limonene to limonene-1,2-diol using *Lasiodiplodiapseudotheobromae.*

2.2.2 Biotransformation of limonene to Perillic-acid

Perillic acid is an attractive target for the pharmaceutical and cosmetic industries due to its cytotoxicity to cancer cells and its antimicrobial properties, respectively. Perillic acid, an almost odorless monoterpenoic acid present as a glycoside in *Perilla frutescens* and as a minor component in essential oils of lemon grass, Citrus, and Perilla, exerts a strong growth-inhibitory effect on bacteria and molds, making it an attractive candidate to be used for natural preservation purposes, e.g., in the cosmetics industry. Eleven different microbial strains were screened for their ability to oxidize the exocyclic methyl group in the *p*-menthene moiety of limonene to perillic acid. *Staphylococcus chonii* IIIMB2707 emerged as the most efficient biocatalyst, producing perillic acid as the major product from the biotransformation of R-(+)-limonene (Fig.8). Optimal conversion, reaching 77%, was achieved in a pH 7 ± 0.2 buffered medium after 48 hours of incubation at 28 °C. The product was characterized using gas chromatography-mass spectrometry (GC–MS) and nuclear magnetic resonance (NMR).

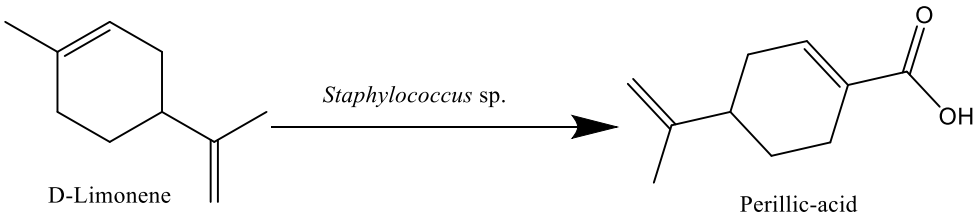


Fig.8: Biotransformation of limonene to perillic acid using *Staphylococcus chonii* IIIMB2707

ASHA CHAUBEY

Dr. Asha Chaubey (Sr. Principal Scientist) with her Research Group

1. Publications/Patents:

Publications:

- Diksha Koul, Devtulya Chander, Ravi Singh Manhas, Mohd. Mehedi Hossain, Mohd. Jamal Dar and **Asha Chaubey**, 2024. Purification, functional characterization and enhanced production of serratiopeptidase from Serratia marcescens MES-4: An endophyte isolated from Morus rubra. *Journal of Biotechnology*, (387), 58-68.
- Natish Kumar, Monika Kumari, Devtulya Chander, Sandeep Dogra, **Asha Chaubey** and Ravi Kumar Arun, 2024. Miniaturized electrophoresis: An integrated microfluidic cartridge with functionalized hydrogel-assisted LAMP for sample-to-answer analysis of nucleic acid. *Biomicrofluidics*, (18*),* 064104.
- Ravi Singh Manhas, Neha Sharma, Safeya Begum, Yedukondalu Nalli and **Asha Chaubey,** 2025**.** (3R)-obscurolide A: a new obscurolide from Streptomyces chartreusis SA-7 isolated from soil of the North Western Himalayas. *Natural Product Research*, (12) 1-8.

Patents

- **Indian Patent Application Number 202411012579**
  A process for the production of Actinomycin D

Chaubey Asha, Sharma Neha, Manhas Ravi S., Nalli Yedukondalu, Verma Mahendra Kumar, Kumar Amit, Reddy SrinavasaDumballa

- **US18703696 EP 4419647**

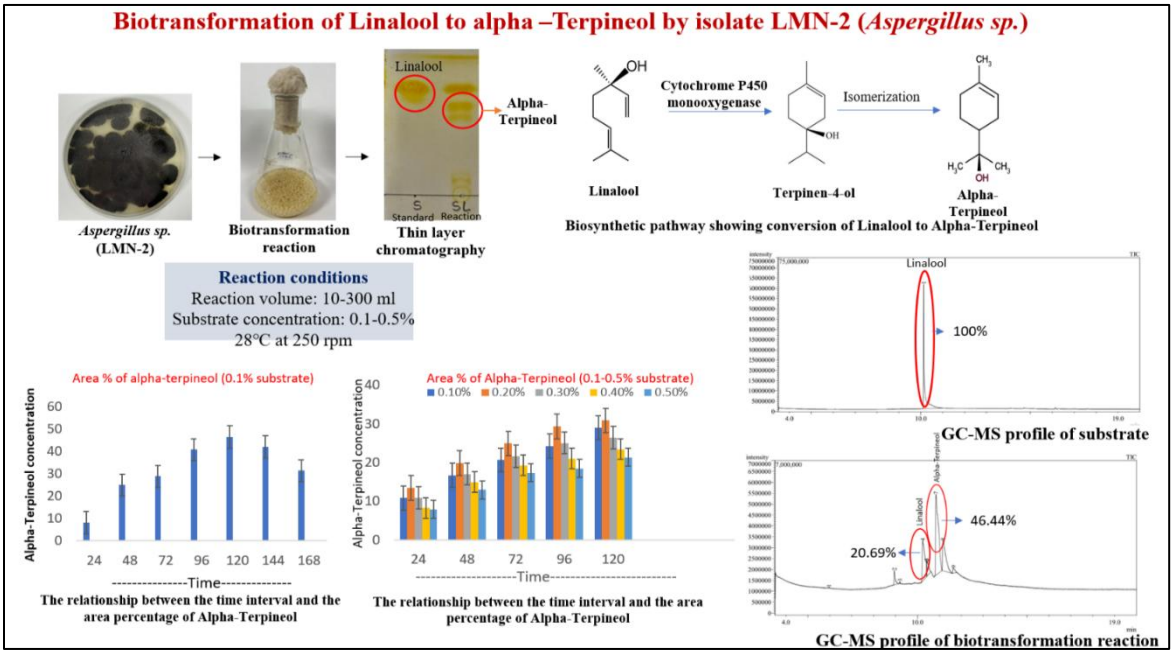
  A process for the preparation of tetrahydroanthracenes from streptomyces spp. And anticancer activity thereof

  Chaubey Asha, Manhas Ravi S., Khosla, Ahmad Ajaz, Ahmad Syed Mudabir, TiwariHarshita, Nargotra Amit, Mukherjee Debaraj and Goswami Anindya

2. Scientific work done:

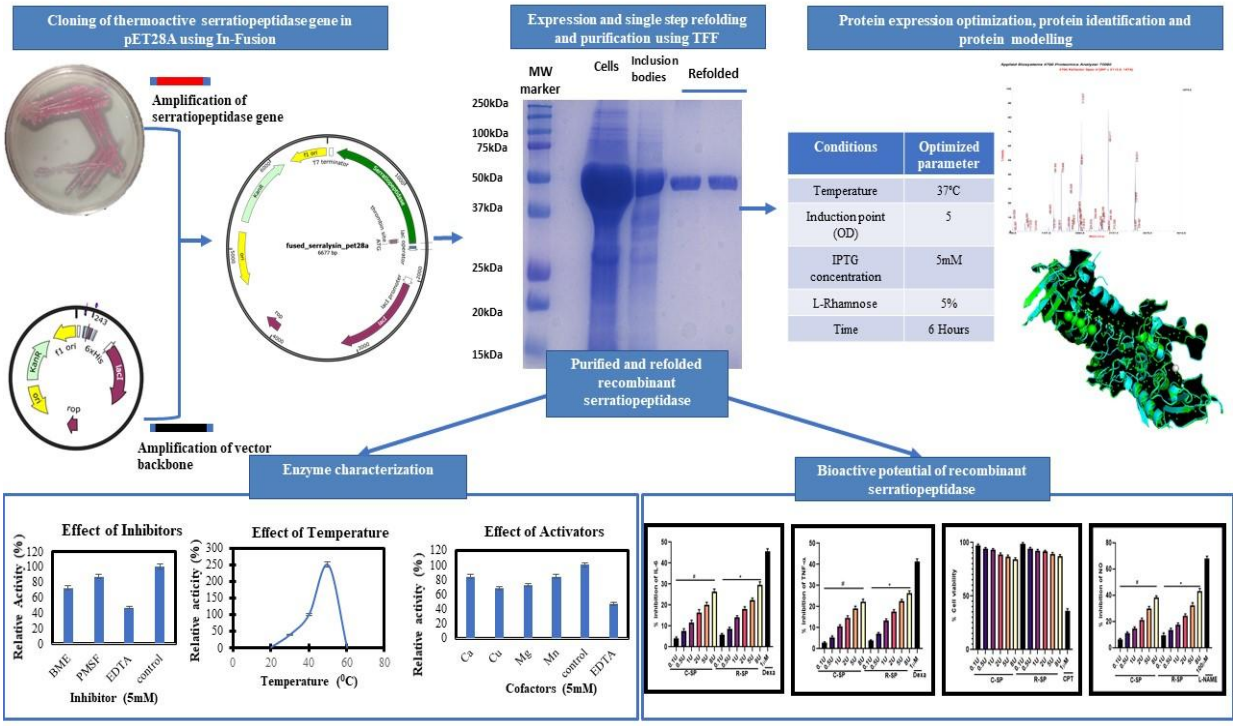
Biotransformation of linalool to alpha-terpineol

This study demonstrates the biotransformation of linalool to alpha-terpineol by the fungal isolate LMN-2 (*Aspergillus sp.*). The process involves culturing the fungus, carrying out the biotransformation reaction under optimized conditions (10–300 ml volume, 0.1–0.5% substrate concentration, 28 °C, 250 rpm), and monitoring the product formation using thin layer chromatography (TLC) and GC-MS. The biosynthetic pathway suggests that linalool is first hydroxylated by cytochrome P450 monooxygenase to yield terpinen-4-ol, which is then isomerized to alpha-terpineol. GC-MS analysis confirmed the conversion, showing a decrease in linalool content from 100% to 46.44%.



Recombinant serratiopeptidase from *Serratia marcescens* AD-W2

Serratiopeptidase, a proteolytic enzyme with therapeutic applications, is traditionally produced from the bacterium *Serratia marcescens*. Recombinant production of serratiopeptidase in *Escherichia coli* offers a safer alternative to the biosafety concerns of the producer. Present study involves cloning and heterologous expression of thermoactiveserratiopeptidase gene from *S. marcescens* AD-W2 in *E. coli* K12 in pET28a plasmid. Optimized expression conditions i.e. 37°C,OD_{600} 5, 5% L-rhamnose, 5mM IPTG and, and 50% dissolved oxygen led to the final yield of 190mg/g serratiopeptidase (4747 mg protein/L) in 9 hours in Bioreactor. Purification and refolding of recombinant serratiopeptidase was performed in a single step using Tangential Flow Filtration (TFF) and diafiltration process. The purified recombinant serratiopeptidase exhibited specific activity of 1800 Units/mg protein, with an optimal activity at pH 9.0 and temperature 50°C. The value of kinetic constant K_m was calculated as 1.38 mg/mL for casein. The recombinant serratiopeptidase demonstrated comparable anti-inflammatory activity to the commercially available serratiopeptidase, inhibiting nitric oxide release and pro-inflammatory cytokine production in LPS-stimulated murine macrophage cell line RAW 264.7. The study reveals that the recombinant serratiopeptidase produced in *E. coli* K12 holds promising source of safe and effective anti-inflammatory agent.



MEENU KATOCH

Dr. Meenu Katoch (Sr. Scientist) with her Research Group

1. Publications/Patents:

Publications:

- Thambi, N. P., Rani, P., Syed Mudassir Ali, Bera, A., & Meenu Katoch. (2024). The mechanism of antifungal effects of *Monarda citriodora* essential oil and trans-cinnamaldehyde as a fumigant against *Aspergillus fijiensis*, a postharvest pathogen of lemon. Journal of Stored Products Research, 106, 102309–102309. https://doi.org/10.1016/j.jspr.2024.102309 (IF 2.7) ·
- Thambi, N. P., Sharma, M., Rajendra Gochar, & Meenu Katoch. (2024). Alternaria sp., a new pathogen causing leaf spot in broccoli, and its management with *Monarda citriodora* essential oil (MEO) and isoeugenol combination. Physiological and Molecular Plant Pathology, 102293–102293. https://doi.org/10.1016/j.pmpp.2024.102293 (IF 2.8)
- Katoch, M., Singh, G., Bijarnia, E., Gupta, A. P., Azeem, M., Rani, P., & Kumar, J. (2024). Biodiversity of endosymbiont fungi associated with a marine sponge *Lamellodysideaherbacea* and their potential as antioxidant producers. 3 Biotech, 14(5), 146. (IF 2.6)
- Gupta, N., Singh, G., Qayum, A., Ovais Dar, M., Singh, S., Katoch, M., & Sangwan, P. L. (2024). In Vitro and In Silico Anticancer Evaluation of Secondary Metabolites from an

Endophytic Fungus *Aspergillus Fumigatus* Isolated from *Monarda Citriodora*. Chemistry Select, 9(13), e202400637. (IF 1.9)

Patents:

- Meenu Katoch, Nidhin Poovathumkadavil Thambi, Mohini Sharma, Rajinder Gochar, Zabeer Ahmed (2024) Antifungal Formulation for Leaf Spot in Broccoli- 202411005915
- Meenu Katoch, Pragya Rani, Mohini Sharma, Zabeer Ahmed (2024) An Alginate Based Coating Composition Comprising Trans-Cinnamaldehyde for the Management of Postharvest Rot of Apples. 202411098113

2. Scientific work done:

Aroma Mission-Phase III

1. **Hydrosol based nano-emulsion for food preservation.**
   Ten Hydrosols were collected from IIIM, Farm, Chatha, Jammu. The antimicrobial activity of the collected hydrosols against food borne pathogens was studied. Hydrosols of *Monarda citriodora*, *Ocimum gratissimum*and *Mentha arvensis* showed positive antimicrobial activities. The chemical composition of active hydrosols was analyzed through GC-MS. Constraints:Chemicals ordered recently and have not yet been delivered (Soybean lecithin, Benzalkonium chloride). Homogenizer is not available.
2. **Microencapsulated essential oil-based formulation as an alternative to antibiotics in animal feed.**
   Contaminated poultry feed was collected from poultry farms in RS Pura/Jammu. Nineteen bacteria and five fungal pathogens were isolated from the contaminated feeds. Essential oils and constituents were screened for antibacterial and antifungal activities against the combined isolates. The combination of essential oil *Monarda citriodora* (MEO) and constituent geraniol (MEO-Ger) showed a synergistic effect against all fungal isolates. Microencapsulation of MEO/geraniol was performed and it was optimized. Microencapsulated MEO/geraniol was evaluated for its antifungal activity in vitro and in vivo. Currently, we are in the process of evaluating its toxicity/adverse effect inside the body of poultry. Next step would be patent filing of antifungal micro-encapsule effective against isolated pathogens of animal feed.

DST-WISE GAP 3173 (project)

Fungal pathogens were isolated from infected stored maize seeds collected from Bihar, Hyderabad, Jammu and Kashmir. The antifungal activity of essential oil/its constituents against isolated pathogens was evaluated and the effective synergistic combination was found. Using this synergistic combination of EO/constituents, a broad-spectrum fungicide formulation was developed, which was found effective against Bihar and Hyderabad combined pathogens in *in vitro* as well as *in vivo* studies for its storage capabilities. Patent filing of this formulation is under way.

REPURPOSING OF TRIFLURIDINE AS ANTIMICROBIAL AGENT against *Staphylococcus aureus*

Staphylococcus aureus is a highly virulent pathogen capable of abruptly evolving and developing antibiotic resistance. It is reported that about 40% of healthy human beings are carriers of *S. aureus* present on their skin, inside their intestine, throat, and nose. This 40 % of carriers are mostly immune-compromised people, children, and older people.

The minimum inhibitory concentration for trifluridine (TRFD) and ciprofloxacin (CIP) was observed at 1.562 mg L^{-1} and 0.195 mg L^{-1} for ciprofloxacin-susceptible *S. aureus* (CSSA) and at 0.0625 mg L^{-1} and 12.5 mg $L^{-1}$for ciprofloxacin-resistant *S. Aureus* (CRSA). Synergistic (0.39 mg L^{-1}(TRFD) + 0.048 mg L^{-1} (CIP)) and partial synergistic (0.03125mg L^{-1} (TRFD) + 3.125 mg L^{-1} (CIP)) effects of TRFD with CIP combination were observed against CSSA and CRSA with fractional inhibitory concentration values of 0.495 and 0.75, respectively. The TRFD + CIP combinations significantly increased the propidium iodide uptake, indicating plasma membrane damage and generated the highest 2′,7′-dichlorofluorescin diacetate signal, indicating increased intracellular ROS accumulation. Furthermore, TRFD + CIP substantially affected the production of the virulence factor staphyloxanthin and altered the surface morphology of CSSA and CRSA with deformation, irregular surfaces, and cracks.
The results indicate that the antibacterial mechanism of TRFD + CIP is multitargeted, involving the generation of intracellular ROS, contributing to plasma membrane damage. The TRFD + CIP combination can be a promising option against *S. aureus*.

Functional Characterization Of MK8, an NRPS Gene Cluster From *T. lixii* Through Heterologous Expression

The 8 genes of MK8 cluster were assembled in yeast and assembled construct was transformed into *Fusarium graminearum* through protoplast mediated method. The integration of construct was validated through colony PCR using primers of nptt and genes present in MK8 cluster (A1-A12). The validated transformant was fermented in shake flask and its extract was analysed through HPLC, HRMS, LCMS. Analytical data is suggesting that it is expressing some different molecule/secondary metabolite. But full characterization is still continued.

VINOD KUMAR

Dr. Vinod Kumar (Sr. Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Sonali Sharma, Ishfaq Nabi Najar, Anu Radha, Nagaraju Nekkala, Varsha Sharma &**Vinod Kumar*(2025).** An effective method for developing cellulose-based polymer from spent lemongrass. Biomass Conversion and Biorefinery.https://doi.org/10.1007/s13399-025-06607-4.
- Ishfaq Nabi Najar, Prayatna Sharma, Rohit Das, Sonia Tamang, Krishnendu Mondal, Nagendra Thakur, Sumit G Gandhi, **Vinod Kumar. (2024).** From waste management to circular economy: Leveraging thermophiles for sustainable growth and global. Journal of Environmental Management. (360):121136
- Ishfaq Nabi Najar, Prayatna Sharma, Rohit Das, Krishnendu Mondal, Ashish Kumar Singh, Sonia Tamang, Nagendra Thakur, Rajendra Bhanwaria, Sumit Gandhi and **Vinod Kumar. (2024). In search of Poly-3-Hydroxybutyrate (PHB): A Comprehensive Review Unveiling Applications and Progress in Fostering a Sustainable Bio-Circular Economy.Food and Bioproducts Processing.** 148:11-30.

Patents:

Title: Fermented composition with anti-inflammation and wound healing properties

Inventors: Zabeer Ahmed, **Vinod Kumar**, Anu Radha, Varsha Sharma, Saurabh Saran, Mahendra Kumar Verma, Nalli Yedukondalu, Boobalan Gopu, Sanket Kumar Shukla, Deepika Singh, Diljeet Kumar, Rajendra Bhanwaria, Jasha Momo Hmsunghel, Sumeet Gairola, Rajendra Gochar

2. Scientific work done:

Research activity 1

(R) 3-hydroxybutyric acid: Process Development, Purification, Scale-up & Potential Applications

Research outcome:

Accordingly, this project aims to develop an efficient bioprocess for the production of (R)-3-hydroxybutyric acid by a novel and robust isolate from halophilic microbes employing batch or fed-batch operations by an isolated strain solid-state fermentation (SSF) and submerged fermentation (SmF) both will be evaluated and compared. In order to reduce the cost of production, several low-cost carbon sources such as oil cakes and agricultural residues rich in starch will be used. Based on the study performed, it can be concluded collected samples showed production of PHB polymer and its monomer R-3-hydroxybutyric acid under low carbon source condition and the most potent was IIIM-VV-H3 with R-3-HB concentration of 1.781(at 96h), 1.017 (at 48hr) and 0.787 (at24h) g/l with 30,10 and 5 g/l sucrose respectively.However, further improvement for higher production is required from the substrate. Concomitantly, intensive research for strain improvement and evaluation of the (R)-3-hydroxybutyric acid produced as a starting material for manufacturing medicines shall be investigated and commercialized.

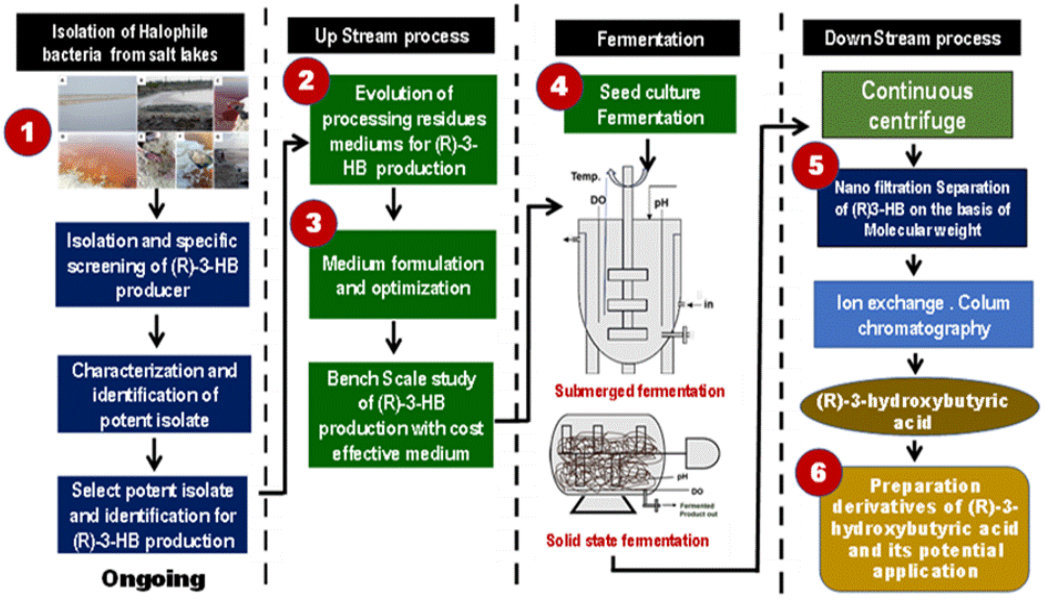


Figure 1: Systematic representation of (R) 3-hydroxybutyric acid production

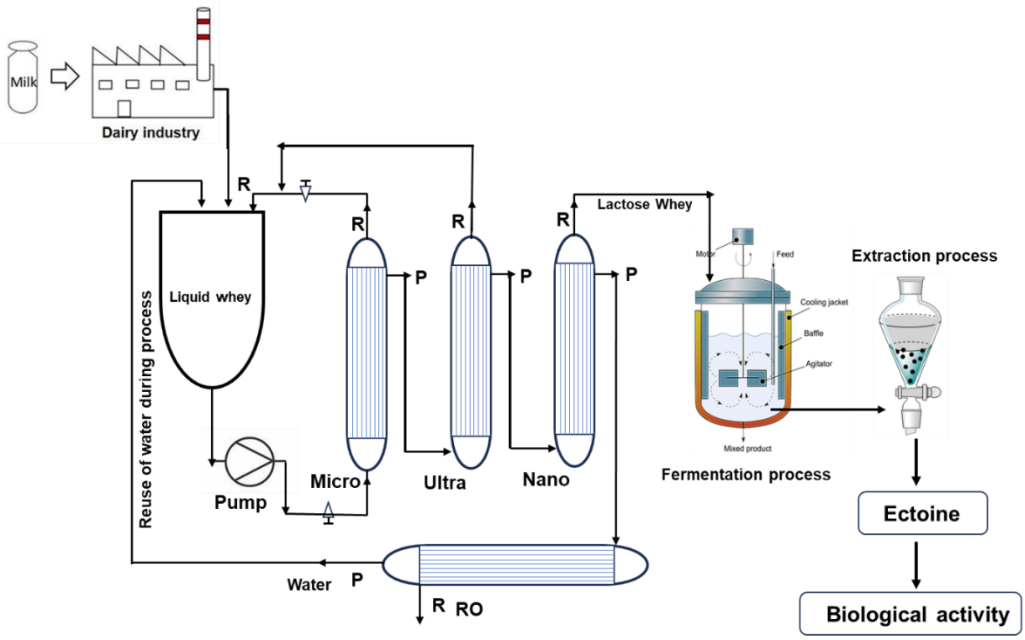
Research activity 2

Ectoine: A Sustainable alternative cell protectant: production, process optimization, purification scale up and evaluation

Research outcome:

Ectoine (1,4,5,6-tetrahydro-2-methyl-4-pyrimidinecarboxylic acid) is a notable compatible solute produced by halophilic microorganisms, a cyclic derivative of aspartate known for its remarkable ability to protect cells from osmotic stress and other environmental challenges. The production of ectoine, a valuable compound with significant potential as an osmoprotectant, anti-inflammatory agent, antioxidant and macromolecule protector, was achieved by a lactose-utilising bacterial strain. We explore the feasibility of using whey, a waste product rich in lactose and amino acids, as a growth medium. Various parameters was optimized to maximise ectoine yield. Initially, the highest ectoine production that is 1.8 g/l was achieved using 75% diluted whey, pH 4.50, 5% NaCl, 250 rpm and 30°C. This is the first study in which whey was efficiently utilised to produce ectoine by ***Halomonassalifodinae BC7***particularly in low-salt conditions and this is the novel approach to used low salt concentration in order to avoid exacerbates the corrosion to fermenters, and more importantly, brings a big challenge to the subsequent dairy waste treatment.

By exploring these and other innovative approaches, we can potentially develop novel methods for the production of ectoine through whey fermentation and low salt concentration that offer advantages in terms of cost-effectiveness, sustainability, productivity, and scalability, however also addressing challenges present in prior art.



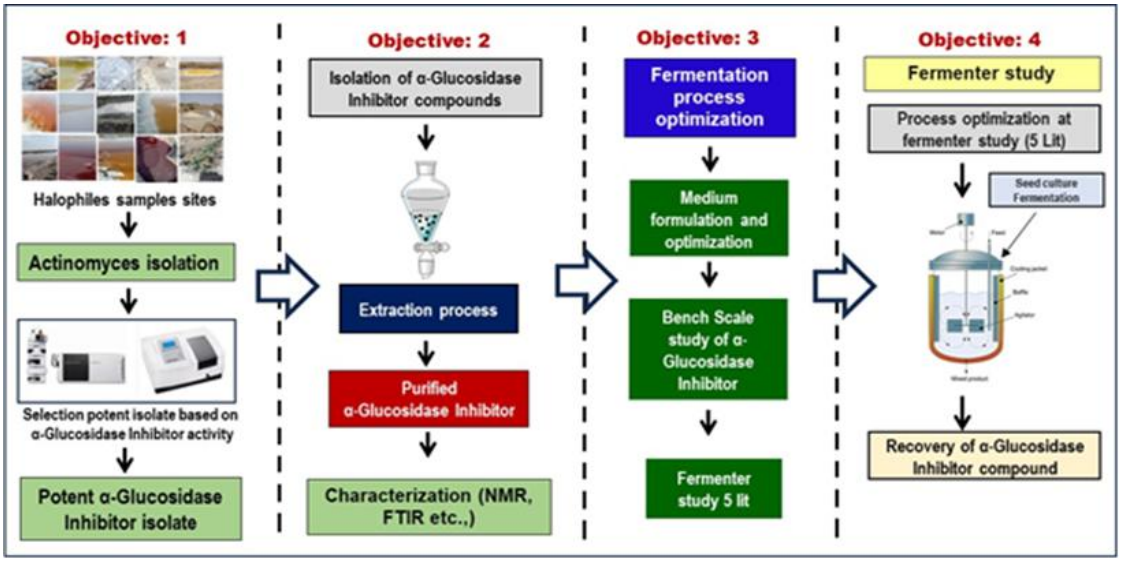
Note: Micro: Micro filtration **Ultra:** Ultrafiltration **Nano:** Nano filtration **RO:** Reverse osmosis **R:** Retantent**P:** Permeate

Figure 2: Ectoine from selected potent *Halomonas* sp.

Research Activity 3

Fermentative production, Isolation, and structure of α-glucosidase inhibitor produced by *Streptomyces* sp., strain

Research outcome:



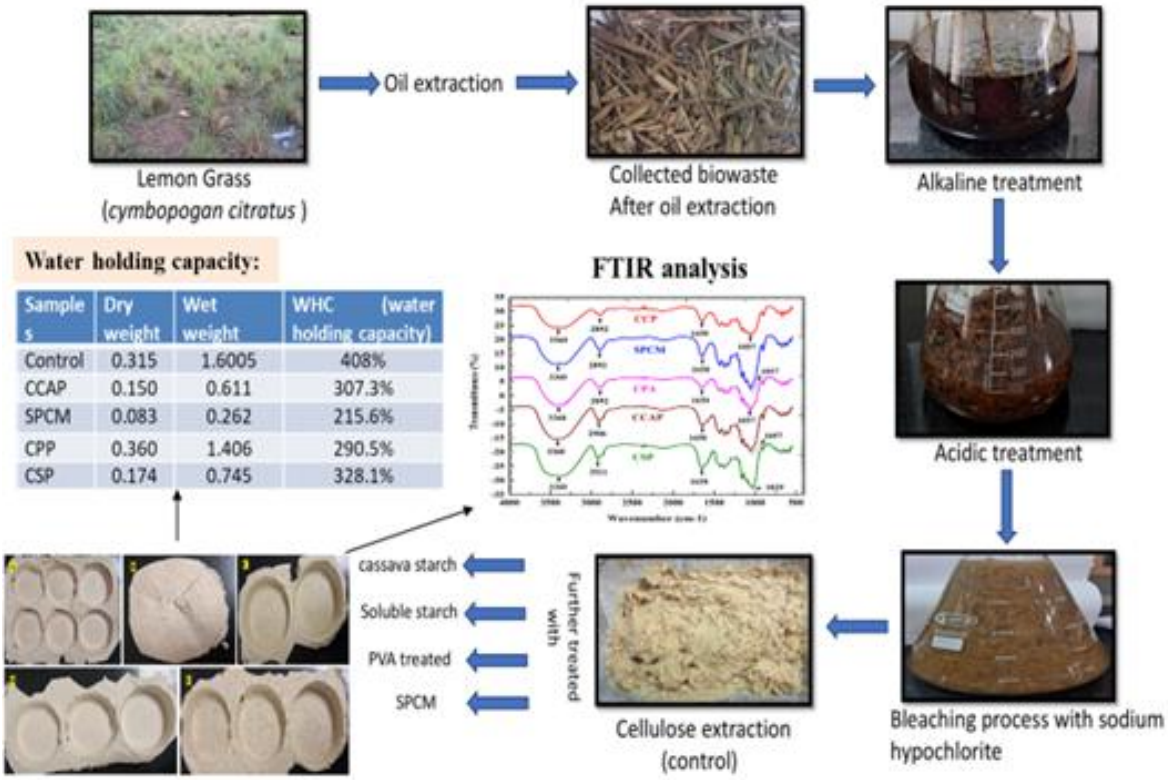
Highlights of the work done/achievements:

- **A new α–glucosidase inhibitor producer strain *Streptomyces coeruleoprunus*IIIM VA-07 in hand.**
- **The α-glucosidase inhibitor substance is present in *Streptomyces coeruleoprunus*IIIM VA-07 aqueous extract.**
- **The aqueous extract was more than 90 % inhibitions, which is better than acarbose (approx. 60 %).**
- **These results suggest aqueous extract of *Streptomyces coeruleoprunus*IIIM-VA07 is the potential source to produce an α-glucosidase inhibitor for the management of postprandial hyperglycemia.**

Research activity 4

An effective method for developing cellulose-based polymer from spent lemongrass for use as packaging material

Research outcome:



Samples	Dry weight	Wet weight	WHC (water holding capacity)
Control	0.315	1.6005	408%
CCAP	0.150	0.611	307.3%
SPCM	0.083	0.262	215.6%
CPP	0.360	1.406	290.5%
CSP	0.174	0.745	328.1%

Highlight:

- The study promotes using lemongrass (LG) lignocellulosic waste as an eco-friendly, biodegradable, and renewable resource for producing cellulose-based packaging material.
- The current study's alkaline pre-treatment, acid hydrolysis, and optimised alkaline treatment effectively removed hemicelluloses, lignin, and cellulose from the sample. The process parameters include sodium hydroxide concentration, nitric acid concentration and sodium hypochlorite solution to enhance cellulose extraction. The optimal conditions identified were a 0.5 w% NaOH concentration and 0.25w% nitric acid concentration, which achieved a maximum cellulose yield of 69.5%.
- Blending cellulose with various additives, particularly soluble starch and PVA, enhances its properties by creating interlinkages, reducing porosity, and strengthening the overall structure. SEM and FTIR analyses provide valuable insights into the material's characteristics.
- The sequential pre-treatments were more effective in breaking down fibres, reducing particle size, and increasing porosity than untreated cellulose, resulting in higher cellulose yield, as demonstrated by SEM results. FTIR analysis confirmed the successful removal of non-cellulosic components, with specific absorption peaks indicating efficient cellulose extraction.

KANHAIYA KUMAR

Dr. Kanhaiya kumar (Senior Scientist)

Research Interests:

Microbial Submerged Fermentation, Metabolomics, API production Bioprocess Development, Microbial Physiology, Waste to Wealth,

1. Publications/Patents:

Publications:

- Vinod Kumar, Varsha Sharma, Anu Radha, Sonali Sharma, Sanket Kumar Shukla, Nagaraju Nekkala, Asha Chaubey, Er. Anil Kumar Katare, Diljeet Kumar, Rajendra Bhanwaria, Kanhaiya Kumar, Zabeer Ahmed. Enhancing Curcumin Bioavailability in Functional Foods via Fermented Turmeric-Whey Protein Complex with Probiotic Strain. CSIR URDIP Ref No: URDIP_202425_IIIM_365006
- Painulia, R., Chauhan, B., Kumar, K., Kumar, C., Phatake, RS., 2025. Pharmacological Diversity in Integrative Medicine: Exploring Sources and Approaches to Drug Discovery Utilizing Natural Products. Secondary Metabolites And Drug Discovery. [Accepted]. Wiley.
- Puneet Kumar, Kanhaiya Kumar, and Jasha Momo H. Anal. 2025. Isolation, Pharmacological Properties, Chemical Syntheses, and Biosynthesis of Isobavachalcone (IBC): A Historical Perspective for the Future Direction. Mini-Reviews in Organic Chemistry. 1-9. [Accepted]. Doi: 10.2174/0118756298360122250320053005

2. Scientific work done:

Industries like pharmaceutical, cosmetic, and cleaning are increasingly looking for sustainable and biologically derived surfactants. Biosurfactants are classified based on their chemical structure, molecular weight, and microbial origin. Key classifications of low molecular biosurfactants include glycolipids (e.g., rhamnolipids, sophorolipids), lipopeptides (e.g., surfactin, iturin), phospholipids (lecithin), polymeric (e.g., emulsan) and particulate (e.g., whole cells) biosurfactants (Sultan et al., 2025). The research has driven towards microbial biosurfactants, especially glycolipids. Glycolipids have several interesting properties, such as their excellent surface activity, biodegradability, biocompatibility, and low toxicity, which make them ideal for pharmaceutical applications. They have been used in diverse biomedical and therapeutic purposes, including antimicrobial, anticancer, and anti-inflammatory activities. These properties can be leveraged for drug delivery, wound healing formulations, and novel therapeutic agents.

In this context, the study was aimed to isolate and screen a promising novel biosurfactant-producing endophyte from the relatively unexplored subtropical plant *Eriobotrya japonica*. This was followed by the study of its physiological growth and biosurfactant production under controlled conditions. Finally, the extracted biosurfactant was identified FTIR, and ^{1}H NMR. The isolated endophytic microbe demonstrated a promising biosurfactant activity up to 65.7 ± 2.4 % emulsification index (E24) and oil displacement of 22 ± 0.5 cm. The isolated microorganism was cultivated under controlled conditions at various pH levels in a multi-bioreactor system equipped with a gas-analyzer. The microbial physiology at pH 8 stands out as revealed through CO_2 evolution, RQ, biomass, and biosurfactant production. The extracted biosurfactant was stable at a wide range of pH, temperatures, and salinities. Further, it exhibited promising antimicrobial activity against both Gram-positive and Gram-negative bacteria, making it a potential candidate for various pharmaceutical and biomedical applications. Chemical and structural characterization revealed the isolated biosurfactant as a glycolipid, exhibiting characteristic molecular features and structural stability. The highest biosurfactant production was 4.6 ± 0.3 g L^{-1} at pH 8.0, 30^{o}C, and 30% DO, demonstrating promising efficiency for potential scale-up.

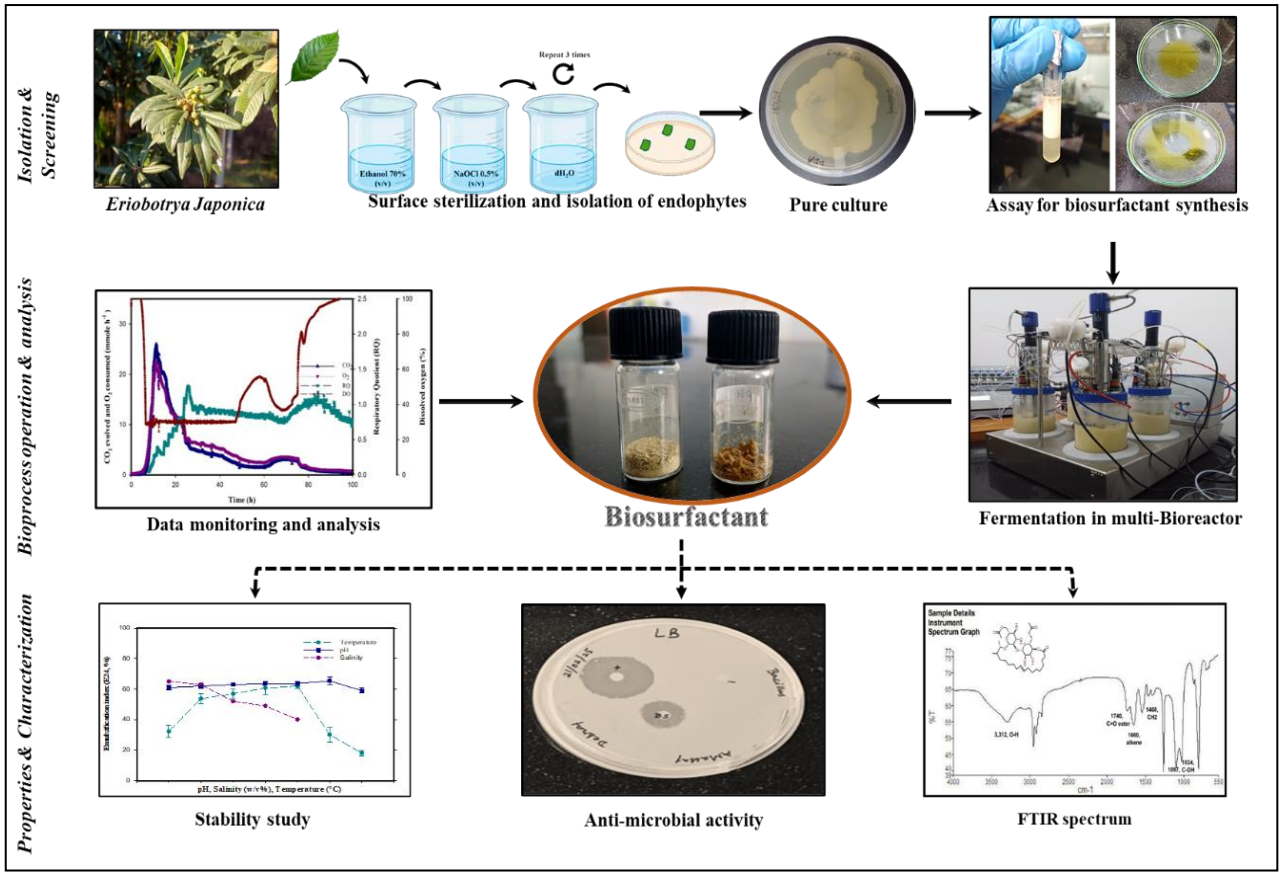


Figure: Overview of the research works for biosurfactants production

SUNDEEP JAGLAN

Dr. Sundeep Jaglan (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Nisha Sharma, MohdMurtaza, WaqasAhmed, Umesh Goutam, **Sundeep Jaglan*** (2025) Isolation, characterization, and diversity of fungal endophytes from *Albizia lebbeck*in Jammu & Kashmir, India. ***Journal of Applied Biology & Biotechnology*, 13 (4),** 89-99. http://doi.org/10.7324/JABB.2025.232699

- Jyoti Chandan, Suruchi Gupta, Zabeer Ahmed, Shashank Kumar Singh, Puneet Kumar, Rupali Choudhary, Sundeep Jaglan, Yogesh Bharitkar, Gurleen Kour, Ekta Nehra, Ravail Singh (2025) Metabolite profiling and bioactivity of fungal endofauna from *Xiphinemanuragicum* in the

rhizosphere of *Withaniasomnifera*. ***Environ Sci Pollut Res*;32**, 8448–8461 https://doi.org/10.1007/s11356-025-36228-3**I.F.: 5.8**

- Vishal Sharma, Vidushi Abrol, Richa, Sundeep Jaglan (2024) Valproic Acid Enhances Antioxidant Potential of *Setosphaeria rostrata*, an Endophytic Fungus of *Datura innoxia* Mill. ***Biol Bull Russ Acad Sci*; 51**, 1622–1630. https://doi.org/10.1134/S1062359024607675**I.F.: 0.4**

- Anshul Grover, Aman Kumar, Priya Kumari, Sundeep Jaglan, Sandeep Yadav, Prashant Singh, Hari Om, Kashmiri Lal (2025) DHA-indole-triazole hybrids: Click mediated synthesis, antimicrobial, antibiofilm and In Silico studies. ***Journal of Molecular Structure*; 1335,** 141953 https://doi.org/10.1016/j.molstruc.2025.141953**I.F.: 4.7**

- Mohd Murtaza, Vidushi Abrol, Ekta Nehra, Poonam Choudhary, Shashank K Singh, **Sundeep Jaglan*** (2024) Biodiversity and Bioactive Potential of Actinomycetes from Unexplored High Altitude Regions of Kargil, India. ***Indian Journal of Microbiology* ;64**, 110–124 https://doi.org/10.1007/s12088-023-01133-1**I.F.: 1.6**

- Vishal Sharma, Shivali Panjgotra, Nisha Sharma, Vidushi Abrol, Umesh Goutam, **Sundeep Jaglan*** (2024) Epigenetic modifiers as inducer of bioactive secondary metabolites in fungi. ***Biotechnology Letters*;46**, 297–314 https://doi.org/10.1007/s10529-024-03478-z **I.F.: 2.1**

2. Scientific work done:

Isolation, characterization, and diversity of fungal endophytes from *Albizia lebbeck*

Endophytes are microorganisms that reside within various plant parts and cause no damage to the host plant. This study aims to isolate and represent the diversity of endophytic fungi associated with the leaves and stem of *Albizia lebbeck*, commonly known as "Siris" or Shirish" in Ayurvedic medicine. Endophytes were isolated and characterized using a combination of morphological and molecular approaches, employing ITS markers. A total of 210 endophytic fungi were successfully isolated (111 from leaves and 99 from stems) from 52 plant samples collected across 13 sites in Jammu and Kashmir. Most of the isolates (99.5%) belonged to the phylum Ascomycota, while only 0.5% was identified as Basidiomycota. Around 82 distinct species were identified, with greater diversity and species richness in leaf samples, which highlights the ecological significance of endophytes in the plant systems. These findings enhance our understanding of the role of fungal endophytes in maintaining plant health and their potential applications in pharmaceuticals.

- Fungal endophytes were characterized from *Albizia lebbeck.*
- 210 isolates were obtained (112 from leaves and 98 from stem) using effective techniques.
- 82 distinct fungal endophytes were identified, with higher diversity in leaves and 42% colonization frequency.
- *Colletotrichum* sp. was the most prevalent genus across sampled tissues.

SAURABH SARAN

Dr. Saurabh Saran (Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

1.	Vandana Sharma, Shifali Chib, Diksha Kumari, Kuljit Singh, **Saurabh Saran,** Deepika Singh	Chromatographic fingerprinting of epiphytic fungal strains isolated from Withaniasomnifera and biological evaluation of isolated okaramine H	2024	Analytical Methods	Royal Society, UK	Vol. 16; Issue 38 Pages 6577-6578 **DOI** https://doi.org/10.1039/D4AY00901K	2.7
2	Manoj Kumar, Shakti Kumar Dhiman, Rahul Bhat &**Saurabh Saran**	In situ green synthesis of AgNPs in bacterial cellulose membranes and antibacterial properties of the	2024	Polymer Bulletin	Springer	Vol 81 Pages 6957–6978 1026-1035 DOIhttps://doi.org/10.1007/s0028	3.11

		composites against pathogenic bacteria				9-023-05046-3	
3	Manoj Kumar, Vinod Kumar &**Saurabh Saran**	Current research and advances in the molecular aspect of bacterial cellulose synthesis with special emphasis on the production of bacterial cellulose from waste and its food applications.	2024	Cellulose	Springer Nature	**31**, 3323–3351 https://doi.org/10.1007/s10570-024-05842-8	4.9
4	Anu Radha, Vivek Ahluwalia, Amit Kumar Rai, Sunita Varjani, Mukesh Kumar Awasthi, Raveendran Sindhu, Parameswaran Binod, **Saurabh Saran**& Vinod Kumar	The way forward to produce nutraceuticals from agri-food processing residues: obstacle, solution, and possibility.	2024	Journal of Food Science and Technology	Springer Nature	61; 429–443 doi.org/10.1007/s13197-023-05729-9	3.11
5	Rahul Bhat, Ashish Dogra, Shifali Chib, Manoj Kumar, Inshad Ali Khan, Utpal Nandi, Saurabh Saran	Development of mupirocin-impregnated bacterial cellulosic transdermal patches for the management of skin infection	2024	ACS omega (ACS Publication)	American Chemical Society, USA	Volume 9 Issue 5 Pages 5496-5508 https://doi.org/10.1021/acsomega.3c07174	4.1

2. Scientific work done:

Isolation, Screening, Production and Scaleup of Okaramines (A-Z) for developing new, safe and eco-friendly insecticides and pesticides

Okaramines (A-Z) are a group of complex indole alkaloids originally isolated from the fermentation broth of the soybean pulp (okara)-degrading fungus *Penicillium simplicissimum* (Matsuda et al., 2018) and *Aspergillus aculeatus* which was isolated from the *Withaniasomnifera* (Sharma et al., 2024). Okaramines exhibit insecticidal activity on a broad range of insects, due to their potent action on glutamate-gated chloride channels (GluCl), which are very crucial for insect nerve function. This makes them strong candidates for developing new, safe and eco-friendly insecticides and pesticides (Matsuda et al., 2018).

Different fungi were isolated from the medicinal plant commonly known as ashwagandha (Withaniasomnifera) using potato dextrose agar plates. For the isolation, different parts of the plant was collected randomly and taken immediately to the laboratory in sterilized perforated polythene bags. With the help of the sterilized forceps and scissor, the plant material was cutted into the small fractions/pieces. Different plant parts were placed and embedded on the surface of the PDA plates at three plates separately. Ampicillin (50 µg/mL) was added to minimize bacterial growth. The plates were properly labeled and incubated in an inverted position at 28°C for 72 h. The emergence and development of colonies was observed after every 24 hours. After the 5 days of the incubation, the different fungal colonies were purified by sub culturing on the fresh PDA plates. From the various isolated fungal strains, the Aspergillus aculeatus (S20) shows the production of Okaramine. The fungal strain S20 showing significant Okaramine production was selected for further studies.

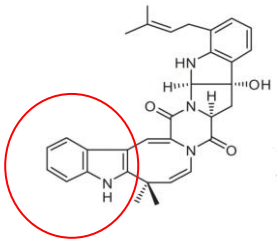
Aspergillus aculeatus S-20

Microscopic view(R)

Production of okaramines

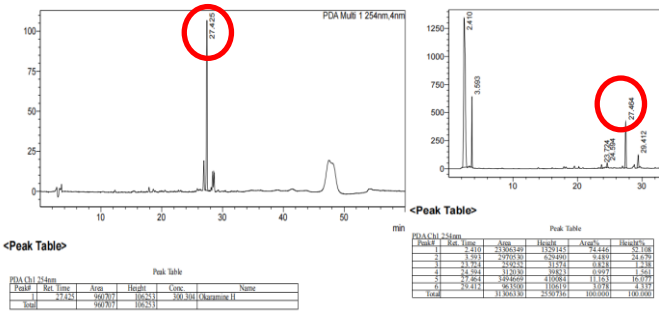
biomass

Separation of



Core structure of Okaramine

Derived from two L-Tryptophan residue, which cyclize to form a diketopiperazine ring



Standard of Okaramine **HPLC analysis of** **Okaramine produced from S20**

Graphical representation of Okaramine

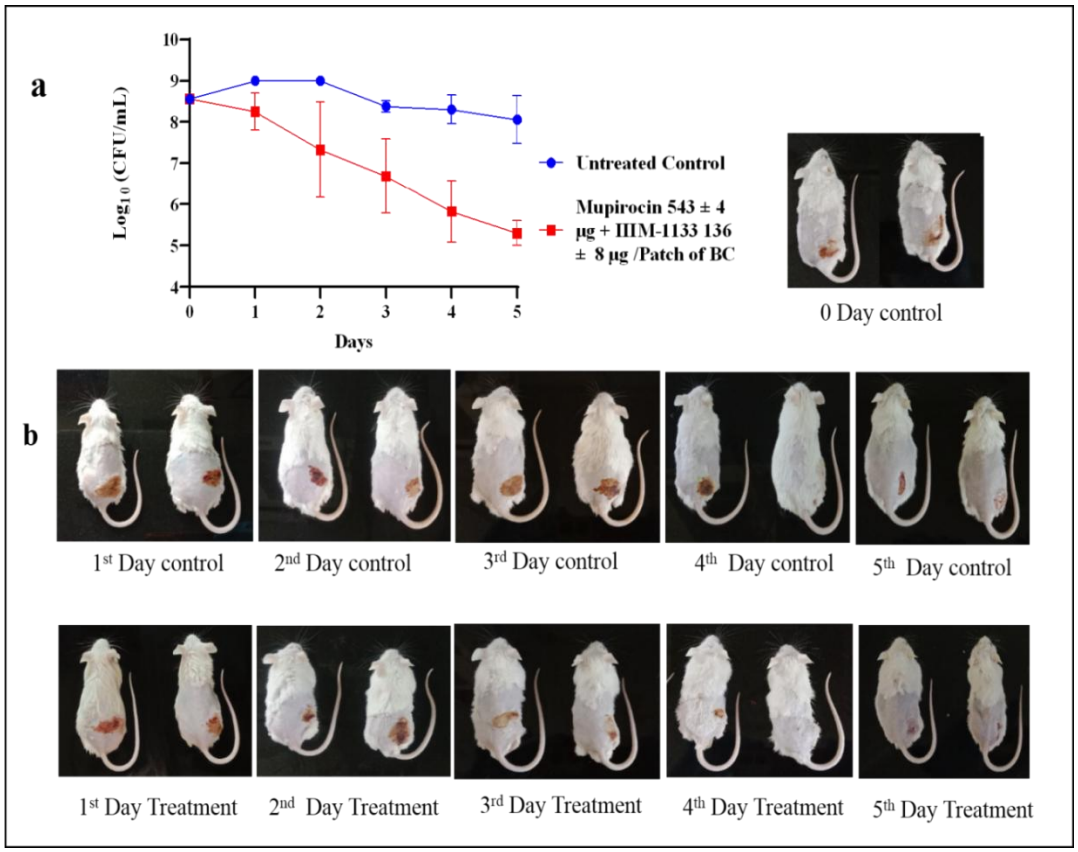
Efficient production of bacterial cellulose-based composites using zein protein extracted from corn gluten meal

Corn gluten meal (CGM) which is a byproduct of corn wet milling has been utilized for the extraction of zein protein which is the main hydrophobic protein present in the corn. The extracted zein protein was used along with bacterial cellulose that is highly pure, biocompatible, and biodegradable for the preparation of composites that have better surface properties and applications. SEM analysis of the synthesized composite showed layering, incorporation of zein protein onto the surface of bacterial cellulose. Maximum production of bacterial cellulose was observed when corn gluten meal and zein protein were used as a cheap nitrogen sources for the production of bacterial cellulose along with other medium components. An increase of approximately 4.0g/l of bacterial cellulose from 13.561g/l to 17.83g/l was observed when corn gluten meal and zein protein were used in the production medium. The prepared BC-based zein protein composites can be utilized for food packaging and storage applications.

Enhancement in antibiotic efficacy using bacterial cellulose membrane with respect to sustained novel multi-drug delivery system

The aim of this study is to produce Bacterial Cellulose membranes by the potent bacteria. Naturally produced bacterial cellulose membrane will be utilized for developing transdermal drug delivery system by impregnating antibiotics along with efficacy enhancer. In-vitro drug release study of the drug impregnated BC membrane using disc diffusion assay against different strains of *S aureus* including

Mupirocin resistant strain mupr-1 and methicillin resistant staphylococcus aureus (MRSA). Accelerated stability study followed by SEM, TEM and pharmacokinetics will be performed. In vivo studies of bacterial cellulose membrane impregnated patch with antibiotic and bacterial efflux pump inhibitor EPI on dermal infection model of mice will also be the important aspect of this project in efficacy studies. One time application of transdermal patch (Mupirocin+EPI) on infected wound may reduce the log10 c.f.u than BC-impregnated mupirocin alone and 2% mupirocin ointment as well. Synergetic work of mupirocin with EPI impregnated on BC-membranes can be a novel medicate as transdermal patch which helps in infected wound recovery in burns, abrasions, skin tears, amputation wounds, exit-site of dialysed patients, surgical cuts as well as other cutaneous infection. Overall the transdermal impregnated patch may have more potency than mupirocin ointment at its single application because of its sustainable drug released property.



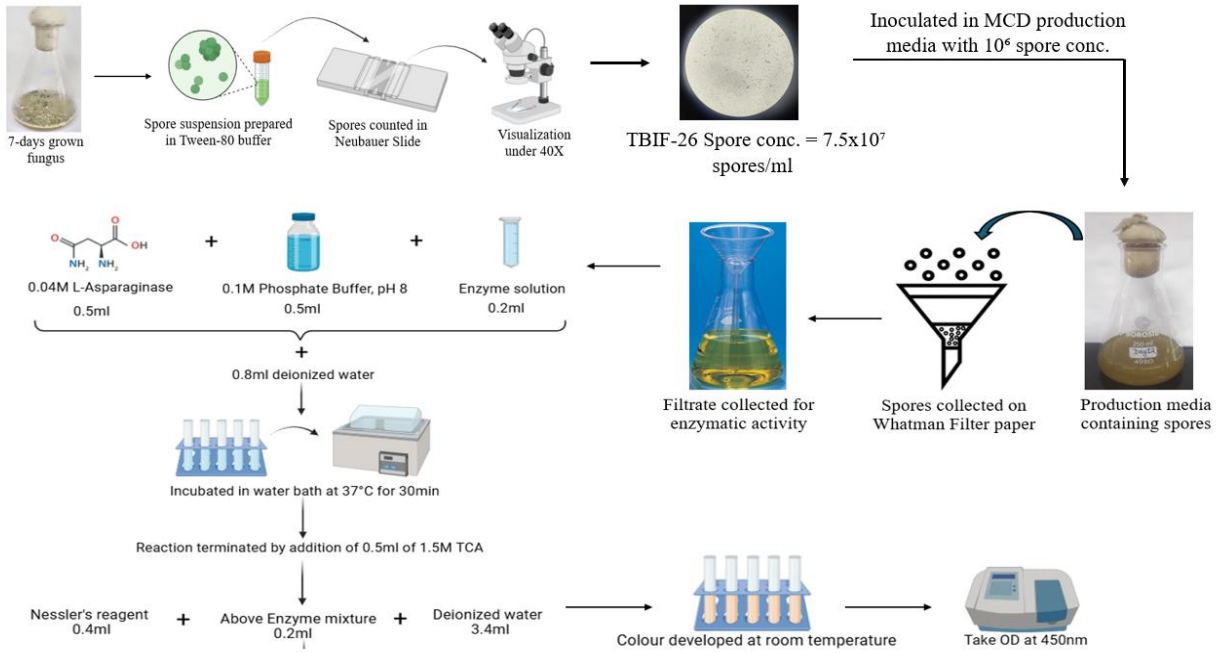
Mutagenesis enhanced Serratiopeptidase, a proteolytic enzyme from Serratia sp. and its anti-inflammatory efficacy studies

In the present investigation, a serralysin type of serratiopeptidase producing microbial strain has been isolated from different samples. The strain has been purified and characterized in terms of its biochemical and physiological growth characteristics. Based on biochemical characterization, the isolate has been identified up to genus level and observed that this strain belongs to Serratia sp and 16sRNA

sequencing confirmed that the isolate is Serratia marcescens. This strain Serratia marcescens MCA-3 has the ability to produce extracellular serratiopeptidase which is known for its commercial importance. In this context, the serratiopeptidase production was optimized by one variable at a time approach to enhance the productivity and yield. The serratiopeptidase was produced with the maximum yield of 363.0 U/ml after 24 h of incubation at pH 9.0, temperature 28o C with the agitation rate of 250rpm by using 2% inoculum size. Therefore, these parameters are crucial for effective production yields. Glucose (2%), yeast extract (1.5%) and tryptone (0.5%) were the favourable Nutrional factors for the production of serratiopeptidase. Moreover, the effects of some metal ions on serratiopeptidase activity were investigated and found that NaCl (0.04%) is the best metal ion source for enhanced production of serratiopeptidase. The down streaming processes for the purification of serratiopeptidase was carried out wherein, a series of processes intended to purify serratiopeptidase. The purification process may separate the protein and non-protein parts of the mixture, and finally separate the desired protein from all other proteins. The STP from S. marcescens MCA-3 was purified by series of steps procedure presenting the specific activity of 3050.414 Units/mg proteins with overall 4.166 fold purification till dialysis step of purification. In order to obtain a high serratiopeptidase producing mutant strain and making the production economically feasible process, random mutagenesis technique was adopted. With the proper dose of UV radiation and EMS, the mutant MCA-3M was screened as a promising serratiopeptidase producer with an enzyme activity of 1521.432 U/ml. This mutant may have wide industrial application.

Microbial Exploration of L-Asparaginase: From Enhanced Production, Scale-up, Purification of L-Asparaginase enzyme for Therapeutic and Industrial Applications

L-asparaginase is a therapeutically useful enzyme best known for its use in treating acute lymphoblastic leukemia (ALL) and other hematologic neoplasms. The anti-cancerous activity of L-asparaginase is due to its ability to remove L-asparagine from blood serum by catalysing the hydrolysis of L-asparagine into aspartic acid and ammonia, required by malignant cells for their growth and hence, cause apoptosis. Originally developed from *Escherichia coli* and *Erwinia chrysanthemi*, conventional products have been hampered by short half-life, immunogenicity and toxicities. The development and optimization of recombinant L-asparaginase with minimized immunogenicity and enhanced therapeutic efficacy, combined with advanced bioprocessing scaleup techniques, will significantly improve treatment outcomes for Acute Lymphoblastic Leukemia (ALL). Recombinant L-asparaginase with reduced glutaminase co-activity and enhanced stability can achieve effective asparagine depletion in cancer cells. Beyond oncology, it can play a crucial role in mitigating acrylamide formation during food processing, thereby addressing important healthcare and food safety concerns.



Qualitative screening and Quantitative analysis revealed that one fungal isolate TBIF-26 exhibited the highest L-Asaparaginase enzyme activity, measuring 817.92 U/mL. Morphologically, the fungal isolate appearance is similar to *Penicillium* sp. Process optimization of TBIF-26 fungal isolate was done on physical parameters like temperature, pH, agitation and inoculum size. At pH 6.2, maximum enzyme activity is attained of 817.27 U/ml with 4.85g/L biomass production. At 28ºC temperature, maximum enzyme activity is attained i.e., 815.31U/ml with 4.81g/L biomass production. At 10^6 inoculum size, maximum enzyme activity is attained i.e., 832.93 U/ml with 4.79g/L biomass production. At 250rpm agitation speed, maximum enzyme activity is attained i.e., 997.98 U/ml with 4.03g/L biomass production.

QAZI PARVAIZ HASSAN

Dr. Qazi Parvaiz Hassan (Sr. Scientist) with his Research Group

1. Publications/Patents:

Publications:

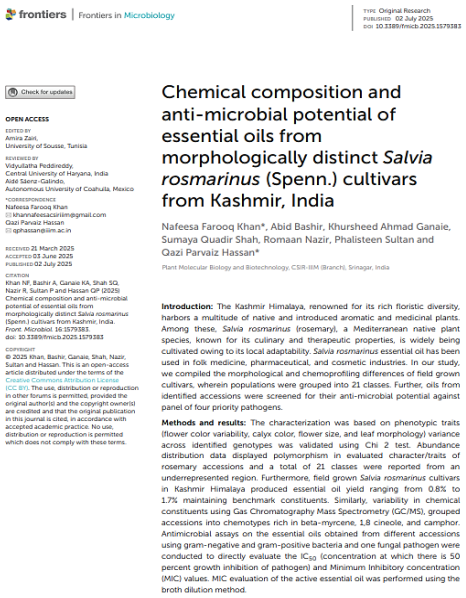
- Khan, N., Abid, B., Khursheed A., Sumaya, Q., Romaan, N., Sultan, P., Hassan, Q. P., (2025). Chemical composition and anti-microbial potential of essential oil from morphologically distinct *Salvia Rosmarinus* (Spenn.), cultivars from Kashmir, India. *Frontiers in Microbiology.*
- Romaan, N.,Roof, U., Mytoullah,Y., Sultan, P., Irshad, A., & Hassan, Q. P.,(2024). Exploring the efficacy of hormonal treatments and pre-sowing techniques on seed germination of *Salvia rosmarinus*Spenn. *Journal of Applied Research on Medicinal and Aromatic Plants.*
- Amin, A., Sharma, N., Sultan, P., Gandhi, S. G., Srinivas, K., Hassan, Q. P., & Ahmed, Z. (2024). In vitro propagation of *Bergenia stracheyi*: an alternative approach for higher production of valuable bioactive compounds. *Vegetos*, 1-10.
- Naseem, N., Khaliq, T., Jan, S., Nabi, S., Sultan, P., Hassan, Q. P., & Mir, F. A. (2024). An overview on Pharmacological significance, Phytochemical potential, Traditional importance, and Conservation strategies of *Dioscorea deltoidea*: A high valued endangered medicinal Plant. *Heliyon*.

- Sabiyah Akhter, Malik Muzafar Manzoor, Sameer Ahmad Mir, Tahira Khaliq, Phalisteen Sultan*, Qazi Parvaiz Hassan*(2024). Extracts and isolated compounds from the *Acorus calamus* (Sweet flag) rhizome showed distinct anti-metastatic activity against MDA-MB-231 breast cancer cells, *Medicinal Plant Biology*.

2. Scientific work done:

Chemical composition and anti-microbial potential of essential oils from morphologically distinct *Salvia rosmarinus* (Spenn.) cultivars from Kashmir, India

Introduction: The Kashmir Himalaya, renowned for its rich floristic diversity, harbors a multitude of native and introduced aromatic and medicinal plants. Among these, *Salvia rosmarinus* (rosemary), a Mediterranean native plant species, known for its culinary and therapeutic properties, is widely being cultivated owing to its local adaptability. *Salvia rosmarinus* essential oil has been used in folk medicine, pharmaceutical, and cosmetic industries. In our study, we compiled the morphological and chemoprofiling differences of field grown cultivars, wherein populations were grouped into 21 classes. Further, oils from identified accessions were screened for their anti-microbial potential against panel of four priority pathogens.



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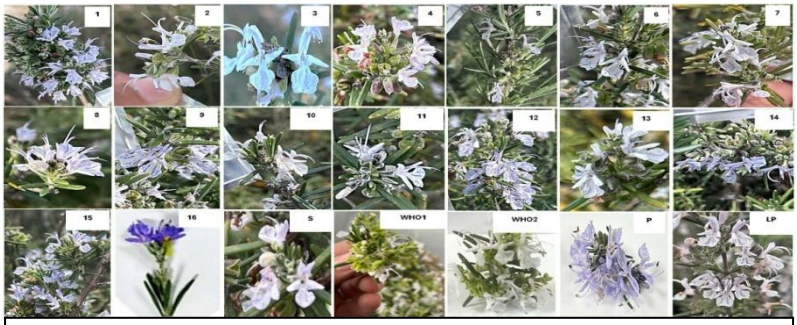
Chemical composition and anti-microbial potential of essential oils from morphologically distinct *Salvia rosmarinus* (Spenn.) cultivars from Kashmir, India

Nafeesa Farooq Khan*, Abid Bashir, Khursheed Ahmad Ganaie, Sumaya Quadir Shah, Romaan Nazir, Phalisteen Sultan and Qazi Parvaiz Hassan*

Plant Molecular Biology and Biotechnology, CSIR-IIIM (Branch), Srinagar, India

Introduction: The Kashmir Himalaya, renowned for its rich floristic diversity, harbors a multitude of native and introduced aromatic and medicinal plants. Among these, *Salvia rosmarinus* (rosemary), a Mediterranean native plant species, known for its culinary and therapeutic properties, is widely being cultivated owing to its local adaptability. *Salvia rosmarinus* essential oil has been used in folk medicine, pharmaceutical, and cosmetic industries. In our study, we compiled the morphological and chemoprofiling differences of field grown cultivars, wherein populations were grouped into 21 classes. Further, oils from identified accessions were screened for their anti-microbial potential against panel of four priority pathogens.

Methods and results: The characterization was based on phenotypic traits (flower color variability, calyx color, flower size, and leaf morphology) variance across identified genotypes was validated using Chi 2 test. Abundance distribution data displayed polymorphism in evaluated character/traits of rosemary accessions and a total of 21 classes were reported from an underrepresented region. Furthermore, field grown *Salvia rosmarinus* cultivars in Kashmir Himalaya produced essential oil yield ranging from 0.8% to 1.7% maintaining benchmark constituents. Similarly, variability in chemical constituents using Gas Chromatography Mass Spectrometry (GC/MS), grouped accessions into chemotypes rich in beta-myrcene, 1,8 cineole, and camphor. Antimicrobial assays on the essential oils obtained from different accessions using gram-negative and gram-positive bacteria and one fungal pathogen were conducted to directly evaluate the IC_{50} (concentration at which there is 50 percent growth inhibition of pathogen) and Minimum Inhibitory concentration (MIC) values. MIC evaluation of the active essential oil was performed using the broth dilution method.



Floral traits of accessions characterized in this study.

Inhibitory concentration (MIC) values. MIC evaluation of the active essential oil was performed using the broth dilution method.

Discussion: The data generated in this study emphasizes the use of morphological and chemical characteristics to characterize and conserve elite *Salvia rosmarinus* cultivars, promoting cultivar R1 (1.7%) in summer season and R14 (0.95%) and R3 (0.93%) in winter season for large-scale cultivation, emphasizing propagation of higher essential oil yielding varieties in Kashmir Himalaya. The diverse rosemary genepool conserved in Kashmir exhibits significant variability in essential oil yield and composition while, certainaccessions demonstrate potent antimicrobial properties. The findings of thestudy are useful for further elaborate studies on the development of natural bioactive compounds to improve human health.

Exploring the efficacy of hormonal treatments and pre-sowing techniques on seed germonation of *Salvia rosmarinusSpenn*

*Salvia rosmarinus*Spenn. (Rosemary) holds significant value in medicinal and aromatic applications, serving as a key ingredient in pharmaceuticals, food products, and cosmetics. While many plant species benefit from seed-based propagation, *S. rosmarinus*poses a challenge due to its mucilaginous seed coating. As a result, germination rates often remain low, ranging from 10 % to 20 %, leading to irregular crop establishment. This study aimed to explore the efficacy of hormonal and other pre-sowing treatments on seed germination of *S. rosmarinus*. Four distinct treatments were evaluated including physical (sandpaper scarification, dry heat, hot and cold water stratification), chemical (sulphuric acid, hydrogen peroxide, and potassium nitrate), hormonal treatments (GA3, IAA, andBAP), combination of pre-chilling and hormonal, as well as different potting media combinations, which were compared against an untreated control. All pre-sowing seed treatments, except for hot water, dry heat, chemical treatments, and nanozim, resulted in increased seed germination percentages in *S. rosmarinus* compared to the control group. Among the different treatments, the combination of pre-chilling +GA3 and prechilling+ soil: sand (1:1) treatment resulted in the highest germination percentages of 59.33 % and 63.83 %, compared with those in the control where the germination was 6.83 % and0.67 %. Potassium nitrate (0.3 % for 3 min) was found to be the most effective chemical treatment with a germinationpercentage of 24.83 %and seedling vigor index of 3.93 ± 0.69. Pre-chilling treatment for 21 days was the most successful physical treatment, with a germination percentage of 36.66 % and a mean germination time of 17.45 ± 1.34 days. The germination percentage improved withincreasing GA3concentration up to 150 ppm, beyond which a decline in trend was seen.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Exploring the efficacy of hormonal treatments and pre-sowing techniques on seed germination of *Salvia rosmarinus* Spenn

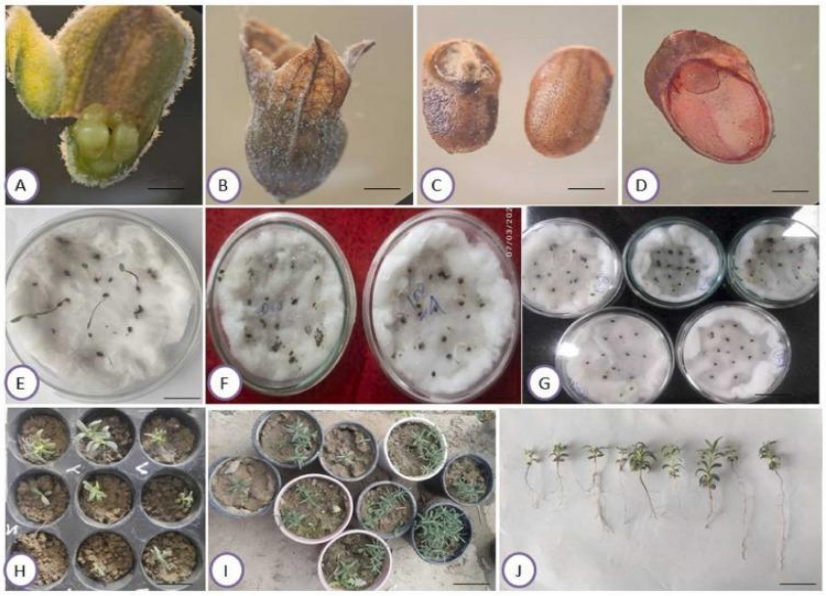
Romaan Nazir, Roof Ul Qadir, Mytoullah Yousuf, Phalisteen Sultan, Irshad A. Nawchoo, Qazi Parvaiz Hassan

ARTICLE INFO

ABSTRACT

1. Introduction

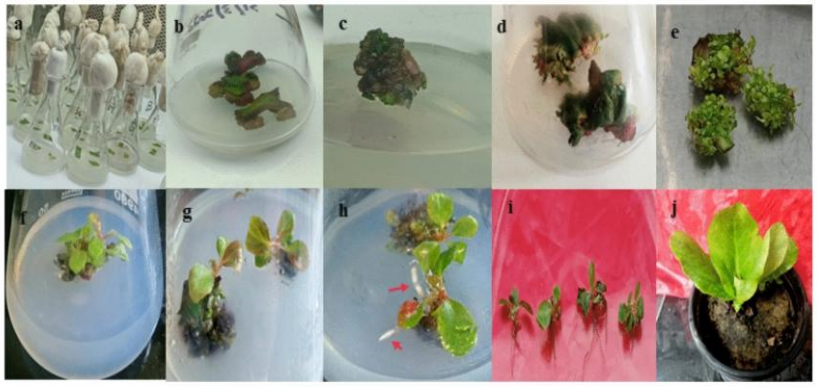
These finding ssuggest that understanding the seed germination ecology of *S. rosmarinus*is crucial for developing seed germination protocols that can enhance mass multiplication with a shorter germination period, ultimately increasing the species' regeneration capability and preserving its variety in nature. This practical and economical approach can help to achieve consistent germination and seedling emergence in nursery raising as well.



Salvia rosmarinus; (A) ovules (B) Capsule (C) Abaxial and adaxial view of seed (D) Embryo (E,F,G) Germination of seeds in different pre-treatments (H) Seedlings transplanted in the plastic trays (I) Seed germination in different potting media (J) Seedling growth in different pre-treatments.

Survey, Domestication and *In vitro* Propagation of *Bergenia stracheyi:* An alternative approach for higher production of valuable bioactive compounds

*Bergenia stracheyi*is high value medicinal plant with immense economical importance. This plant species has been shrinking in their natural habitat due to over exploitation for medicinal purposes and habitat destruction. Therefore a rapid and productive micropropagation protocol was developed by using leaf explant. For shoot induction and multiplication MS media was supplemented with BAP (6- benzyl amino purine), IAA (indole -3- acetic acid) and NAA (1-naphthalene acetic acid). The most positive response for the callus induction was observed on MS media supplemented with BAP (1.5mg/L) + NAA (1mg/L). The highest number of shoots was observed on solid MS media supplemented with BAP (2mg/L) + IAA (2mg/L). Maximum shoot response was obtained on MS media supplemented with BAP (2.5mg/L).

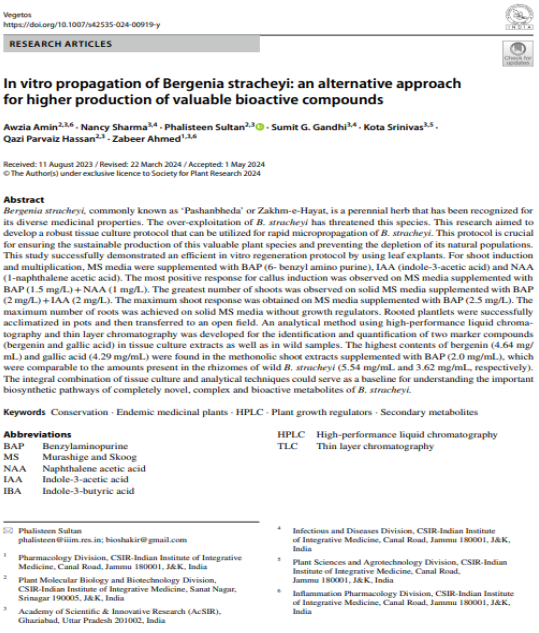


In vitro propagation of *Bergenia stracheyi*: an alternative approach for higher production of valuable bioactive compounds

Maximum number of rooting was achieved on solid MS media without growth regulators. Rooted plantlets

were successfully acclimatized in pots and then transferred to open field.The presence of two marker compounds (Bergenin 4.64and gallic acid 4.29 mg/ml*)* treated withBAP (2.0 mg/L) was confirmed in invitro shoot extracts by HPLC and TLC analysis.

The amount of Bergenin and gallic acid present in the wild samples of *Bergenia stracheyi*was found to be (5.54 and 3.62mg/l) respectively. The percentage of gallic acid was found in higher concentrations in invitro raised shoot extracts compared to wild sample. The present study revealed that these invitro grown plantlets are capable of synthesizing valuable secondary metabolites. This could be an alternative approach for the industrial production of plant derived bioactive compounds and a potential supplement for minimising the over exploitation of wild populations of *Bergenia stracheyi.* For the first time an efficient protocol has been established for *Bergenia stracheyi*which will be important for conservation and mass propagation of this plant on large scale industrial level.



Vegetos
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RESEARCH ARTICLES

In vitro propagation of Bergenia stracheyi: an alternative approach for higher production of valuable bioactive compounds

Awzia Amin[2,3,6] · Nancy Sharma[3,4] · Phalisteen Sultan[2,3] · Sumit G. Gandhi[3,4] · Kota Srinivas[3,5] · Qazi Parvaiz Hassan[2,3] · Zabeer Ahmed[1,3,6]

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Abstract
Bergenia stracheyi, commonly known as 'Pashanbheda' or Zakhm-e-Hayat, is a perennial herb that has been recognized for its diverse medicinal properties. The over-exploitation of *B. stracheyi* has threatened this species. This research aimed to develop a robust tissue culture protocol that can be utilized for rapid micropropagation of *B. stracheyi*. This protocol is crucial for ensuring the sustainable production of this valuable plant species and preventing the depletion of its natural populations. This study successfully demonstrated an efficient in vitro regeneration protocol by using leaf explants. For shoot induction and multiplication, MS media were supplemented with BAP (6- benzyl amino purine), IAA (indole-3-acetic acid) and NAA (1-naphthalene acetic acid). The most positive response for callus induction was observed on MS media supplemented with BAP (1.5 mg/L) + NAA (1 mg/L). The greatest number of shoots was observed on solid MS media supplemented with BAP (2 mg/L) + IAA (2 mg/L). The maximum shoot response was obtained on MS media supplemented with BAP (2.5 mg/L). The maximum number of roots was achieved on solid MS media without growth regulators. Rooted plantlets were successfully acclimatized in pots and then transferred to an open field. An analytical method using high-performance liquid chromatography and thin layer chromatography was developed for the identification and quantification of two marker compounds (bergenin and gallic acid) in tissue culture extracts as well as in wild samples. The highest contents of bergenin (4.64 mg/mL) and gallic acid (4.29 mg/mL) were found in the methonolic shoot extracts supplemented with BAP (2.0 mg/mL), which were comparable to the amounts present in the rhizomes of wild *B. stracheyi* (5.54 mg/mL and 3.62 mg/mL, respectively). The integral combination of tissue culture and analytical techniques could serve as a baseline for understanding the important biosynthetic pathways of completely novel, complex and bioactive metabolites of *B. stracheyi*.

Keywords Conservation · Endemic medicinal plants · HPLC · Plant growth regulators · Secondary metabolites

Abbreviations

BAP	Benzylaminopurine
MS	Murashige and Skoog
NAA	Naphthalene acetic acid
IAA	Indole-3-acetic acid
IBA	Indole-3-butyric acid
HPLC	High-performance liquid chromatography
TLC	Thin layer chromatography

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An overview on Pharmacological significance, Phytochemical potential, Traditional importance and Conservation strategies of *Dioscorea deltoidea*: A high valued endangered medicinal Plant

Dioscorea deltoidea Wall. ex Griseb. is an endangered species of the Dioscoreaceae family. It is the most commonly consumed wild species as a vegetable due to its high protein, vital amino acid, vitamin, and mineral content. There are approximately 613 species in the genus *Dioscorea* Plum. ex L., which is found in temperate and tropical climates. This plant has nutritional and therapeutic uses and also contains high amounts of steroidal saponins, allantoin, polyphenols, and most notably, polysaccharides and diosgenin. It has both expectorant and sedative properties. It is employed in the treatment of cardiovascular diseases, encompassing various ailments related to the heart and blood vessels, skin disease, cancer, immune deficiencies, and autoimmune diseases. Additionally, it finds application in managing disorders of the central nervous system and dysfunctional changes in the female reproductive system. Furthermore, it is valued for its role in treating bone and joint diseases. Metabolic disorders are also among the ailments for which *D. deltoidea* is employed. It has traditionally been used as a

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Review article

An overview on pharmacological significance, phytochemical potential, traditional importance and conservation strategies of *Dioscorea deltoidea*: A high valued endangered medicinal plant

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ABSTRACT

Dioscorea deltoidea Wall. ex Griseb. is an endangered species of the Dioscoreaceae family. It is the most commonly consumed wild species as a vegetable due to its high protein, vital amino acid, vitamin, and mineral content. There are approximately 613 species in the genus *Dioscorea* Plum. ex L., which is found in temperate and tropical climates. *Dioscorea deltoidea*, a plant species widespread across tropical and sub-tropical regions, called by different names in different languages. In English, it is commonly referred to as "Wild yam" or "Elephant foot". The Sanskrit name for this plant is "Varahikand," while in Hindi, it is known as "Gun" or "Singly-singly." The Urdu language refers to it as "Qanis," and in Nepali, it is called "Tarul," "Bhyakur," or "Ghoswar." *Dioscorea deltoidea* has been used to cure a wide range of human ailments for centuries. This plant has nutritional and therapeutic uses and also contains high amounts of steroidal saponins, allantoin, polyphenols, and most notably, polysaccharides and diosgenin. These bioactive chemicals found in *D. deltoidea* have been associated with a range of beneficial biological activities, such as antibacterial, antioxidant, anti-inflammatory, immunomodulatory, hepatoprotective, and cytotoxic properties. Sapogenin steroidal chemicals are highly valued in the fields of medicine, manufacturing, and commerce. It has both expectorant and sedative properties. It is employed in the treatment of cardiovascular diseases, encompassing various ailments related to the heart and blood vessels, skin disease, cancer, immune deficiencies, and autoimmune diseases. Additionally, it finds application in managing disorders of the central nervous system and dysfunctional changes in the female reproductive system. Furthermore, it is valued for its role in treating bone and joint diseases. Metabolic disorders are also among the ailments for which *D. deltoidea* is employed. It has traditionally been used as a vermifuge, fish poison, and to kill lice. Diosgenin, a

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vermifuge, fish poison, and to kill lice. Diosgenin, a steroidal compound found in *D. deltoidea*, plays a crucial role as a precursor in the chemical synthesis of various hormones. Due to the presence of valuable bioactive molecule, like corticosterone and sigmasterol, *D. deltoidea* is cultivated specifically for the extraction of these beneficial phytochemicals. The current study aims to assess *D. deltoidea's* medicinal properties, ethnobotanical usage, phytochemicals, pharmacological properties, threats, and conservation techniques.

Fig. 1 *Dioscorea deltoidea* Wall. ex Griseb.

Extension Activities Done under CSIR Aroma Mission – III.

Total Material distributed: 3,00,000

Total area covered under cultivation: 50 acres

Extension activities during 2024

Transplantation of material

Survey and monitoring infarmersland :

Extension activities done in year 2025

Total Material distributed: 1,50,000
Total area covered under cultivation: 25 acres

List of Beneficiaries - District wise

- Baramulla: 29
- Budgam: 15
- Anantnag: 4
- Kulgam: 3
- Srinagar: 3
- Kupwara: 2
- Shopian: 1

Awareness cum Training programmes:

1. **Awareness & Promotion of Aroma Mission activities by Aroma Team in collaboration with Agriculture Production Department**

   - Around 80 farmers from nearby areas of Chadoora, Budgam participated and gained valuable insights into the cultivation, importance, and market potential of various aromatic and medicinal plants.
   - Field demonstration & detailed information was given to visiting farmers on benefits of cultivation & marketing of Aroma crops.

Students visit from Govt. Degree College visited IIIM Srinagar (Br.) on 4th Dec., 2024

College student's along with some faculty members to CSIR IIIM, Srinagar in December, 2024. The students had a highly enriching experience during their visit to IIIM Srinagar. They toured various labs, including the *Chemistry, Biochemistry, and Biology* labs, where they had the opportunity to interact with expert scientists.

SYED RIYAZ-UL-HASSAN

Dr. Syed Riyaz-UL-Hassan (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Bashir A, Bhat SA, Manzoor MM, Bhatti F, Bhat KA, Riyaz-Ul-Hassan S (2025) Secalonic acid F1 derived from an endophytic fungus *Periconia verrucosa* as a potential antimicrobial agent against *Staphylococcus aureus*. *Journal of Applied Microbiology*. **136 (5):** lxaf120. https://doi.org/10.1093/jambio/lxaf120

- Bashir A, Manzoor MM, Bhatti, Banoo M, Riyaz-Ul-Hassan S (2025) Ecological functions, inter-organismal interactions, and underlying mechanisms of fungal endophytes. *Plant and Soil* https://doi.org/10.1007/s11104-025-07444-0

2. Scientific work done:

I. Studies on bacterial-fungal inter-organismal interactions in the saffron pathogen *Fusarium* species

We isolated twenty-seven strains of fungal pathogens from *Crocus sativus* (saffron crocus) diseased corms. Cultural and morphological characteristics like septate hyphae, cylindrical conidiophores bearing sickle-shaped macroconidia, and the presence of microconidia placed these strains under the genus *Fusarium.* The strains showed variability in growth patterns, colony morphology, and color. Molecular identification based on the acquisition of ITS1-5.8S-ITS2 ribosomal gene sequence and analysis revealed that most of the isolates causing disease in saffron were strains of *Fusarium oxysporum,* which is regarded as the primary pathogen of saffron crocus. However, other species of *Fusarium,* like *Fusarium acuminatum*, *Fusarium citricola*, *Fusarium tricinctum*, and *Fusariumavenaceum,* were also associated with the corm-rot disease. We attempted the isolation of EHB from twenty strains of these isolated strains, among which five strains yielded bacterial partners. The endohyphal bacteria were purified and characterized by 16S ribosomal gene sequence analysis. Phylogenetic analysis revealed that the EHB were strains of *Bacillus pumilus*, *Lysinibacilluscapsici*, *Brevibacillusnitrificans, Alcaligenes faecalis, Bacillus velezensis* and *Bacillus cereus.* Thus, the EHB were predominantly Gram-positive bacteria. EHB were found in the following strains. *Fusarium oxysporum CSP3 – Bacillus pumilus*

i. *Fusarium acuminatum CSP4*
ii. *Fusarium oxysporum CSP11*
iii. *Fusarium oxysporum CSP12*
iv. *Fusarium avenaceum CSP14*

Interestingly, three species of *Fusarium*harbored EHB and CSP14 housed two EHB together.

II. *Fusarium oxysporumCSP3 – Bacillus pumilus* association: Role of the EHB in fungal biology

In order to study the role of EHB in fungal biology, we developed an axenic strain of *Fusarium oxysporum* CSP3 by amending it with a consortium of antibiotics to develop an EHB-free strain. The confirmation was done by 16S ribosomal gene-based, bacteria-specific PCR reaction, producing a positive amplification of bacterial DNA in the wild-type strain and no amplification of the EHB-negative strain developed by the antibiotic treatment. The presence and absence of the EHB (*Bacillus pumilus*) in both these strains were also confirmed by fluorescence *in situ* hybridization (FISH), which shows fluorescence after hybridizing with the bacterial DNA within the fungal hyphae.

The EHB regulated the sporulation of the fungal partner, but it did not significantly affect the colony size (hyphal proliferation) of the fungal partner. The EHB induced sporulation, thus facilitating the asexual reproduction and dissemination of the fungus. Similar effects were found

on different carbon sources as well. The results imply that the EHB profoundly affects the host fungal biology, as it regulates the spore formation and catalyzes the reproduction of *Fusarium oxysporum* CSP3.

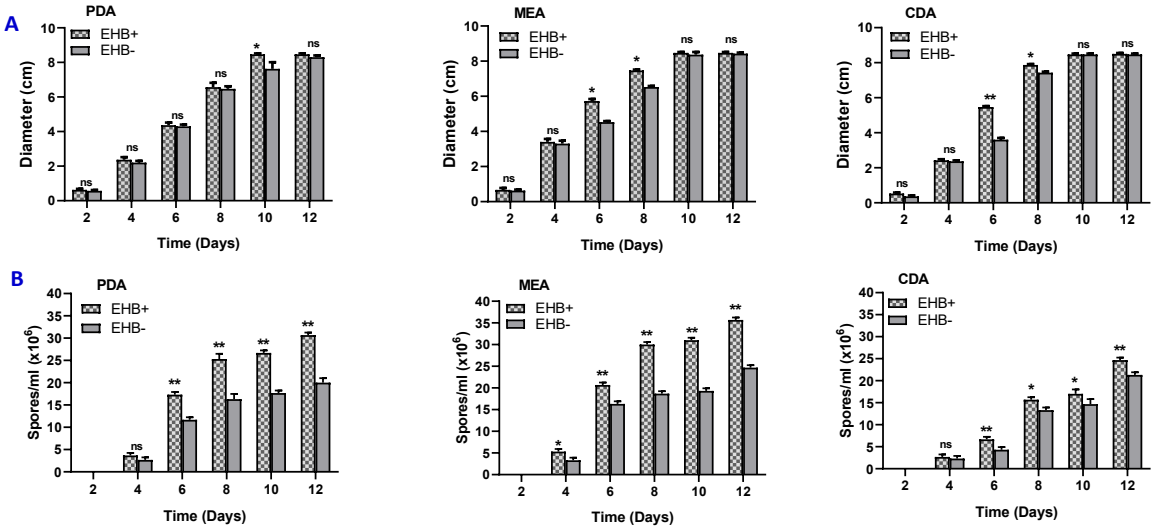


Fig 1: Effect of EHB 1 (*B. pumilus*) on (A) Colony size (B) Sporulation of EHB^{+} and EHB^{-} *Fusariumoxysporum*CSP3 grown on different growth media at 25°C.

III. Chemoprofiling of *Fusarium* species by GC/MS analysis

Selected strains of the *Fusarium* spp., causing the saffron corm-rot, were analyzed by GC/MS after preparing their extracts—the isolates produced batteries of volatile organic compounds (VOCs). The most common VOCs were butylphenol, Hexadecanoic acid, Hexacosene, Eicosene, and Octacosanol, which were produced by most strains. *Fusarium acuminatum* CSP4produced a unique set of VOCs that were distinct from those of the other strains. The role of these compounds in pathogenicity and the role of EHB in the production of these VOCs is under study.

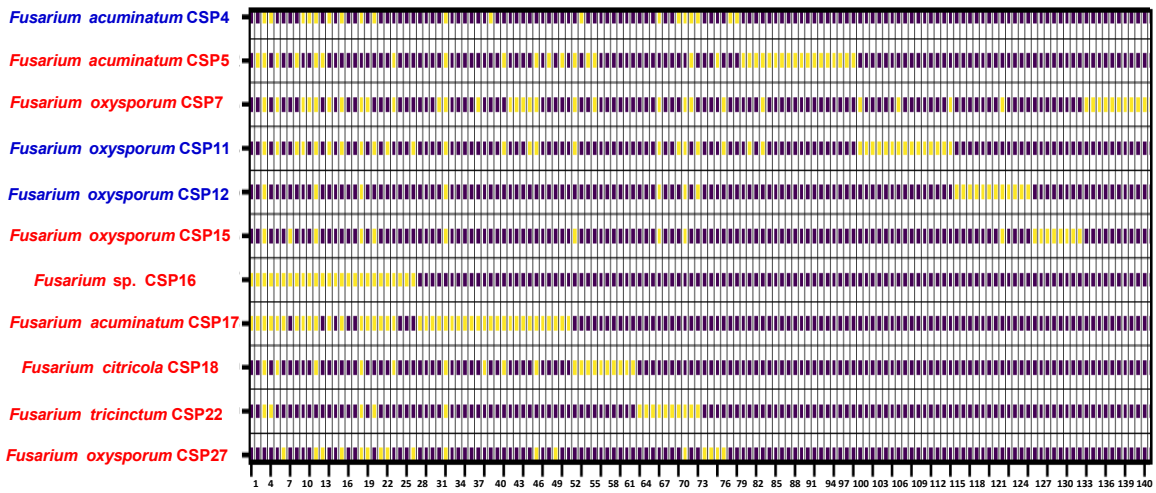


Fig 2: Heat Map showing the diversity of VOCs produced by different phytopathogenic Fusarium species.

V. Secalonic acid F1derivedfrom an endophytic fungus *Periconia verrucosa* asa potential antimicrobial agent against *Staphylococcus aureus* (In collaboration with NPC Division)

We investigated the antimicrobial potential of a Secalonic acid F1 derivative produced by an endophytic *Periconia verrucosa.* The endophyte RDE85 was characterized as *P. verrucosa* by morphological and phylogenetic analysis. We characterized a major compound from RDE85 as Secalonic acid F1 (SF1) with a 2,4′-linkage. SF1 demonstrated antimicrobial activity with an $IC_{50}$of 7.6 µg ml^{-1}against *S. aureus*. It inhibited the biofilm formation, causing morphological changes and disruption of cell membrane integrity in the pathogen, confirmed by scanning electron microscopy (SEM). The compound depicted strong synergistic potential with ciprofloxacin and reduced DNA and RNA synthesis. The time-kill kinetics demonstrate that SF1 is an effective concentration-dependent bactericidal agent. Further, SF1 severely affected the respiratory chain dehydrogenase activity, confirmed by *in-silico* studies, revealing its interaction with respiratory chain succinate dehydrogenase. The treatment with this compound downregulated the staphylococcal accessory gene regulator and enterotoxin gene, two important virulence factors of the organism, and reduced the staphyloxanthin production, which is also an important virulence trait. SF1 is a potential antimicrobial agent against *S. aureus.* The study highlights the antimicrobial potential of Secalonic acid F1, a secondary metabolite produced by the fungal endophyte.

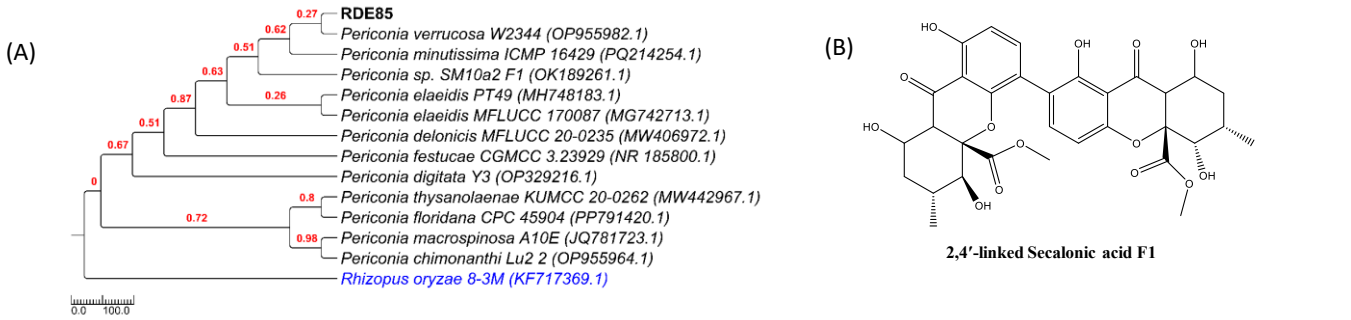


Fig. 3: The phylogenetic position of the fungal isolate RDE85 and molecular structure of the secondary metabolites characterized: (A) Molecular phylogeny based on ITS1-5.8S-ITS2 DNA gene sequence. The phylogenetic trees were constructed in MEGA 6.0, with *Rhizopus oryzae* and *Rhizopusarrhizus* serving as outgroups, respectively. (B) The molecular structure of the secondary metabolite, SF1. The compound was characterized as 2,4′-linked Secalonic acid F1.

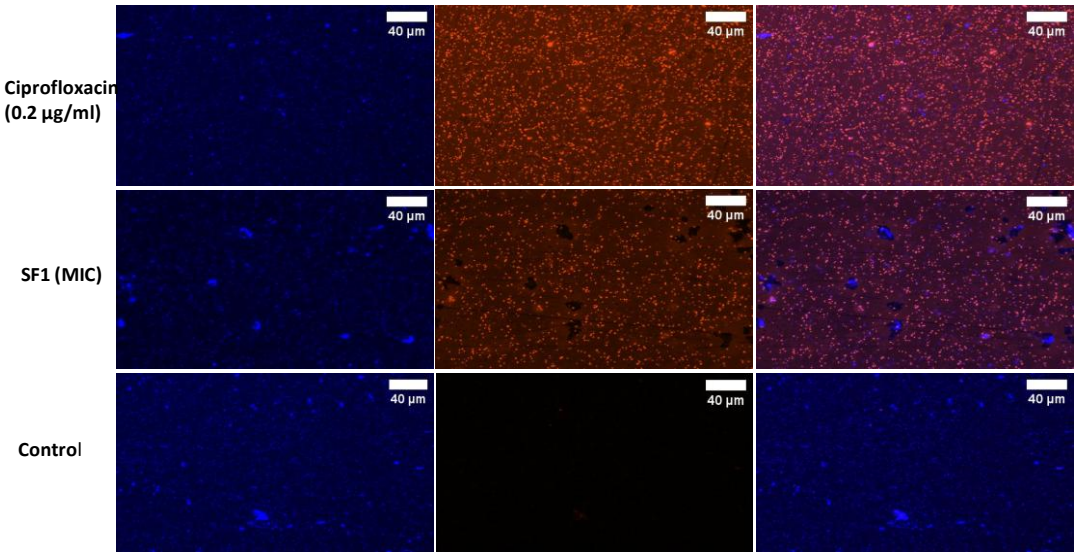


Fig. 4:*S. aureus* biofilm inhibition by SF1. (A) SF1 inhibited biofilm formation by 80.7% and 64.5% at the MIC and 0.5 × MIC, respectively. The inhibition was dose-dependent, reaching 17% at the one-sixteenth concentration of MIC (0.06 µg/mL) (** = p <0.05; *** = p <0.001; **** = p <0.0001; ns = nonsignificant). (B) Representative micrographs, as documented under the light microscope, depict the dose-dependent biofilm inhibition. (C) Biofilms observed under SEM. The cellular surfaces showed significant perturbations, leading to the formation of blebs, rough surfaces, and irregularly shaped cells, with insignificant biofilm formation at MIC and sub-MIC concentrations, while the control cells are regular, forming a thick biofilm. The micrographs were captured at 20000× magnifications.

NAZIA ABBAS

Dr. Nazia Abbas (Scientist) with her Research Group

1. Publications/Patents:

Publications:

S. No	Author(s)	Title	Name of Journal	Volume	Page	Year
1.	Khan, R. A., Kumar, A., &**Abbas, N.**	AaGL3-like is jasmonate-induced bHLH transcription factor that positively regulates trichome density in Artemisia annua.	Gene	904	148213	2024
2.	Hurrah, I.M., Kumar, A. and **Abbas, N.**	"Functional characterisation of Artemisia annua jasmonic acid carboxyl	Planta	259	152	2024

		methyltransferase: a key enzyme enhancing artemisinin biosynthesis."				
3.	Khan, R. A., Kumar, A., &**Abbas, N.**	"AbHLHtranscriptionfactorAaMYC2-typepositivelyregulatesGlandulartrichomedensityandartemisininbiosynthesis in*Artemisia annua"*	Physiologia Plantarum	176	e14581	2024
4.	Hurrah, I. M., Mohammad, Kumar, A., &**Abbas, N.**	"Synergistic interaction of AaMYC2 and AaMYC2-LIKE enhances artemisinin production in *Artemisia annua.*"	Journal Of Biotechnology	402	69-78	2025

2. Scientific work done:

A bHLH transcription factor AaMYC2-type positively regulates glandular trichome density and artemisinin biosynthesis in *Artemisia annua*

RameezAhmadKhan, AmitKumarandNaziaAbbas

Artemisinin-based combinational therapies (ACTs) constitute the first line of malaria treatment. However, due to its trichome-specific biosynthesis, low concentration, and poor understanding of regulatory mechanisms involved in artemisinin biosynthesis and trichome development, it becomes very difficult to meet the increased demand for ACTs. Here, we have reported that a bHLH transcription factor, AaMYC2-type, plays an important role in regulating GSTs development and artemisinin biosynthesis in *Artemisia annua*. AaMYC2-type encodes a protein that is transcriptionally active and is localized to the nucleus. It is prominently expressed in aerial parts like leaves, stems, and inflorescence and least expressed in roots. AaMYC2-type expression is significantly increased under different hormonal treatments. In transgenic overexpression lines, a significant increase in the expression of trichome development and artemisinin biosynthesis genes was observed. While in knockdown lines (*Aamyc2-type*), expression of trichome development and artemisin biosynthesis genes were significantly reduced. Yeast one hybrid assay clearly shows that the AaMYC2-type directly binds to the E boxes in the promoter regions of *ADS* and *CYP71AVI*. Finally, we reported an increase in GST density and artemisinin content in stable overexpression lines of AaMYC2-type as compared to control plants. As in *Aamyc2-type* lines, the GST density and artemisinin biosynthesis were significantly reduced as

compared to the wild type. These findings suggest that the AaMYC2-type drastically increases the final accumulation of artemisinin content by regulating both GST developmental and artemisinin biosynthetic genes.

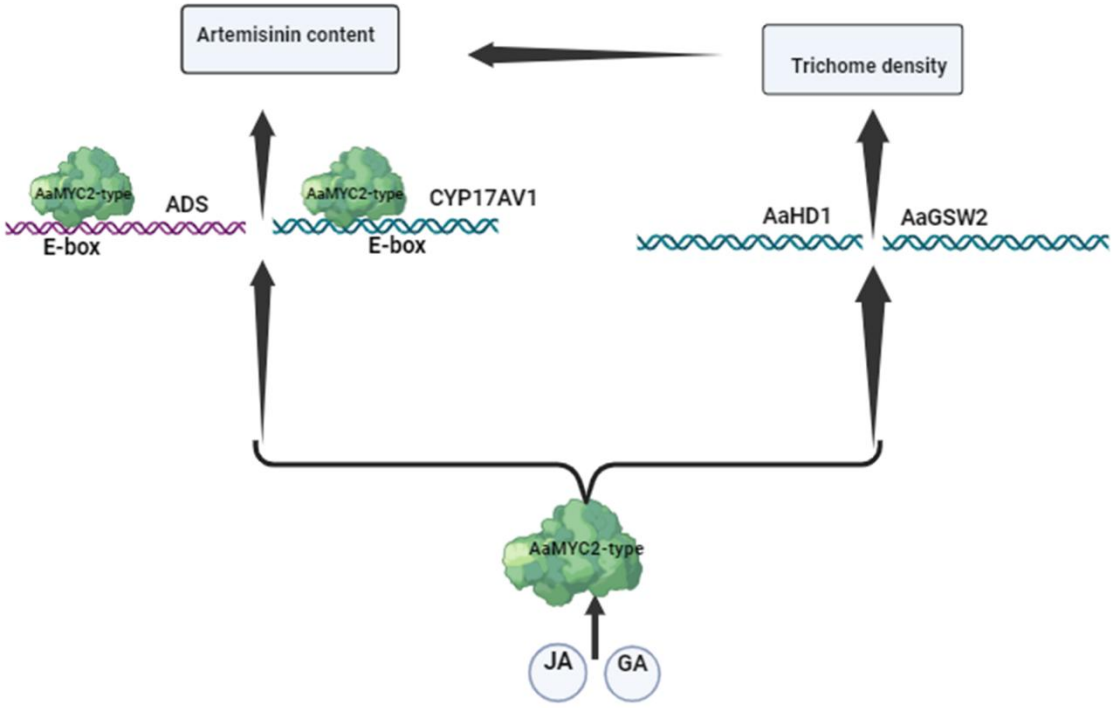


Fig. A simplified model of AaMYC2-type on the regulation of artemisinin biosynthesis and GST development in *Artemisia annua.*

MJ and GAactivate the expression of AaMYC2-type which binds to the promoters of ADS and CYP17AV1 and enhances their expression. Increased expression of ADS and CYP17AV1 intern enhances the artemisinin content in overexpression lines of AaMYC2-type. Model also shows AaMYC2-type also increases GST density on the leaves of *Artemisia annua* which also accounts increase in artemisinin content in overexpression lines.

FAYAZ AHMAD MALIK

Dr. Fayaz Ahmad Malik (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Mir, Shabir Ahmad, Sameera Firdous, Mir Shahid Maqbool, Gulzar Hussain, Mohammad Yaqoob Bhat, **Fayaz A. Malik**, and Syed Khalid Yousuf. "Sonogashira coupling-based synthesis

and in vitro cytotoxic evaluation of C-2 alkynyl derivatives of withaferin A." *Steroids* 212 (2024): 109526.

- Khaliq, Tahirah, Loveleena Kaur, Malik A. Waseem, Phalisteen Sultan, **Fayaz A. Malik**, and Qazi Parvaiz Hassan. "In Vitro Neuroprotection Against Corticosterone Prompted Impairment Activating BDNF–TrkB Pathway Through Bioactive Secondary Metabolites Isolated From Rumex dentatus." *Chemistry & Biodiversity* (2025): e00147.
- Jameel, Salman, Loveleena Kaur, Henna Amin, Showkat Ahmad Bhat, **Fayaz A. Malik**, and Khursheed Ahmad Bhat. "Design, synthesis and neuroprotective evaluation of nitrogen heterocyclic and triazole derivatives of sarracinic acid." *Natural Product Research* 39, no. 3 (2025): 405-414.

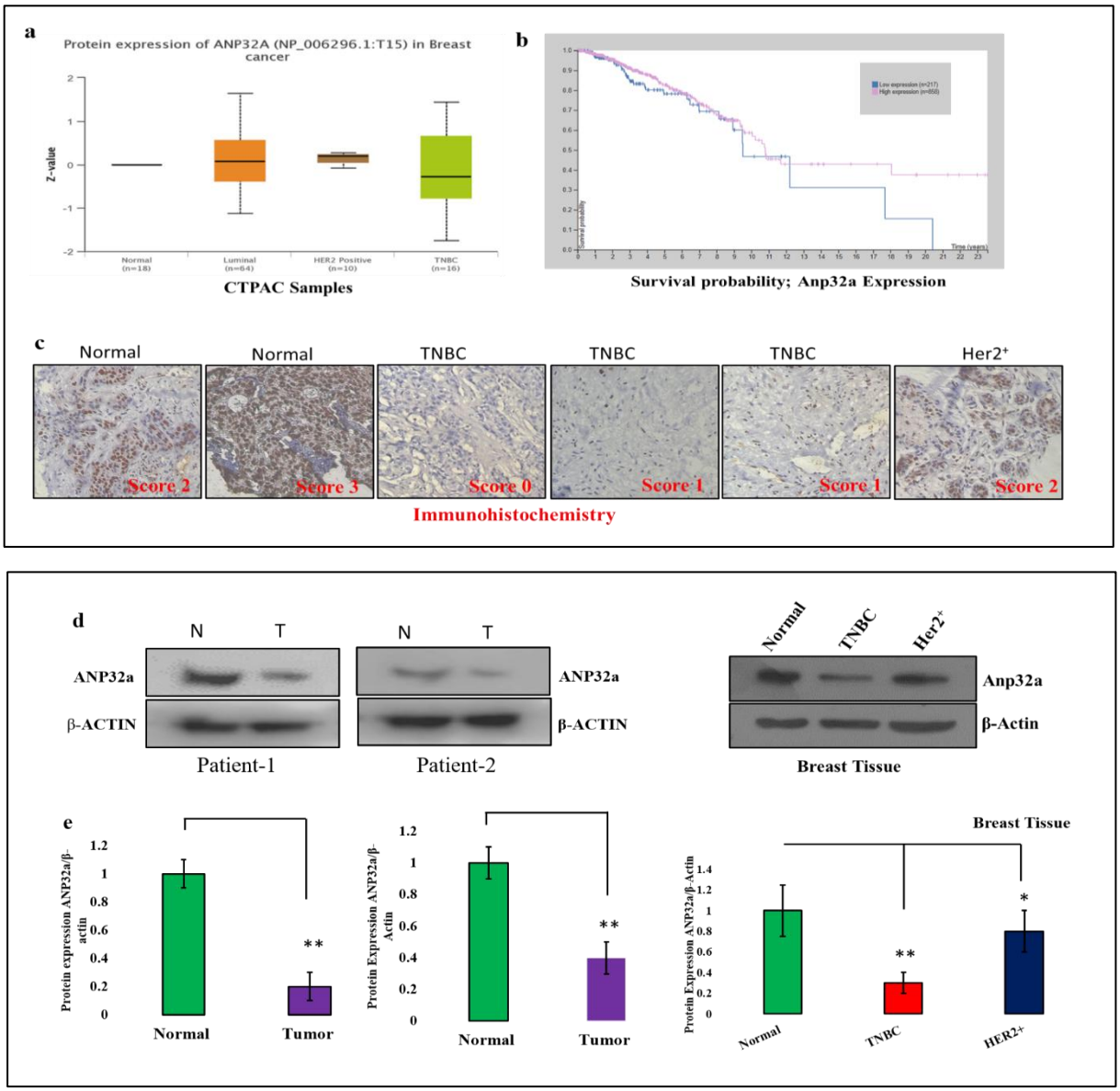
Patents:

- 2'-{Heterocyclyl (Aryl/Alkyl) Methyl}-Cannabidiol Compounds And Process For Preparation Thereof. Pankaj Singh Cham, Loveleena Anand, Yassir Arfath, Nadia Rashid, Mir Shahid Maqbool, Ria Gupta, Zaheen Akhter, Varun Pratap Singh, Zabeer Ahmed, Sheikh Rayees Rafiq, **Fayaz A Malik**, Parvinder Pal Singh. (2024) ***WO2024231957***
- Composition for treating paclitaxel-resistant breast cancer and method for preparation thereof Sameer Ahmad Mir, Shahnawaz Khan, Sameer Ullah Khan, Masroor Ahmad Paddar, Loveleena Kaur Anand, Mir Shahid, Atul Kumar, Anil Padala, GousiaChashoo, Utpal Nandi, Gurdarshan Singh, Bhahwal Ali Shah, Qazi Naveed Ahmed, Baseerat Hamza, Kaneez Fatima, Nadiem Nazir, Ashish Dogra, Amit Kumar, Govind Yadav, **Fayaz Malik, (2024) *WO2024105699A1.***

2. Scientific work done:

Comparative analysis of ANP32A demonstrates lower expression of the protein in TNBC clinical samples and cell lines.

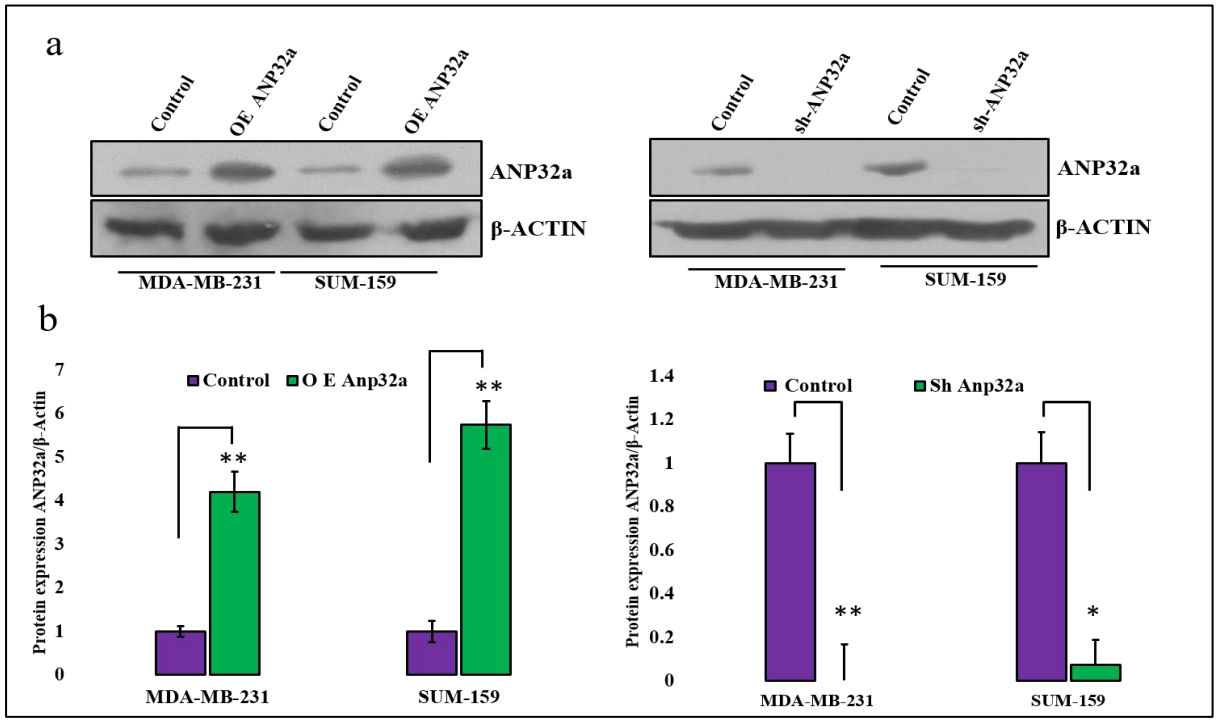
The role of the ANP32A protein in breast cancer has not yet been explored much, and the mechanism of action by which it regulates different biological functions is not yet known. Analysis of TCGA data showed low expression of ANP32A in TNBC compared to normal and other breast cancer subtypes (luminal and $HER2^+$) (**Fig. a**). As per the Kaplan-Meier survival curve, it was seen that low expression of ANP32A in breast cancer patients has a lower survival probability than patients having high expression of ANP32A (**Fig. b**). Analysis of ANP32A expression in adjacent non-tumour breast tissues and cancerous tissues of TNBC and $HER2^+$ subtypes of breast cancer by using immunohistochemistry (IHC) and immunoblotting (**Fig. c, d, e**), these results showed that ANP32A expression was low in TNBC tissue samples compared to normal and $HER2^+$ samples, and the same was compared by using immunoblotting.

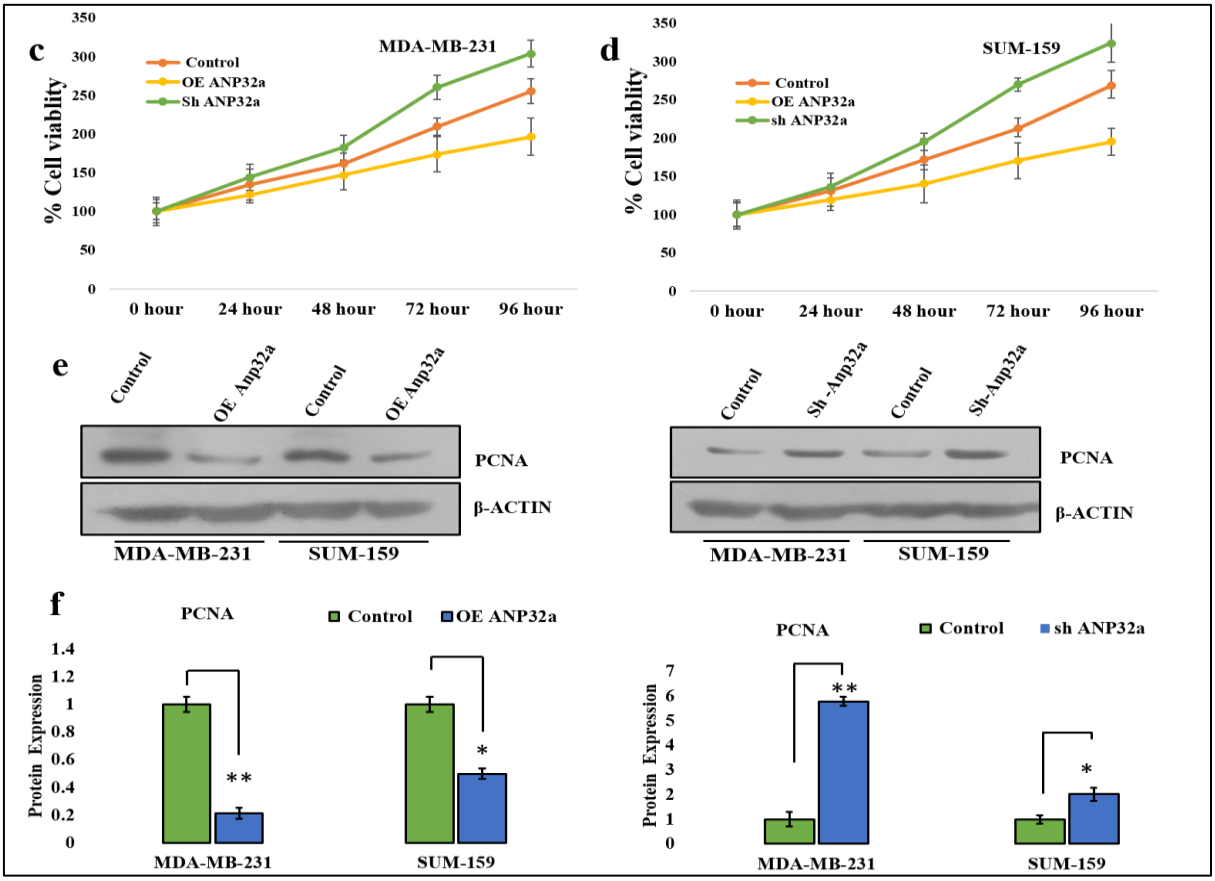


Overexpressing ANP32A inhibited cell proliferation and induced cell cycle arrest in Triple-Negative Breast Cancer Cell lines

We observed in TNBC cell lines that the expression of ANP32A is very low compared to other breast cancer subtypes, which may be a reason for its highly aggressive and metastatic nature when we overexpressed and silenced the ANP32A gene in MDA-MB-231 and SUM-159 cell lines using CRISPR Cas-9 activation and lentiviral knockdown plasmid respectively. The overexpression and knockdown of ANP32A in both cell lines MDA-MB-231 and SUM-159 were confirmed by western blot analysis (**Fig. a, b**). To check the effect of overexpression and knockdown of *ANP32A* on cell proliferation in (MDA-MB-231 and SUM-159), we performed the MTT cell viability assay, and it was found that compared to

respective controls, overexpression of ANP32A showed inhibition, and knockdown led to increased cellular proliferation (**Fig. c, d**). The role of ANP32A on cellular proliferation was further confirmed by the expression analysis of PCNA and Ki67 (**Fig e, f, g, h**). Next, we tried to evaluate the role of ANP32A on cell cycle by analyzing the expression of different cell cycle-regulating proteins through immunoblotting. We found that expression of two important Cyclin-dependent kinase (CDK) inhibitor proteins, like p27 and p21, was significantly increased in the case of overexpressed ANP32A, which led to a decrease in the proteins (CDK-6, CDK-4) critical for the progression of the G1 phase of the cell cycle. On the other hand, a reverse trend was observed in the case of silenced ANP32A (**Fig. I; Fig. k**). These results depict that ANP32A inhibited cell proliferation and induced cell cycle arrest at the G1 phase in TNBC cells.

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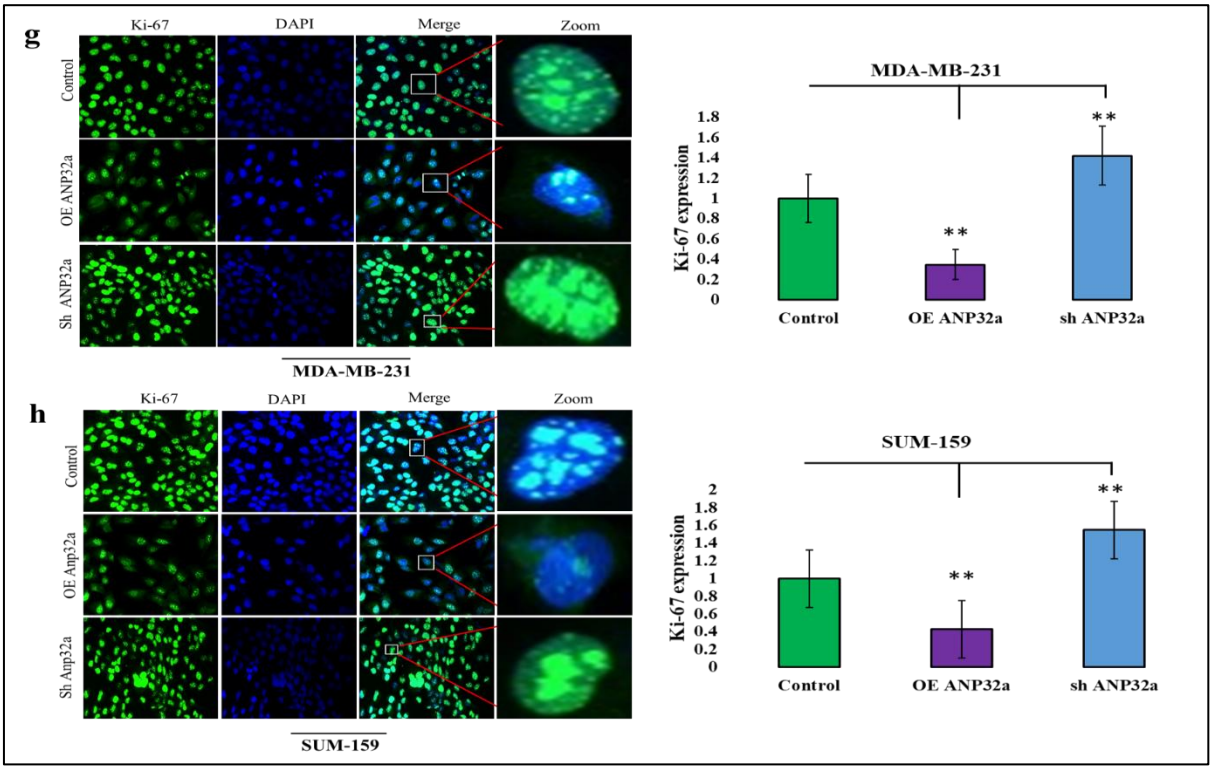
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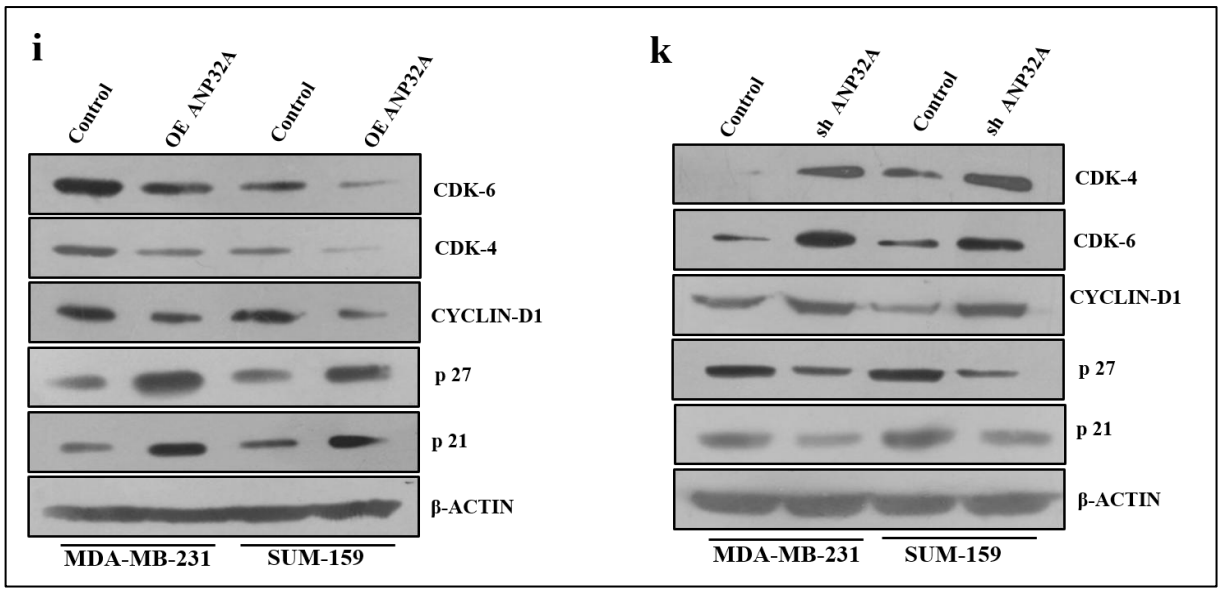
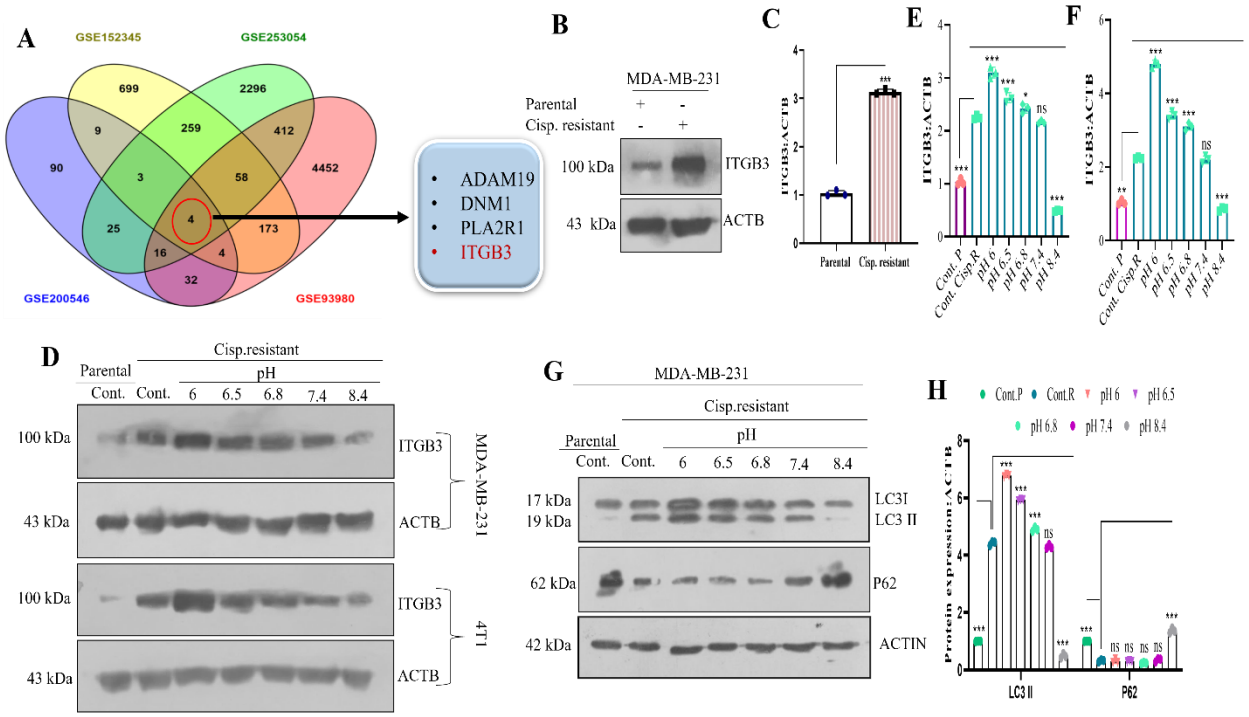


A low pH TME triggers autophagy mediated survival in chemo-resistant TNBCs

During the generation of chemoresistant cells, we observed a decrease in the extracellular pH of the media in cisplatin-resistant cells, being approximately 6.8, compared to around 7.0 in the parental cell media. To explore gene expression under acidic conditions favoring resistance, we conducted a differential gene expression analysis using four publicly available microarray datasets: GSE200546, GSE152345, GSE253054, and GSE983980. These datasets provide valuable insights into how gene expression is affected by low-pH environments. Using GEO2R, we identified differentially expressed genes (DEGs), both upregulated and downregulated. The number of DEGs from each dataset was as follows: GSE200546 (184 upregulated, 225 downregulated), GSE152345 (1,210 upregulated, 774 downregulated), GSE253054 (3,074 upregulated, 1,739 downregulated), and GSE983980 (7,694 upregulated, 6,827 downregulated). Notably, four genes—ADAM19, DNM1, PLA2R1, and ITGB3—were consistently upregulated in response to low pH across all datasets (**Fig. 1A**). Among these, we selected ITGB3 for further investigation due to its potential relevance, as cisplatin-resistant cells exhibited increased adherence to the culture dish compared to parental cells. Although previous research has demonstrated the activation of integrins, including ITGB3, in low-pH environments, no studies to date have directly linked low pH to ITGB3 overexpression. To confirm this, we first assessed ITGB3 expression in vitro via immunoblotting. We observed that Cisplatin-resistant MDA-MB-231 cells showed significantly elevated ITGB3 levels compared to their parental counterparts (**Figure 1 B & C**). To further validate ITGB3 expression under acidic conditions, we subjected both MDA-MB-231 Cisplatin-resistant and 4T1 Cisplatin-resistant TNBC cell lines to varying pH levels (**Figure 1 D-F)**). ITGB3 expression was markedly higher at a pH of 6.0 compared to control-resistant conditions, and it gradually decreased as the pH increased. This pattern suggests a clear link between ITGB3 upregulation and acidic microenvironments, consistent with our analysis from the microarray datasets. Furthermore, we checked the expression pattern of LC3 II and p62, autophagy markers, in cisplatin-resistant cells and under acidic conditions. It was found that in cisplatin-resistant cells, there was an increased expression

of LC3 II and decreased expression of p62, and in acidic conditions, the expression of LC3 II was further increased and the expression of p62 was decreased. However, increasing pH decreases the expression of LC3 II and increases the expression of p62 (**Figure 1 G-H)**. This indicates that expression of ITGB3 and LC3 II under low pH favors the survival pathways in cancer cells.



KHURSHEED AHMAD BHAT

Dr. Khursheed Ahmad Bhat (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Amin H, Kaur G, Goswami A, **Bhat KA**. Facile Synthesis of Ureidic Derivatives of Betulinic Acid With Antiproliferative Effects on Colorectal and Prostate Cancer Cells. **Chemistry & Biodiversity**. **2025** Mar 15:e202402669.

- Jameel S, Kaur L, Amin H, Bhat SA, Malik FA, **Bhat KA**. Design, synthesis and neuroprotective evaluation of nitrogen heterocyclic and triazole derivatives of sarracinic acid. **Natural Product Research**. **2025** Feb 1;39(3):405-14.
- Bashir A, Bhat SA, Manzoor MM, Bhatti F, **Bhat KA**, Riyaz-Ul-Hassan S. Secalonic acid F1 derived from an endophytic fungus Periconia verrucosa as a potential antimicrobial agent against Staphylococcus aureus. **Journal of Applied Microbiology**. **2025** May;136(5):lxaf120.
- Amin H, Kantroo HA, Mubarak MM, Bhat SA, Ahmad Z, **Bhat KA**. Design and synthesis of betulinic acid–dithiocarbamate conjugates as potential antifungal agents against Candida albicans. **RSC advances**. **2024**;14(51):38293-301.
- Gani I, Sofi ZI, Kaur G, Goswami A, **Bhat KA**. Hemisynthesis and cytotoxic evaluation of manoyl oxide analogs from sclareol: effect of two tertiary hydroxyls & Heck coupling on cytotoxicity. **Natural Product Research**. **202**4 Apr 13:1-0.
- Bhat SA, Ahmed QN, **Bhat KA**. DMSO–KOH mediated stereoselective synthesis of Z-enamides: an expeditious route to Z-enamide bearing natural products. **Chemical Communications**. **2024**;60(1):114-7

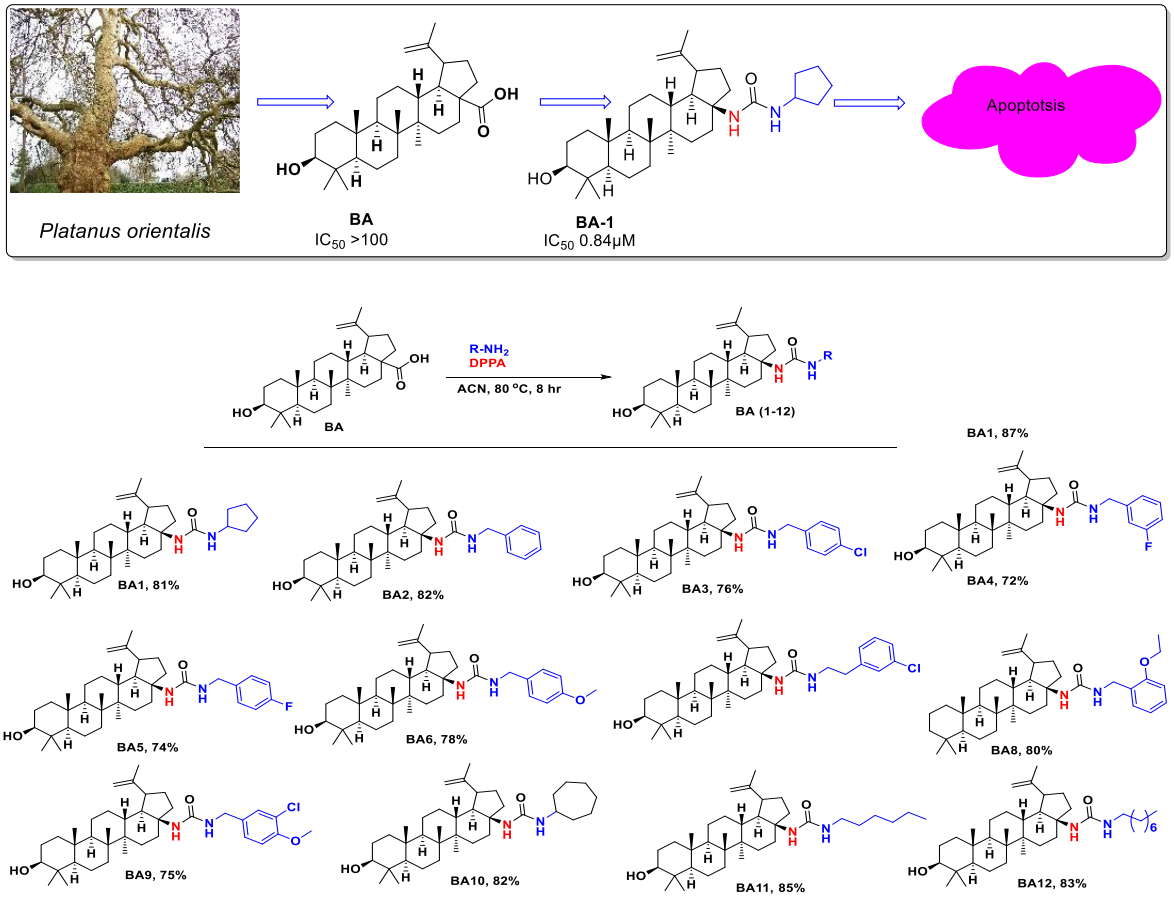
2. Scientific work done:

- Diverse betulinic acid–dithiocarbamate conjugates were synthesized and evaluated for antimicrobial activity. The most active analog (**DTC-2**) demonstrated the best antifungal activity against *Candida albicans*, with an MIC of 4 mg mL^{-1}. **DTC-2** exhibited synergistic effects with the antifungal drugs fluconazole and nystatin, resulting in a significant decrease in MIC by 64 and 16 folds, respectively, when co-administered. Notably, the molecule displayed time- and concentration-dependent kill kinetics, sterilizing *C.albicans* within 8 hours at 8× MIC (**RSC advances 2024**).
- Betulinic acid isolated from *Platanus orientalis*bark was modified in one-pot reaction to furnish 12 ureidic derivatives. The synthesized derivatives were tested against an array of cancer cell lines, colon HCT-116, breast MCF-7, pancreatic MIA PaCa-2, and prostate PC-3 cancer cell lines. Among the synthesized compounds, **BA1** exhibited potent anti-cancer activity with $IC_{50}$of 0.84 and 3.87 µM against HCT-116 and PC-3 using doxorubicin as standard. Our study demonstrates the anti-proliferative and anti-metastatic role of **BA1**, thus inducing apoptosis in prostrate and colorectal cell lines (***Chemistry & Biodiversity*, 2025**).
- An expeditious route to Z-enamide bearing natural products was developed using KOH-DMSO reagent system. The method was successfully applied for the facile synthesis of natural products Lansiumamide A, Lansiumamide B and Z-alatamide. The developed method features operational simplicity, excellent functional group tolerance, broad substrate scope and fast kinetics to furnish Z-enamides (**ChemComm*2024***).
- Manoyloxide was prepared from labdane diterpene natural product –sclareol and its SAR studies revealed that the two tertiary hydroxyls of sclareol are necessary for its cytotoxic activity. It was

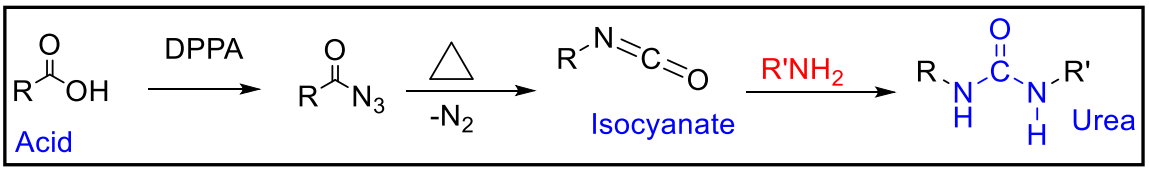
also observed that Heck coupling enhances cytotoxicity of parent molecule (**Nat. Prod. Res2024**).

- Nitrogen heterocyclic and triazole derivatives of natural product sarracinic acid were designed, synthesized and evaluated for neuroprotection which resulted in the identification of two strong neuroprotective molecules (**Nat. Prod. Res2025**).
- Published A critical review entitled 'Sclareol: isolation, structural modification, biosynthesis, and pharmacological evaluation' (*Pharmaceutical Chemistry Journal* **2024**).

Facile Synthesis of Ureidic Derivatives of Betulinic Acid with Antiproliferative Effects on Colorectal and Prostate Cancer Cells

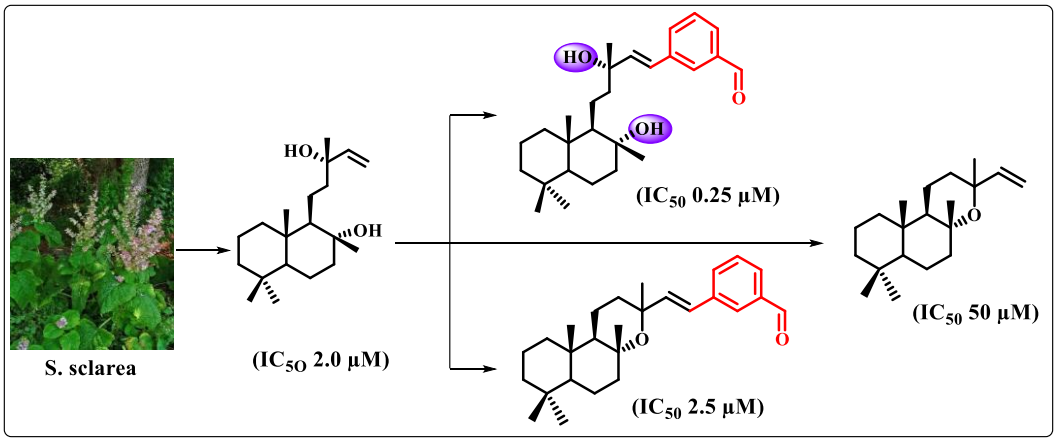


Mechanism:



Betulinic acid isolated from *Platanus orientalis*bark was modified in one-pot reaction to furnish 12 ureidic derivatives. The synthesized derivatives were tested against an array of cancer cell lines, colon HCT-116, breast MCF-7, pancreatic MIA PaCa-2, and prostate PC-3 cancer cell lines. Among the synthesized compounds, **BA1** exhibited potent anti-cancer activity with $IC_{50}$of 0.84 and 3.87 µM against HCT-116 and PC-3 using doxorubicin as standard. Our study demonstrates the anti-proliferative and anti-metastatic role of **BA1**, thus inducing apoptosis in prostrate and colorectal cell lines.

Hemisynthesis and cytotoxic evaluation of sclareol analogs: Effect of two tertiary hydroxyls & Heck coupling on cytotoxicity



Sclareol, a bioactive diterpene alcohol isolated from *Salvia sclarea*, was subjected to structural modification and cytotoxic evaluation. Boron-Heck-coupled analogs of manoyl oxide were prepared from sclareol in a two-step reaction scheme. In the first step manoyl oxide was prepared from sclareol using cerium (IV) ammonium nitrate. Further the structural modification of manoyl oxide *via* Palladium (II) catalysed Boron-Heck coupling reaction produced a new series of compounds. All the synthesised compounds were screened for *in vitro* cytotoxic evaluation against four cancer cell lines HCT-116, MCF-7, MDA-MB231and MDA-MB468. The results showed that manoyl oxide is less active than sclareol. Sclareol shows an IC_{50} of 2.0µM compared to manoyl oxide with an IC_{50} of 50µM against the MCF-7 cell line. From the results it was inferred that the presence of two tertiary hydroxyls in sclareol are necessary for its cytotoxic activity and Heck coupled analogs are more active than sclareol and manoyl oxide.

Ultrasound-assisted facile synthesis of Boron-Heck-coupled sclareol analogues as potential antibacterial agents against *Staphylococcus aureus*

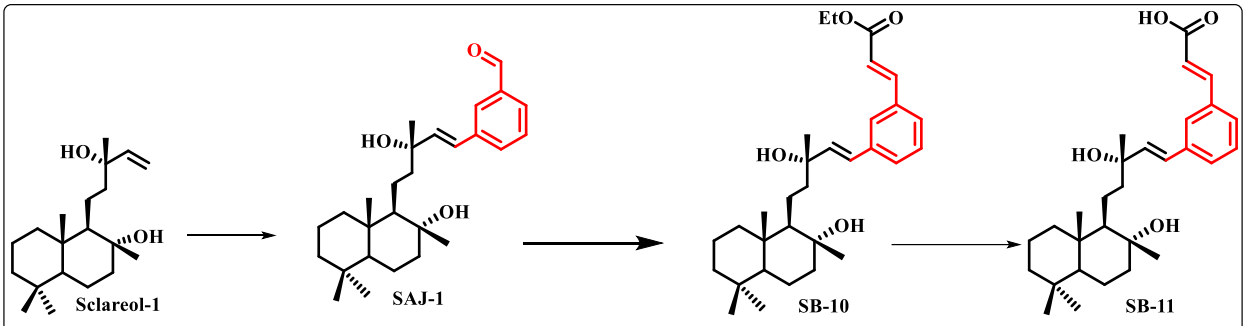


Fig ii) : Heck coupling of sclareol and preparation of Wittig product (SB-11) from Heck coupled sclareol analog SAJ-1

A new series of Heck-coupled sclareol analogs were prepared by structural modifications at C-15 terminal double bond of sclareol using ultrasonication (fig ii). The structural modifications were designed to keep the stereochemistry of all the five chiral centres of sclareol intact. A two-step reaction scheme consisting of Heck coupling of sclareol followed by Wittig reaction was carried out to produce novel sclareol congeners for antimicrobial evaluation. Three compounds SAJ-1, SAJ-2, and SB-11 exhibited strong antibacterial activity against *Staphylococcus aureus* and Methicillin-resistant strain (MRSA) with MIC values between 3 to 11 µM (fig ii).

DMSO–KOH mediated stereoselective synthesis of Z-enamides: an expeditious route to Z-enamide bearing Natural Products

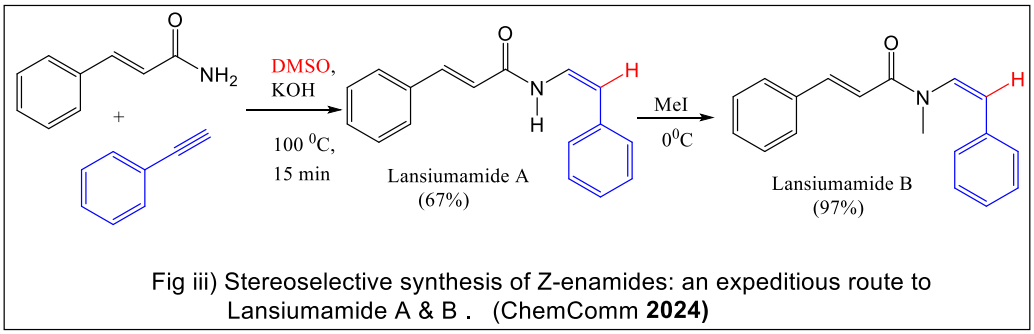


Fig iii) Stereoselective synthesis of Z-enamides: an expeditious route to Lansiumamide A & B . (ChemComm **2024)**

An efficient strategy towards stereoselective amidation of alkynes is reported. The given method features operational simplicity, excellent functional group tolerance, broad substrate scope and fast kinetics to furnish Z-enamides. Moreover, the method was successfully applied for the facile synthesis of the natural products lansiumamide A, lansiumamide B and Z-alatamide. Notably, DMSO plays two vital roles: hydrogen source and solvent (fig iii).

Design, Synthesis and Neuroprotective Evaluation of Nitrogen Heterocyclic and Triazole derivatives of Sarracinic Acid

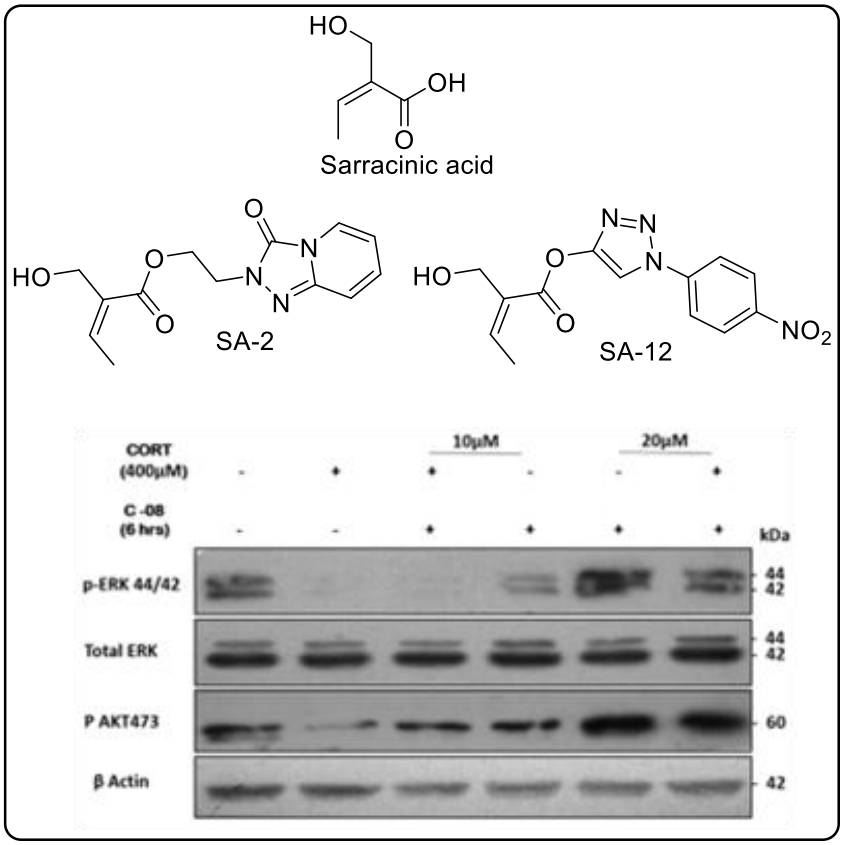
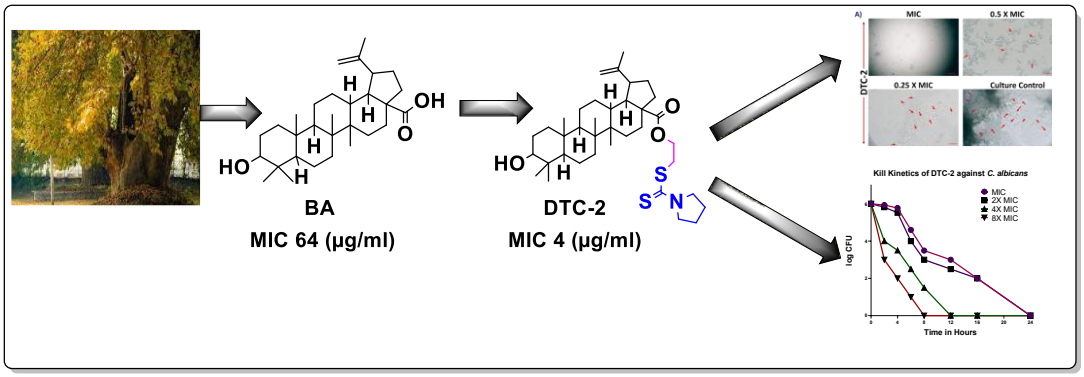


Fig. iv) Structures ofsarracinic acid, SA-2 and SA-12. Sarracinic acid (C-08) functions through the activation of ERK/AKT pathways. C-08 incubated with differentiated SH-SY5Y cells showing the induced expression of p-ERK44/42 along with p-AKT

Nine natural products: gallic acid, stigmasterol, β-sitosterol, sarracinic acid, 2β-(angeloyloxy) furanoeremophilane,1-hydroxypentan-2-yl-4-methylbenzoate,β-{[(*Z*)-2-hydroxymethylbut-2-enoyl]oxy}furanoeremophilane, 3, 4-di-*tert*-butyl toluene, and sitosterol 3-*O*-β-d-glucopyranoside were isolated for the first time from *Senecio graciliflorus*DC. Among various isolated compounds, three natural products (sarracinic acid, gallic acid, and β-sitosterol) displayed better neurotropic activity.The compounds increased neuronal cell survival in differentiated neuroblastoma cells (SH-SY5Y) from high-dose corticosterone (400 µM)–induced cell death. Two analogs of sarracinic acid- SA-2 and SA-12 exhibited strong neuroprotective activity (fig iv).

Design and synthesis of betulinic acid-dithiocarbamate conjugates as potential antifungal agents against Candida albicans



Diverse betulinic acid–dithiocarbamate conjugates were designed and synthesized via a two-step reaction at room temperature. Among the fourteen dithiocarbamate analogs of betulinic acid, **DTC2** demonstrated the best antifungal activity against *Candida albicans*, with a minimum inhibitory concentration (MIC) of 4 mg mL^{-1}, achieving 99% fungicidal activity at the same concentration. These compounds were found to be ineffective against common Gram-negative and Gram-positive pathogens, suggesting their specificity to fungi. Furthermore, **DTC2** exhibited synergistic effects with the antifungal drugs fluconazole and nystatin, resulting in a significant decrease in MIC by 64 and 16 folds, respectively, when co-administered.

NASHEEMAN ASHRAF

Dr. Nasheeman Ashraf (Principal Scientist) with her Research Group

1. Publications/Patents:

Publications:

- Khurshaid N, Shabir N, Pala AH, Yadav AK, Singh D, **Ashraf N**. "Transcriptome wide analysis of MADS box genes in Crocus sativus and interplay of CstMADS19-CstMADS26 in orchestrating apocarotenoid biosynthesis" **Gene** (2025) 10;932:148893. doi:10.1016/j.gene.2024.148893.

- Malik A, Khurshaid N, Shabir N and **Ashraf N**. "Transcriptome wide identification, characterization and expression analysis of PHD gene family in Crocus sativus" **Physiologyand Molecular Biology of Plants** (2024) https://doi.org/10.1007/s12298-024-01410-3

- Mir JA, Yadav AK, Singh D, **Ashraf N**. A novel mutation in non-constitutive lycopene beta cyclase (CstLcyB2a) from Crocus sativus modulates carotenoid/apocarotenoid content, biomass and stress tolerance in plants. **Planta** (2024) 260(4):80. doi: 10.1007/s00425-024-04515-x.PMID: 39192071

2. Scientific work done:

Weidentified a novel mutation in stigma specific lycopene-β-cyclase of *Crocus* (CstLcyB2a) at A^{126}whichsterically hinders its binding of δ-carotene but does not affect lycopene binding thereby diverting metabolic flux towards β-carotene formation. Thus A126L-CstLcyB2a expression results in enhanced production of β-carotene and β-branch apocarotenoids. The mutation also enhanced phyto-hormones like abscisic acid (ABA) which imparts stress tolerance. This mutation can therefore, lead to better quality and stress resilient saffron. These findings provide a platform for development of new generation crops with improved productivity, quality and stress tolerance.

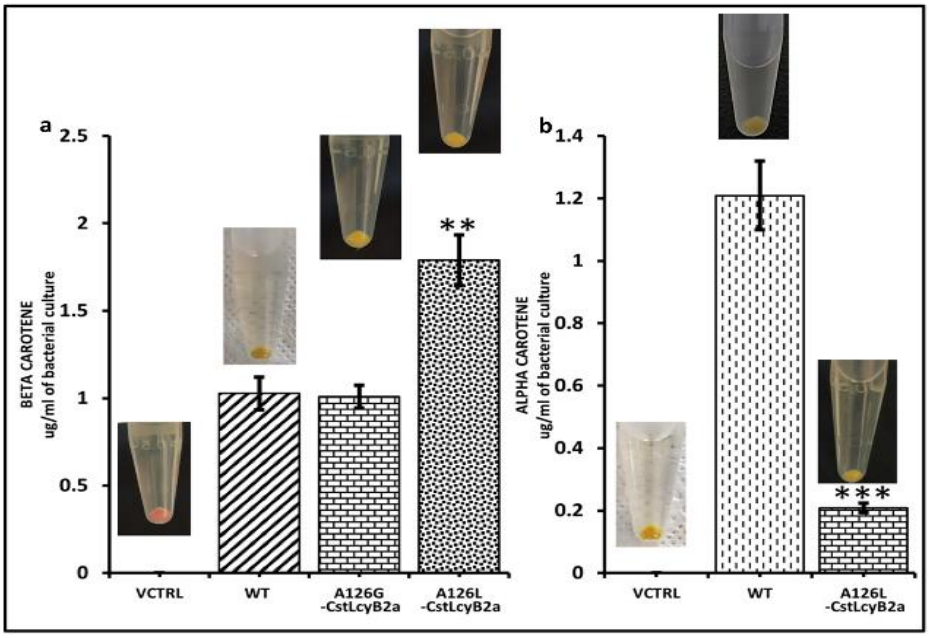


Figure. Color complementation assay and HPLC quantification of carotenoids in pAC-LYC &pAC-DELTA bacterial strains (a) β-carotene content in CstLcyB2a, A126L-CstLcyB2a and A126G-CstLcyB2a transformed pAC-LYC bacterial strains (b) α- carotene content in pAC-DELTA bacterial strains.

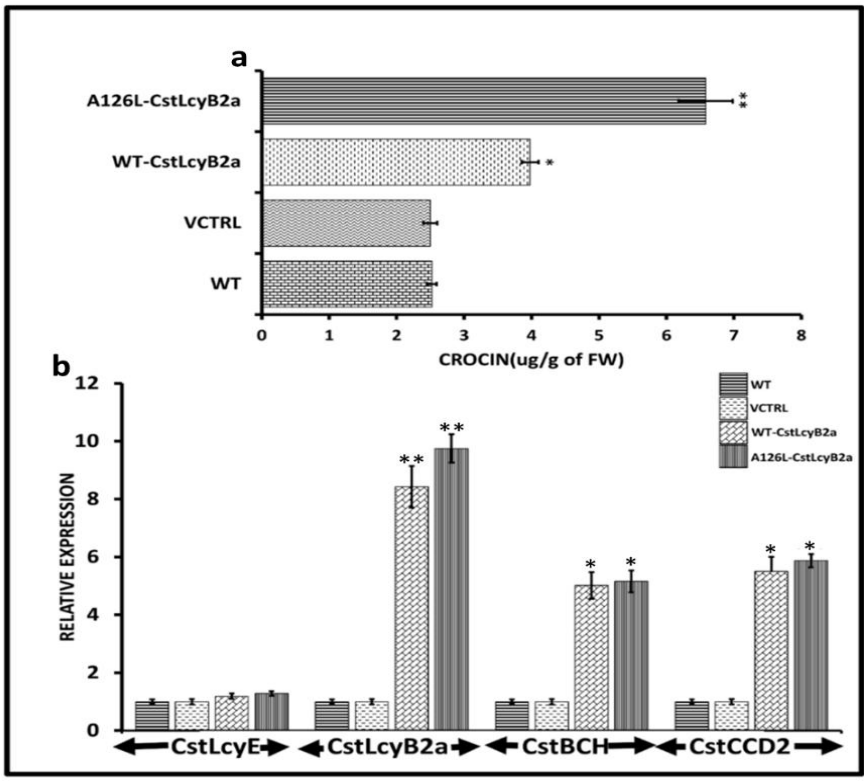


Figure. Quantification of crocin and pathway gene expression in wild type, vector control, CstLcyB2a and A126L-CstLcyB2a transformed *Crocus* stigmas

We also identified MADS box gene family in *Crocus*. Moreover, interplay of two genes i.e., *CstMADS19* and *CstMADS26* work together to enhance apocarotenoid content and hence quality of saffron.

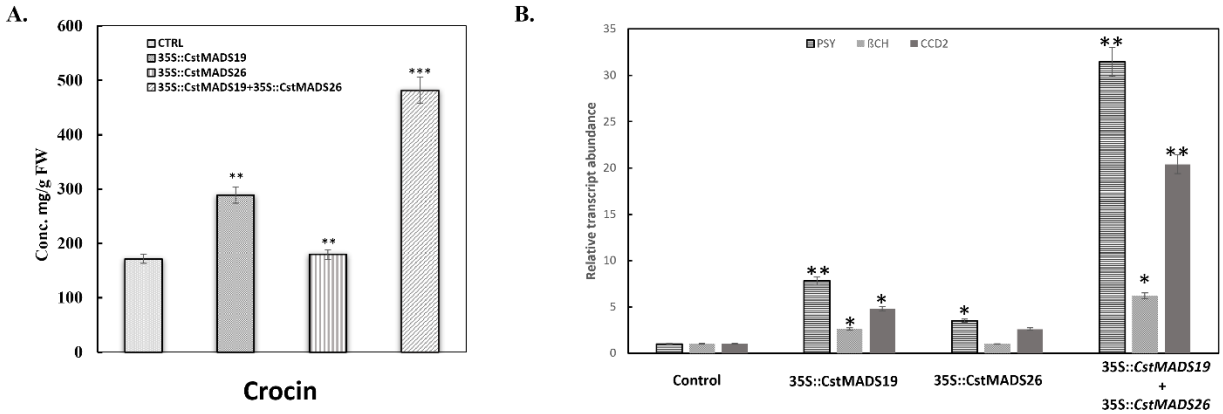


Figure: Overexpression of CstMADS26 in *Crocus*(A)Effect of over-expression of *CstMADS26* and co-overexpression of CstMADS19 and CstMADS26 on crocin content as quantified using HPLC (B) expression of apocarotenoid pathway genes using qPCR.

SHOWKAT RASHID

Dr. Showkat Rashid (Senior Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Chemoselective Oxidation of Aldehydes to Carboxylic Acids: Potassium tert-butoxide as an Anomalous Source of Oxygen
  Waseem I. Lone, Auqib Rashid, Bilal A. Bhat* and **Showkat Rashid***, *Chem Comm.*, **2024**, ***60***, 6544-6547.

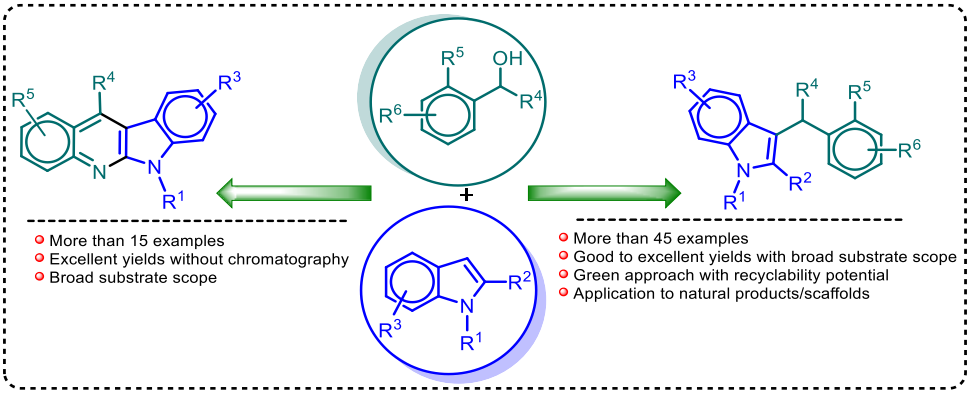
- $NaIO_4$-Driven Oxidative Dimerization and Cu(I)-Catalyzed Oxidative Decarbonylation: Modular Synthesis of 1,2-Naphthoquinones and Aryl Naphtho[2,b]furans
  Mudassir Ahmad, Gowhar Ahmad Rather, Amir Rashid Tarray, Waseem I. Lone, **Showkat Rashid***, *Org. Biomol. Chem.*, **2025***, DOI: 10.1039/D5OB01064K*.

- Polycyclitol Derivatives Restore Long-Term Memory Via cdk5/p25 Activation of Tau Signaling in Experimental Cerebral Malaria.
  Praveen Kumar Simhadri, **Showkat Rashid**, Shailaja Karri, Bilal A. Bhat, Goverdhan Mehta, Phanithi Prakash Babu, *Neurochemical Research*, **2025**, 50, 250.

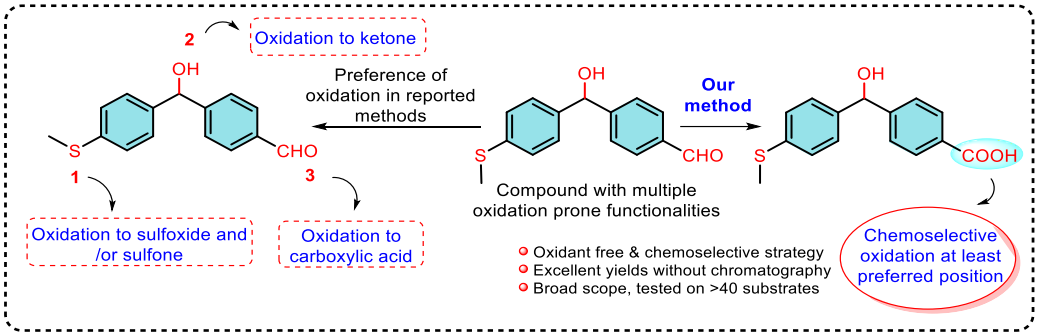
- Rashid, A.; Lone, W. I.; Dogra, P.; **Rashid, S.;*** Bhat, B. A.;* HFIP-mediated C-3-alkylation of indoles and synthesis of indolo[2,3-b]quinolines & related natural products, *Org. Biomol. Chem.*, **2024**,*22*,3502-3509.

2. Scientific work done:

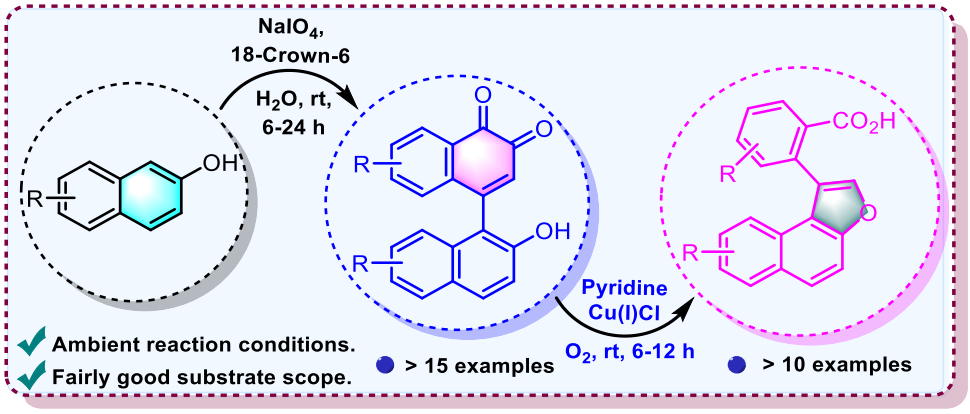
a) We have developed a metal-free C3-alkylation protocol for indoles, along with an NIS-mediated pathway that diverges toward the synthesis of indolo[2,3-b]quinolones. This methodology, carried out in aqueous HFIP, features a broad substrate scope and aligns well with the principles of green and sustainable chemistry. The utility of this strategy was demonstrated through the synthesis of privileged bioactive natural products such as vibrindole, norcryptotakeine, neocryptolepine, and indenoindolone scaffolds. The resulting highly functionalized and diverse indole derivatives were screened for activity against multidrug-resistant microbial strains, yielding promising results. Our ongoing efforts are focused on optimizing these scaffolds to generate more potent hits in this domain.



b) A robust, chemoselective, and gram-scale oxidation protocol for the conversion of aromatic and heteroaromatic aldehydes to their corresponding carboxylic acids has been recently developed in our research group. This method employs potassium tert-butoxide as an unconventional oxygen source, delivering the desired acids without the need for chromatographic purification. Key advantages of this strategy include the use of readily available, table-top reagents, broad substrate compatibility, operational simplicity, and excellent chemoselectivity, particularly in selectively oxidizing less reactive aldehyde functionalities in the presence of more oxidation-prone groups. Notably, the protocol is well-suited for large-scale and potential industrial applications.



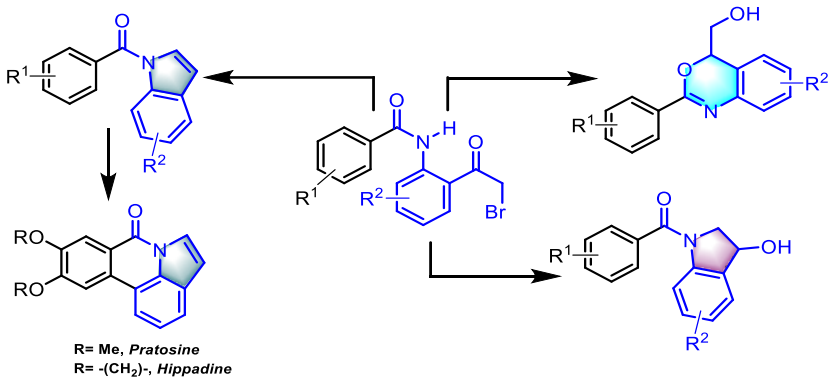
c) We have developed an efficient two-step oxidative strategy for the transformation of readily available β-naphthols into valuable aryl naphthofuran scaffolds via cyclic 1,2-diketone intermediates. The first step involves sodium metaperiodate-mediated oxidative homocoupling of β-naphthols in an aqueous medium, facilitated by 18-crown-6, to afford 1,2-naphthoquinones. In the second step, a Cu(I) chloride-catalyzed oxidative decarbonylation under an oxygen atmosphere converts these intermediates into aryl naphthofurans in good yields. This orthogonal oxidation protocol provides a practical, modular, and scalable approach for synthesizing functionalized naphthofurans from simple 2-naphthol precursors.



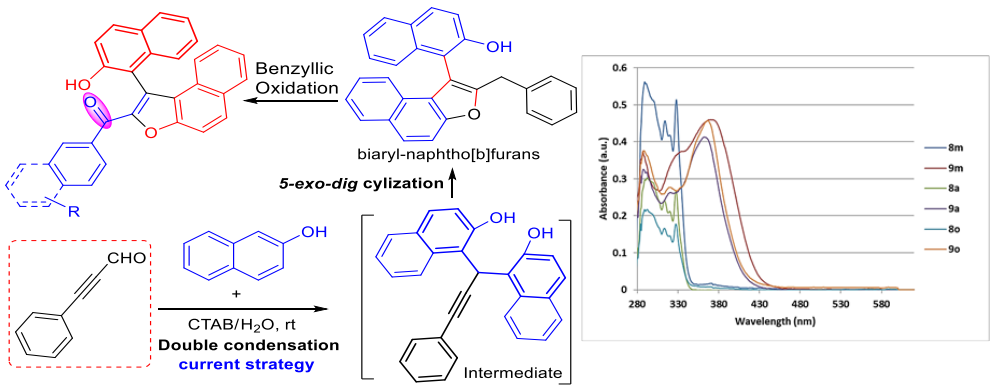
d) A scalable and commercially viable synthesis of the potent histone deacetylase (HDAC) inhibitor panobinostat and its close congener, dacinostat, has been accomplished in our research group under the Centre for Marine Therapeutics (CMT) project. The synthesis proceeds via a non-infringing route and involves the efficient preparation of key advanced intermediates, such as 2-methyltryptamine, tryptamine, and ethyl (E)-3-(4-formylphenyl)acrylate, on a multigram scale from inexpensive, commercially available starting materials. The process features minimal reliance on column chromatography, employs benchtop reagents, and delivers good to excellent yields, with clear potential for scale-up. Owing to its practical applicability in industrial production, this strategy is currently being pursued for patent protection.

e) A chemodivergent synthetic strategy has been developed for the selective construction of three distinct classes of compounds, 1,3-benzoxazines, indolin-3-ols, and indoles, from readily accessible designer amides. This divergence is achieved by employing three different reagent systems: $NaBH_4$ at –5 °C; $NaBH_4$ with 2 equivalents of TFA at 85 °C; and $NaBH_4$ with more than 5 equivalents of

TFA at 85 °C. The protocol is highly versatile, enabling efficient molecular diversification and the streamlined synthesis of structurally varied compounds within each class. The strategy has been successfully demonstrated on the gram scale, and its utility was further highlighted through post-synthetic transformations and a unified approach to the synthesis of phenanthridine-based natural products.



f) We have developed an unprecedented and efficient synthetic protocol for accessing biarylnaphthofurans via a cascade transformation of β-naphthols and ynals in a CTAB (cetyltrimethylammonium bromide) micellar medium. This one-pot process involves a sequence of key steps: an initial double condensation between β-naphthol and the ynal, followed by an intramolecular 5-exo-dig cyclization to forge the naphthofuran core. The unique reactivity observed in this transformation is critically dependent on the micellar environment, which acts as a nano-reactor. Notably, the reaction does not proceed in conventional organic solvents or in purely aqueous media, underscoring the essential role of the CTAB micelles in facilitating substrate organization, enhancing local concentrations, and stabilizing reactive intermediates. This method not only demonstrates a novel reactivity paradigm for naphthofuran synthesis but also highlights the power of micellar catalysis in enabling sustainable and environmentally benign chemical transformations. The resulting biarylnaphthofurans, bearing diverse substitution patterns, represent valuable scaffolds for further exploration in medicinal and materials chemistry.



DHIRAJ VYAS

Dr. Dhiraj Vyas (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Ali, V., & Vyas, D. (2025). A transplantation study in the high-altitude ecosystem of Ladakh suggests site-specific microenvironment is key for physiological adaptation than altitude. *Plant Physiology and Biochemistry*, *220*, 109532.
- Ali, V., Mandal, J., & Vyas, D. (2025). Insights into light-driven dynamics of phytochemicals in sprouts and microgreens. *Plant Growth Regulation*, *105*(1), 129-152.

Patent

- A nutraceutical formulation for improving qualitative and quantitative sleep (PCT/IN2025/050040)

2. Scientific work done:

A. **<u>Site-specific microenvironment is key for physiological adaptation than altitude in Ladakh</u>**

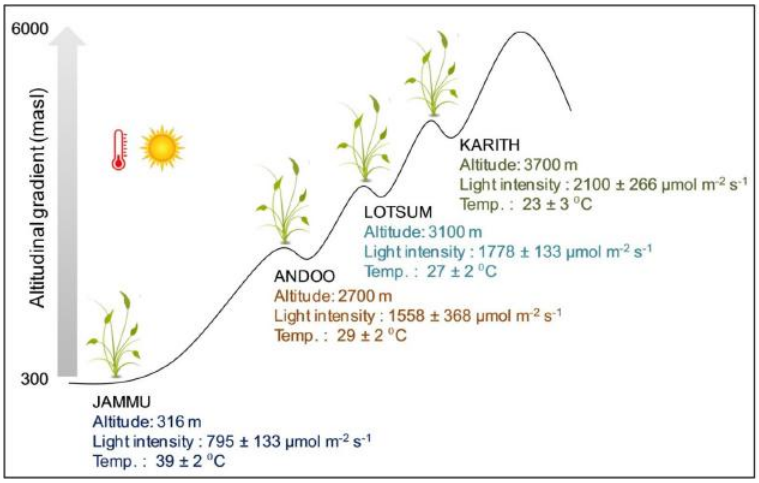
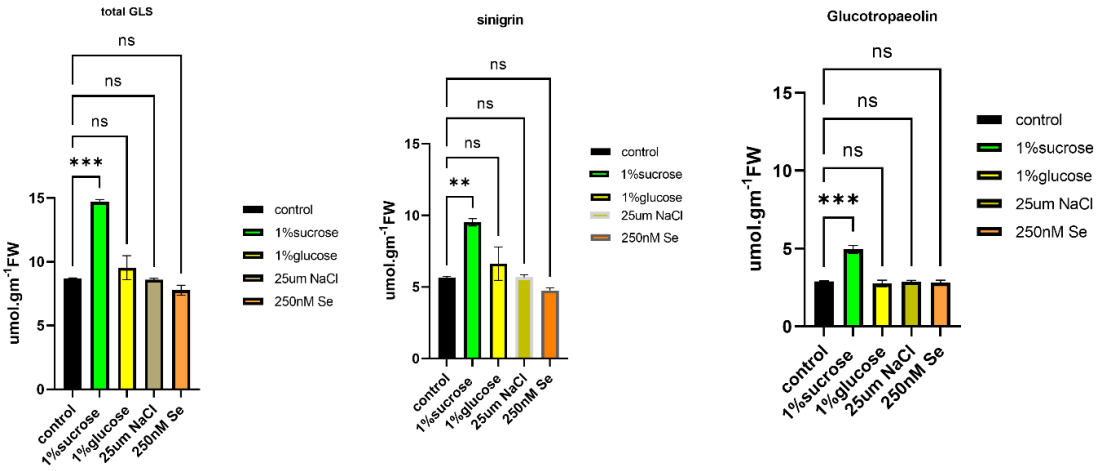


Figure. Attributes of the area selected for the study.

Transplantation experiments conducted in high altitude ecosystems are rising as key strategy to examine the response of individual plant transplanted across distinct elevations. However, plant physiological and biochemical performance in response to changes in abiotic factors across different species and mountain ranges is still lacking. So, in the present study, we have made an attempt to link physiological performance with that of altitudinal gradient in Ladakh by transplanting *Lepidium latifolium*at four different altitudinal sites. The plant was found to maintain photosynthesis even at high altitudes by modulating photochemical efficiency of photosystem II. Various physiological processes including performance index (PIABS), increase in energy fluxes, closing of the reaction centres and decrease in chlorophyll content play a crucial role in the adaptation of this plant. The efficient and dynamic non-photochemical quenching (NPQ) involving carotenoids particularly zeaxanthin mediated dissipation of excess light energy at high altitudinal sites of Ladakh led the plant to withstand extremely strong light radiation. As a photoprotective mechanism, decreases in chlorophyll content and increase in carotenoids could lead to a reduction in the absorption of high light energy and avoid photo damage to the chloroplasts. Higher content of redox metabolites such as GSH, ASC, GSH/GSSG ratio and ASC/DHA ratio in plants transplanted at high altitudinal sites further suggests the resilience ability of *Lepidium latifolium*against harsh environmental stresses. Furthermore, increase in glucosinolate content in plants transplanted at high altitudes suggests the involvement of glucosinolates in the establishment of *Lepidium latifolium*in Ladakh. Overall, no specific altitudinal trend was observed in the present study indicating the adaptation strategy of *Lepidium latifolium*to different altitudinal sites can be attributed to the combined effects of multiple environmental factors/ microenvironments.

B. **Insights into bio-fortification mechanisms of glucosinolates and other phytochemicals in *Lepidium* sprouts**

Glucosinolates, are secondary metabolites are present in family Brassicaceae and are known for environmental interactions and nutraceutical value. Pepperweed, or *Lepidium latifolium*, has drawn interest in its potential as a nutraceutical with high glucosinolate content. Glucosinolates and the byproducts of their hydrolysis, such as isothiocyanates, have anti-inflammatory, anti-cancer, and antioxidant qualities. The use of biotic or abiotic elicitors that activate plant defense pathways to increase glucosinolates and related compounds is a recent development in biofortification processes. On the other hand, little is known about how these elicitors affec*t Lepidium latifolium*seedlings. The sprouts of this plant have many more neutraceutically important compounds compared to mature ones. The current work assesses how various elicitors modulate glucosinolate content and links these modifications to changes in important nutraceutical characteristics, including antioxidant potential.



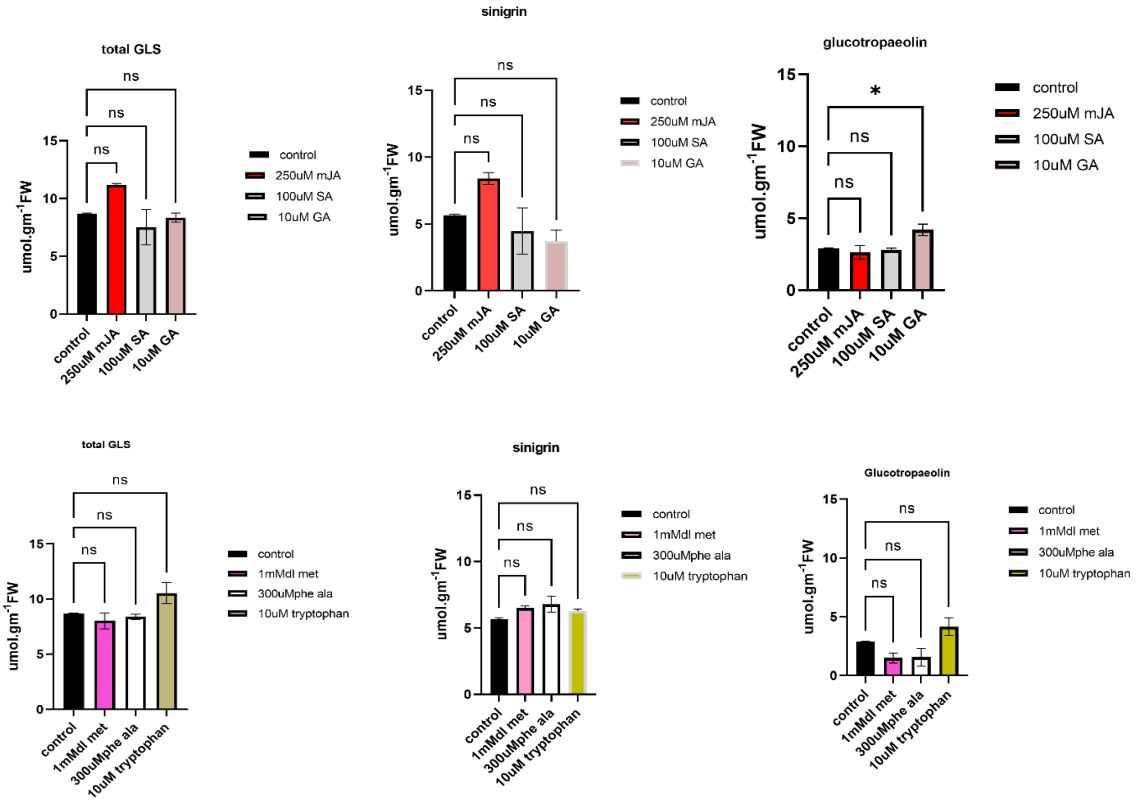


Figure. Metabolic content of total glucosinolates, sinigrin and glucotropaeolin with different elicitors.

We have observed significant enhancement in the health-promoting compounds in *Lepidium latifolium* sprouts when treated with different elicitors. For instance, Sucrose (1%) has shown significant positive impact on glucosinolate level enhancing its content up to 70%. Similarly, Gibberellic acid (10 µM) was found to enhance a typical benzyl glucosinolate, glucotropaeolin up to 44%.

Apart from Glucosinolates, elicitors such as sugars and salts were found to have significant impact on Vitamin C. The metabolic content of Vitamin C was found to be increased by 4-fold when treated with NaCl (25µM) whereas the glucose (1%) and 250nM Selenium (Se) treatment led to increase the content by 1.5-fold in sprouts of *Lepidium latifolium*. The Vitamin C content corroborates to the DPPH antioxidant activity with lowest IC_{50} value (0.2mg ml^{-1}) in NaCl (25µM) treated sprouts. The total phenol content was found to be increased by all the elicitors, however significantly highest enhancement was observed in sprouts treated with Gibberellic acid (10 µM).

C. **Understanding Cannabinoid Regulation in *Cannabis sativa* L.**

Cannabis sativa L., a dioecious member of the Cannabaceae family, is one of the oldest cultivated plants, historically used for food, fiber, fuel, and medicine. Recent metabolomic studies have revealed over 6000 chemical constituents in *Cannabis*, with cannabinoids and terpenes being the most pharmacologically significant classes (Wishart et al., 2024). Alongside cannabinoids, *Cannabis sativa*produces over 150 terpenes—including monoterpenes and sesquiterpenes—that contribute to the

plant's aroma and therapeutic synergy, often referred to as the "entourage effect" (Russo, 2011; Livingston et al., 2020). Recent studies have shown that these terpenes may modulate or enhance the pharmacological effects of cannabinoids, and that their biosynthesis shares common precursors, suggesting a complex metabolic and regulatory interplay. As the global legal cannabis market is projected to surpass USD 100 billion by 2030, understanding the molecular basis of cannabinoid and terpene biosynthesis has become a research priority.

The seeds of different accessions were procured from sites of Himachal Pradesh and Madhya Pradesh, labelled as natural accessions. Some commercial varieties of differential cannabinoid content were also procured based on the desired THC and CBD profile and availability of plant material. The seeds collected were grown in controlled conditions at CSIR-IIIM Jammu. Plants grown in a light duration of 12h day and 12h night photoperiod at 25 ±2°C having light intensity of 150±20 µmol photons m-2 s-1 and a RH of 70%. The topmost mature inflorescence from female plants was collected 90 days after sowing and immediately frozen with liquid nitrogen and stored at -80 °C for further analysis.

This data reveals significant chemotypic variation across ecologically distinct accessions of *Cannabis sativa* L. A total of 30 terpenes, primarily monoterpenes and sesquiterpenes, were identified, with clear quantitative differences between accessions H and M. PCA confirmed distinct metabolic profiles, highlighting key discriminatory terpenes such as α-Pinene, β-Ocimene, and caryophyllene. Major cannabinoids such as THC and CBD also show differential accumulation in both accessions, correlating with the terpene diversity, suggesting coordinated regulation of these secondary metabolites. For understanding cannabinoid regulation in *Cannabis sativa* L., highlighting how environmental and genetic factors influence metabolite biosynthesis will lay a foundation for future molecular studies and can aid breeding programs aimed at optimizing cannabinoid and terpene profiles for medicinal and industrial purposes. Further studies on the light regulations and the involvement of WRKY and other transcription factors will be studied in differential accessions.

D. Insect interaction studies <u>Bioassay of glucosinolates and their hydrolysis products on specialist and generalist herbivores</u>

The Brassicaceae family, comprising approximately 3,200 species, represents a highly diverse group of plants with significant roles in global food systems, agriculture, and pharmaceuticals. The family includes both cultivated and wild species, ranging from vegetable crops such as cabbage, radish, and cauliflower to oil-producing mustard plants and various ornamentals. However, these species' agricultural and ecological success is continually threatened by herbivorous insects. In response, Brassicaceae plants have evolved various defense mechanisms, most notably the production of glucosinolates, a group of sulfur- and nitrogen-containing secondary metabolites characteristic of the family. Upon tissue damage, typically caused by herbivore feeding, glucosinolates are hydrolyzed by the enzyme myrosinase to produce a range of biologically active compounds, including isothiocyanates, nitriles, and thiocyanates. These hydrolysis products are toxic or deterrent to many herbivores and pathogens and form the chemical basis of the so-called "mustard oil bomb" defense system.

The chemical defense is essential in shaping interactions with generalist and specialist herbivores. Generalist feeders, such as *Spodoptera litura* (Fabricius), are highly polyphagous pests that attack over 120 plant species, including economically important crops like tobacco, cotton, tomato, and soybean. Their feeding behavior, ranging from leaf defoliation to fruit boring and stem damage, can lead to severe yield losses. While glucosinolate-derived compounds can deter or impair such generalists, specialists like *Plutellaxylostella* (L.) have evolved mechanisms to tolerate or exploit these chemical defenses. These insects, which feed almost exclusively on Brassicaceae, not only cause significant foliage damage but have also developed widespread resistance to insecticides, making them one of the most challenging pests in Brassica crop production, with estimated annual losses approaching US$1 billion. The co-evolutionary arms race between Brassicaceae plants and their herbivores, shaped mainly by glucosinolate-mediated defenses, highlights the complexity of plant–insect interactions and underscores the importance of understanding these mechanisms for sustainable crop protection.

Initial laboratory cultures were established for *Plutellaxylostella* (L.) and *Spodoptera litura* (Fabricius), two lepidopteran pests of considerable economic importance worldwide due to their destructive impact on major crops. Both pests were reared and maintained under controlled conditions of 25±2 °C temperature, 65-70% relative humidity, and a 14-hour light:10-hour dark photoperiod. These pests are of significant concern as they have developed resistance to multiple classes of conventional chemical insecticides, creating an urgent need for alternative control methods, such as novel biocontrol agents, biopesticides, and integrated pest management strategies. Both pests serve as important model organisms in studying insect physiology, feeding behavior, host–plant interactions, and insecticide resistance mechanisms. Establishing and maintaining their colonies at CSIR-IIIM ensures a continuous supply of uniform experimental material, eliminating the variability and unpredictability of seasonal field collections.

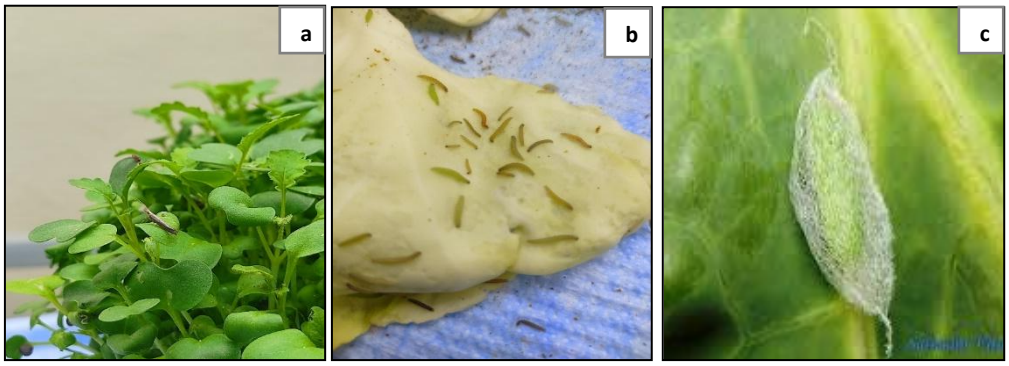


Figure. (a) *Plutellaxylostella* moth laying eggs on *Brassica* plants, (b) Larvae feeding, and (c) Pupa.

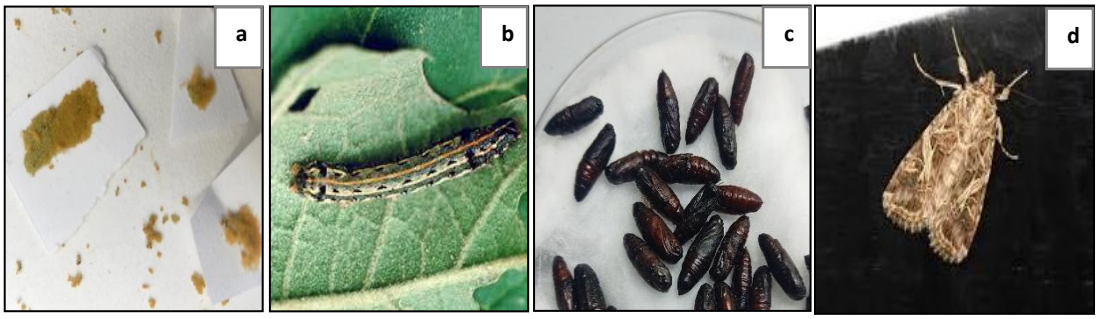


Figure. (a) Egg masses of *Spodoptera litura*,(b) Larvae feeding, (c) Pupae, and (d) Adult moth

To assess the impact of glucosinolate-derived hydrolysis products on herbivore performance, a bioassay was conducted using two different concentrations of allyl isothiocyanate (AITC), a major volatile breakdown product of sinigrin, on the leaves of *Arabidopsis thaliana* and cabbage (*Brassica oleracea var. capitata*). The treatments were designed to evaluate the deterrent or toxic effects of AITC against the specialist lepidopteran herbivore *P. xylostella.* Leaves from both plant species were treated with varying concentrations of AITC and subsequently exposed to *P. xylostella* larvae under controlled laboratory conditions. Larval feeding behavior and leaf damage were monitored over a designated period. Among the treatments, higher concentrations of AITC significantly reduced larval feeding, particularly on *Arabidopsis* leaves. In contrast, no significant reduction in feeding behavior was observed on cabbage leaves, suggesting that while AITC can deter *P. xylostella* on specific hosts, its effectiveness may vary across Brassicaceae species. These findings indicate that, despite *P. xylostella*'s adaptation to glucosinolate-rich plants, AITC can still significantly impact larval performance, particularly at elevated concentrations, with the potential for varying efficacy depending on the plant species.

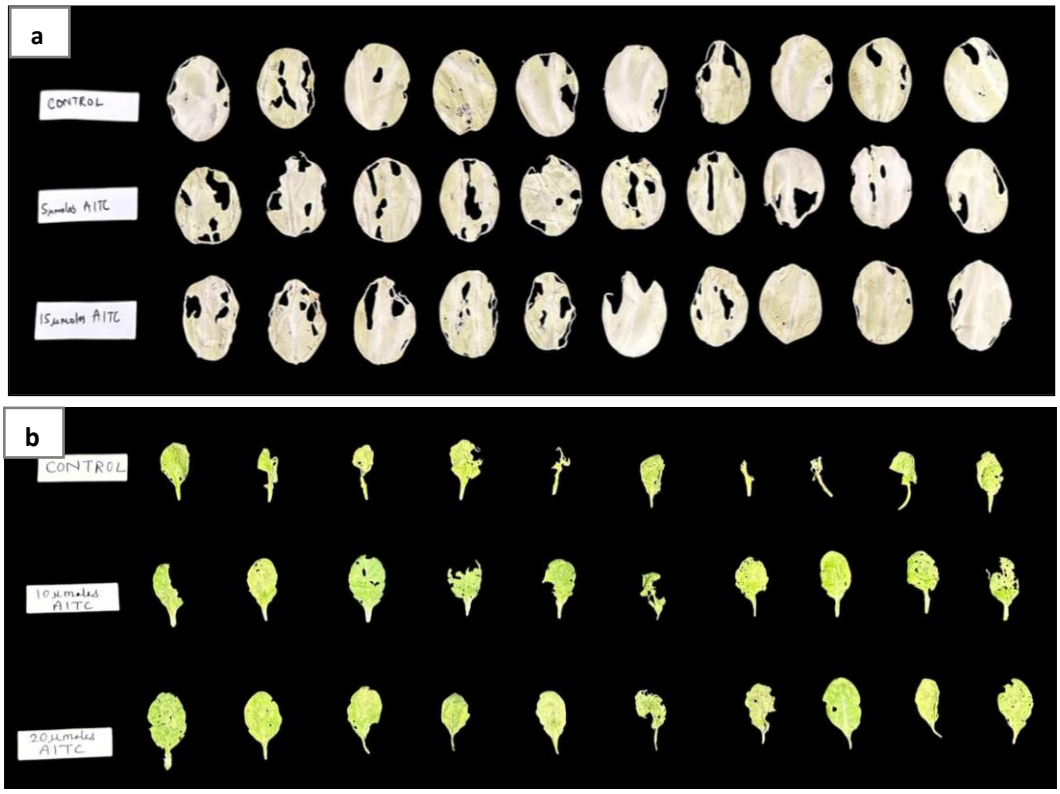


Figure. Allyl isothiocyanate (AITC) treatment against *Plutellaxylostella* on (a) cabbage (*Brassica oleracea var. capitata*) leaves and (b) *Arabidopsis thaliana* leaves

CSIR Aroma Mission-2024-25

Kamlesh Negi, Jyotsana Sharma, Neelisha Ambardar, Vanshika Bhagat, Shiksha, Amulaya Gandotra, Sandeep Charak, Suphla Gupta and Zabeer Ahmed.

The Aroma Mission has significantly boosted Agri startups by offering science-backed planting materials and agronomic practices that ensure high yields and consistent quality to the farmers reaching remote areas converting barren lands to lush aromatic areas. Under CSIR Aroma Mission Phase III, during the second year (2024-25), more than 105 awareness programs were held in different Indian states, sensitizing over 4000 participants, more than 30% of them were women participants. These initiatives sought to promote aromatic crops as a lucrative and sustainable substitute for conventional farming by educating farmers, gardeners, and rural business owners about their economic potential. The Hon'ble Prime Minister's goal of doubling farmers' earnings through the promotion of industrially important crop production is in accordance with this strategy.

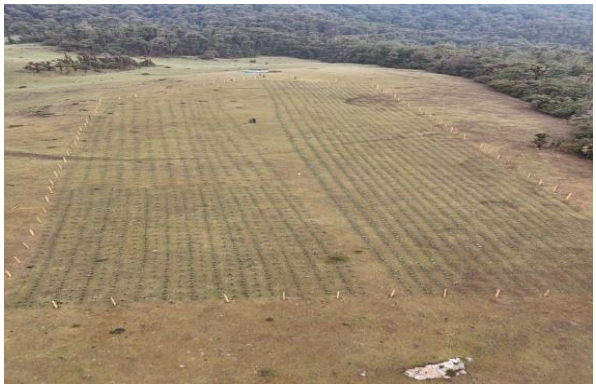
Aligning with the laid down objectives for the extension of the aroma crops more than 600 hectares area have been covered in the IInd year of the IIIrd Phase. The largest coverage was seen in Uttarakhand (more than 100 ha) for Lavender and Rosemary, closely followed by Jammu & Kashmir on the same

two crops. The farmers of the state of Punjab were keen on cultivating Mentha, while Rajasthan and Haryana farmers showed interest in cultivating Ocimum and Lemongrass. Aromatic grasses also attracted the farmers of Jharkhand, Chhattisgarh, Madhya Pradesh, Uttar Pradesh, Haryana, and Maharashtra. North-East region, although comparatively smaller in land area under aromatic crop cultivation, enthusiastically participated in cultivating Lavender.

The mission not only enhanced farmer awareness but also supports them by facilitating access to quality planting material, guiding them in scientific cultivation practices, and helping to establish market linkages for aromatic products. These combined efforts aim to strengthen the rural economy, create employment opportunities, and promote environmentally sustainable farming practices. Looking ahead, CSIR-IIIM Jammu, under the CSIR Aroma Mission, plans to expand its outreach to newer regions, continuing to provide technical support and capacity building to farmers and stakeholders. Overall, the Aroma Mission plays a pivotal role in transforming rural livelihoods by leveraging India's rich biodiversity and the growing global demand for aromatic and medicinal plants.

Awareness Cum Training Program

Quality Planting MaterialDistribution



Plantation of Lavender in Tehri

Lavender cultivation in Tehri

Lavender Festival-2025

Third Lavender Festival | June 1–2, 2025 | Bhaderwah, J&K

CSIR-IIIM Team

As part of its continued efforts to promote aromatic crop-based rural development under the **CSIR-Aroma Mission Phase III**, **CSIR–Indian Institute of Integrative Medicine (CSIR–IIIM), Jammu** organized the **Third Lavender Festival** from **1st to 2nd June 2025** at **Bhaderwah**, in the **Doda district of Jammu & Kashmir**.

The event was inaugurated by **Dr. Jitendra Singh**, Hon'ble **Union Minister of Science & Technology** and **Vice-President, CSIR**, whose sustained leadership has been pivotal in advancing the **"Purple Revolution"** and mainstreaming lavender cultivation as a viable livelihood option in temperate Himalayan regions.

The festival witnessed the participation of over **1,200 stakeholders**, including **farmers, scientists, entrepreneurs, investors, industry representatives, and policymakers** from across the country. Designed to function as a comprehensive knowledge-exchange and market-connect platform, the two-day event included, **Technical sessions** on scientific cultivation, post-harvest protocols, essential oil extraction, quality parameters, and product formulation; **Live distillation demonstrations**, featuring both mobile and fixed distillation units, to educate stakeholders on efficient oil recovery techniques; **Field visits** to lavender cultivation sites and CSIR–IIIM-supported farms, offering practical exposure to best practices; and **buyer-seller meet**, facilitating direct market access and enabling long-term trade partnerships.

Experts from CSIR–IIIM and collaborating institutions provided technical guidance to growers and agri-startups, further reinforcing the mission's focus on **value chain integration, quality assurance**, and **market-driven production**.

The Lavender Festival 2025 successfully demonstrated the economic and ecological benefits of lavender cultivation in the **hill and mountain agro-climatic zones**. It also underlined CSIR–IIIM's role in **technology dissemination, rural entrepreneurship development**, and the **creation of a sustainable aroma economy** in line with national priorities.

Awards and Honours

Buyer-seller Meet

MOU Signing Between CSIR-IIIM and IBSD Imphal

Lavender Field Visit

SUPHLA GUPTA

Dr. Suphla Gupta (Sr. Principal Scientist) with her Research Group

1. Publications/Patents:

Publications:

a) Arora, P., Tabssum, R., Gupta, A. P., Kumar, S., & Gupta, S. (2024). Optimization of indole acetic acid produced by plant growth promoting fungus, aided by response surface methodology. **Heliyon,** 10(14).

b) Devi, R., Arora, P., Verma, B., Hussain, S., Chowdhary, F., Tabssum, R., & Gupta, S. (2025). ABCB transporters: functionality extends to more than auxin transportation. **Planta,** 261(4), 1-22.

c) Hussain, S., Verma, B., Manzoor, M. M., Goyal, P., Devi, R., Gupta, A. P., ... & Gupta, S. (2025). Identification and functional characterization of a cold-inducible UDP-Glycosyltransferase (GgUGT72L11) from Glycyrrhiza glabra**. Journal of Plant Biochemistry and Biotechnology**, 1-17.

2. Scientific work done:

Deciphering the Role of Differentially Expressed UDP-Glycosyltransferases in Abiotic Stress Tolerance of *Glycyrrhiza glabra* L

Hussain, S., Verma, B., Manzoor, M. M., Goyal, P., Devi, R., Gupta, A. P., Manoj K. Dhar, Shakti Kumar Dhiman, Fariha Chowdhary, Debaraj Mukherjee & Gupta, S.

In this pioneering transcriptome-wide study, 83 UDP-glycosyltransferase (UGT) genes were identified in *Glycyrrhiza glabra*. These GgUGTs showed conserved domain architecture, with PSPG motifs,

except in GgUGT80A30, GgUGT80A28, and GgUGT80A31, which formed an out-group linked to lipid and sterol biosynthesis. Phylogenetic analysis grouped GgUGTs into 15 clades, revealing both primitive (OG) and advanced (R group) members, such as GgUGT708D8, implicated in trihydroxyacetophenone*C*-glycosylation. A unique Group Q member, GgUGT95B14 previously thought to be monocot-specific was identified, expanding the UGT lineage in legumes (Fig.1a).

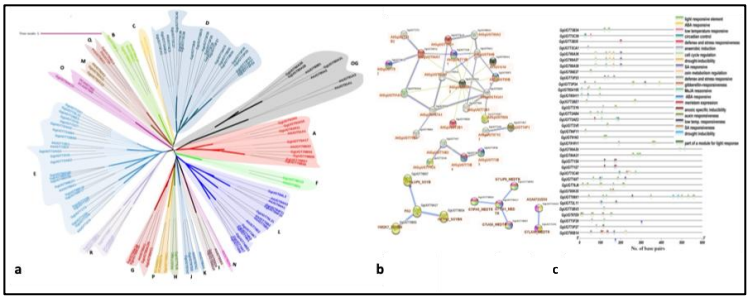


Fig.1 a) Phylogenetic analysis of *Glycyrrhiza glabra* UDP-glucosyltransferase (UGT) family members. b) Protein–protein interaction (PPI) networks and c) cis-regulatory element (CRE) distribution in selected *Glycyrrhiza glabra* UGT (GgUGT) genes.

Functional Annotation and Promoter Architecture

Functional clustering aligned well with known biosynthetic pathways, such as flavonoid, lignin, and hormone metabolism. STRING-based protein–protein interaction networks, particularly with *Medicago truncatula* and *Glycine max*, provided high-confidence functional predictions and co-expression links relevant to flavonol and anthocyanin biosynthesis (Fig.1b). Comprehensive analysis of upstream regulatory regions revealed enrichment in cis-acting elements responsive to abiotic (ABA, low temperature, wounding) and biotic (pathogen) stresses, indicating strong transcriptional regulation potential (Fig.1c).

3. Stress Responsiveness, Heterologous Validation, and Application Potential

qRT-PCR-based expression profiling under various stresses revealed six key GgUGTs: *GgUGT73B34, GgUGT72AE2, GgUGT72AG2, GgUGT708D8, GgUGT88F16, and GgUGT88F17* as differentially expressed in a tissue- and condition-specific manner. Among them, GgUGT73B34 exhibited remarkable transcriptional induction under drought (1041-fold), pathogen infection (255-fold), methyl jasmonate (34-fold), and ABA (18-fold), highlighting its central role in stress signaling. This gene likely operates via two distinct hormonal pathways: methyl jasmonate-mediated secondary metabolite biosynthesis and ABA-driven glycosylation to ABA-glucose ester (ABA-GE), aiding in oxidative stress mitigation. Other GgUGTs responded to additional stimuli such as senescence, UV, salinity, and auxin, underscoring their multifunctional roles in stress adaptation (Fig.2).

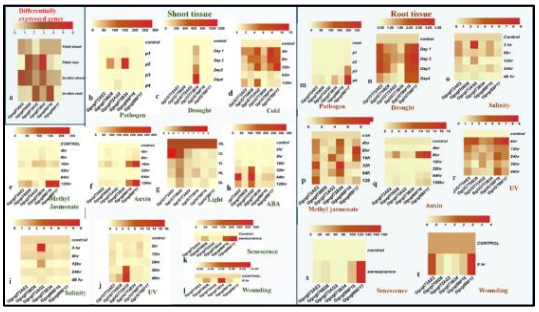


Fig. 2 Heat map representation of differential gene expression patterns of selected *Glycyrrhiza glabra* UGT (GgUGT) genes under different conditions, and various stresses.

To validate the functional relevance of *GgUGT73B34*, a transient expression system was established in *Nicotiana benthamiana* via Agrobacterium-mediated transformation. Promoter-reporter assays confirmed that the *GgUGT73B34* upstream region was transcriptionally activated under individual and combined stresses (mannitol, pathogen, and methyl jasmonate). Notably, the GgUGT73B34 promoter induced strong and sustained GUS expression in response to mannitol-induced drought and combined stress treatments, outperforming the constitutive CaMV35S promoter, thus confirming its potential as a robust, stress-inducible regulatory element for crop improvement strategies (Fig.3).

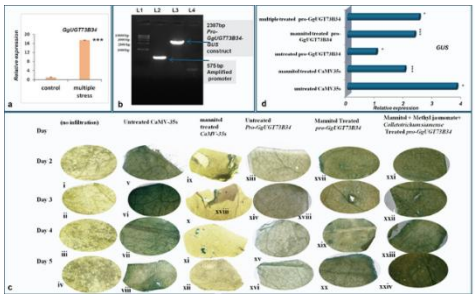


Fig.3 (a) The relative expression level of the Gg*UGT73B34* gene analyzed by qRT-PCR in the *Glycyrrhiza glabra u* under multiple combined stress (300mM mannitol, *Colletotrichum siamens,* and 100µM methyl jasmonate) **(b):**Gel electrophoresis of PCR products of **pBI121**-*pro-UGT73B34-GUS* construct. **(c):** Histochemical assay of GUS activity driven by the promoter in transiently expressed *Nicotiana benthamiana* leaves from day 1 to day 5. **(d)**: representing the relative expression level of GUS gene analyzed by qRT-PCR in the *Nicotiana benthamiana*transformed with *pro-UGT73B34* and CaMV 35s promoter of day 3, when the gus intensity was seen to be maximum. The x-axis indicates the treated and infiltered leaf tissue and the y-axis indicates the relative expression value of GUS. The mean value was represented as three measurements for each plant, and three plants were used for each experiment. The error bars indicated standard deviation. Significant differences were shown by ** and *** ($P < 0.05$ or $P < 0.001$. respectively).

Anthracnose as a metabolic trigger unveiling the role of Colletotrichum in modulating

Diosgenin and CYP90 expression

Anthracnose disease caused by *Colletotrichum spp*. in *Dioscorea spp.* significantly impacts crop productivity and medicinal compound accumulation. The present study was aimed at evaluating the pathogenicity of three *Colletotrichum* isolates (PP1, PP2, and PP3) associated with anthracnose disease in *Dioscorea composita* and exploring their influence on the modulation of secondary metabolites (Fig.4a-b). Based on ITS sequencing, morphological traits, and virulence testing, isolate PP3 was identified as the most virulent, followed by PP2 and PP1. In vitro and detached leaf assays confirmed differential pathogenic potential among isolates (Fig.4c). UPLC-MS/MS quantification revealed that diosgenin content decreased significantly in PP3-infected plants compared to control, while total

phenolic content (TPC) and total flavonoid content (TFC) increased, indicating a possible metabolic shift under stress. Expression analysis of CYP90, a gene involved in diosgenin biosynthesis, showed downregulation under PP3 infection (Fig.4d). These findings suggest that anthracnose severity not only compromises plant health but also modulates the biosynthesis of key secondary metabolites. The study provides novel insights into pathogen-induced metabolic modulation in *Dioscorea composita*, highlighting the need for integrated disease management and future mechanistic studies on host-pathogen interaction.

This study investigates how Colletotrichum-induced anthracnose disease affects secondary metabolism in D. composita. Among three isolates tested (PP1, PP2, and PP3), PP3 showed the highest virulence. The infection caused a decrease in diosgenin content and downregulation of CYP90 gene expression, while phenolic and flavonoid content increased, indicating stress-induced metabolic shifts. The work highlights a critical link between pathogen virulence and the modulation of medicinal compound biosynthesis, providing a foundation for future studies on disease-resistance mechanisms and the development of improved crop protection strategies.

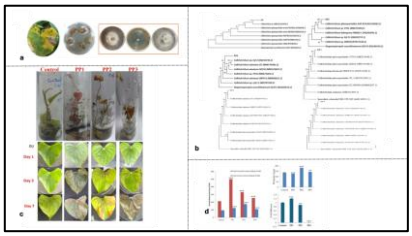


Figure 4(a): (i) Symptoms of anthracnose disease on *Dioscorea* leaf showing characteristic lesions and necrosis. (ii) Growth of fungal colonies from diseased leaf explants cultured on Potato Dextrose Agar (PDA) medium. (iii) Pure cultures of three isolated fungal pathogens designated as PP1, PP2, and PP3. (4b) Phylogenetic analysis of Colletotrichum isolates based on ITS and β-tubulin sequences. **(4c)** Pathogenicity assay of three Colletotrichum isolates. **(4d):** (i) total flavonoid and phenolic content (ii) Diosgenin concentration in response to pathogenic infection. UPLC-MS/MS analysis of diosgenin content in control and pathogen-inoculated Dioscorea leaves. (iii) Relative expression of the CYP90 gene involved in diosgenin biosynthesis. The expression of CYP90 was analyzed using β-actin as an endogenous control. Statistical analysis was performed using GraphPad Prism 8.4.2 with t-tests. Significance levels are indicated as $^{**}p < 0.01$ and $^{***}p < 0.001$

Understanding the Organization and Function of Selected ABC Transporter genes from *Glycyrrhiza glabra* L under the Influence of Abiotic elicitors

ATP Binding Cassette (ABC) Transporter constitutes one of the largest families of membrane proteins which translocates substrate across the membrane, using energy released from ATP hydrolysis. Structural architecture possesses highly diverse trans-membrane domains (TMDs) and conserved nucleotide-binding domains (NBDs). According to phylogenetic relationships and domain organization ABC transporters are categorized into eight subfamilies (ABCA to ABCH) with ABCH uncharacterized in plants. These transporters mediate the transportation of plant hormones, metal ions, lipids, secondary metabolites, and exogenous substances. ABCB subfamily involved in auxin transport (Geisler et al., 2005). Auxin production directly affects the biosynthesis of the secondary metabolite Glycyrrhizin in *Glycyrrhiza glabra*, a medicinally important plant known for its benefits for ages. From the

transcriptome resource of *G.glabra*, 181 full length genes were mined which were phylogenetically categorized into different subfamilies (A to I).

Phylogenetic analysis of GgABCB transporters

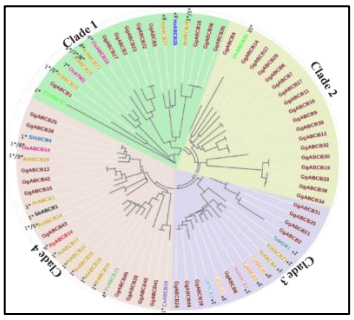


Fig 1. Phylogenetic analysis of the N-terminal Nucleotide Binding Domains of 32 functionally characterized ABCB proteins from various plant classes, along with 45 GgABCBs from *G. glabra*. The phylogenetic tree was conducted in MEGA 11 software.

Phylogenetic analysis grouped GgABCB proteins into four clades: Clade I (GgABCB3, 17, 22, 23 clustered with OsABCB24) associated with heavy metal detoxification; Clade II (GgABCB14 grouping with ZmABCB15) with pathogen resistance; Clade III (GgABCB6 grouping with MdABCB1 and CjABCB2) with auxin and berberine transport; and Clade IV (GgABCB25, 26 aligned with SlABCB4, AtABCB19, and OsABCB14) with auxin, brassinosteroid transport, and iron homeostasis.

Expression analysis of *GgABCB*transporter genes under auxin and inhibitor (NPA) treatment

Shoot tissue exhibited higher expression of *GgABCBs* compared to root, with *GgABCB14* (147.5-fold), *B15* (6-fold), *B25/B26* (18-fold), *B40* (1273-fold), *B42* (51-fold) under auxin treatment. The NPA (10 µM) downregulated expression of all the selected *ABCB* genes along with associated proteins- *GgTWD1* (0.4 folds), *GgPIN1* (0.3 folds) and *GgPIN3/4/7* (0.2 folds).

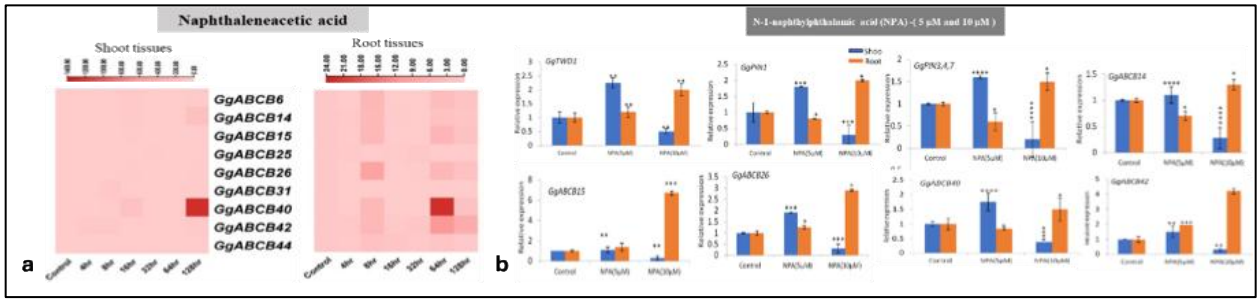


Fig 2. Expression analysis of selected *GgABCB*subfamily genes in shoot and root tissues under auxin (a) and (b) N-1-Naphthylphthalamic acid treatment.

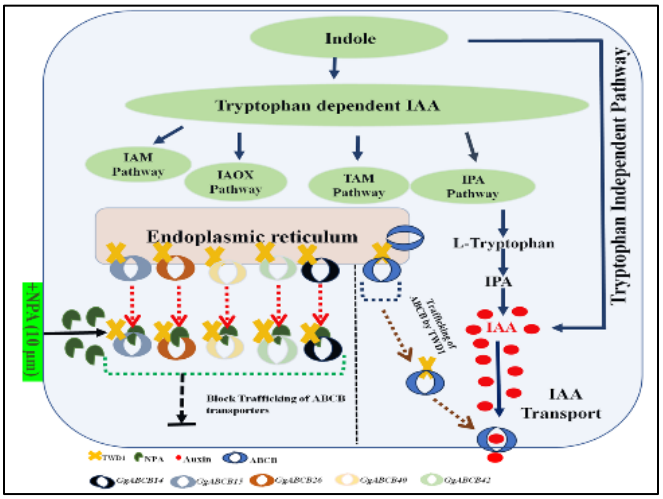


Fig 3. Schematic representation of IAA transportation under the influence of NPA. IAA transportation is mediated by ABCBs. A positive regulator, TWD1, PGP1-mediated auxin transporter, acts as a chaperone in association with ABCB subfamily for transportation from ER to PM. N-1-naphthylphthalamic acid (NPA), a polar auxin transport inhibitor, binds with high affinity to ABCBs and TWD1 complex of plant membranes NPA (10 µM) disrupts TWD1-ABCB interaction resulting in inhibition of auxin transportation. Blue arrows indicate auxin biosynthesis pathways. Brown dotted arrows indicate trafficking of ABCB transporter by TWD1 from Endoplasmic reticulum to Plasma membrane, when no NPA is present. In the presence of NPA (10µM), its binds to the ABCB – TWDI Complex and blocks the transportation.

PRASHANT MISRA

Dr. Prashant Misra (Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Rajput R, Tyagi S, Anchal K, Singh S, Laxmi A, **Misra P**, Pandey A **(2025)** Cytokinin-mediated repression of anthocyanin biosynthesis in banana fruits. **The Plant Journal** 122, e70267. DOI: 10.1111/tpj.70267.
- Sharma P, Wajid MA, Pal K, Fayaz M, Majeed A, Yadav AK, Singh D, Bhat S, Bhat WW, **Misra P* (2025)** Functional characterization of 1-deoxy-D-xylulose-5-phosphate synthase (DXS) genes from *Monarda citriodora* establishes the key role of McDXS2 in specialized terpenoid biosynthesis. **Plant Physiology and Biochemistry.** DOI: 10.1016/j.plaphy.2025.109961.
- Fayaz M, Angmo T, Katoch K, Majeed A, Kundan M, Wajid MA, Pal K, **Misra P* (2025**) The promoter regions of CBDAS and PT genes of cannabinoid biosynthesis in *Cannabis sativa* respond to phytohormones and stress-related signals. **Planta.** doi: 10.1007/s00425-025-04709-x.
- Sen Y, Sharma V, Singh S, Bulle M, **Misra P**, Kota S **(2024)** MetaTopolin-driven breakthrough in lemon beebalm (*Monarda citriodora*) regeneration: A molecular fidelity study for genome

engineering applications. **Journal of Medicinal and Aromatic Plant Sciences.** 46: 123-132, Doi: https://doi.org/10.62029/jmaps.v46i3.sen

- Wajid MA, Sharma P, Majeed A, Bhat S, Angmo T, Fayaz M, Pal K, Andotra S, Bhat WW, **Misra P*(2024).** Transcriptome-wide investigation and functional characterization reveal a terpene synthase involved in γ-terpinene biosynthesis in *Monarda citriodora*. **Functional and Integrative Genomics**. 26; 24(6):222. DOI: https://doi.org/10.1007/s10142-024-01491-z.

2. Scientific work done:

(A) Identification and functional characterization of genes involved in the biosynthesis of components of essential oil in *Monarda citriodora*

Our earlier work led to the identification of four *DXS* genes (*McDXS1* to *McDXS4)* from the transcriptome resource of *M. citriodora*. The full-length CDS regions corresponding to these genes were cloned. All the four genes were demonstrated to encode functional DXS proteins, based on the complementation assay in mutant *E.coli* strain, defective in DXS gene function (Fig. 1). Further, based on the phylogentic analysis, gene expression and metabolite correlation, we predicted that out of the four (McDXS1, 2, 3, and 4), McDXS2 could be involved in the biosynthesis of specialized monoterpenes in *M. citriodora* (Fig. 2).

Transient overexpression and silencing of *McDXS2* were carried out in *M. citriodora* leaves using Agroinfiltration. The silencing of the *McDXS2* led to a decrease in the content of volatile monoterpenes, whereas its overexpression increases the content of volatile monoterpenes in *M. citriodora* (Fig. 3). *McDXS2* was constitutively expressed in the *N. tabacum*. Transgenic *N. tabacum* lines expressing *McDXS2* were reported to have decreased content of chlorophyll and carotenoids, as compared to that of WT (wild-type) control plants (Fig. 4). The *McDXS2* expressing transgenic lines displayed enhanced content of specialized diterpenoids (labdanoids and cembranoids) as compared to WT plants. These results established *McDXS2* as a key gene involved in the biosynthesis of specialized terpenes in *M. citriodora*.

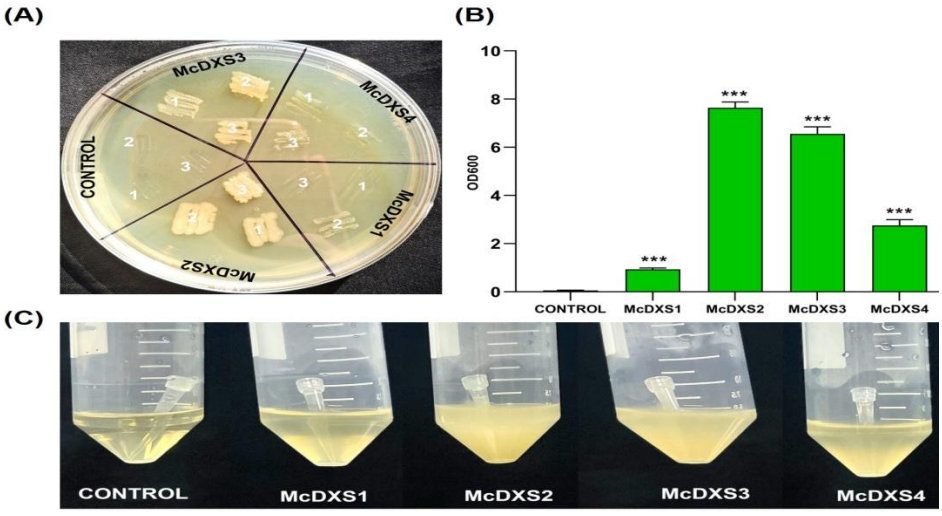


Fig. 1: Results of bacterial complementation test. Panel **A** and **C** represents the different section on the culture plate and the culture tubes representing the growth of *E. coli* strain EcAB4-2 transformed with McDXS1, McDXS2, McDXS3 and McDXS4 plasmids and empty vector. The culture plates and culture tubes contained the LBA and LB, medium, respectively, without mevalonate. Growth of the bacteria was observed in the case of EcAB4-2 strain transformed with McDXS1, McDXS2, McDXS3 and McDXS4 plasmids. No

growth was observed in empty vector control, which serves as a negative control. Panel **B** represents bar plot showing the quantitative growth measured in terms of optical density (OD) of the culture at 600 nm.

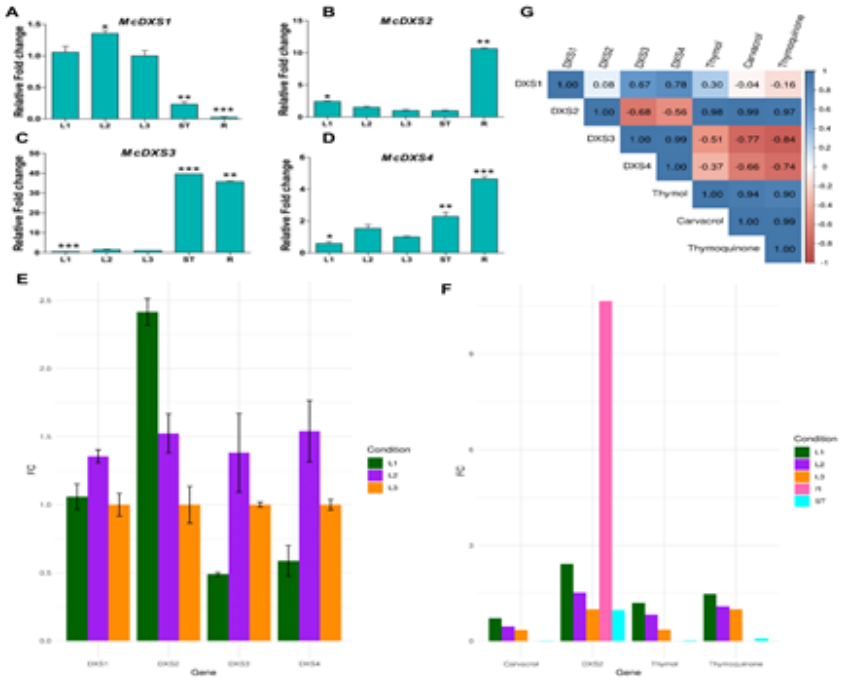


Fig 2. Gene expression and metabolite correlation. Panels A-D depict the qRT-PCR expression analysis of **(A)** *McDXS1*, **(B)** *McDXS2*, **(C)** *McDXS3*, **(D)** *McDXS4*, in different tissues of *M. citriodora*. L1, early stage of leaf development; L2, mid stage of leaf development; L3, later stage of leaf development; S, stem, and R, root. The expression of *McElongation factor* gene has been used as an internal control for normalization. The results are the mean and SD of three replicates. The statistical significance was calculated using Student's t-test. The asterisks ***P, **P and *P denote the significance of the fold change at the p-values < 0.0001, 0.001 and 0.05, respectively. Panel **E** shows the real time PCR expression results of the *McDXS*1-4 across different developmental stages of leaf only. Panel **F** represents GC-MS based the quantitative measurements of carvacrol, thymol, and thymoquinone, across the different *M. citriodora* tissues. Panel G shows the correlation between the expression of different *McDXS* genes and metabolite accumulation of carvacrol, thymol, and thymoquinone. FC represents fold-change.

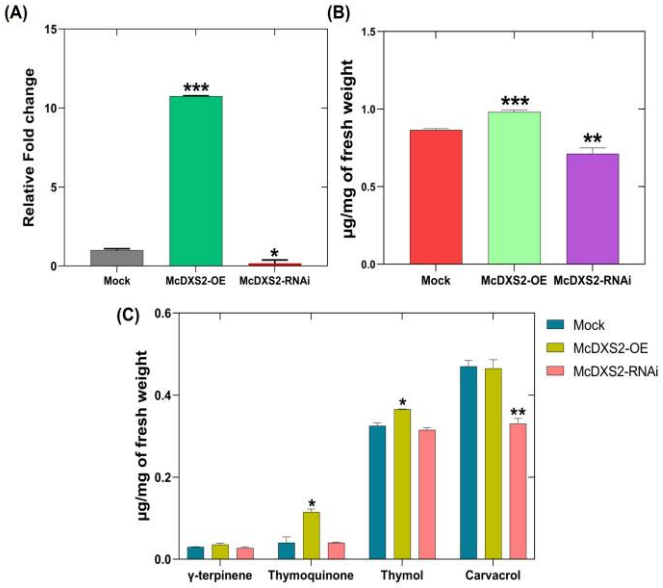


Fig 3(A) Expression analysis of *McDXS2* in agroinfiltarted leaves of *M. citriodora* with overexpression (McDXS2-OE), silencing (*McDXS2*-RNAi) and empty vector construct (Mock). The relative expression of McDXS2 in *McDXS2*-OE, *McDXS2*-RNAi, and mock was analysed by qRT-PCR, using *McEIF* gene as normalization control. The relative expression values are presented in comparison to the mock, with results expressed as the mean ± SD from three replicates. Statistical significance was determined using Student's t-test, with asterisks denoting significant differences compared to the mock: *P≤0.05, **P<0.01, ***P<0.001. **(B)** Quantitative analysis of total terpenoids in *McDXS2*-OE and *McDXS2*-RNAi transiently expressed in *M. citriodora leaves*, compared to the mock control, was performed using GC-MS. The concentration of total terpenoids was determined through area base quantification using authenticated standards and expressed as ug/mg of fresh tissue weight. The results are expressed as the mean ± SD from three replicates. Statistical significance was determined using Student's t-test, with asterisks denoting significant differences compared to the mock: *P≤0.05, **P<0.01, ***P<0.001. **(C)** shows the quantitative GC-MS analysis of individual monoterpenes in *McDXS2*-OE, *McDXS2*-RNAi, and mock.

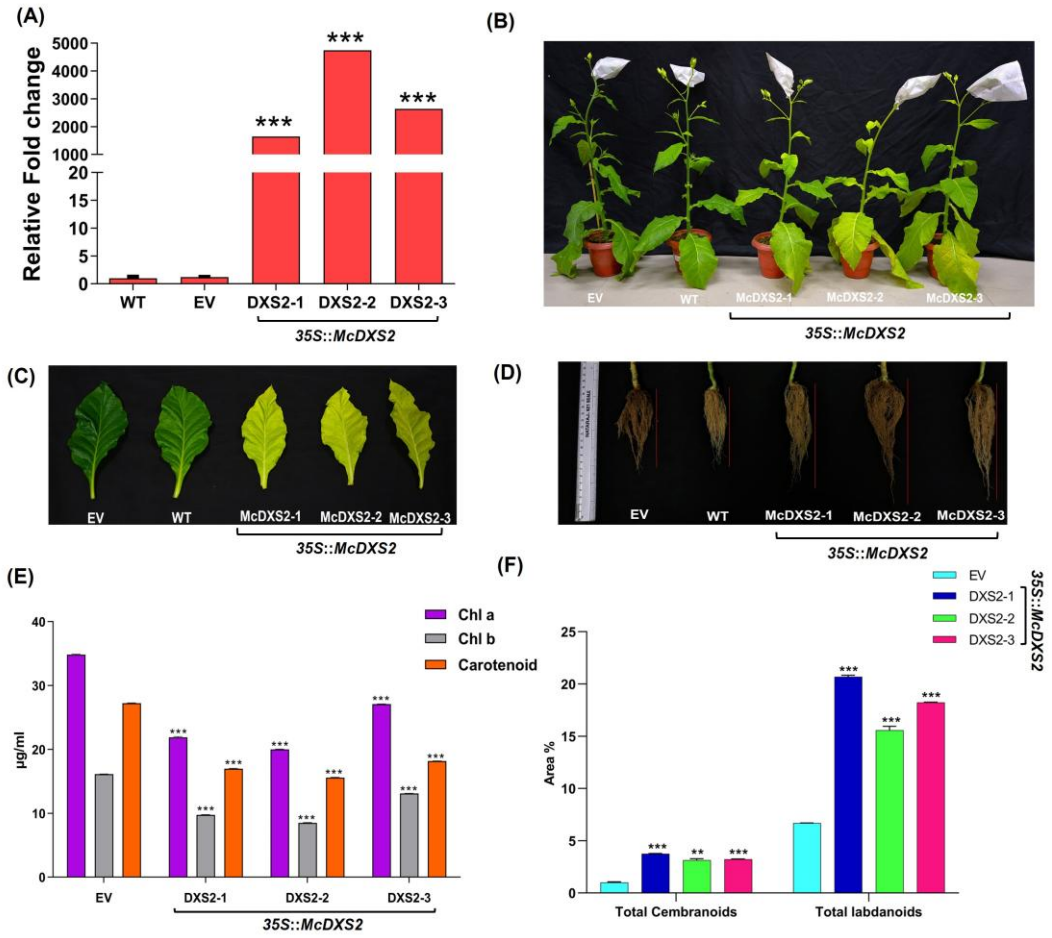


Fig. 4. Development and analysis of *Mc-DXS2*-expressing transgenic *N. tabcaum*lines. Panel A expression of *McDXS2* in *Mc-DXS2* expressing transgenic, wild-type (WT) and empty vector (EV) *N. tabcaum* plants. Panel B shows the phenotypic changes in different McDXS2-expressing different transgenic N. tabcaum plants as compared to wild-type (WT) and empty vector (EV) N. tabcaum plants. Panel C shows yellowing phenotype in the leaves of McDXS2-expressing transgenic *N. tabacum* over-expression. Panel D shows the effect of McDXS2 expression in transgenic N. tabcaum roots. Panel E shows the bar graph representing chlorophyll (Chlorophyll a and chlorophyll b) and carotenoid content in the leaves of *McDXS2*-expression transgenic N. tabcaum (*McDXS2-1*, *McDXS2-2*, and *McDXS2-3*) and WT plant (X-axis). The Y-axis represents the chlorophyll and carotenoid content (µg/ml). The results are the mean and SD of three biological replicates. The statistical significance was calculated using Student's t-test. The asterisks ***P and **P denote the significance at the p-values < 0.0001 and < 0.001, respectively. Panel F depicts the qualitative GC-MS analysis of leaf tissue of McDXS2 expression transgenic tobacco lines (*McDXS2-1*, *McDXS2-2*, and *McDXS2-3*) and empty vector (EV) tobacco plant. The Y-axis represents the relative area % of diterpenoids (total cembranoids and labdanoids). Cembraboids and labdanoids were identified following GC-MS analysis of hexane extract of leaves. The total content of cembranoids and labdenoids was calculated by adding the peak area percentages of cembranoids and labdanoids.

A promoter region of *McDXS2* was cloned through genome-walking approach. The *in silico* analysis of the promoter region suggested the presence of several putative *cis*-acting elements. Expression of *McDXS2 promoter-GUS* fusion in the *M. citriodora* leaf revealed that *McDXS2* promoter is primarily active in the glandular trichomes of *M.citriodora* (Fig. 5).

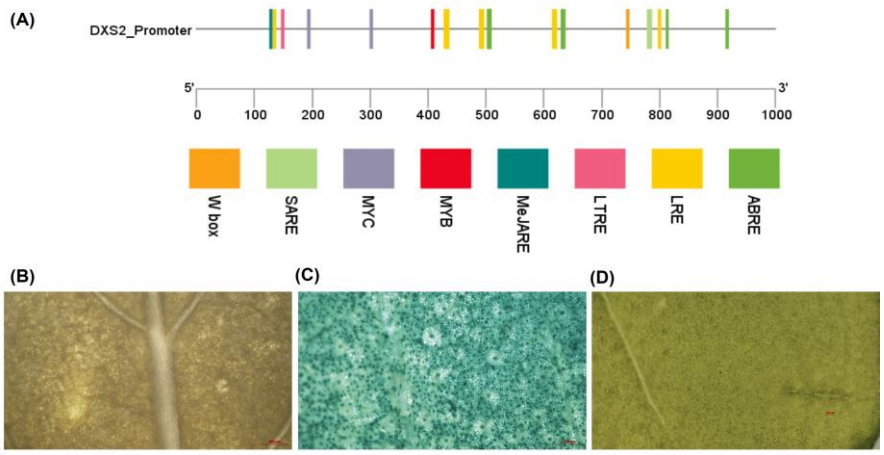


Fig. 5. (**A)** Represents the distribution of key non-overlapping motifs in the *McDXS2* promoter sequence. **(B)** Shows GUS staining of empty vector (EV) agroinfiltrated in *M. citriodora* leaves. **(C)** GUS staining of *M. citriodora* leaves infiltrated with *CaMV35Spro::GUS*, serving as a positive control. **(D)** Shows GUS staining under *McDXS2pro::GFP-GUS* agroinfiltration.

In order to study the biosynthesis of γ-terpinene in *M. citriodora*, the terpene synthase gene family was identified using the in house transcriptome resource of *M. citriodora*. Based on the phylogenetic analysis, gene expression and metabolite profile, *McTPS22* was selected as a candidate gene involved in the biosynthesis of γ-terpinene in *M. citriodora* (Fig. 6). *McTPS22* was expressed as a recombinant protein in *E.coli*, and purified. When incubated with geranyl diphosphate (GPP), the recombinant McTPS22 converted it into γ-terpinene, confirming that McTPS22 is γ-terpinene synthase. McTPS22 was localized into the plastids as confirmed by agro-infiltration of McTPS22-YFP fusion construct in the *Nicotiana benthamiana*levaes (Fig. 7). The co-expression of *DXS2*, *GPP*, and *McTPS22* in the *Nicotiana benthamiana* leaves led to the production of γ-terpinene. Further, the promoter region of *McTPS22* was reported to be primarily active in the glandular trichomes of *M. citriodora*.

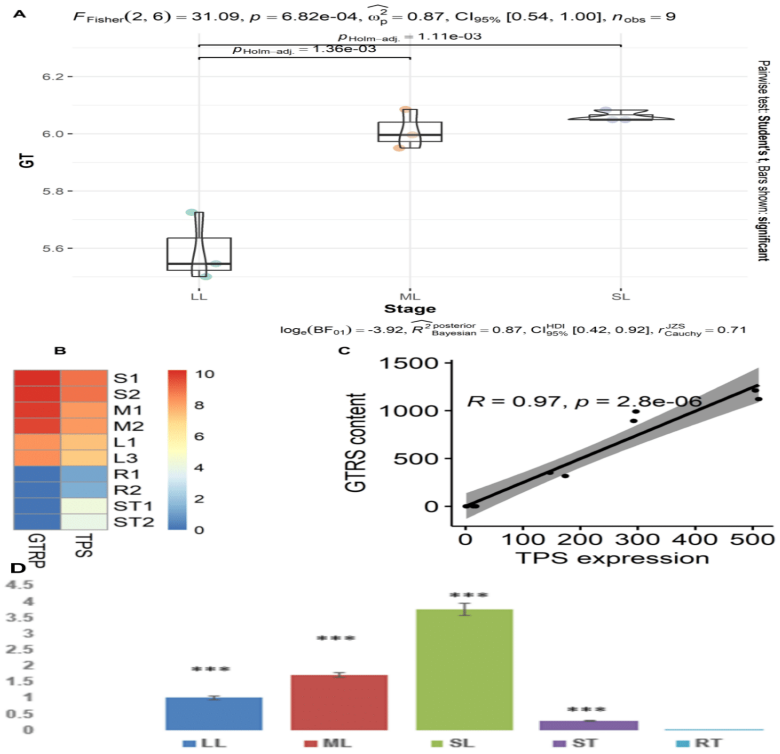


Fig. 6: Relationship between the *TPS* gene expression and γ-terpinene accumulation in *M. citriodora.* (A) Graphical summary of ANNOVA showing influence of leaf stage on γ-terpinene accumulation. The bars connecting the stages depict significant differences in mean γ-terpinene accumulation between those stages. (B) Heatmap showing tissue specific variation in TPS gene expression and γ-terpinene accumulation. Color legend is based on log10 scale. (C) Correlation between γ-terpinene accumulation and TPS gene expression. (D) Tissue-wide qRT-PCR expression analysis of *McTPS22* in SL: Small leaf, ML: Medium leaf, LL: Large leaf, ST: Stem, and RT:Root. The expression levels have been expressed as fold change with respect to the expression level in the large leaf (Large leaf). The expression of the *McELF* gene was used for the normalization of the expression. The results reflect the mean and standard deviation of three replicates. Student's t-test was used to calculate statistical significance. The asterisks * **P, * *P, and *P denote the significance of the fold change at the p-values of < 0.0001, 0.001, and 0.05, respectively. GTRS: gamma terpinene.

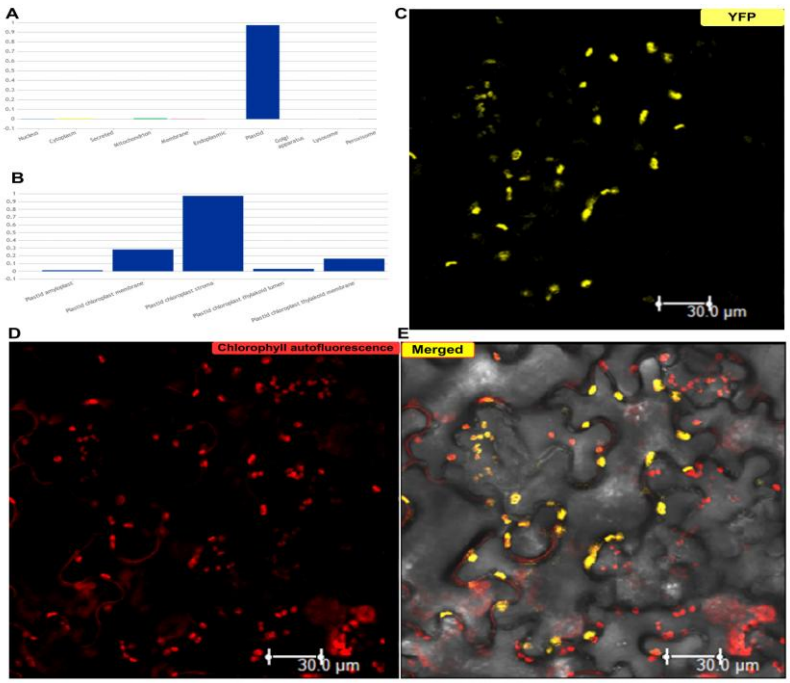


Fig. 7: Summary of sub-cellular prediction and co-localization analysis of *McTPS22* gene in *N. benthamiana.* (A) & (B) show *in-silico* predicted sub-cellular localization of *McTPS22* using DeepLoc&MULocDeep. (C) Represents emitted fluorescence signal by the McTPS22 C-terminally tagged with e-YFP. (D) Represents the autofluorescence signal of chlorophyll. (E) Represents the merged chlorophyll autofluorescence and e-YFP signals.

(B) Identification of molecular regulators of glandular trichome development in the family Lamiaceae

Homology searches led to the identification of putative homologs of the regulators of glandular trichome development in *M. citriodora*. These regulators include McHDZ1 and McHDZ8, belonging to the HD-ZIP family of transcription factors. The phylogentic analysis grouped them with the AaHD1 and AaHD8, of *A.annua*, which act as positive regulators of glandular trichome development (Fig. 1). Full-length CDS corresponding to *McHDZ1* and *McHDZ8* genes have been cloned and their plant expression constructs have been developed (Fig. 2) The plant expression constructs of *McHDZ1* and *McHDZ8* have been transformed in *N. tabacum*. Currently, transgenic lines expressing McHDZ1 and McHDZ8 are being developed. Two more putative regulators of glandular trichome development in *M. citriodora* have been identified. These regulators show homology with *MIXTA* and *MYC2* genes. The full-length CDS of these two genes have been cloned.

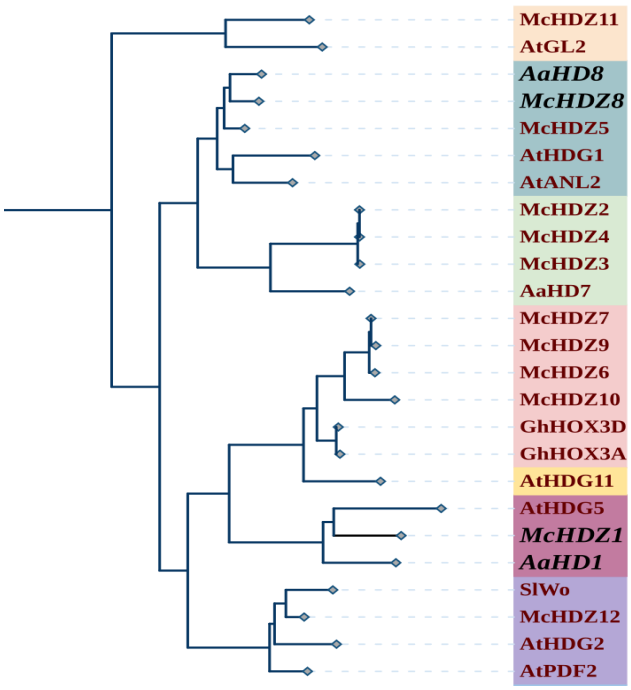


Fig. 1: Phyolgentic analysis of HDZIP-IV family genes showing the homologs of AaHD8 and AaHD1, which are involved in the glandular trichome development.

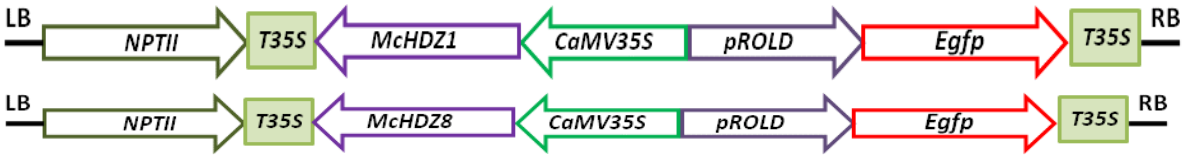


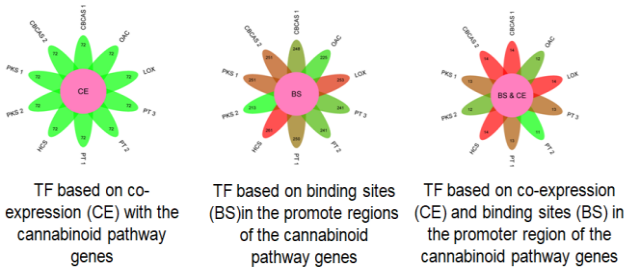
Fig. 2: Schematic representation of T-DNA regions of the developed plant expression vector for McHDZ1 and McHDZ8 in pK7WG2D vector. The developed constructs were transformed in *Agrobacterium tumefaciens* (strain GV3101). The transformed A. *tumefaciens* was used for the genetic transformation of *N. tabacum*.

(C) Identification of candidate transcription factors involved in the regulation of cannabinoid biosynthesis in *Cannabis sativa*

Using publically available transcriptome resource of *C. sativa* (More than 300 transcriptomes), co-expression analysis of structural genes of cannabinoid biosynthesis with the transcription factor genes was carried out. The analysis led to the identification several transcription factor genes displaying close positive correlation with the genes of cannabinoid biosynthesis. Based on the co-expression analysis and the putative binding sites, present in the promoter regions of the genes of cannabinoid biosynthesis, 10

candidate transcription factors belonging to DOF, MYB, ERF, SBP and TCP, bHLH families were identified. These TFs showed co-expression with the genes of cannabinoid biosynthesis, and could be involved in the regulation of cannabinoid biosynthesis (Fig. 1).

(A)



TF based on co-expression (CE) with the cannabinoid pathway genes

TF based on binding sites (BS)in the promote regions of the cannabinoid pathway genes

TF based on co-expression (CE) and binding sites (BS) in the promoter region of the cannabinoid pathway genes

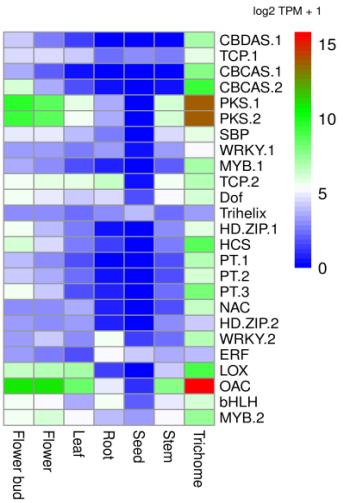


Fig. 1: Co-expression analysis of the genes of cannabinoid biosynthesis and transcription factors. (A) The identified transcription factor genes coexpressing with the genes of cannabinoid biosynthesis (B) Heat map showing expression of coexpressed TF genes with the genes of cannabninoid biosynthesis. The expression values are in the form of log2 transformed TPM (transcript per million) in different tissues of *C. sativa.*

RAJENDRA BHANWARIA

Dr. Rajendra Bhanwaria (Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

S. No	Authors	Title of the Article	Name of Journal
1.	Tamanna Bhardwaj, Ruby Singh, Harpreet Singh, Rajendra Bhanwaria, Sumit G Gandhi, Renu Bhardwaj, Ajaz Ahmad, Parvaiz Ahmad (2024)	Pseudomonas consortium improves soil health and alleviates cadmium (Cd) toxicity in Brassica juncea L. via biochemical and in silico approaches	Plant Stress Volume :14 Pages :100611

2.	Ishfaq Nabi Najar, Prayatna Sharma, Rohit Das, Krishnendu Mondal, Ashish Kumar Singh, Sonia Tamang, Palash Hazra, Nagendra Thakur, Rajendra Bhanwaria, Sumit G Gandhi, Vinod Kumar	In search of poly-3-hydroxybutyrate (PHB): A comprehensive review unveiling applications and progress in fostering a sustainable bio-circular economy	Food and Bioproducts Processing Volume: 148 Pages: 11-30
3.	Sabha Jeet, Ravindra Verma, Gajendra Kumar Yadav, Sonali Bhagat, Shahina Tabassum, Kamlesh Kumar, Rajendra Bhanwaria	Morphological and phenological characteristic, oil yield, quality and economics of Lemon bee balm (*Monarda citriodora* Cerv. ex-Lag) at diverse environment	Journal of Essential Oil-Bearing Plants Volume: 27 Issue: 4 Pages: 1079-1101
4.	Sabha Jeet, Ravindra Verma, Sonali Bhagat, Rajendra Bhanwaria, Shahina Tabassum, Gajendra Kumar Yadav	Physicochemical Properties of Soil and Plant Geometry in Oil Yield, Quality and Economics of Lemongrass in Rainfed Bundelkhand Region, India	Journal of Scientific & Industrial Research (JSIR) Volume: 84 Issue: 02 Pages: 136-147
5.	Chahat Chopra, Sabha Jeet, Sonali Bhagat, Shahina Tabassum, Rajendra Bhanwaria	Morphological and phytochemical characteristics of *Cymbopogon flexuosus* (Nees ex Steud.) W.Watson cultivars at different harvest intervals in the Western Himalayas, India	Journal of the Science of Food and Agriculture DOI-https://doi.org/10.1002/jsfa.14354

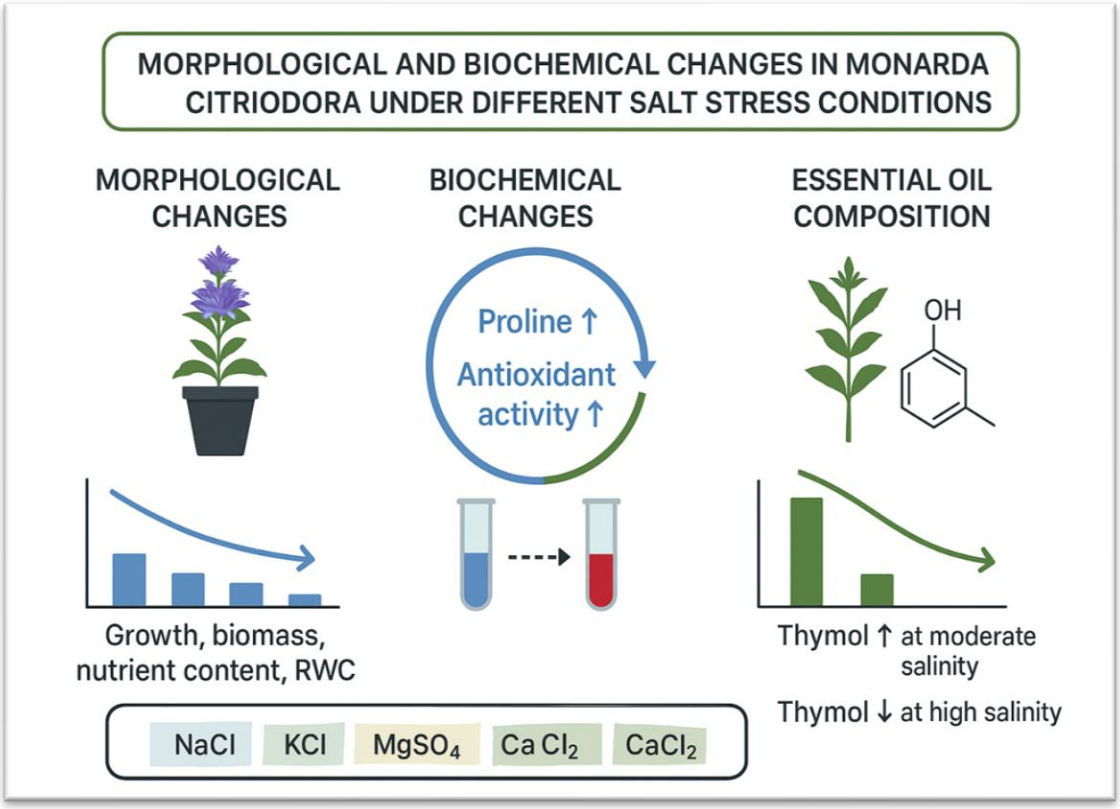
2. Scientific work done:

Morphological and Biochemical changes in Monarda citriodora under different salt stress conditions.

This study investigated the effects of four distinct salts—sodium chloride (NaCl), potassium chloride (KCl), magnesium sulfate ($MgSO_4$), and calcium chloride ($CaCl_2$)—applied at five concentrations (0, 25, 50, 100, and 200 mM) on various physiological, biochemical, and phytochemical attributes of

Monarda citriodora. The evaluated parameters included growth characteristics, biomass production, nutrient content, relative water content (RWC), proline accumulation, antioxidant activity, and the chemical composition of essential oil. The experiment was conducted in pots under a completely randomized design (CRD), where plants were irrigated with the respective salt solutions for 60 days following two months of transplanting.

The results demonstrated that increasing salinity levels, regardless of salt type, adversely affected nutrient uptake, growth, biomass accumulation, chlorophyll content, and RWC. In contrast, stress-responsive metabolites showed a marked increase under salinity stress. Proline concentration and antioxidant activity increased proportionally with salt concentration, suggesting their role in osmotic adjustment and oxidative stress mitigation. The highest proline content (83.50 mg g^{-1} fresh weight) was recorded under 200 mM NaCl treatment, while maximum antioxidant activity, measured as DPPH radical scavenging (43.24% inhibition), was observed with 200 mM MgSO4.



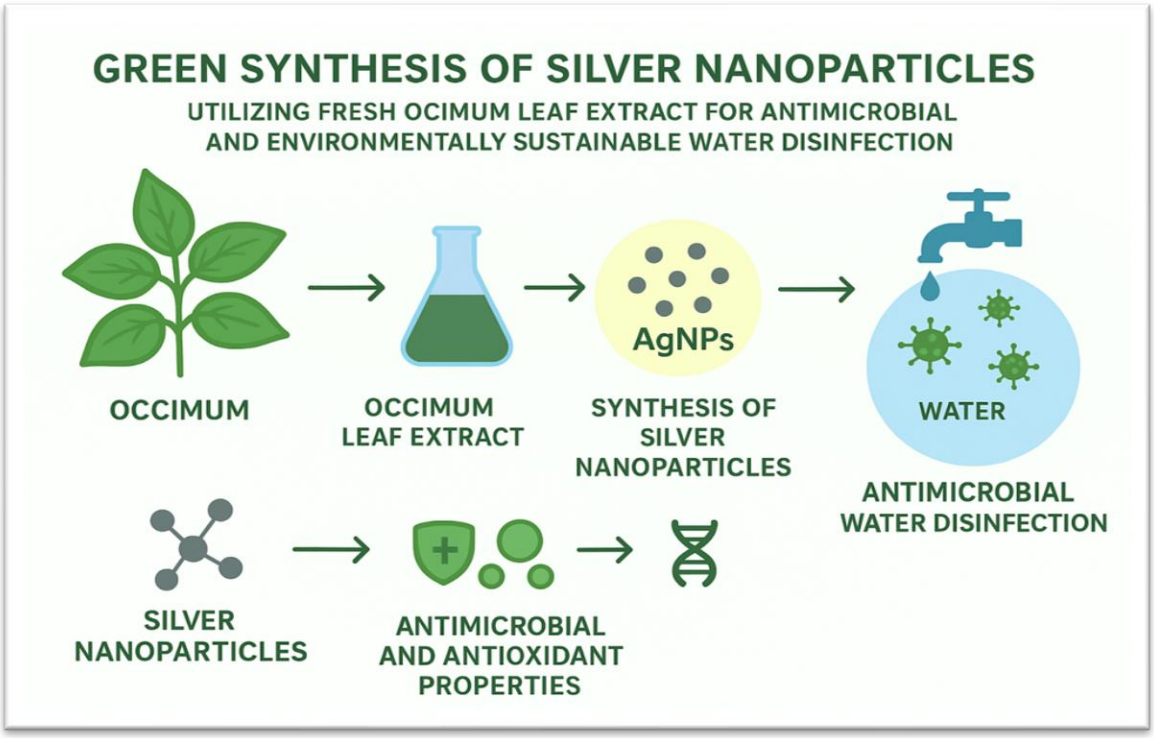
Gas Chromatography–Mass Spectrometry (GC–MS) analysis revealed thymol as the predominant essential oil constituent, accounting for 39.26–91.36% of the total oil composition. Interestingly, moderate salinity (50 mM) enhanced thymol content, with the highest levels detected under 50 mM KCl (91.36%), followed closely by 50 mM NaCl (91.07%) and 100 mM KCl (88.58%). Conversely, severe salinity (200 mM $CaCl_2$) led to the lowest thymol percentage (39.26%). These findings indicate that moderate salt stress can act as a metabolic modulator, enhancing thymol biosynthesis and, consequently, essential oil quality.

Furthermore, salt treatments significantly altered the overall chemical profile of *M. citriodora*, with the appearance of novel compounds in the essential oil under stress conditions. This suggests that salinity not only affects quantitative yield but also qualitatively modifies secondary metabolite composition. However, further research is necessary to elucidate the biosynthetic pathways underlying these changes and to determine the functional roles and potential applications of the newly induced compounds.

Overall, the study underscores the profound influence of environmental stressors, such as salinity, on plant metabolite profiles. It also highlights the possibility of strategically manipulating salt concentrations to optimize essential oil yield and quality in *M. citriodora*.

Green synthesis of Silver Nanoparticles utilizing Ocimum leaf extract for antimicrobial and environmentally sustainable water disinfection purposes. Due to extensive pollution, natural water bodies require sustainable treatment for effective purification. So, the synthesis of silver nanoparticles [AgNPs] was achieved through eco- friendly methodologies. The silver nanoparticles displayed a crystalline structure and had a spherical geometry further consisting of alkanes, flavonoids, and phenols as key components. The findings indicates that silver nanoparticles are highly effective against multiple pathogens and also exhibits strong antimicrobial properties. Therefore, it has a significant impact on the remediation of polluted wastewaters. At the nano scale nanoparticle shows distinct physical and chemical properties. These unique properties have significant implications for commercial and industrial applications. Silver nanoparticles have been shown to possess both antioxidant and antimicrobial properties against both the types of bacterial strains of Gram-positive and Gram-negative bacteria.

To avoid the drawbacks of traditional physical and chemical synthesis methods which require high energy consumption and lead to the generation of toxic byproducts, the production of silver nanoparticles has shifted towards biological methods. One such approach is green synthesis, a method that employs plants for nanoparticle synthesis. Plant based Phytochemicals possess natural reducing and stabilizing agents allowing for the synthesis of nanoparticles with enhanced bioactivity and therapeutic potential. Ocimum is renowned for its well documented therapeutic benefits and therefore considered a prominent medicinal plant.



In this research, leaf extract of Ocimum was used as a bio-reductant for the synthesis of silver nanoparticles by adopting a green chemistry approach which is both economical and eco-friendly. The characterisation of silver nanoparticles synthesised from Ocimum leaf extract was performed using various techniques which included: UV- Visible spectroscopy, FTIR, XRD, FESEM and HRTEM. Additionally, the green synthesised silver nanoparticles were investigated for their potential uses in antimicrobial and photocatalytic processes.

RAVAIL SINGH

Dr. Ravail Singh (Principal Scientist) with his Research Group

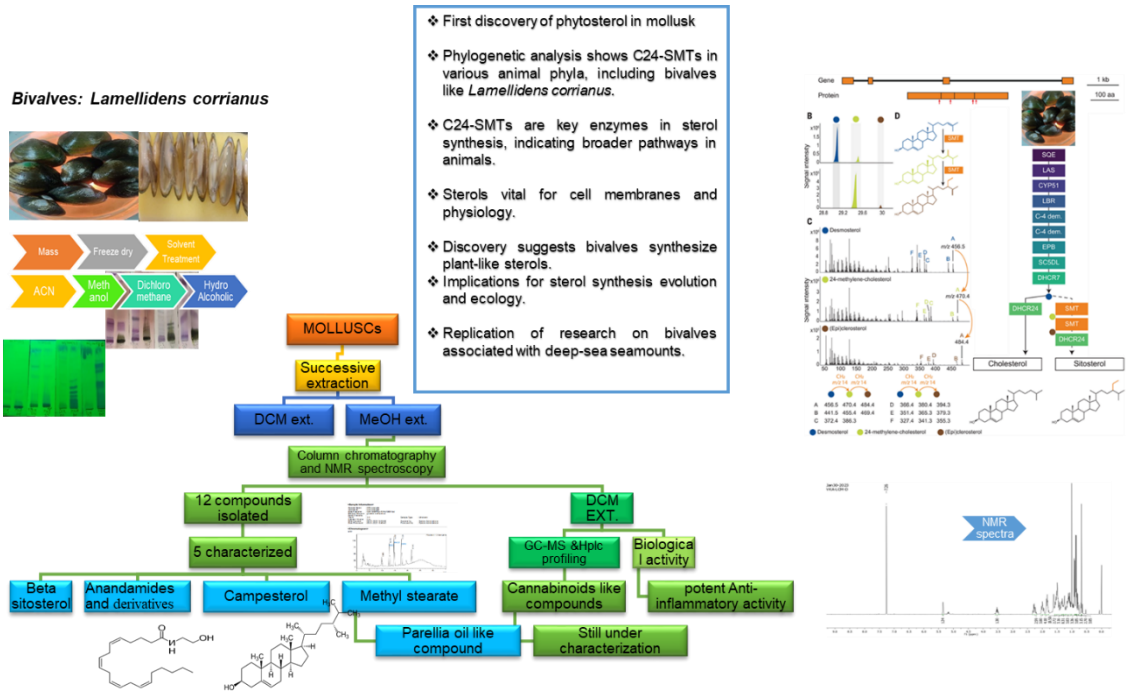
1. Publications/Patents:

Publications:

- Shamsun Nisa, Bhawna Ghora, Vanila Sharma, Jyoti Chandan, Parvinder Pal Singh, Mohd Hassan, Ravail Singh* 2024 Codon usage in Cannabis sativa and pathogens Ecological Genetics and Genomics Netherlands 33, 100296 10.1016/j.egg.2024.100296
- Waqas Ahmed, Ajaz Ali Ahmed Khan, Gourav Sharma, Deepika Singh, Ravail Singh*2024 Heavy metal impact on Limnodrilus cervix. Process Safety and Environmental Protection UK 188, 595–607 10.1016/j.psep.2024.05.147
- Chandan J., Gupta S., Ahmed Z., Ravail Singh*, et al. 2025 Metabolite profiling from Xiphinemanuragicum endofauna Environmental Science and Pollution Research Germany 32, 8448–8461 10.1007/s11356-025-36228-3
- Edwin Dach, Daniela Zeppilli, Jozée Sarrazin, Ravail Singh, et al. 2025 MarNemaFunDiv: marine nematode functional traits database Nature-Scientific Data UK 12, 222 10.1038/s41597-025-05105-6

2. Scientific work done:

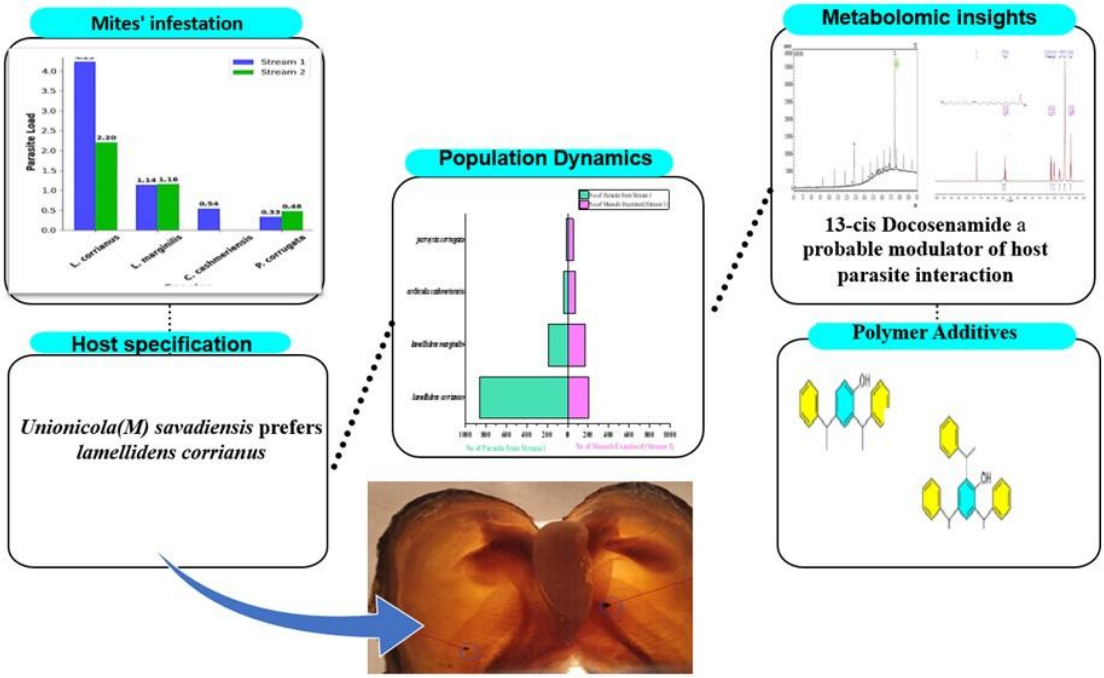
At CSIR-Indian Institute of Integrative Medicine (CSIR-IIIM) Jammu, my team has established a pioneering research group, “Freshwater Invertebrate Community from Jammu and Kashmir: Dynamics from Ecological Significance to Therapeutic Potential”. This initiative investigates the biodiversity, ecological roles, and therapeutic potential of aquatic invertebrates in Jammu and Kashmir’s marine and freshwater ecosystems, aligning with CSIR-IIIM’s mandate to advance scientific discovery, drug development, and sustainable biotechnological solutions through integrative research. A landmark achievement—the isolation of phytosterols from mollusks—has unveiled a novel domain for pharmaceutical innovation, reinforcing CSIR-IIIM’s mission to harness natural resources for health and industrial applications. Globally, this work contributes to biodiversity conservation, drug discovery, and ecological research, addressing pressing challenges in healthcare and environmental sustainability.



Key Objectives and Achievements:

Aquatic Invertebrate Community Database: We are developing a comprehensive, open-access inventory of aquatic invertebrates across Jammu and Kashmir’s rivers, lakes, and coastal marine habitats. This database catalogs species diversity, distribution, population dynamics, and ecological interactions, providing a robust resource for conservation, ecosystem management, and bioprospecting. By documenting endemic and rare species, it supports global biodiversity initiatives like the Convention on Biological Diversity, enhancing understanding of aquatic ecosystems and informing international conservation strategies. This aligns with CSIR-IIIM’s goal of fostering knowledge-driven solutions for sustainable development.

Bioprospection Ventures: Our bioprospecting efforts target marine and freshwater invertebrates to identify novel bioactive compounds and genetic resources. The isolation of phytosterols from mollusks, with potential applications in anti-inflammatory, anticancer, and cholesterol-lowering therapies, exemplifies our success. This work advances CSIR-IIIM's mandate to develop natural product-based therapeutics, contributing to global drug discovery by providing lead molecules for pharmaceutical pipelines. It also supports biotechnological innovations, such as nutraceuticals and cosmeceuticals, addressing global health demands.

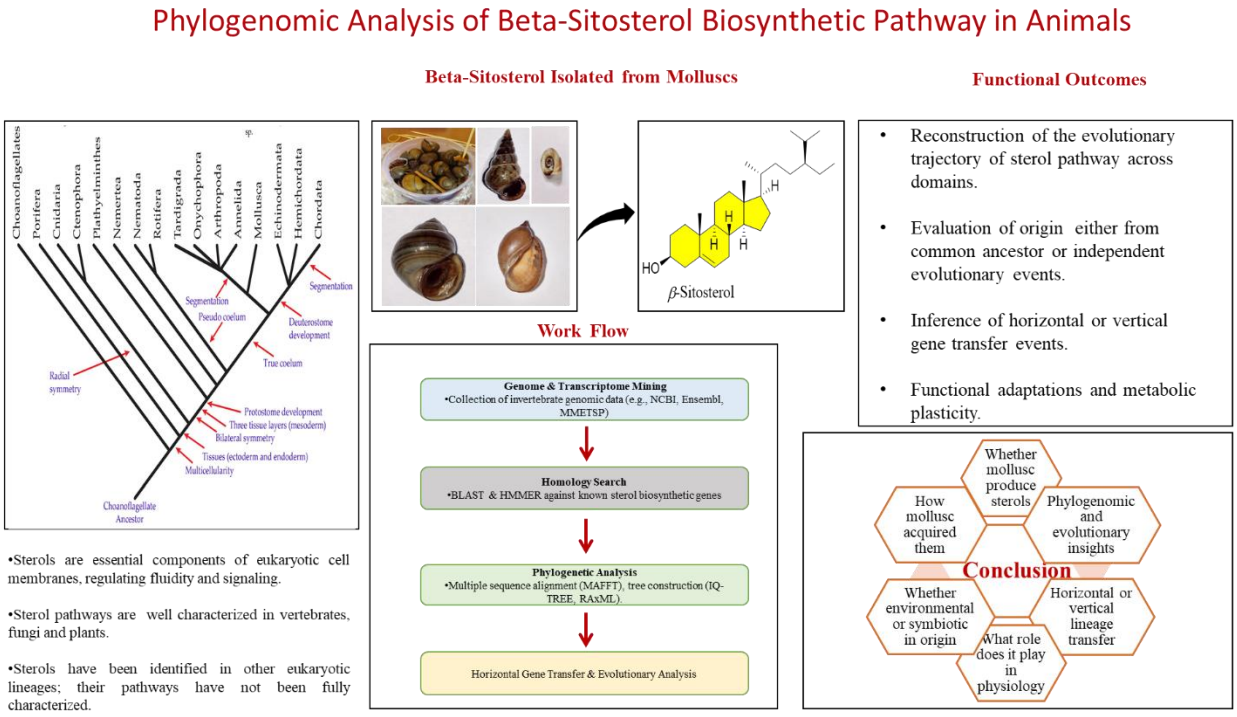


Establishment of Benthic Invertebrate Research Laboratory: We have launched the first benthic invertebrate research laboratory at CSIR-IIIM Jammu, equipped with state-of-the-art molecular tools, high-resolution microscopes, and culturing facilities for morphological and molecular taxonomic identification of aquatic and soil invertebrates. The laboratory's research includes:

Morphological and Molecular Strategies: We explore the adaptive mechanisms of invertebrates like earthworms, mollusks, and nematodes, focusing on their morphology and gut microbiota. This research elucidates their roles in nutrient cycling, sediment stabilization, and ecosystem resilience, aligning with CSIR-IIIM's focus on bioresource utilization. Globally, it informs ecological restoration and sustainable agriculture by leveraging invertebrates' ecosystem services.

Genome Mining for Bioactive Compounds: Using genome mining, we identify pharmaceuticals and bioactive molecules within benthic invertebrates. This work supports CSIR-IIIM's drug discovery goals by uncovering novel compounds for biotechnology, pharmaceuticals, and environmental remediation.

Globally, it contributes to bioprospecting frameworks, offering solutions for antibiotic resistance, chronic diseases, and ecosystem health.



Screening of bioactive molecules and investigating their therapeutic potential

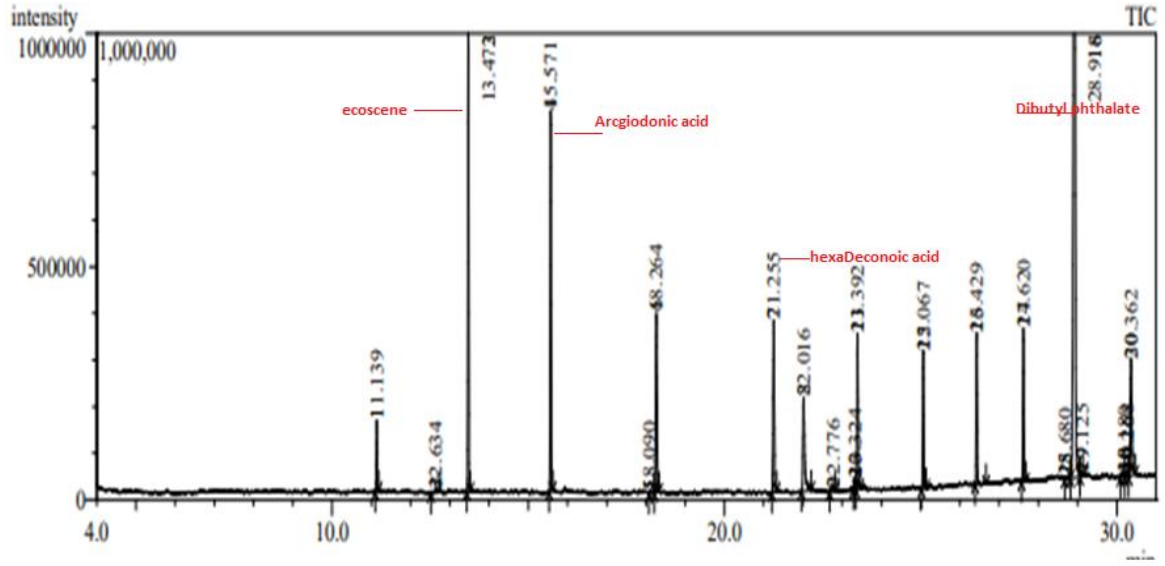
Objective: The objective of this study is to screen bivalve organisms, specifically Lamellidenscorrianus and Lamellidensmargenilis, for their bioactive molecules and investigate their therapeutic potential.

Methodology: The research begins with the screening of the dominant species, Lamellidenscorrianus, to fulfill the objective. Untargeted metabolomics profiling using GC-MS and LC-MS techniques is employed for preliminary analysis. The satisfactory results obtained in the initial phase of analysis lead to the next step, where the crude extract is loaded onto a column packed with neutral alumina.

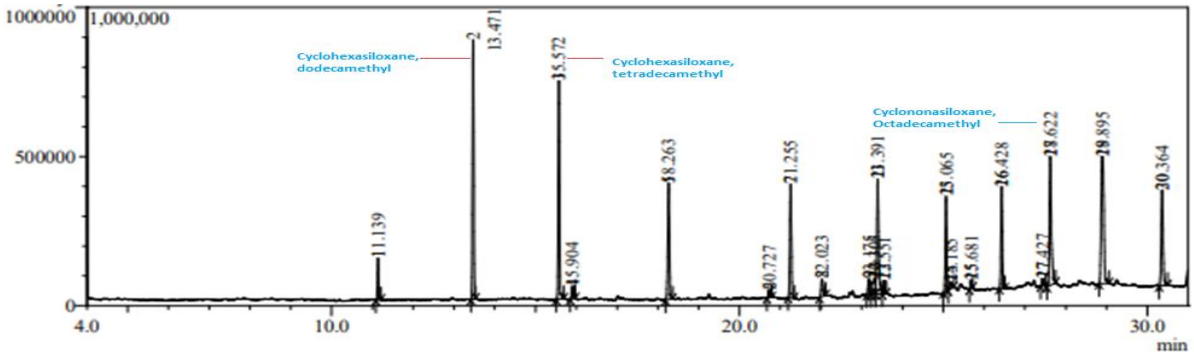
A total of 10 compounds have been isolated so far, with the majority of them being phyto products of mysterious occurrence and origin. These compounds, including phyto cannabinoids and phyto sitosterol (beta sitosterol), are characterized using NMR spectroscopy. Additionally, various types of annandamides have been characterized in this study.

Significance: This research aims to uncover bioactive molecules present in bivalve organisms, particularly Lamellidenscorrianus and Lamellidensmargenilis, and explore their therapeutic potential. The isolation and characterization of these compounds will contribute to the understanding of their origin, structure, and potential applications in medicine. The study utilizes advanced analytical techniques and highlights the diverse nature of bioactive molecules found in these bivalve species. The

findings have the potential to pave the way for the development of novel therapeutic agents and enhance our knowledge of the naturalresources available in aquatic ecosystems.



GCMS Spectra of Crude MeOH extract of Lamellidenscorrianus



GCMS Spectra of Crude DCM extract of Lamellidenscorrianus

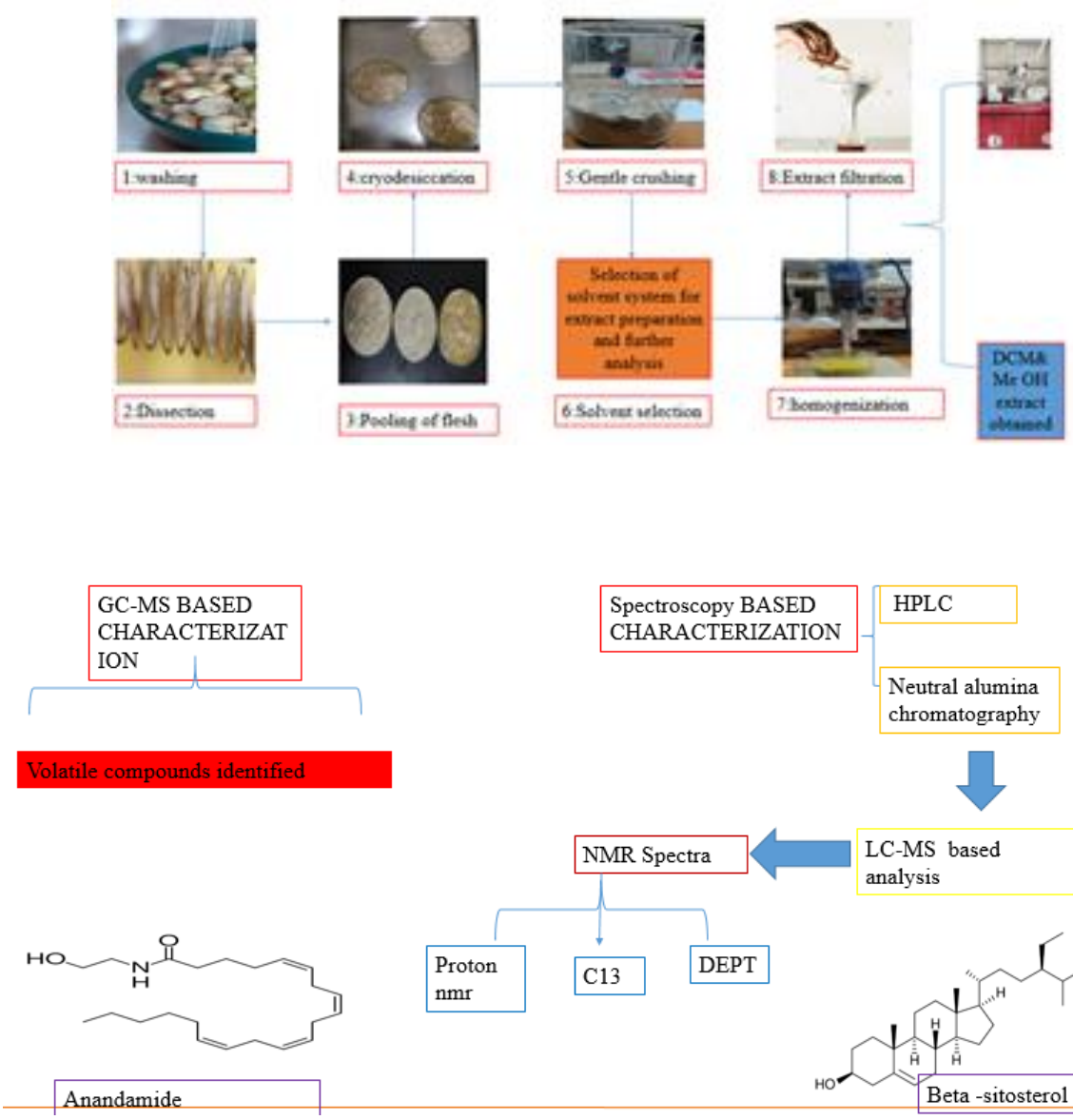


Fig: methodology and characterized compounds

Genome mining of the invertverates:

Lamellidenscorrianus, a freshwater mussel belonging to the class Bivalvia, is prominently distributed in the aquatic ecosystems of the Indian subcontinent. Noteworthy for its significant pearl-producing capabilities, this mussel holds economic, nutritional, medicinal value, and substantial environmental importance. Despite its relevance in freshwater aquaculture, a comprehensive exploration of its genomic, evolutionary, and ecological perspectives remains elusive. The current study aimed to bring forth insights into the genomic structure and complexity of L. corrianus through de novo genome assembly. The genomic revelations highlighted an inclination towards AT richness and a wealth of

enriched pathways, as indicated by Gene Ontology and KEGG analysis. Furthermore, evolutionary aspects were investigated, examining the role of forces such as mutation and natural selection in shaping codon Usage Bias (CUB) through various codon indices like ENC, CAI, and CBI. Besides, the study also encompassed population dynamics and the impact of hydrological parameters on these mussels. Temperature, pH, and alkalinity emerged as dominant factors affecting the species. In addition the current investigation contribute to our understanding of the evolutionary processes shaping the genomes of mollusc species, shedding light on the dynamics of gene family evolution, phylogenetic relationships. Overall, this study contributes valuable insights into the ecological, genomic, and evolutionary dimensions of L. corrianus. The findings provide a foundation for future studies, highlighting the significance of this mussel species in ecological contexts and suggesting its potential for further practical applications in diverse research areas.

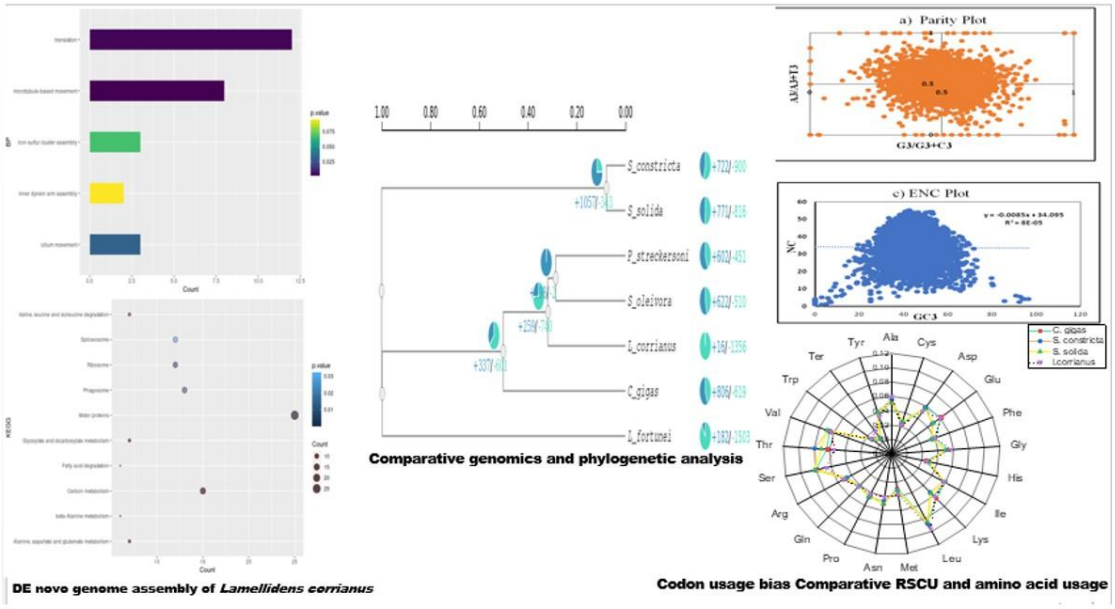


Figure Analysis of predicted genes for gene ontology (a) CC: Cellular component (b) BP: Biological process (c) MF: Molecular function (d) KEGG enrichment pathway

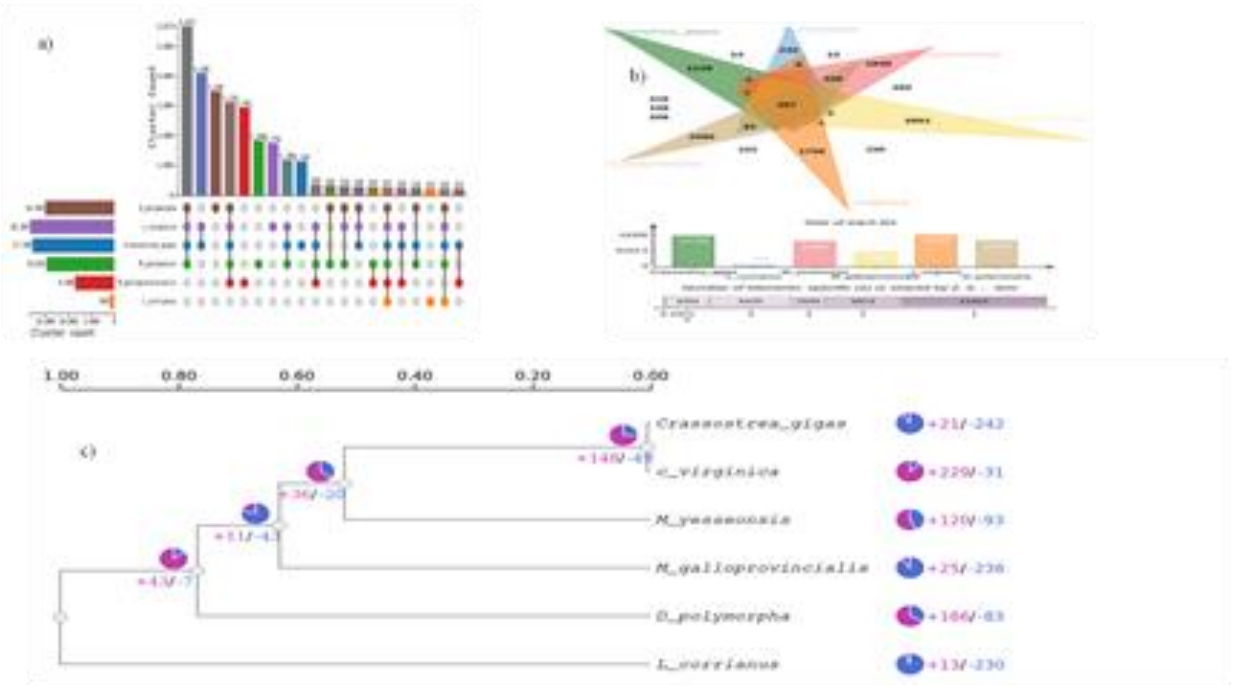
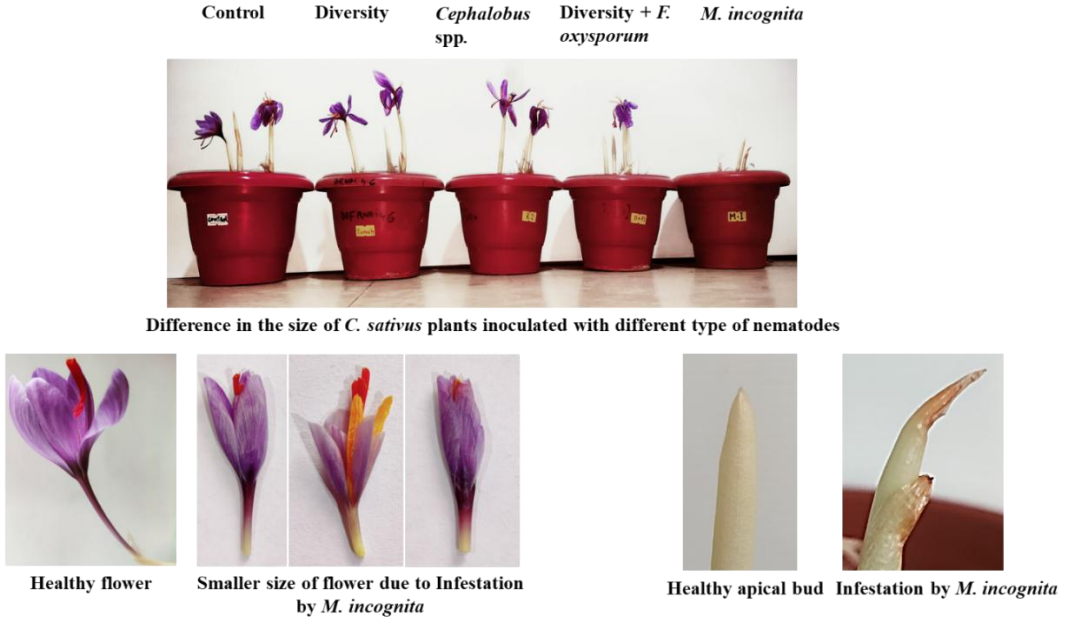


Figure Comparative genome analysis between *Lamellidenscorrianus* and other selected mollusk species (a) orthologous gene clusters (b) Venn diagram (c) Phylogenetic tree of gene families.

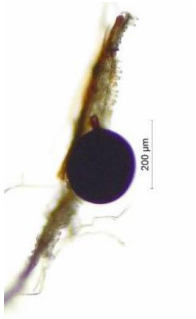
Investigating the Impact of Nematode and Fungal Interactions on Saffron (*Crocus sativus*) Secondary Metabolites: A Pot Experiment.

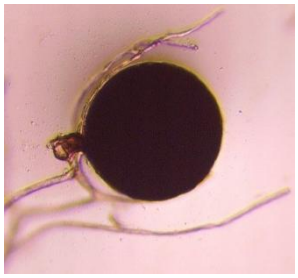
Plant parasitic nematodes induced phenotypic variation in *C. sativus* flowers and apical buds



Aim and Objectives

This study aimed to elucidate the complex interactions between the rhizosphere nematode community, fungal pathogens, and *Crocus sativus* (saffron), focusing on their influence on plant growth, phenotypic traits, and secondary metabolite production, particularly crocin, a key therapeutic compound. Our objectives were: (1) to assess the effects of beneficial (*Cephalobus* spp.) and pathogenic (*Meloidogyne incognita*) nematodes, natural nematode diversity, and their interactions with *Fusarium oxysporum* on saffron's phenotypic traits, (2) to quantify variations in crocin content across treatments using high-performance liquid chromatography (HPLC), and (3) to explore the ecological and therapeutic implications of these interactions for sustainable saffron cultivation.






- **Free-Living Nematodes:**

- Bacterial feeders (nutrient cycling).
- Fungal feeders (organic matter decomposition).
- Predators (ecosystem balance).

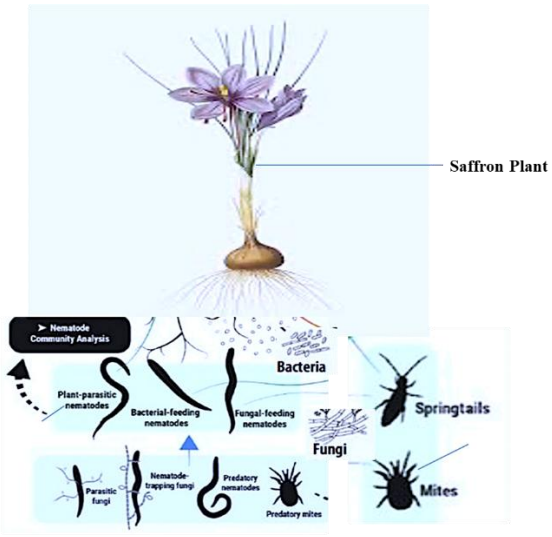
- **Plant-Parasitic Nematodes (PPNs)** : Indicate poor soil health.

- **Applications of Nematodes in Soil Health Monitoring:**

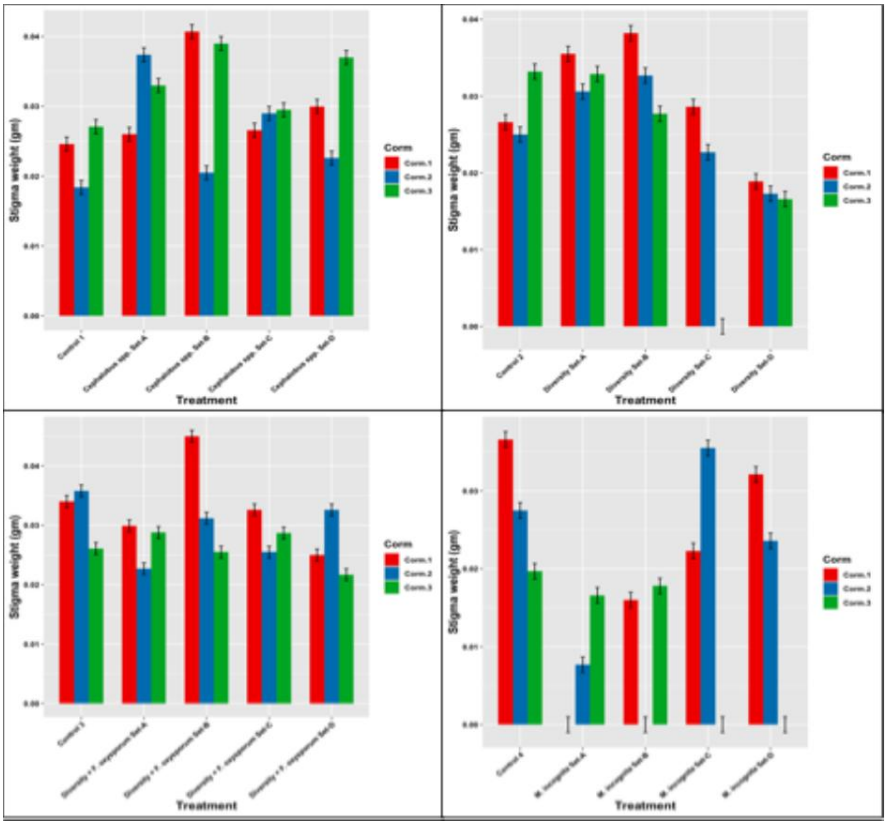
- **Soil Management:** Farmers and ecologists can use nematode population analysis to evaluate the impact of agricultural practices and develop strategies for soil restoration.

- **Pollution Assessment:** Nematode diversity can help identify soil contamination from heavy metals, pesticides, or other pollutants.

- **Climate Change Studies:** Nematodes are also used to study the effects of climate change on soil ecosystems, as they respond to changes in temperature and moisture levels.

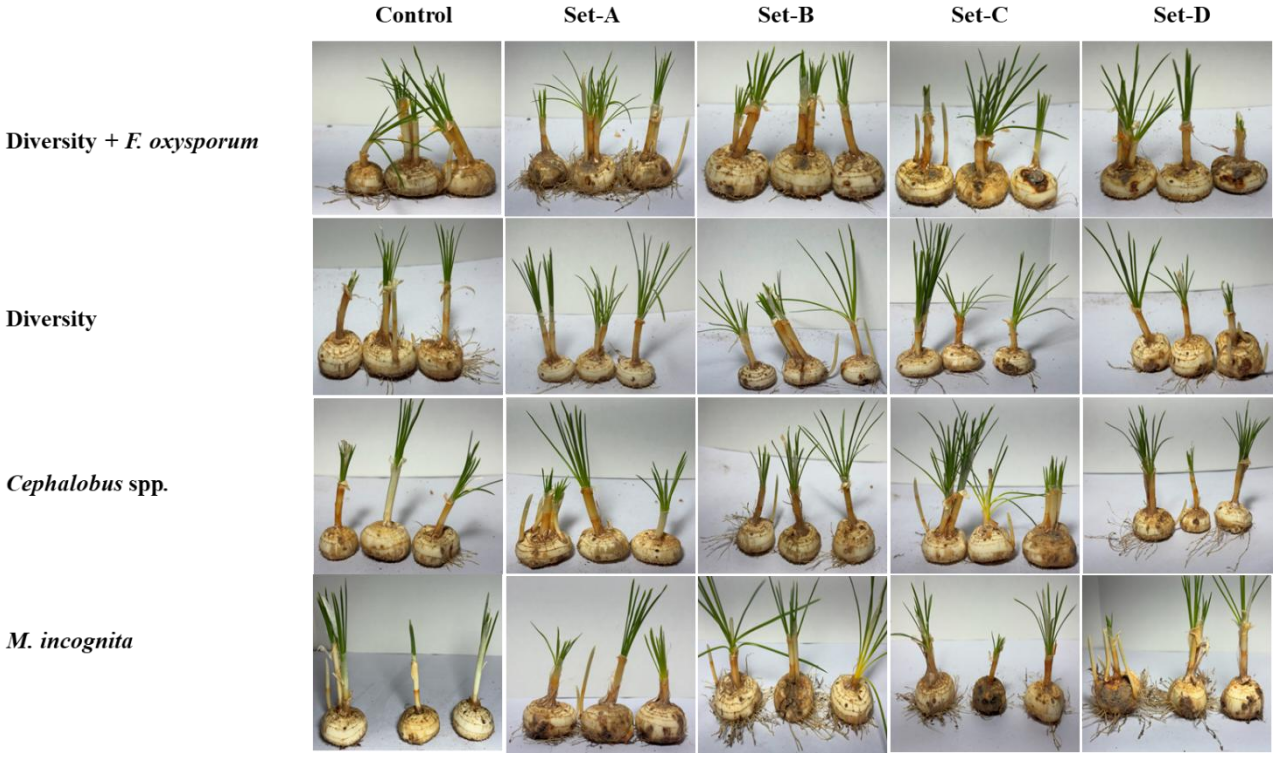


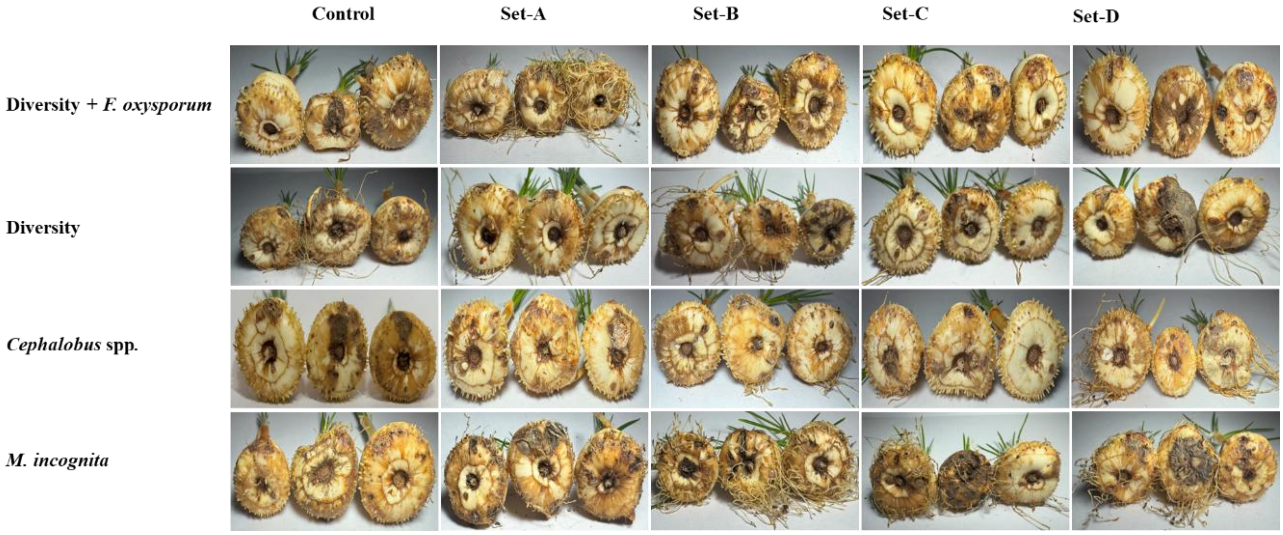
Schematic diagram of the underground invertebrate community attached to the *crocus sativus*



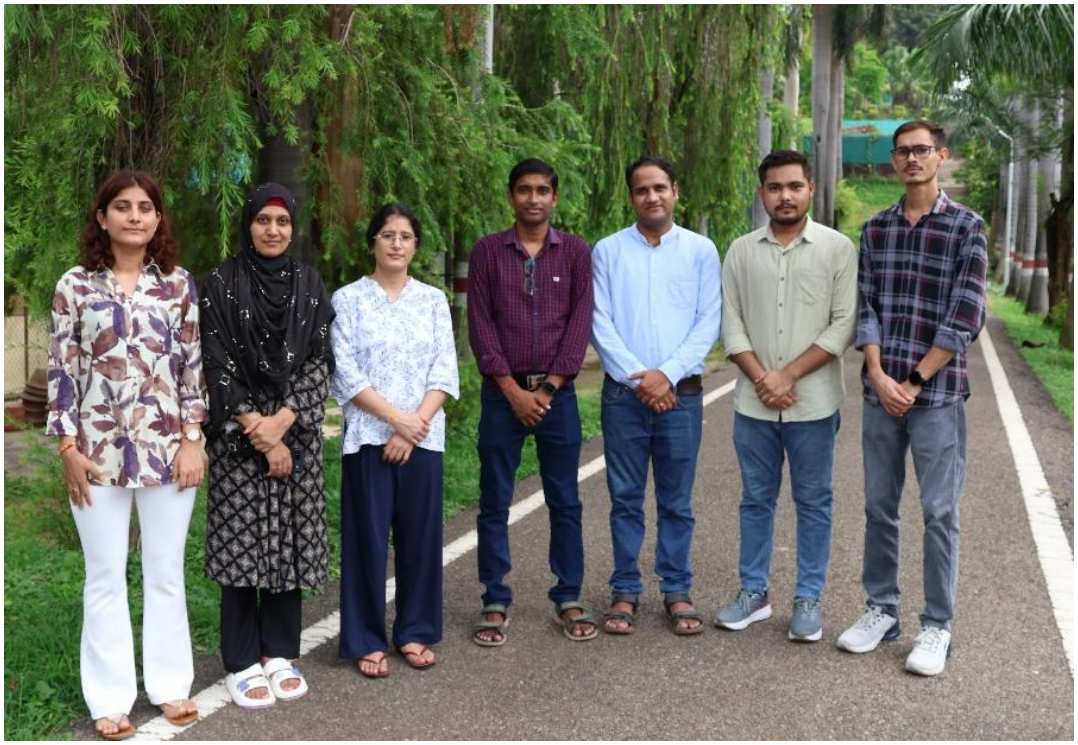
What We Did

At the CSIR-Indian Institute of Integrative Medicine in Srinagar, India, we conducted a controlled pot experiment using sterilized soil to eliminate pre-existing biotic influences. Healthy saffron corms,





KOTA SRINIVAS



Dr. Kota Srinivas (Sr. Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Yadunandan Sen, Vanila Sharma, Suman Singh, Mallesham Bulle, Prashant Misra, **Srinivas Kota*** (2024) metaTopolin-driven breakthrough in lemon beebalm (Monarda citriodora) regeneration: A molecular fidelity study for genome engineering applications. Journal of Medicinal and Aromatic Plant Sciences. 46 (3) : 123-132.
- Kumar Bushan.; Wani Ishfaq Ahmed, Lone Javid.F, **Srinivas Kota**, Gairola Sumeet (2025) Chemical Diversity in Essential Oils of 40 Artemisia Species from Western and Trans Himalayan Regions of India. Resources. 14, 42
- Prasanna Dhondi, **Srinivas Kota**, Gulab Khan Rohela, Kiranmayee Kasula (2025) Development of efficient micro propagation, assessment of genetic fidelity and biochemical fidelity in Curcuma longa L. Vegetos. https://doi.org/10.1007/s42535-025-01290-2
- Awzia Amin, Nancy Sharma, Phalisteen Sultan, Sumit G.Gandhi, **Kota Srinivas**, Qazi Parvaiz Hassan, Zabeer Ahmed (2024) In vitro propagation of Bergenia stracheyi: an alternative approach for higher production of valuable bioactive compounds. Vegetos. 1-10

2. Scientific work done:

I. Genomic improvement of *Bacopa monnieri*by modification of LAS1 and CAS1 genes for the high production of Bacoside A and B through CRISPR Cas genome editing". (Completed in October, 2024)

Vanila Sharma, Suman Singh, Prashant Misra and Kota Srinivas

Regeneration and antibiotic sensitivity of Bacopa using leaf explant

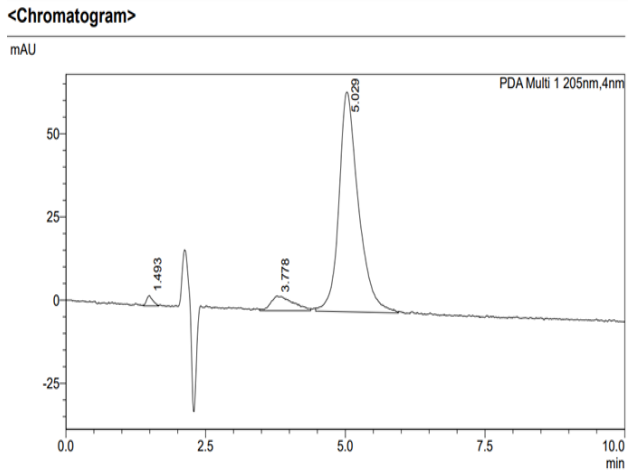
- Bacopa regeneration was reconfirmed using leaf explant. MS medium supplemented with 6 mg/L BAP and 0.2 mg/L IAA was used to reconfirm the leaf regeneration.
- Along with the regeneration reconfirmation different antibiotics sensitivity also examined for further screening and selection process of genome edited lines.
- Various concentrations of antibiotics like Kanamycin and Spectinomycin from 25, 50, 75 and 100 mg/L was added to the regeneration medium to check the sensitivity of Bacopa leaf explant.

Figure: Regeneration of *Bacopa monnieri*

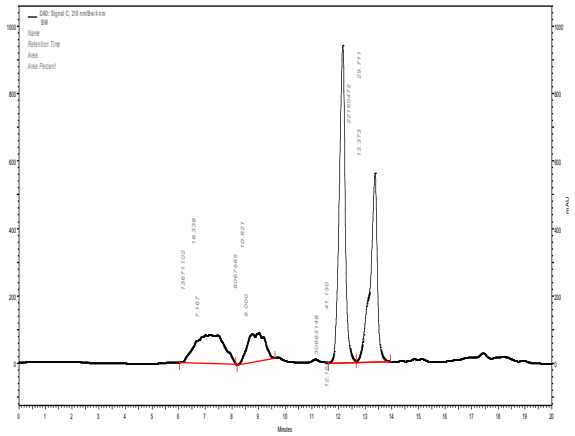
Quantification of bacoside content through column chromatography and high performance liquid chromatography.

- Extraction with different solvent (methanol and chloroform)
- Isolation from methanolic extract via column chromatography by using 60-120 silica gel
- High performance liquid chromatography

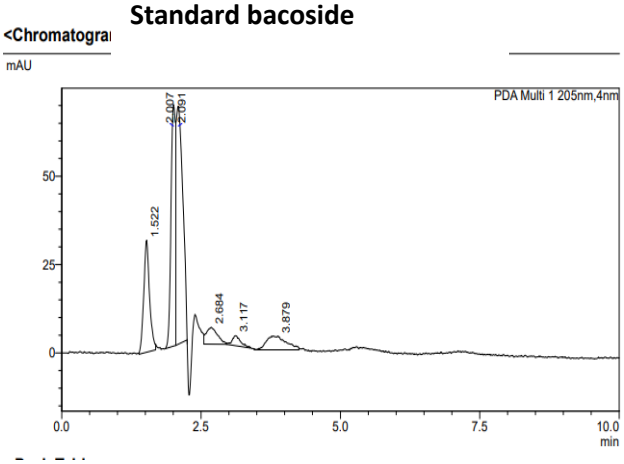
Semipreparative RP HPLC on Discovery® C18was performed and we isolated BM-01, BM-02, BM-03, and BM-04 using acetonitrile: water (40:60) as a solvent. Further analytical HPLC RP was performed on BM-01, BM-02, BM-03, and BM-04 and the chromatogram obtained was compared with the chromatogram of bacopside II (commercial).



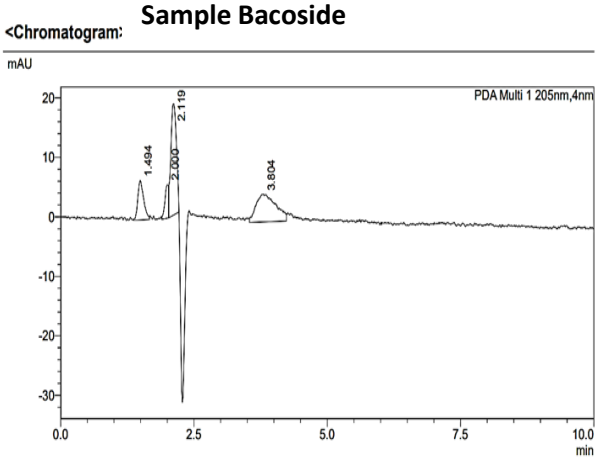
Standard bacoside



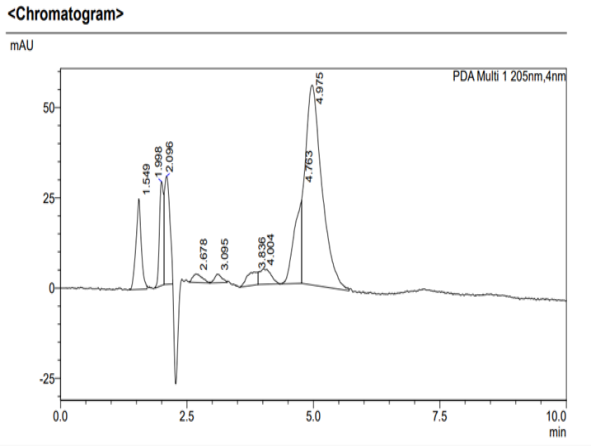
Sample Bacoside



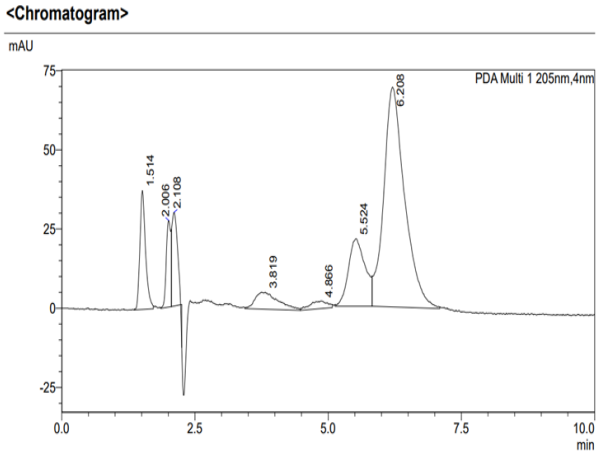
BM-01



BM-02



BM-03



BM-04

RNA Isolation

- Total RNA was isolated using total RNA isolation kit (Zymo) from various plant parts of *Bacopa monnieri* like whole plant, leaf tissue and root tissue for transcriptome analysis to get targeted genes sequences.
- Isolated total RNA was quantified and subjected to electrophoresis to check the quality and quantity.
- Verified RNA samples were sent to transcriptome sequencing.
- RNA Quantification using ThermoScientific Nanodrop2000.

S.No	elution 1	sample	Concentration (ng/l)	Volume
I	B1	Whole Plant	539.4	25µl
II	B2	Whole Plant	338.6	25µl
III	B3	Whole Plant	246.3	25µl
IV	B4	Whole Plant	426.5	25µl
V	L1	Leaf	1350	25µl
VI	L2	Leaf	959.1	25µl
VII	L3	Leaf	1829.3	25µl
VIII	L4	Leaf	1303.5	25µl
IX	R1	Root	467.2	25µl
X	R2	Root	380.9	25µl
XI	R3	Root	628.6	25µl
XII	R4	Root	534.8	25µl

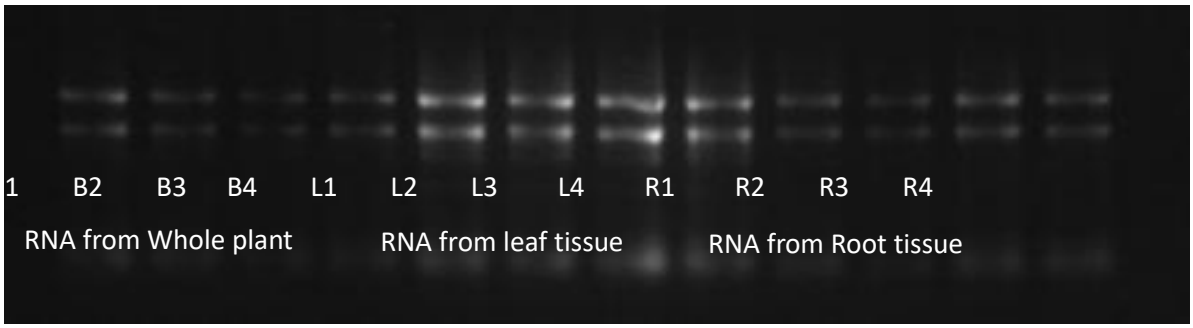


Figure: Gel picture of RNA (1µL)

- RNA extraction from biological sample (whole plant, leaf, root)
- Qualitative and Quantificational Analysis of RNA

- RNA sent for transcriptome
- Synthesis of first strand cDNA using RNA
- Optimization of annealing temperature for *LAS, CAS, BAS, LUP1, LUP2* gene amplification.
- Amplification of DNA of interest using its primers for ligation.

Transcriptome Analysis

Transcriptome analysis was carried out using next-generation sequencing (Illumina platform) to gain in-depth information about the genome of *Bacopa monnieri.* A total of 95464570 and 77140968 raw reads were obtained from stolen and leaf sample respectively. Raw reads were processed (adapter sequence removal) to obtain clean reads 70385290 with Q30 as 96.44; GC as 52.30 from stolen and 63756450 with Q30 as 96.18; GC as 50.25 from leaf sample. These high-quality reads were further used to generate assembled transcriptome. Trinity assembly resulted in mm111015 transcripts and 110962 unigenes with an average GC content of 51.27%. Number of transcripts with more than 2Kbp constituted 23179 unigenes. The unigene sequence alignment and functional analysis displayed the annotation of 110962 unigenes with different databases.

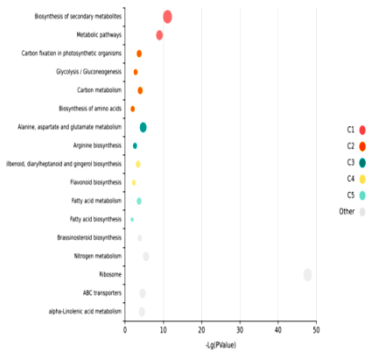
To understand the distribution of *Bacopa monnieri* gene functions at a macro level, the unigenes were classified using the GO database. The resulting GO annotation classification yielded 53624 unigenes which were categorized into genetic molecular function, cellular component, and biological process. The unigenes were further divided by biological process into 26 categories, the two most abundant being cellular process and metabolic process. To further investigate the metabolic pathways associated with the identified unigenes, pathway enrichment analysis was performed using the KEGG database. Among the identified pathways, biosynthesis of metabolic pathway was among the most enriched pathways.

Transcriptome of *Bacopa monnieri* was mined to identify the genes of interest including *LAS, CAS, BAS* and *LUP*s. Complete gene sequences were retrieved from the transcriptome that was further used to design the primers to amplify the gene of interest. Further, phylogenetic analysis of *LAS, CAS* and *BAS* genes was carried out in order to identify and authenticate genes in *Bacopamonnieri*. Different sequences of same genes belonging to related plant species were retrieved from NCBI to construct phylogenetic tree.

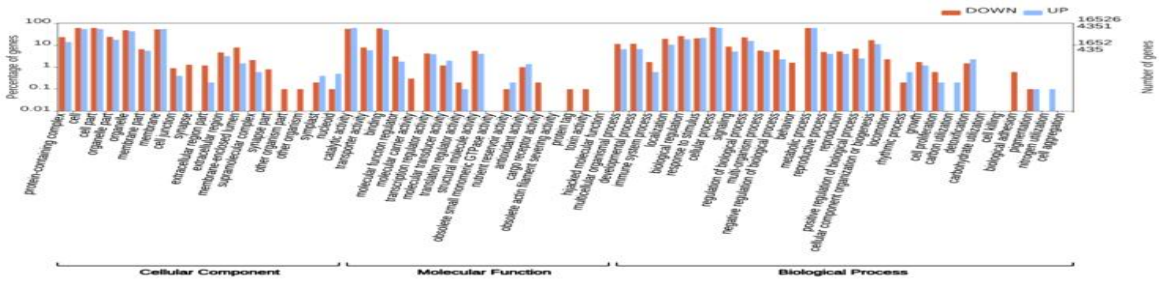
Summary of Transcriptome Assembly

Number of raw reads	66207526
Number of filtered reads	6370183
GC percentage	45
% Alignment	92%
Total sequence	185675
Total no. of sequence with blast hit	184355
Percentage of sequence annotated	99.28%

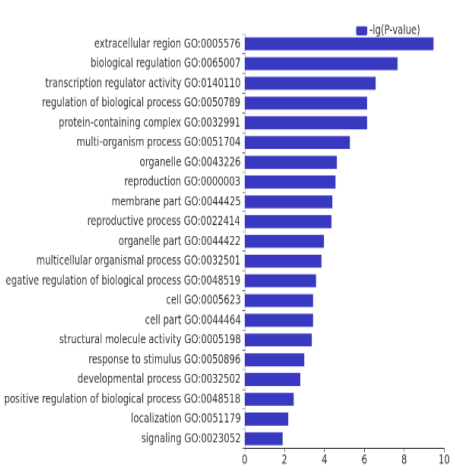
KEGG Annotation

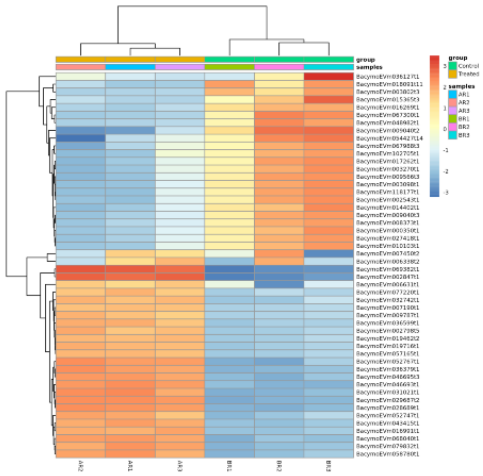


Phylogenetic Analysis



GO Annotation





GO Bar graph Heatmap

Heatmap showing top 50 genes exhibiting the highest variance across different tissue sample. Out of these genes our study was mainly focused on *LAS, CAS* and *BAS*. The data retrieved from the transcriptome analysis regarding the variance in gene expression for *LAS, CAS* and *BAS* is summarized in table form.

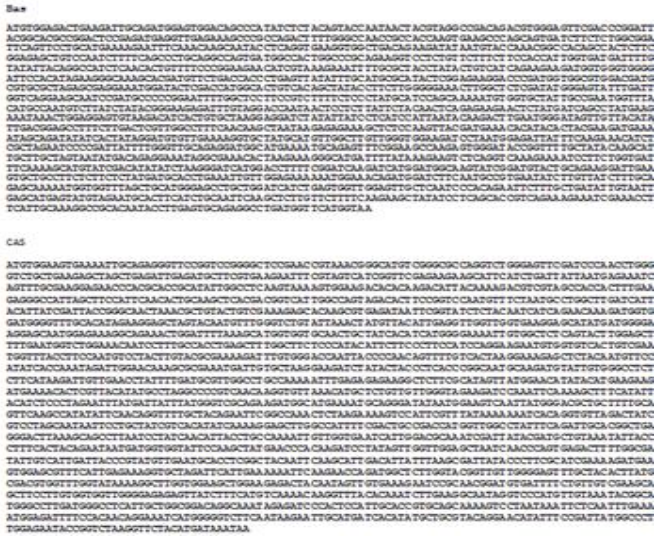
Table1:*LAS* did not show any variation, while *CAS* and *BAS* did show the variance.

Tissue	*Gene*	*DOWN regulated*	*UP regulated*
Whole plant compared to leaf	*CAS*		✓
	BAS	✓	
Whole plant compare to roots	*BAS*	✓	
Leaf compare to roots	*CAS*	✓	

This variance data reflects the differential gene expression across various plant tissues, providing insights into the tissue-specific regulation of these genes.

Identified genes with their sequences

Genes/Proteins	Contig id
Cycloartenol synthase	BacymoEVm003035t3
Beta amyrin synthase	BacymoEVm002921t4
Lanosterol synthase	BacymoEVm048748t1



- Complete gene sequence of *LAS, CAS* and *BAS* was retrieved from the transcriptome which was further used to design the primers to amplify genes.
- Primers were designed against the gene sequence.

Table 2: Forward and Reverse primers used for amplification of target genes

Genes	***Forward primer***	***Reverse primer***
Beta amyrin synthase (BAS)	*ATGTGGAGACTGAAGATTGCAGA*	*TTACCATGAACCATCAGGCCTCT*
Cycloartenol synthase (CAS)	*CAAGGCGAAAACTATATATCTTCAAGATC*	*ATAATGTGGAAGCTGAAAATTGCAGAGGG*
Lanosterol synthase (LAS)	*ATGGACGTGCTGCACGTAGTTCTA*	*TCAATTTTTCAAGTAGCTTAACACCTTGTTGA*
LUP1	*ATGTGGAAGCTGAAGATTGCCGAA*	*TTAAATATTGTCGCAACTAACCTGTC*
LUP2	*ATGTGGAGGCTAAAGATTGCGGAA*	*CTATTTCATCAATTTGTTTACGAGTATCTG*

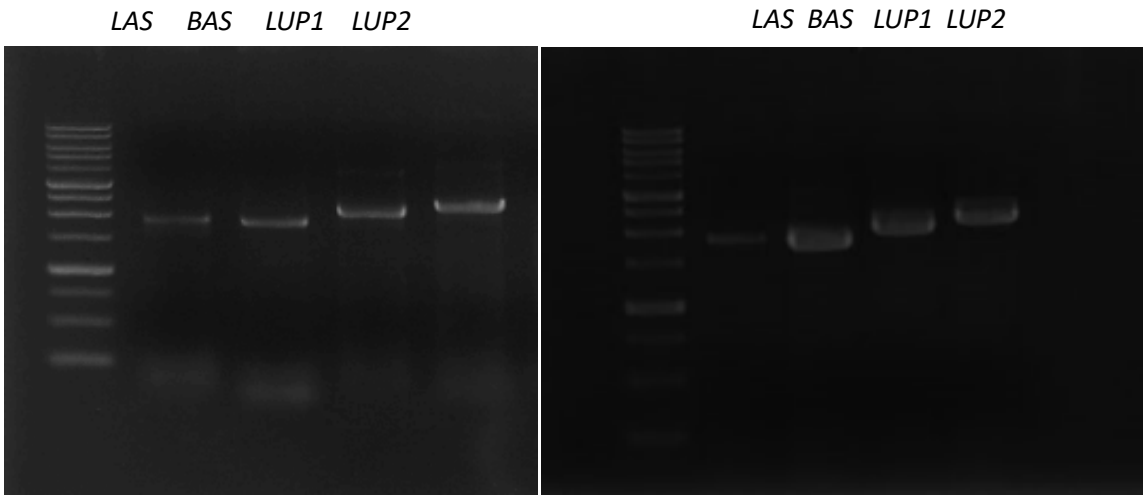
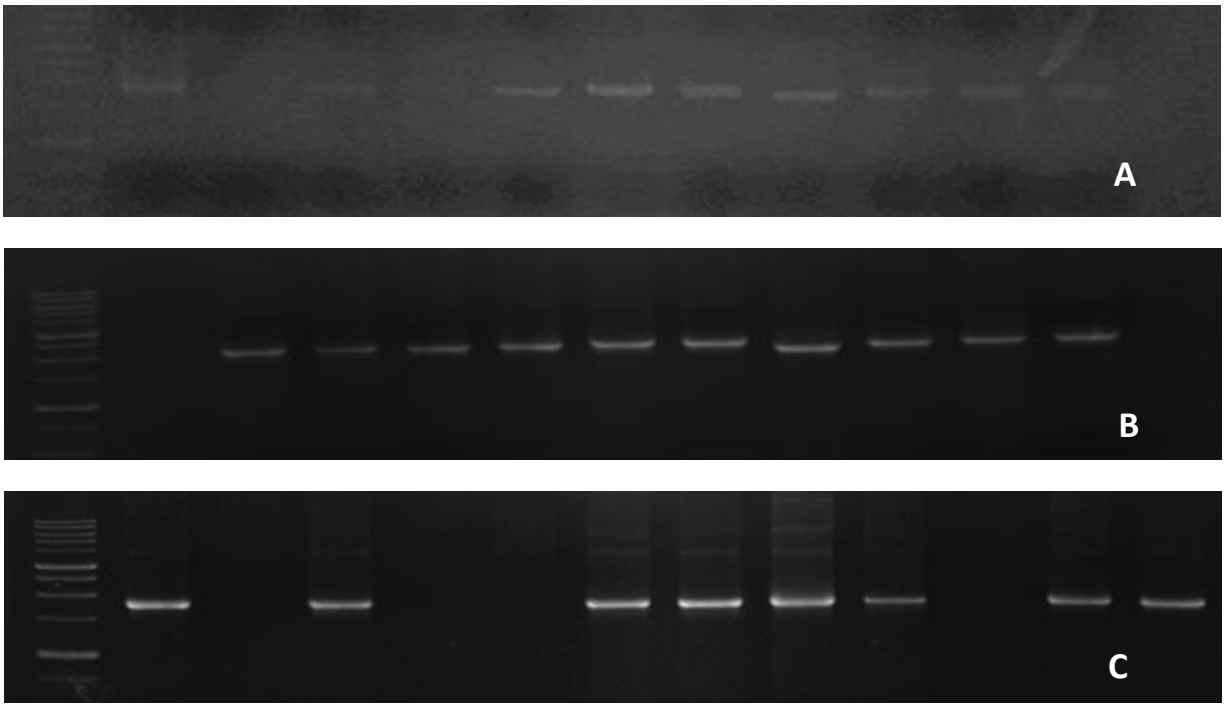
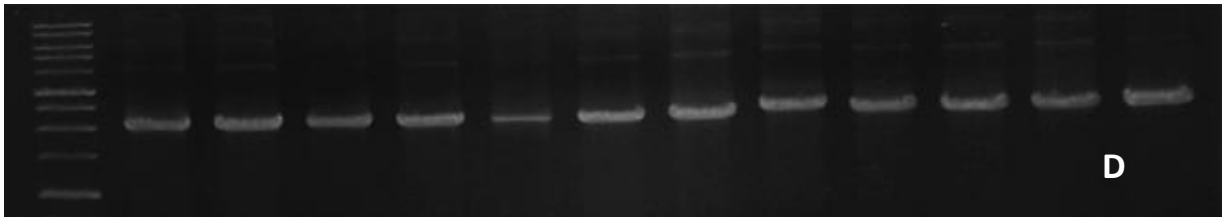


Figure: PCR using taq polymerase **Figure:** Hi-fidelity polymerase

- Ligation of gene of interest into pJET cloning vector.
- Transformation in *E.coli*.
- Screened transformed colonies using gene specific primers (*LAS CAS BAS LUP1*)





Figures: Screened transformed colonies using gene specific primers shows the presence of A) 1878bp amplicon size of *LAS*, B) 2271bp amplicon size of *CAS*, C) 1827bp amplicon size of *BAS*, D) 2100bp amplicon size of *LUP1*.

- Plasmid isolation along with its quantification.
- PCR conformation of gene presence in plasmid
- Sanger's sequencing
- Sequence was then retrieved and BLAST in NCBI.

gRNA Designing

The targeted gene sequences were used as an input for different online tools for designing target guide RNA sequence (sgRNA). We outsourced the gRNA as per the given criterion

- Identify a 20 nucleotide sequence within gene of interest that is unique to the genome
- The PAM sequence, typically 5'NGG3', was identified at or near the desired edit site to ensure precise targeting.
- Lack of availability of full genomic sequence, off targets was check against the exons available from transcriptome results.

CDS LAS Bacopa

ATGGACGTGCTGCACGTAGTTCTACAAGAAGAGCATCAAAAGGAGATGCGCCGATATATCTATAACCATCAAAAT
GTTGATGGAAGGTTGGGGATTGCATATAGAAGGGCATAGCACCATGTTTTGCACAGCCTTGAACTATGTATCTTTGA
GACTTCTTGGAGAACAAATGGAGGGTGGAGATGAGGCTATAGAGAATGCCAGAACATGGATTCTTGATAGAGGT
GGTGCTATCTATATACCATCATGGGGAAAATTTTTGTTATCAGTTCTTGGAGTGTATGAATGGGGTGGGAATAATC
CTCTACCACCAGAATTATGGCTTCTTCCTTACTCCCTTCCTATCCATCCAGGTCGTGCATGGTGTCACTGTCGGATGG
TCTACCTGCCTATGTCATATTTGTACGGAAAGAGATTCATAGGGCCAATCAATGCCACTATTCTATCTCTGAGAAAA
GAGCTATATATTCAAGCTTATAATCAGATTGATTGGGATTTGGCCAGAAATCAGTGTGCTAAGGAGGATTTATACT
ATCCACACCCACTTGTACAAGACATTTTGTGGACGTGTTTGCACAAATTTTCAGAACCTCTTCTTATGCAATGGCCTT

Figure: Yellow line corresponds to fifth exon, purple line 20nucleotide gRNA target and Light blue NGG PAM site

CAS

S.NO.	Primer Name	(2 GRNA CRISPR) Primers Sequence	No. of nucleotides
1.	DT1-BsF	5' ATATATGGTCTCGATTGCGTAGCCACCACTTTGAAGGTT 3'	39
2.	DT1-F0	5' TGCGTAGCCACCACTTTGAAGGTTTTAGAGCTAGAAATAGC 3'	41
3.	DT2-R0	5' AACGGTAATCGATAATGTAATGCAATCTCTTAGTCGACTCTAC 3'	43
4.	DT2-BsR	5' ATTATTGGTCTCGAAACGGTAATCGATAATGTAATGCAA 3'	39

LAS

S.NO.	Primer Name	(2 GRNA CRISPR) Primers Sequence	No. of nucleotides
1.	LDT1-BsF	5' ATATATGGTCTCGATTGGTTGGGGATTGCATATAGAGTT 3'	39
2.	LDT1-F0	5' TGGGTTGGGGATTGCATATAGAGTTTTAGAGCTAGAAATAGC 3'	42
3.	LDT2-R0	5' AACTGTTCTGGCATTCTCTATAGCAATCTCTTAGTCGACTCTAC 3'	44
4.	LDT2-BsR	5' ATTATTGGTCTCGAAACTGTTCTGGCATTCTCTATAGCAA 3'	40

Assembly of cas9 constructs

The vector with Cas9 protein was used to assemble the construct. The primers harboring appropriate restriction sites were ligated to sgRNA under the control of U6 promoter. The final construct was prepared in vector having Cas9 via the Golden Gate cloning system.

- Once the gRNA has been cloned in destination vector (PKSE401).
- Transformed into *E.coli* DH5α following its confirmed by colony PCR
- Insertion of gRNA into the destination vector was confirmed by Sanger's sequencing.

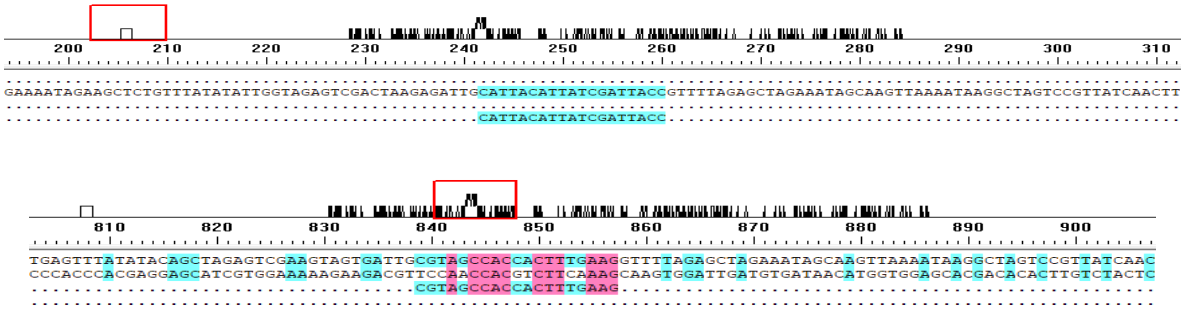
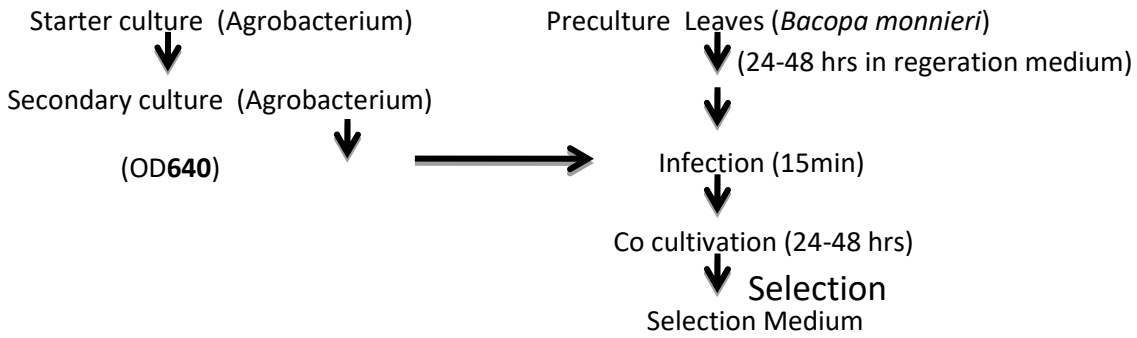


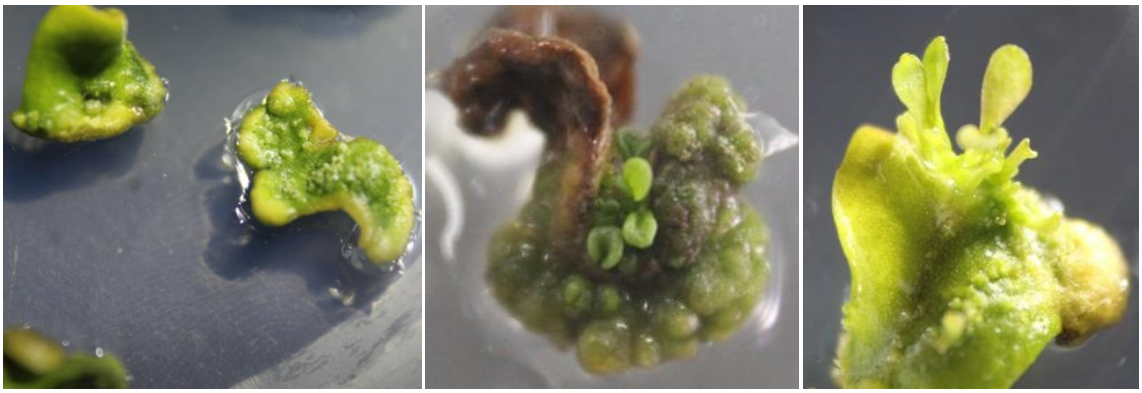
Figure: Indicates successful insertion of 20 bp gRNA (*CAS*) into the vector sequence

- Transformation of CRISPR/Cas9 vector containing gRNA (*CAS*) into Agrobacterium strain GV3101 and confirmation of positive colonies by colony PCR method.
- Standardized protocol of Agrobacterium mediated genetic transformation with leaf as explant was used for infection with Agrobacterium strain containing CRISPR/Cas9 vector.
- The same procedure of ligation of gRNA into PKSE401 destination vector and transformed into *E.coli* DH5α was repeated with *LAS* gene as well followed by sanger's sequencing and transformation into the Agrobacterium strain.

Agrobacterium mediated transformation of CRISPR vector in to Bacopa for the genome editing of the target



genes



After 1month of infection **After 1.5 month of infection** **After 2 months of infection**

Figure: Selection of leaf explants after infection on selection medium

II. Establishment of plastid transformation platform in millets

Suman Singh, Vanila Sharma and Kota Srinivas

1. Regeneration studies:

Callus regeneration has been obtained and organogenesis is yet to be achieved.

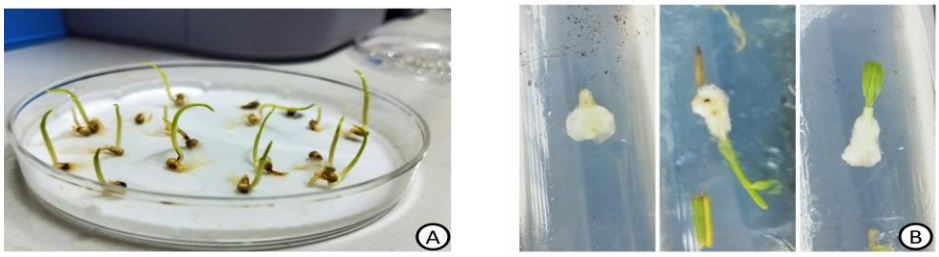
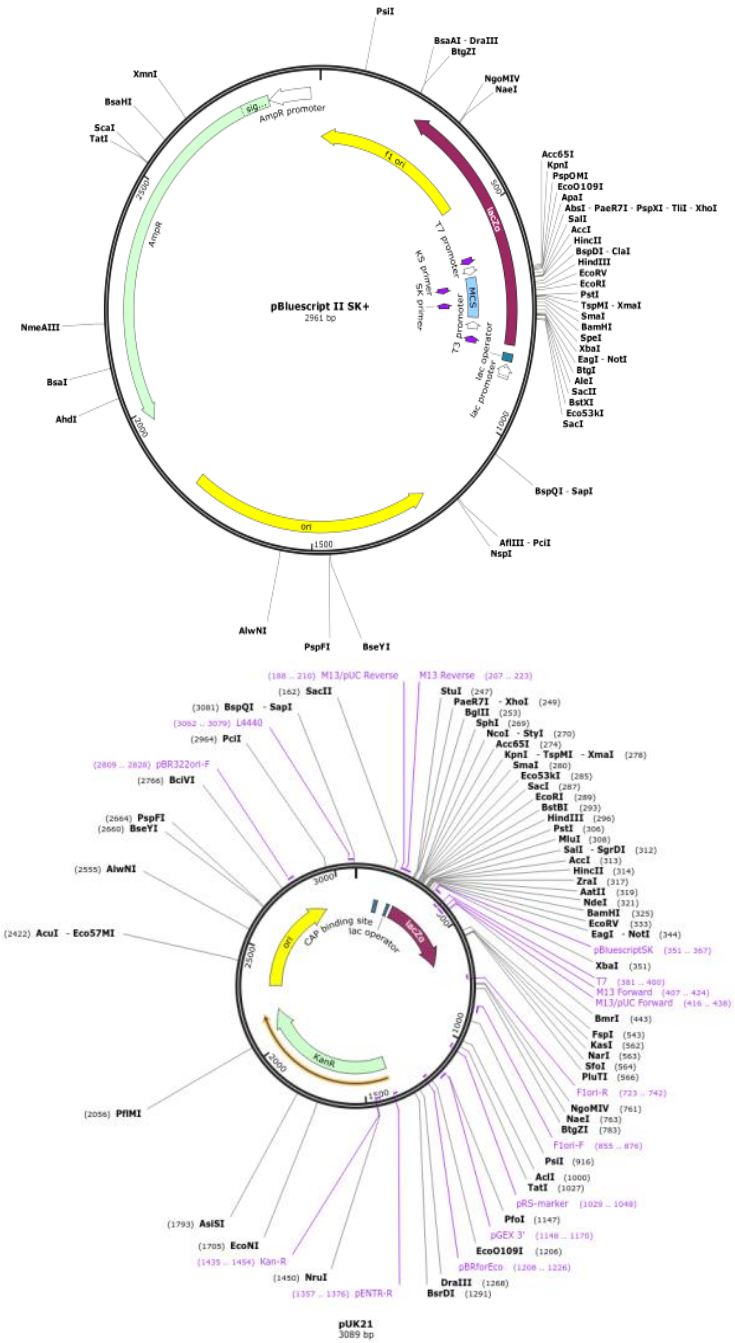


Figure 2: A) Millet seeds germinated on MS. B) Callus mediated regeneration observed within 15 days of SAM explants put on regeneration media (MS+ 3mg/L 2,4D+ 1mg/L Kn+ 0.1 mg/L BAP).

Vector construction:

Cloning under progress using golden gate as well as conventional cloning techniques with pBluescript II SK(+), pUK21 and pUC12 vectors. Cloning involves the segments of left flank, right flank and the marker gene.



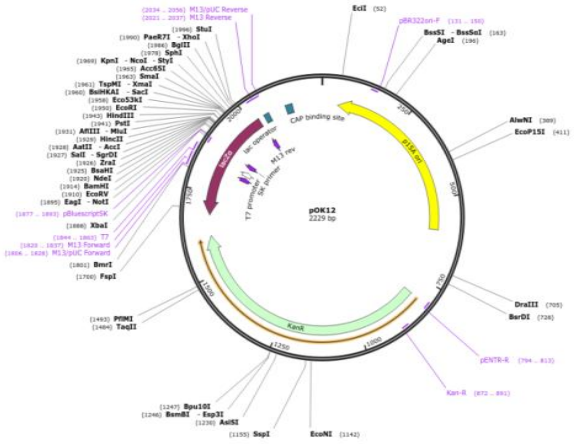


Figure 3: Vectors: pBluescript II SK+, pUK21 and pOK12.

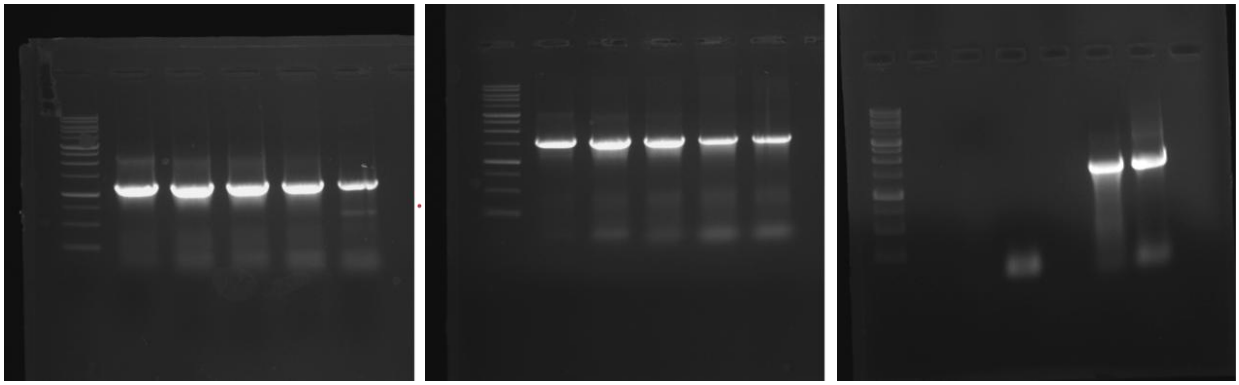


Figure 3: Amplified genes to be cloned in vectors: A) AADA gene (1.1 kb) from CaIA vector B) Right flank made of trnA+rrn23 (1.5 kb) from millet plastid genome C) Left flank made of trnI+rrn16 (1.5 kb) from millet plastid genome.

2. Spectinomycin-resistant mutation induction:

To induce the point mutation, seeds were germinated at high doses of spectinomycin and leaves of the germinated seedlings have been put on regeneration medium with higher spectinomycin concentration. Sequencing would be performed for the shoots so obtained to identify the regions of point mutation that induced resistance to spectinomycin.

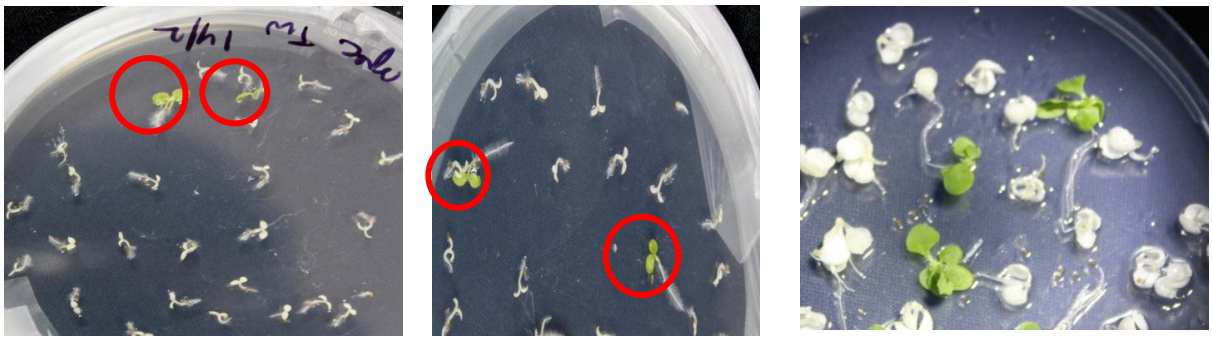


Figure 4: Wild tobacco seeds germinated on MS media with 300 mg/l spectinomycin concentration (putative mutants show green leaves).

Figure 5: Shoot initiation from leaf explants on regeneration media with higher doses of spectinomycin; A) 400 mg/l B) 450 mg/l C) 500 mg/l.

Figure 6: Leaves from healthy grown shoots at different spectinomycin doses have been put on regeneration media having spectinomycin concentration 500 mg/l, 550 mg/l, 600 mg/l and 650 mg/l.

MANU KHAJURIA

Dr. Manu Khajuria (Scientist) with her Research Group

1. Publications/Patents:

2. Scientific work done:

1. Phytopharmaceutical Mission Phase-III (MMP075201)

Field Preparation and Transplantation of *Dysoxylumbinectariferum*at CSIR-IIIM Chatha Farm

Prior to transplantation, field preparation was carried out through tractorization and leveling to ensure uniform ground conditions. Weeds were manually removed, and soil clods were broken to facilitate better aeration and root penetration.

- **Pit Formation:** Planting pits measuring approximately 1.5 to 2 feet in depth were excavated to accommodate the root systems of the saplings.
- **Sapling Procurement and Conditioning:** A total of approximately 185 healthy *Dysoxylumbinectariferum*saplings were procured from Pune on 7th September 2024. Upon arrival, the saplings were subjected to an acclimatization process for 2–3 days under the

ambient climatic conditions of Jammu to mitigate transplant shock and ensure successful establishment.

- **Transplantation:** The acclimatized saplings were transplanted at the CSIR-Indian Institute of Integrative Medicine (CSIR-IIIM) Chatha Farm on 12th September 2024.

Figure1.Field related work: phenotypic data recording timely Intercultural operation including (irrigation, weeding etc).

Due to the limited vegetative growth exhibited by the plant under study, an experimental approach was undertaken to enhance biomass accumulation through exogenous application of gibberellic acid (GA_3). Prior to GA_3 application, the endogenous content of routhikine - a key secondary metabolite—was quantified in leaves collected from different positions (apical, middle, and basal) to assess the spatial distribution of the compound within the plant canopy. This baseline data was essential for evaluating the effect of GA_3 treatment on both growth and metabolite accumulation.

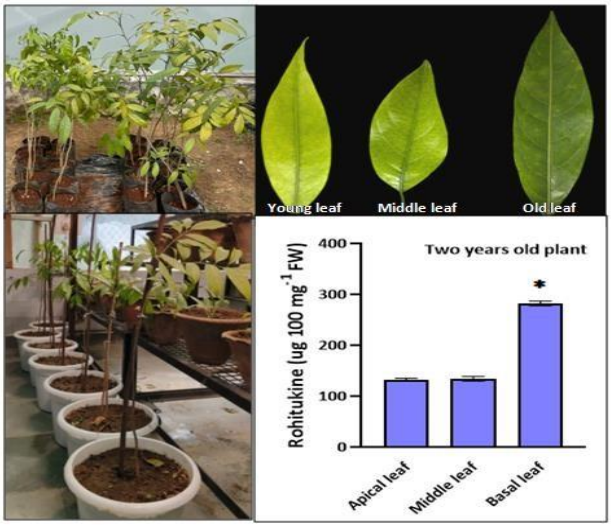


Figure 2. Rohitukine content in different leaves (apical, middle and basal) of Dysoxylumbinectariferum.

GA_3, a well-known plant growth regulator, was applied at three different concentrations: 25 mg/L, 75 mg/L, and 100 mg/L. The treatments were administered as foliar sprays at regular intervals (15 days) under controlled environmental conditions. Chlorophyll fluorescence parameters were measured after 2 months.

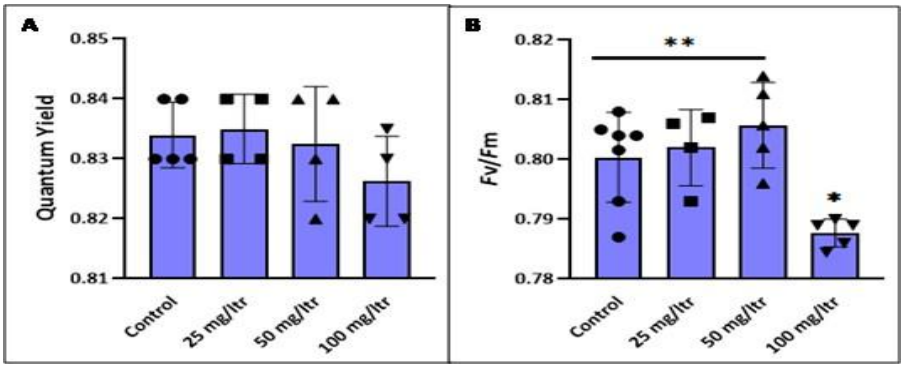


Figure 3. Chlorophyll fluorescence parameters:Quantum yield (A) and *F*v/*F*m (B) in the leaves of *Dysoxylumbinectariferum*after 2 months of treatment.

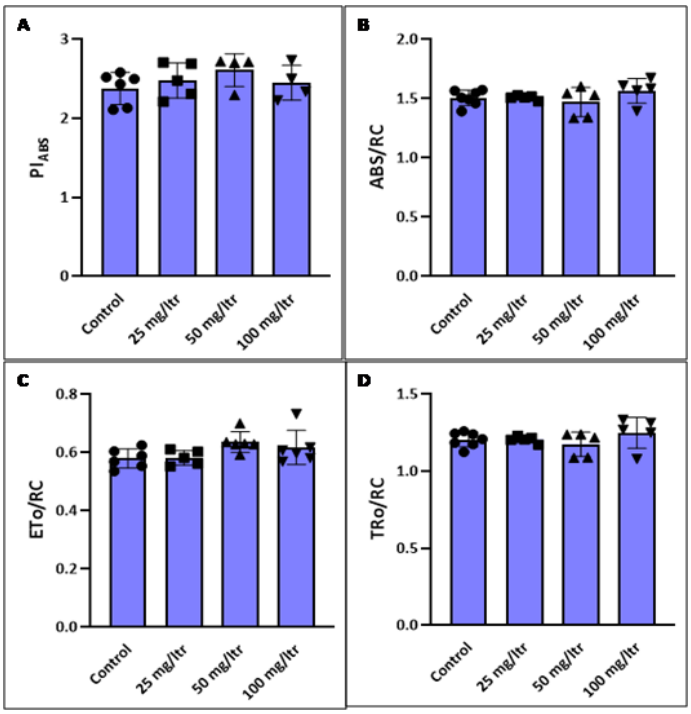


Figure 4. Chlorophyll fluorescence parameters: Performance index (A), Absorption per reaction centre (B), Electron transport rate per reaction centre (C) and Trapping rate per reaction centre in the leaves of *Dysoxylumbinectariferum*after 2 months of treatment.

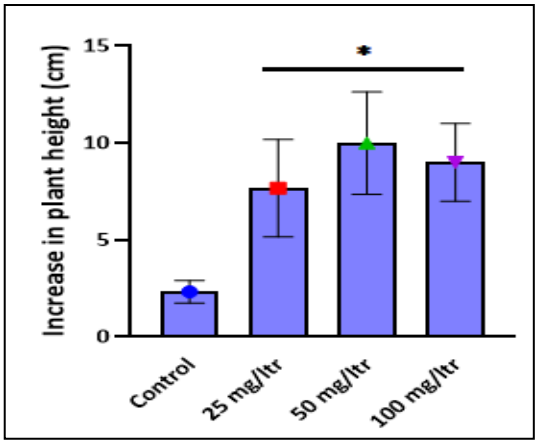


Figure 5. Increase in plant height of *Dysoxylumbinectariferum*after 2 months of treatment

The experiment is designed to span a period of three months and is currently in progress. This preliminary data set will contribute to evaluating the potential of GA_3 in promoting biomass production and modulating secondary metabolite accumulation in the plant. Further analyses are ongoing and will provide insights upon completion of the experimental timeline.

2. Aroma Mission Phase-III (HCP0007)

Authenticated seeds of *Salvia sclarea* were obtained from the CSIR-IIIM seed bank. Seeds were sown in 30 cm-wide pots filled with autoclaved Soilrite and maintained in a controlled environmental chamber under a photosynthetic photon flux density (PPFD) of 120 µmol m^{-2} s^{-1}, with a 16/8 h light/dark photoperiod and 70% relative humidity. After germination, seedlings were transferred to individual pots and supplied with water and Murashige and Skoog (MS) medium as needed. Subsequently, plants were shifted to a greenhouse and grown under standard conditions. Experimental treatments were initiated 30 days after germination. Two different concentrations of methyl jasmonate (0.1mM and 1mM) were given for different intervals of time (3 hr, 24 hr and 48 hr) to study its effect on squalene content. Chlorophyll fluorescence parameters were measured after different intervals.

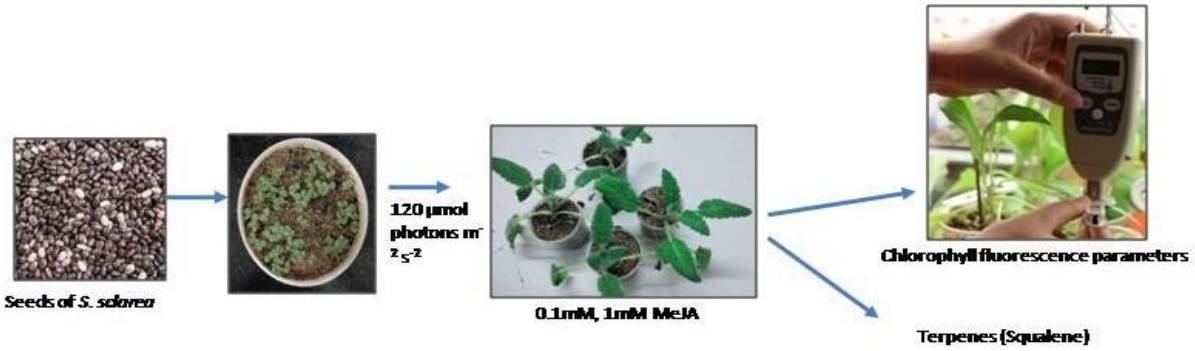


Figure 6. Overview of the experiment

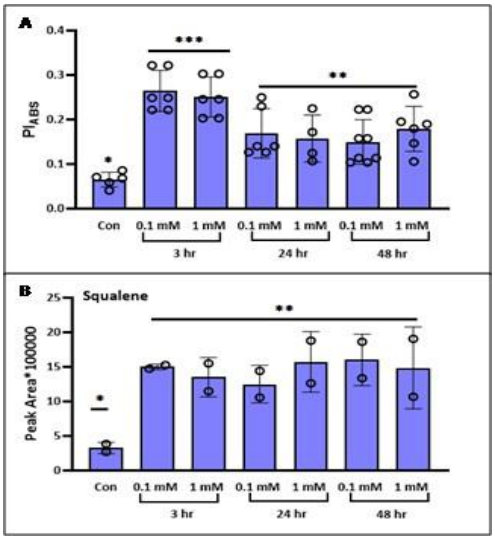


Figure 7. Chlorophyll fluorescence parameters: Quantum yield (A), Absorption per reaction centre (B), Dissipation rate per reaction centre (C) and Electron transport rate per reaction centre (D) in the leaves of *Salvia sclarea.*

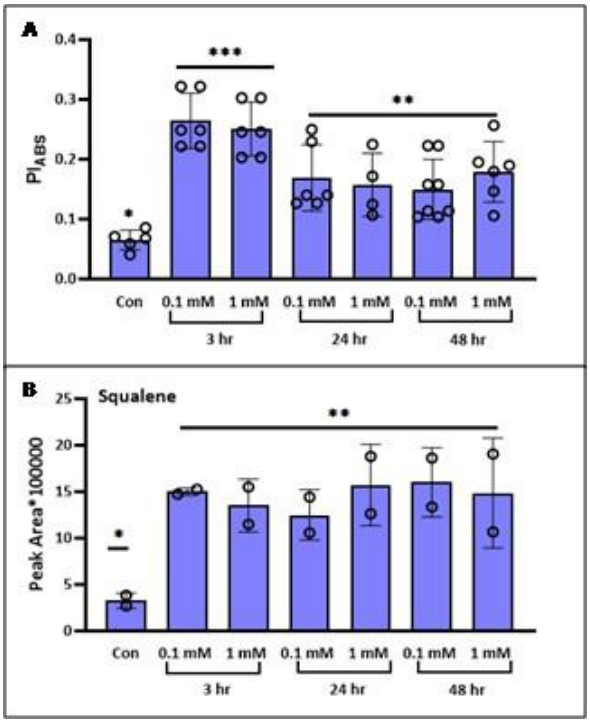


Figure 8. Performance index (A) and Squalene (B) in the leaves of *Salvia sclarea*.

3. Plant Adaptive Biology

The Himalayan herb *Inula racemosa* has long been valued for its therapeutic benefits, which are largely attributed to the bioactive compounds present in its roots. However, the chemical and medicinal potential of its leaves have remained largely unexplored. Herein, we report a new 4,5-epoxy-guaien-

12,8-olide (**2**), along with ten known (**1** and **3** – **11**) sesquiterpene lactones from the leaves of *Inula racemosa* grown at CSIR–IIIM, Jammu, India.

Leaves of *I. racemosa* were taken for the current investigation. N-hexaneextract from leaves of *I. racemosa* was prepared, and then separated into 26 fractions using Silica gel column chromatography. These fractions were purified using Sephadex LH20 column, silica gel, and high-performance liquid chromatography (HPLC). The known compounds were identified as 4,5-epoxy-11(13)-guaien-12,8-olide (**1**), tomentosin (**3**), xanthinosin (**4**), 8-epiconfertin (**5**), inuloxins A (**6**), carpespene C (**7**), 1*β*-hydroxyalantolactone (**8**), 1-epi-inuviscolide (**9**), 11a,13-dihydrotomentosin (**10**) and 11(13)-dehydroivaxillin (**11**) by comparing their spectroscopic data with reported in the literature values.

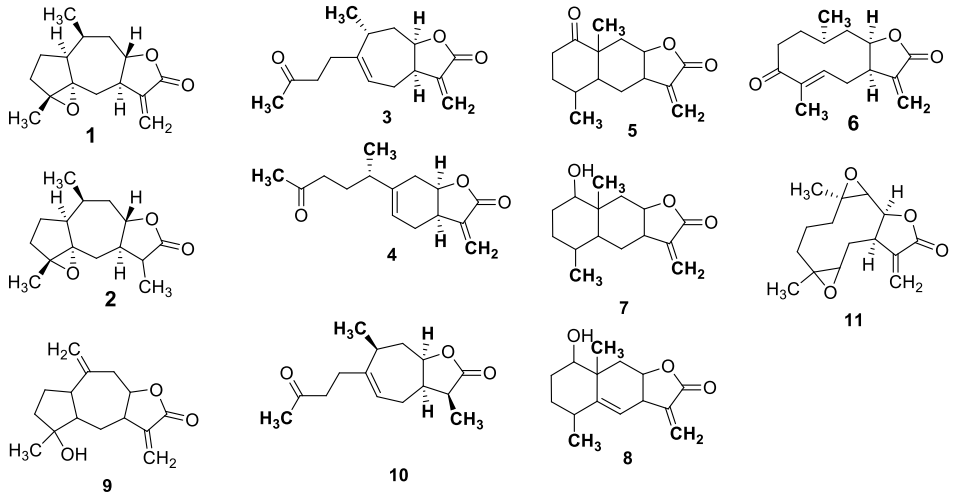


Figure 9. Structures of sesquiterpene lactones (**1**–**11**) from the leaves of *Inula racemosa*

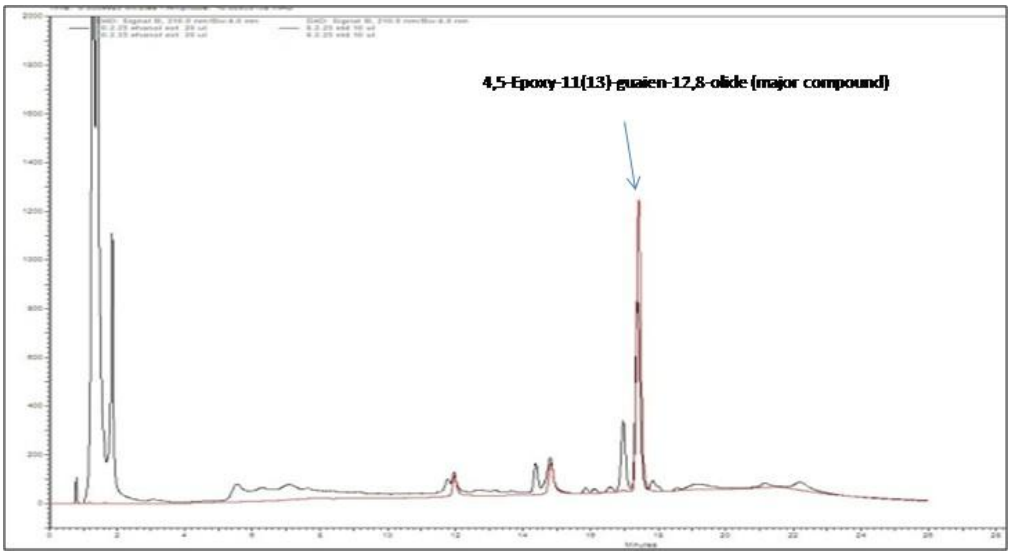


Figure 10.Chromatogram showing major compound isolated from the leaves of *Inula racemosa*

Arabidopsis thaliana seeds were treated with different concentrations of major compound and significant results were obtained.

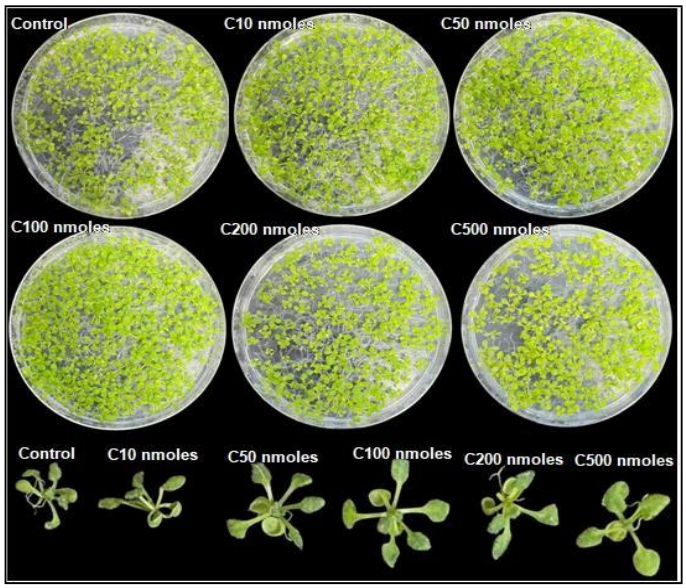


Figure 11. Changes in the shoot portion of *Arabidopsis thaliana* after treatment with major compound isolated from the leaves of *Inula racemosa.*

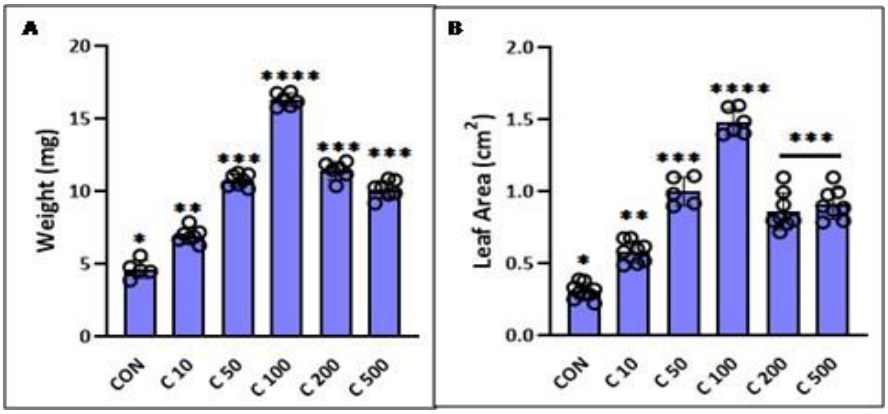


Figure 12. Changes in the shoot portion (weight, A and leaf area B) of *Arabidopsis thaliana* after treatment with major compound isolated from the leaves of *Inula racemosa.*

BOOBALAN GOPU

Dr. Boobalan Gopu (Sr. Scientist) with his Research Group

1. Publications/Patents:

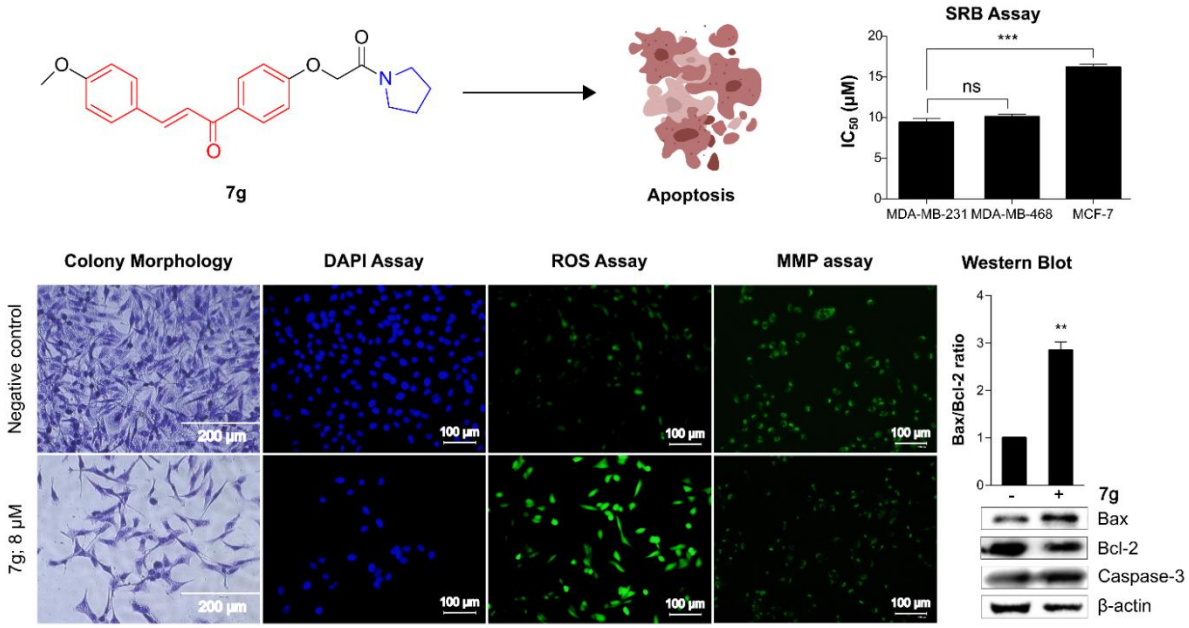
Publications:

- Kumar P, Singh R, Sharma D, Hassan QP, **Gopu B*,** Anal JMH. Design, synthesis, and biological evaluation of chalcone acetamide derivatives against triple negative breast cancer. Bioorg Med Chem Lett. 2024 Jul 15;107:129795. doi: 10.1016/j.bmcl.2024.129795. Epub 2024 May 13. PMID: 38750906.
- Singh R, Singh B, Singh A, Rana S, Sharma K, Viswakarma P, **Gopu B*,** Nalli Y. Canniprene B, a new prenylated dihydrostilbene with cytotoxic activities from the leaves of *Cannabis sativa*. Nat Prod Res. 2024 Jul 11:1-9. doi: 10.1080/14786419.2024.2376348. Epub ahead of print. PMID: 38989798.
- Singh B, Thappa C, Komal, Laasya Priya P, Begum S, Nalli Y, **Gopu B***. Two new dibenzyl-γ-butyrolactone lignans with cytotoxic activity from *Himalaiella heteromalla*, an Indian Himalayan

plant. Nat Prod Res. 2025 Apr 17:1-8. doi: 10.1080/14786419.2025.2491122. Epub ahead of print. PMID: 40241524.

2. Scientific work done:

1. Design, synthesis, and biological evaluation of chalcone acetamide derivatives against triple negative breast cancer

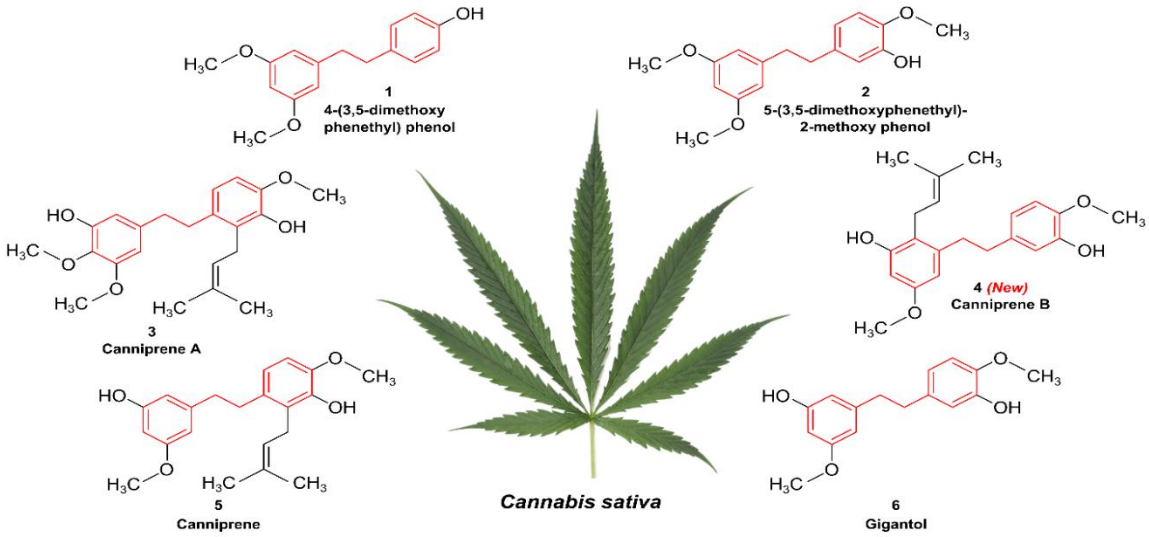


Chalcones are chemical scaffolds found in natural products, particularly in plants, and are considered for structural diversity in medicinal chemistry for drug development. Herein, we designed and synthesized novel acetamide derivatives of chalcone, characterizing them using 1H NMR, 13C NMR, HRMS, and IR spectroscopic methods. These derivatives were then screened against human cancer cells for cytotoxicity using the SRB assay. Among the tested derivatives, 7g, with a pyrrolidine group, exhibited better cell growth inhibition activity against triple-negative breast cancer (TNBC) cells. Further assays, including SRB, colony formation, and fluorescent dye-based microscopic analysis, confirmed that 7g significantly inhibited MDA-MB-231 cell proliferation. Furthermore, 7g promoted apoptosis by upregulating cellular reactive oxygen species (ROS) levels and disrupting mitochondrial membrane potential (MMP). Elevated expression of pro-apoptotic proteins (Bax and caspase-3) and a higher Bax/Bcl-2 ratio with downregulation of anti-apoptotic (Bcl-2) protein levels were observed in TNBC cells. The above results suggest that 7g can promote cellular death through apoptotic mechanisms in TNBC cells.

2. Canniprene B, a new prenylated dihydrostilbene with cytotoxic activities from the leaves of *Cannabis sativa.*

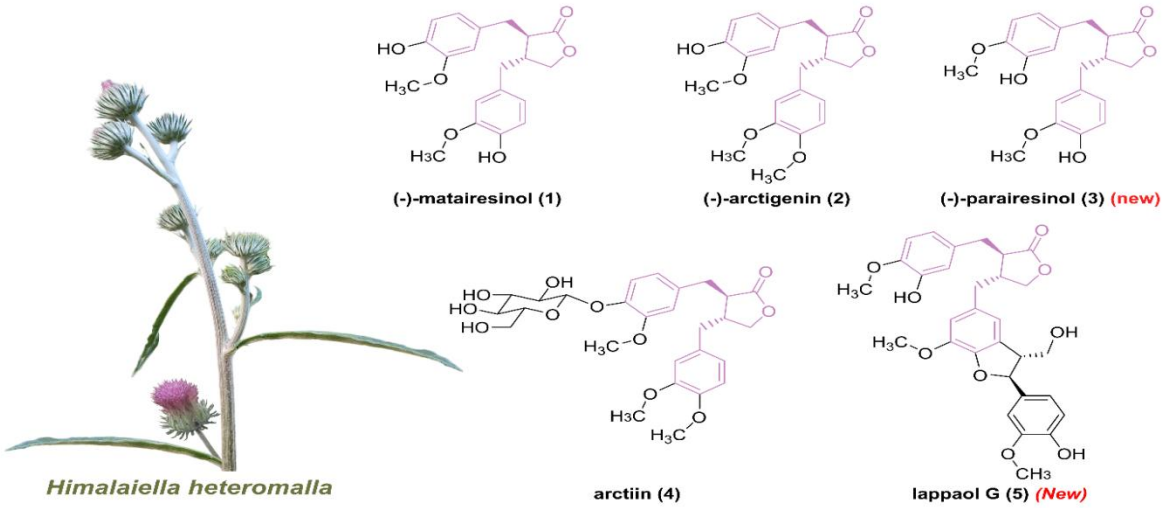
A new, canniprene B (**4**), along with five known (**1** – **3** and **5** – **6**) dihydrostilbenes were isolated from the leaves of *Cannabis sativa* collected at CSIR – IIIM, Jammu, India. Structures of all isolated compounds were elucidated by spectroscopic data analysis, including 1D and 2D NMR, and HR-ESI-MS. Canniprene B is a new prenylated dihydrostilbenes, a positional isomer of the known

compound canniprene (**5**). The cytotoxic activities of these compounds (**1** – **6**) were evaluated using the SRB assay against a panel of five human cancer cell lines. Notably, canniprene B (**4**) exhibited varying levels of cytotoxicity with IC_{50} values ranging from 2.5 – 33.52 µM, demonstrating the most potent activity against pancreatic cancer cells.



3. **Two New Dibenzyl-γ-butyrolactone Lignans with Cytotoxic Activity from Himalaiella heteromalla, an Indian Himalayan Plant.**

Two new (-)-parairesinol (**3**), lappaol G (**5**), and three known (**1**, **2**, and **4**) dibenzyl-γ-butyrolactone lignans were isolated from the Indian Himalayan herb *Himalaiella heteromalla*. Their structures were characterized by NMR and mass data analysis. *In vitro* cytotoxic study revealed that arctiin (**4**) showed promising growth inhibition across seven human cancer cells, with potent activity against Mia-PaCa-2 cells. Notably, compounds **3** and **5** did not demonstrate significant cytotoxicity up to 80 µM concentrations.



ZAHOOR AHMAD PARRY

Dr. Zahoor Ahmad Parry (Sr. Principal Scientist) with his Research Group

1. Publications/Patenets:

Publications:

- Mubarak M. M and **Ahmad Z ***. The Role of Astrocytes in Neurological Infections: Mechanisms, Responses, and Implications for Disease Progression. *Current Neuropharmacology*. 2025.Accepted (**JIF: 5.3**).
- Baba IA, Wani AZ, MM Mubarak and **Ahmad Z ***.Actinomycetes from High Altitude Salt Lake Tso-Kar of Ladakh offers bright prospects for antimycobacterial drug discovery especially for drug resistant Mycobacteria. *Extremophiles.* 2025. (**JIF: 2.6**).
- Kantroo H, Mubarak MM and**Ahmad Z***. Exploring Therapeutic Strategies for Candidiasis: From Current Treatments to Future Perspectives. *Bioorg. Chem*. 2025.In(**JIF: 4.7**)
- Mubarak MM, Chowdhary R, Rahim JR, Kantroo HA, Wani AZ, Malik A, shah S, Baba IA, Sarkar AR,Rai Rand **Ahmad Z***. Lauric acid conjugated ureido derivatives of 2-(4-aminopiperidin-4-yl) acetic acid ($\beta^{3,3}$-Pip): Overcoming resistance and outperforming standard antibacterials.*Eur. J. Med. Chem. Rep*. 2025.14, August 2025, 100260(**JIF: 4.1**)
- Mubarak MM, Baba IA, Wani AZ, Kantroo HA, and **Ahmad Z***. Matrix metalloproteinase-9 (MMP-9): A macromolecular mediator in CNS infections: A review. *Int. J. Biol. Macromol* 2025.311, Part 2, June 2025, 143902(**JIF: 8.5**)
- Mubarak MM, Kantroo HA, Mir FA, Kumar C and **Ahmad Z*.** Targeting InhA in Drug-Resistant *Mycobacterium tuberculosis*: Potent Antimycobacterial Activity of Diaryl Ether Dehydrozingerone Derivatives. Arch Microbial 2025.(**JIF: 2.6**).

- Mubarak MM, Majeed S, Wani AZ, Kantroo HA, Malik MA, Baba I, Mhatre R and **Ahmad Z*.** Modulating Sonic Hedgehog (SHH) Pathway to Create a Rapid CNS-TB Model: Facilitating Drug Discovery.*J. Neuroimmunology.*2025. **(JIF: 3. 4**).
- Amin H, Kantroo H, Mubarak MM, Bhat S, Bhat KA and**Ahmad Z***. Design and Synthesis of Betulinic acid Dithiocarbamate conjugates as potential antifungal agents against Candida albicans. RSC Advances 2025 **(JIF: 3.9**).
- Kantroo H, Mubarak MM, Chowdhary R, Rai R, **Ahmad Z***. Antifungal Efficacy of Ultra-Short β-Peptides against Candida Species: Mechanistic Understanding and Therapeutic Implications. *ACS Infect. Dis*. 2025 **(JIF: 4.3).**
- Baba IA, Wani AZ, Ali S, MM Mubarak and **Ahmad Z ***.Actinomycetes - The Repertoire of Diverse Bioactive Chemical Molecules: From Structures to Antibiotics. *Curr. Top Med. Chem*. 2024. (**JIF: 3. 4**).
- Waseem A, Agarwal M, Jamal S, Gangwar R, Sharma R, Mubarak MM, AZ Wani, **Ahmad Z***, Khan A, Sheikh JA, Grover A, Bhaskar A, Dwivedi VP and Grover S. Revitalizing antimicrobial strategies: paromomycin and dicoumarol repurposed as potent inhibitors of *M. tb's* replication machinery via targeting the vital protein DnaN. *Int. J. Biol. Macromol.* 2024;278(3):134652. Doi: 10.1016/j.ijbiomac.2024.134652. (**JIF: 7.7**).
- Mubarak MM, Majeed S, Wani AZ, Kantroo HA, Malik MA and **Ahmad Z*.** DecipheringTuberculous Meningitis: From Clinical Challenges to Novel Models and Pathogenic Pathways. *Curr. Top Med. Chem*.2024. (**JIF: 3. 4**).
- Mehraj S and **Ahmad Z***; Enterococcus Unleashed: Decoding the Rise of a Formidable Pathogenic Force. *Acta Scientific Microbiology*. 2024: 58-77. (**JIF: 1.5**).
- Teli B, Mubarak MM, **Ahmad Z***, Bhat BA. Trifluoroacetic acid-mediated synthesis of xanthene constructs and their extensive anti-tuberculosis evaluation. *RSC Med Chem*. 2024. 12;15(4):1295-1306.(**JIF: 4.1**).

2. Scientific work done:

The year 2024–25 has seen several GOI funded projects, as well as lab initiatives, deliver high-impact outcomes across CNS-TB, MDR-TB, antifungal discovery, and antibacterial drug development with strong translational potential, reinforcing their role in shaping the future landscape of infectious disease therapeutics.

The **ICMR-GOI funded project on CNS-TB** has significantly advanced our understanding of neuroinfectious disease biology. Three major publications emerged, including (i) a comprehensive review positioning astrocytes as central regulators and therapeutic targets in neuropathogenesis, (ii) a critical appraisal of MMP-9 as both a biomarker and druggable mediator of blood–brain barrier disruption, and (iii) an original study uncovering the protective role of Sonic Hedgehog (SHH) signaling in CNS-TB and introducing a novel, rapid mouse model of CNS-TB through SHH inhibition. Together, these outputs not only reveal key host–pathogen interactions but also establish methodological innovations with strong translational value.

The **DBT-GOI funded project on new MDR-TB regimens**, though long-standing, continues to yield high-quality data. Recent work has identified diaryl ether dehydrozingerone derivatives as potent InhA inhibitors with robust activity against drug-susceptible, resistant, and MDR *M. tuberculosis*, alongside synergism with frontline drugs. Complementary drug-repurposing strategies revealed paromomycin and dicoumarol as inhibitors of the replication clamp protein DnaN, while novel dioxohexahydroxanthenes exhibited selective and rapidly sterilizing antimycobacterial activity. These advances underscore the project's enduring contributions to MDR-TB drug discovery.

In parallel, the DBT-GOI bioprospecting initiative exploring extremophilic actinomycetes from the high-altitude Leh–Ladakh ecosystem has uncovered 23 active isolates, with 15 extracts exhibiting potent bactericidal activity against both drug-susceptible and resistant *M. tuberculosis*. Metabolite profiling revealed diverse bioactive classes, underscoring extremophilic actinomycetes as a vital reservoir for novel anti-TB and antibacterial agents.

In antifungal drug discovery, the group has made notable progress. A 2025 *ACS Infectious Diseases* study reported ultrashort β-peptide P3 as a promising antifungal scaffold with broad anti-*Candida* efficacy, synergistic interactions, and inhibition of virulence traits. Complementary work on betulinic acid derivatives identified DTC2 as a potent fungicidal candidate. A 2025 *Bioorganic Chemistry* review further charted innovative antifungal strategies. Importantly, efforts have now been extended beyond *Candida* to clinically and industrially relevant *Aspergillus* species (*A. fumigatus, A. flavus, A. niger*), broadening the translational impact of this pipeline.

The **CSIR-GOI funded β-hairpin peptidomimetics project** has culminated in the discovery of compound 3 (LAU-β3,3-Pip-PEA), which demonstrated exceptional antibacterial activity, outperformed multiple standard drugs against MRSA and MDR *E. coli*, and showed superior efficacy in a murine wound infection model. Its stability, synergism with existing antibiotics, and mechanistic versatility (membrane disruption, DNA binding, post-antibiotic effect) highlight its translational promise as a next-generation anti-infective agent.

Finally, the **ongoing project on a novel anti-TB molecule, 3-Cinnamoyl-4-hydroxy-pyran-2-one,** is poised to provide pivotal insights into TB therapeutics. By integrating WGS, metabolomics, and proteomics of resistant mutants, it aims to validate this molecule as a strong candidate against drug-susceptible, tolerant, and MDR-TB, while also uncovering new druggable targets. This effort represents a forward-looking step toward filling critical gaps in MDR-TB drug development.
The sustained flow of high-quality publications, along with the expansion of horizons to additional fungal pathogens and the integration of omics-driven approaches **reflects the lab's strong momentum and** promise to generate powerful new insights and transformative advances in infectious disease therapeutics.

GURLEEN KOUR

Dr. Gurleen Kour (Scientist) with her Research Group

1. Publications/Patents:

Publications:

- Rupali Choudhary, Puneet Kumar, Jasha Momo H. Anal , Sanket K Shukla , Asha Bhagat, **Gurleen Kour**, Zabeer Ahmed. Synthesis and potential anti-inflammatory response of indole and amide derivatives of ursolic acid in LPS-induced RAW 264.7 cells and systemic inflammation mice model: Insights into iNOS, COX2 and NF-κB. *Bioorganic Chemistry*. 2025;155:108091. (IF:4.5)

- Diljeet Kumar, Ahmed M, Andrabi NI, Singh CP, Saroch D, Bharitkar YP, **Gurleen Kour**, Madishetti S, Asha Bhagat, Shukla SK, Zabeer Ahmed. Anti-inflammatory and anti-oxidant potential of dispiro-indanedione hybrid of parthenin via regulating Nrf2 and NF-κB/MAPK pathways. *European Journal of Pharmacology*. 2025 Jun 5; 996:177547. (IF:4.3)

- Manas Ranjan Barik, Harjot Kaur, Tanzeeba Amin, Harshita Tiwari, **Gurleen Kour**, Anindya Goswami, Zabeer Ahmed, Amit Nargotra. Network pharmacology and in vitro validation to elucidate the molecular mechanism of *Boswellia serrata* phytoconstituents on inflammation. *Journal of Proteins and Proteomics.* 2024; Vol 15; 473-459.

- Sharma BK, Sharma Y, Manzoor A, Ahmed M, Choudhary S, Rawal RK, Shukla SK, Ahmed Z, **Gurleen Kour**, Ravi Shankar . Design and synthesis of C-17 benzylidene derivatives of 14 deoxyandrographolide (14-DAG) and their TNF-α and IL-6 expression inhibitory activities. *Journal of Molecular Structure.* 2024, 1323: 140770. (IF:4.0)

- Ghazala Khanum, Shaghaf Mobin Ansari, Rupali Choudhary, **Gurleen Kour**, Vivek Gupta, Saleem Javed, Zabeer Ahmed, Bhahwal Ali Shah. Computational and biological evaluation of naphthofuran-based scaffold as an anti-inflammatory agent. *Journal of Molecular structure*, 2025, Vol 1321, 139989. (IF:4.0)

- Majid Ahmad Ganie, Shaghaf Mobin Ansari, Rupali Choudhary, Faheem Fayaz, **Gurleen Kour**, Vivek Gupta, Zabeer Ahmed, Saleem Javed, Bhawal Ali Shah. Investigation of an aminothiazole-based scaffold as an anti-inflammatory agent: Potential application in the management of cytokine storm in SARS-CoV-19. *Journal of Molecular structure*, Vol 1303, 2024, 137562. (IF:4.0).

2. Scientific work done:

Core Capabilities and Strengths

As a Scientist in the Pharmacology division, my primary focus is to identify and evaluate the therapeutic potential of in-house synthesized NCEs, extracts, fractions and institutional leads with further substantiation of their anti-inflammatory and anti-rheumatic potential. In this regard, I have developed an *in-vitro* osteoclastogenesis model using receptor activator of nuclear factor-κB ligand (RANKL)-stimulated osteoclast differentiation in RAW264.7 cells. We have further developed the Collagen Induced Arthritic (CIA) mice model using C57/BL6 mice while elucidating the effect of identified hits/lead on inflammation, cartilage erosion, bone destruction, paw swelling and the progression of arthritis in CIA mice while exploring their mechanism of action with a special emphasis on JAK/STAT signaling pathway.

Assays Established

- *In vitro*: RANKL-induced osteoclast differentiation
- *In vivo*: Collagen induced arthritic model

1. Work Highlight

- Determined the effect of novel chemical compounds and phytochemicals on receptor activator of nuclear factor-κB ligand (RANKL)-induced osteoclast formation in RAW264.7 cells and collagen-induced arthritis (CIA) in mice.
- To effectively study the expression of tartrate-resistant acid phosphatase (TRAP) and cathepsin K, on osteoclast formation and NF-κB signaling pathway.
- Estimation of the pro-inflammatory cytokine (TNFα, IL-6, IL-1β, IL-17 and interferon-γ) levels *in vitro* and *in vivo.*

- Elucidating the effect of the compounds/phytochemicals on inflammation, cartilage erosion, bone destruction, paw swelling and the progression of arthritis in CIA mice while exploring their regulation by matrix metalloproteinase and JAK–STAT signaling pathway.

2. Projects received

S.No	Title of the Project	Coordinating Agency	Contribution being made by you as representative of your organization*
1.	Mechanism based approach comprising concomitant administration of chlorogenic acid, a natural JAK/STAT inhibitor with leflunomide (DMARD) for the management of adverse drug reactions and improved efficacy in the treatment of rheumatoid arthritis.	Start-up Research grant (SRG) DST-SERB	PI (GAP-3161)
2.	Pre-IND enabling studies on *Adhatoda vasica* extracts for treatment of pulmonary fibrosis through hypoxia response modulation.	CSIR, Phytopharmaceutical Mission Project (2024-2026)	PI (MMP075201)
3.	Isolation, Pharmacopeial Standardization and Immunomodulatory activity of Unani drug *Habb-e-suranjan* and *Habbe-e-Asgand.*	Central council for Research in Ayurvedic Sciences (CCRAS)	Co-PI (GAP-2143)
4.	Optimisation of ursolic content in Lavender *Marc*, and its derivatives for anti-inflammatory and anti-arthritic potential.	SEED Grant, CSIR (2024-2026)	Co-PI

5.	Development of phyto pharmaceutical from withaferin A and withanolide-enriched fractions as a leptin sensitizer for obesity associated diabetes.	SEED Grant, CSIR (2024-2026)	Co-PI
6.	Towards discovery and development of novel drugs and pharmaceuticals (Deep Ocean Mission)	Ministry of Earth Sciences, Government of India	Team Member

SYED KHALID YOUSUF

Dr. Syed Khalid Yousuf (Sr. Scientist) with his Research Group

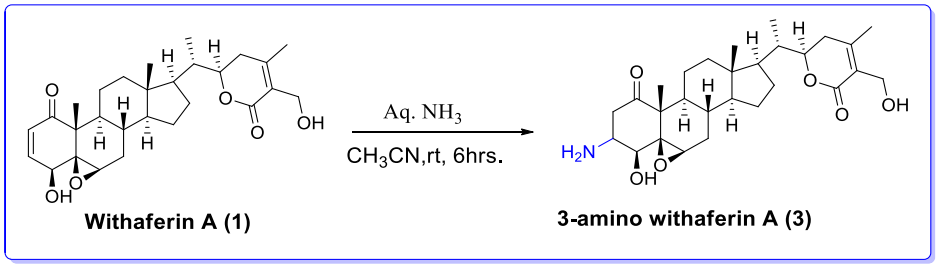
1. Publications/Patents:

Publications:

- Ahmad Mir S, Firdous S, Shahid Maqbool M, Hussain G, Yaqoob Bhat M, Malik FA, Khalid Yousuf S. Sonogashira coupling-based synthesis and in vitro cytotoxic evaluation of C-2 alkynyl derivatives of withaferin A. **Steroids** 2024, **212**, 109526
- Gulzar Hussain, Manzoor Ahmed, Sundas Chowdhary, Sanket K. Shukla & Syed Khalid Yousuf. *Synthesis and in vitro antiproliferative evaluation of novel drimane oxepinyl triazoles from labdane diterpene sclareol*. ***Med. Chem. Res***. 2025, **34**, 240–251
- Gulzar Hussain, Umar Ul Islam, Yogesh P. Bharitkar, Avinash Madhesiya, Tejender S. Thakur, Syed Khalid Yousuf. Drimane based substituted pyrano-oxepines from labdane diterpene sclareol; stereoselective synthesis, molecular docking simulations and in silico ADMET prediction studies. Tetrahedron, 2025, 184, 134758.

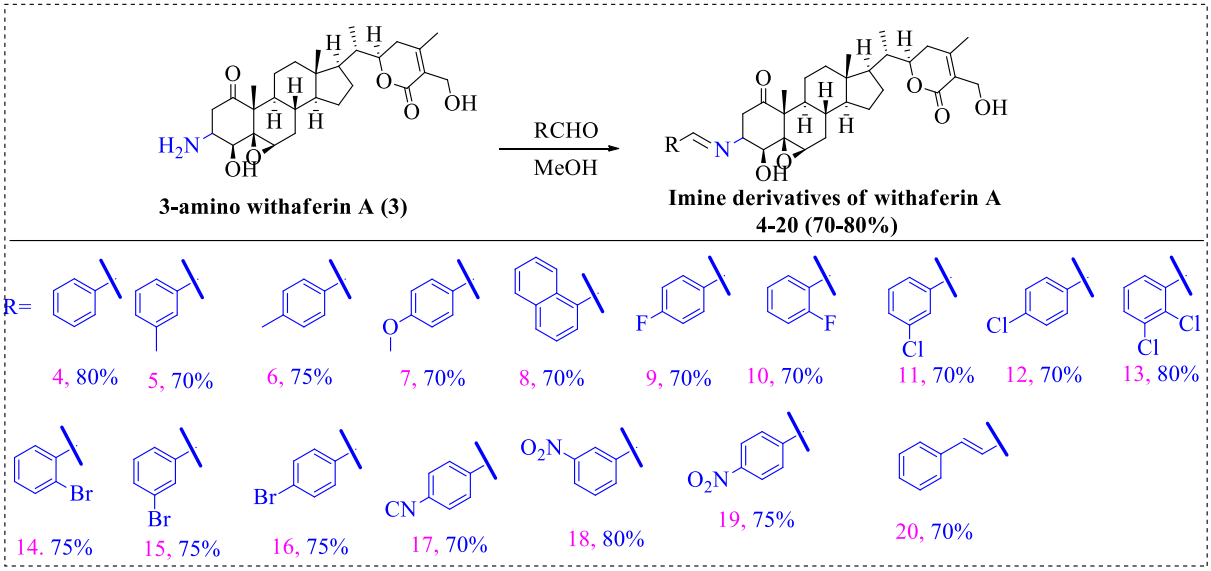
2. Scientific work done:

i) A synthetic strategy has been developed to synthesize 3-amino withaferin A (Scheme 1) and its amine derivatives. The resulting amine derivative is then subjected to an addition-elimination reaction with various aldehydes in ethanol, forming imine congeners of withaferin A (Scheme 2). The amine analog and its derivatives are evaluated for their cytotoxicity against eight cancers and one normal cell line. Compound **13**, the imine derivative of withaferin A demonstrated significant



Scheme 1. Synthesis of 5-amino withaferin A from withaferin A using liq. NH_3.

antiproliferative and anti-metastatic properties across various cell lines such as Breast cancer, colon cancer, prostate cancer, pancreatic and lung cancer cell lines. Breast cancer is the second leading cause of cancer-related deaths among women worldwide. Specifically, triple-negative breast cancer (TNBC) has been a challenge to treat owing to its aggressive behavior and has a poor prognosis with a median overall survival (OS) of less than two years. The results from the

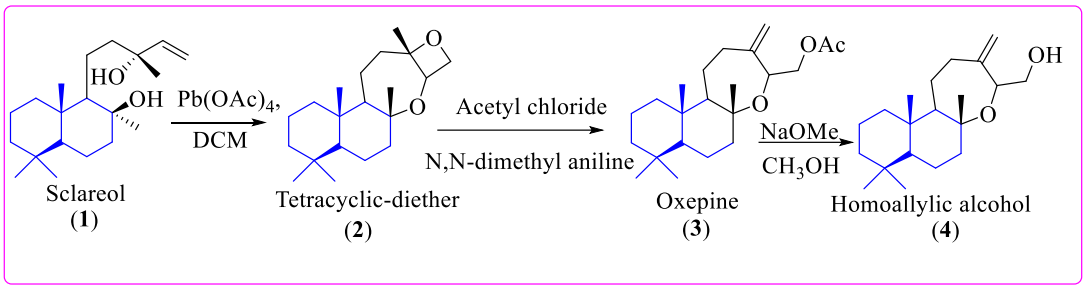


Scheme **2**. Reaction of 3-amino withaferin A with aldehydes

cell scattering assay, Boyden chamber assay, and wound healing assay support the antimigratory effect of compound **13**. Compound **13** robustly inhibited the formation of invadopodia and filopodia, highlighting its strong anti-invasive properties. Additionally, Immunoblotting studies showed

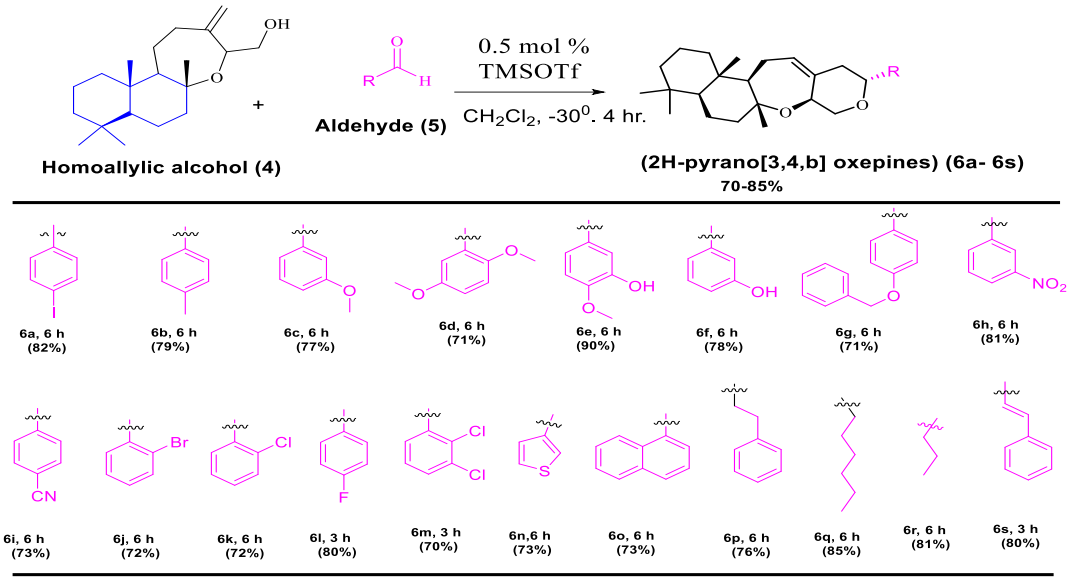
a consistent decline in the expression of various EMT markers in the presence of compound **13**, thus confirming the anti-metastatic properties of compound **13**.

ii) Heteroatoms and heterocyclic scaffolds are frequently present as the common cores in a plethora of active pharmaceuticals natural products. Statistically, more than 85% of all biologically active compounds are heterocycles or comprise a heterocycle and most frequently. These facts disclose and emphasize the vital role of heterocycles in modern drug design and drug discovery. Scalreol has been used as versatile starting material for the synthesis of various industrially important materials like ambrox along with other diterpenes containing the labdane core. We also envisioned the conversion of scalreol to homoallylic alcohol **4** containing a labdane core along with an oxepane ring using the reaction **scheme 3**.



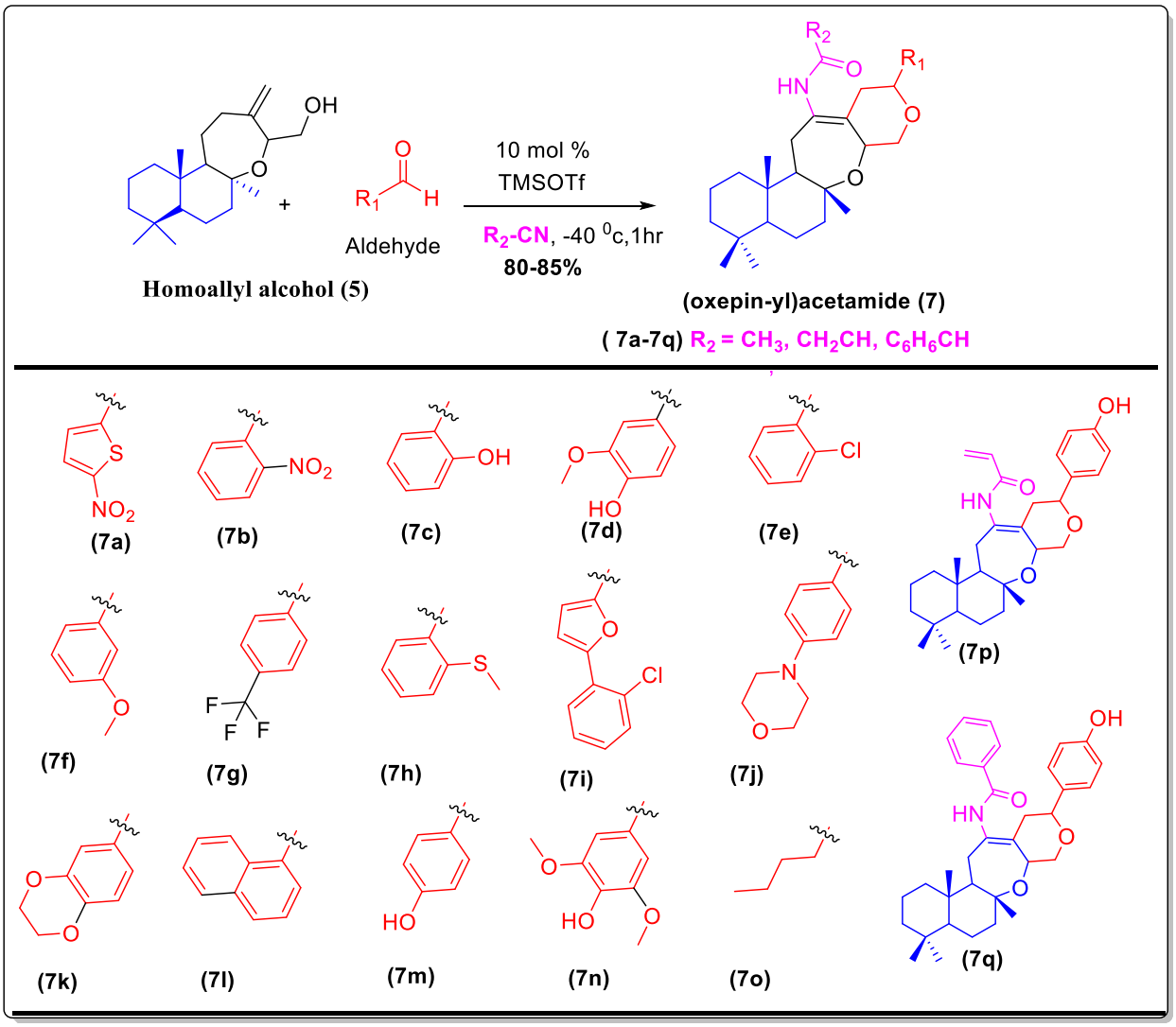
Scheme 3. Synthesis of homoallylic alcohol **4** from sclareol.

Keeping in view the synthetic importance of homoallylic alcohols, we explored the synthetic potential of Prins cyclisation and the associated reactions including aza-Prins, Ritter-Prins etc. to afford the new heterocycles (scheme 4).



Scheme 4: The synthetic route for the synthesis of oxepine fused tetrahydropyrans.

Encouraged by these results, we explored the Prins-Ritter[41] reaction for the preparation of amido-derivatives of 2H-Pyrano[3,4,b]oxepines from scalreol through the key intermediate homoallylic alcohol **4**. The Prins-Ritter reaction involves a three-component coupling of homoallylic alcohol, aldehyde, and nitriles to afford amido-tetrahydropyrans. The general reaction strategy for the synthesis of targeted molecules is as follows (Scheme 5).With respect to substrate scope various aldehydes bearing electron donating, electron-withdrawing groups smoothly reacted under the optimised reaction conditions to afford the targeted amido-derivatives of 2H-Pyrano[3,4,b]oxepines. Heterocyclic aldehydes also reacted to yield the corresponding desired products. In the study, besides acetonitrile, acrylonitrile and benzo nitrile were also used for diversification. All synthesized compounds were characterized through various spectroscopic techniques.



Scheme 5: Synthesis of amido-derivatives of 2H-Pyrano[3,4,b]oxepines

FARINA SULTAN

Dr. Farina Sultan (Scientist) with her Research Group

1. Publications/Patents:

Publications:

- Tanwar J, Ahuja K, Sharma A, Sehgal P, Ranjan G, **Sultan F**, Agrawal A, D'Angelo D, Priya A, Yenamandra VK, Singh A, Raffaello A, Madesh M, Rizzuto R, Sivasubbu S, Motiani RK. Mitochondrial calcium uptake orchestrates vertebrate pigmentation via transcriptional regulation of keratin filaments. PLoS Biol. 2024 Nov 11;22(11):e3002895. doi: 10.1371/journal.pbio.3002895. PMID: 39527653; PMCID: PMC11581414.

2. Scientific work done:

Currently, the lab we are working on two diseases – obesity and skin pigmentation.

Obesity: Obesity is complex chronic health problem of 21st centaury which has become doomed to the mankind due to associated risk of type II diabetes, cardiovascular diseases and MAFLD. Medically obesity is a metabolic disorder of excessive fat accumulation by adipocytes and chronic low-grade inflammation affecting peripheral tissues like muscles and the liver. Clinically, the treatment of obesity is a challenging task and is not very successful due to the associated side effects and weight regain after the removal of the therapy. A need to revisit the current treatment regime and identify natural molecules

and plant based products will hold the future of obesity therapeutics. In first project, we are working on identifying targetable pathways and redirecting the natural molecules to target these pathways. We have shortlisted molecules to target adiponectin pathway from the IIIM repository using in-silico screening and further validated their effect in C2C12 muscle differentiation model. In second project, we are also working on *Withania somnifera* plant extract standardization and its effect on fat accumulation in 3T3-L1 muscle cells. Our study demonstrates that root extract is more efficient in targeting lipid accumulation. Overall our lab is working on synthetic molecules, natural compounds and plant extract to target different aspect of obesity.

Skin pigmentation disorders: skin pigmentation is a most evident evolutionary trait in human race that has selected in shorted few thousand years based on exposure to sunlight. Skin pigmentation is protective against UV radiation and its harmful effects such as skin cancers. Skin pigmentation disorders comprises of patchy skin tone either hyper or hypopigmentary. It is crucial to understand these disorders because of the high prevalence in Indian subcontinent, their impact on quality of life, and their potential link to underlying systemic diseases. Metabolic diseases such as obesity and diabetes may causes hyper-pigmentation patches on neck. Lab work revolve around a keen interest to understand how these metabolic disorders can impact skin pigmentation and identifying novel natural products for targeting skin pigmentation disorders. One of the project aims to identify the role of flaxseed oil/ extract in modulating skin pigmentation. We have established B16 pigmentation model. Our overall aim is to develop natural product based formulation of skin pigmentation disorders.

AMOL B. GADE

Dr. Amol B. Gade (Scientist) with his Research Group

1. Publications/Patents:

Publications:

- One-pot oximation-Beckmann rearrangement under mild, aqueous micellar conditions
  Maryam Nabi, Kirti Sharma, Raj S. Wandre and Amol B. Gade
  Green Chem., **2025***, 27*, 5332.

Patents:

- A Process for the Preparation of Lenalidomide and Intermediates Thereof Amol B. Gade, Ahemad M. Pathan, Raj S. Wandre, Zabeer Ahmed 202411100693 (18-Dec-2024).

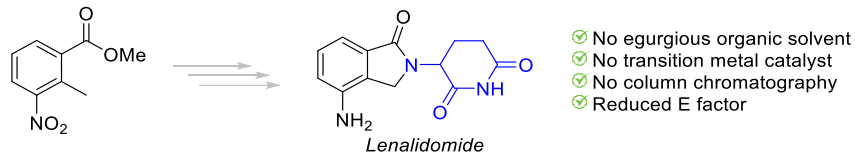
- Pyridine-3-yl quinolin-2(1H)-one Derivatives as Anti-Viral Agent Maryam Nabi, Raj S. Wandre, Yogesh Sardana, Alna K. Martin, Gunjan Lakhanpal, Bokara K. Kumar, Amit Nargotra, Qazi N. Ahmed, Amol B. Gade, Zabeer Ahmed 202411101808 (20-Dec-2024).

2. Scientific work done:

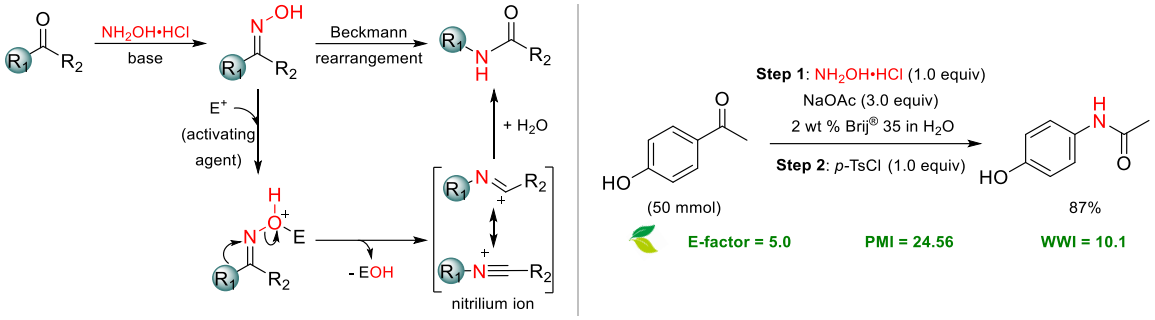
The research group is engaged in sustainable organic synthesis and process development, with a strong emphasis on developing pharmaceutically relevant compounds through environmentally responsible and scalable methodologies. As part of the CSIR-Active Pharmaceutical Ingredient—Affordable Health Care (API-AHC) mission, we developed a green, sustainable, and scalable synthetic process for

Lenalidomide, an essential immunomodulatory drug widely used in the treatment of multiple myeloma and various hematologic cancers such as mantle cell lymphoma, follicular lymphoma, and marginal zone lymphoma. Given the growing demand for cost-effective oncology treatments and the strategic need for self-reliance in critical APIs, this mission project directly supports national initiatives like Atmanirbhar Bharat, Ayushman Bharat, and Make in India.

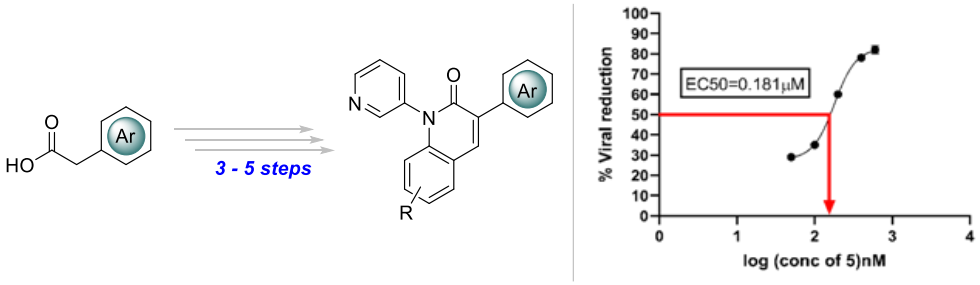
The newly developed route overcomes the environmental and economic challenges associated with conventional Lenalidomide synthesis, which typically relies on toxic polar solvents (e.g., DMSO, NMP), hazardous reagents, and expensive palladium-based catalysts. The process not only minimizes environmental footprint but also enhances safety, lowers energy requirements, and significantly reduces the cost of production. Furthermore, the process eliminates palladium catalysis by employing metal-free reduction strategies, which mitigates concerns related to residual metal contamination and simplifies purification. The process has been validated up to the decagram scale in the laboratory, achieving >99.5% purity with high yields and simplified crystallization. Enhanced green chemistry metrics—including low E-factor and process mass intensity—confirm its applicability.



Yet another work highlighting a novel, green, and scalable synthetic protocol for the one-pot oximation–Beckmann rearrangement has been reported under mild aqueous micellar conditions. This sustainable methodology enables the efficient transformation of readily available ketones into valuable amides—such as paracetamol and ε-caprolactam—in a single-pot operation, with yields up to 96%. The process utilizes biodegradable nonionic surfactants (e.g., Brij® 35) to form nanomicelles, replacing conventional toxic solvents and harsh acidic conditions typically used in traditional Beckmann rearrangements. The protocol was optimized using *p*-toluenesulfonyl chloride as an activating agent and buffered reaction media to control pH and avoid undesired hydrolysis. A wide substrate scope was demonstrated, including electron-rich, electron-deficient, heteroaryl, aliphatic, and steroidal ketones, showcasing excellent chemoselectivity and functional group tolerance. Notably, gram-scale synthesis of API like paracetamol and commercially valuable compound (ε-caprolactam) validated the scalability and robustness of the process. Additionally, the method facilitates direct conversion of aldehydes to nitriles and was successfully extended to pharmaceutically relevant ketones such as testosterone and ketoprofen. Environmental metrics for the gram-scale synthesis of paracetamol—E-factor (5.0), process mass intensity (24.56), and wastewater intensity (10.1)—underscore the greenness of this protocol. Moreover, the aqueous micellar medium was recyclable for up to three cycles with minimal loss in yield.



In parallel, contributing to the CSIR-Antiviral mission, we designed and synthesized a novel class of 3-aryl-1-(pyridin-3-yl) quinolin-2(1H)-ones as potential inhibitors of SARS-CoV-2. These compounds are inspired by the structural framework of perampanel-derived non-covalent inhibitors, which have shown strong affinity for main protease (M^{pro}) by engaging key catalytic residues such as His41 and Cys145 through hydrogen bonding and hydrophobic interactions. The rational design integrates the quinolin-2-one core known for its broad antiviral and pharmacologically relevant activity with pyridinyl and aryl substituents to enhance binding affinity and selectivity. Preliminary in vitro assays indicate that these molecules exhibit promising viral inhibition, supporting their potential as selective antiviral agents. Their non-covalent mode of action also suggests reduced toxicity and a lower likelihood of resistance development compared to covalent inhibitors. These findings contribute significantly to the development of next-generation small-molecule therapeutics against COVID-19 and may offer a platform for broader antiviral drug discovery.



GOVIND YADAV

Dr. Govind Yadav (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- **Qasam, I**; Nawaz, S; Kumar, C; Kumari, H; Dhiman, S; Wazir, P; **Yadav, G.** Novel Semisynthetic Derivative of Dehydrozingerone (DHZ-15) Modulates Lipopolysaccharide-Stimulated Macrophages by Targeting the NF-κB/p65 Pathway and In Vivo Evaluation in a Sepsis BALB/c Model, Clinical and Experimental Pharmacology and Physiology, 2025; 52:e70063, https://doi.org/10.1111/1440-1681.70063
- Rahul Bhat, Neha Jeena, Samsher Singh, Nitin Pal Kalia, **Narendra Singh Chauhan**, Surrinder Koul, **Govind Yadav,** Saurabh Saran, Inshad Ali Khan, 5-(3, 4-methylenedioxyphenyl)-4-ethyl-2E, 4E-pentadienoic acid piperidide as MdeA efflux pump inhibitor of Staphylococcus aureus,Biochimie,Volume 237,2025,Pages 125-137,ISSN 0300-9084, https://doi.org/10.1016/j.biochi.2025.07.016.
- Clement Odunayo Ajiboye, Dorcas Olufunke Moronkola, **Arfan Khalid**, Akinbo Akinwumi Adesomoju, Sagar S. Bhayye, Yogesh P. Bharitkar, **Govind Yadav**, Mahendra Kumar Verma. Isolation, characterization, HPLC quantification, in-vitro and in-silico evaluations of coumarins and coumarolignans from Blighia unijugata stem with their chemotaxonomic significance, Biochemical Systematics and Ecology.2025, 120,104950,ISSN 0305-1978, https://doi.org/10.1016/j.bse.2024.104950.

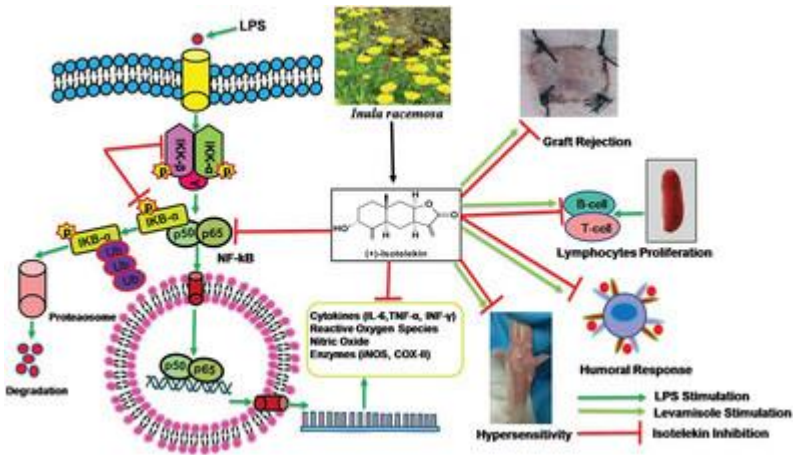
- **Qasam I**, Nawaz S, Kumari H, Chauhan N, Nalli Y, **Yadav G.** Evaluation of Anti-Inflammatory and Immunosuppressant Potential of Isotelekin in Lipopolysaccharide (LPS) Stimulated Macrophage (RAW 264.7) and Sheep Red Blood Cells (SRBC) Sensitized Murine Models. Adv Biol (Weinh). 2024 Oct 16:e2400386. doi: 10.1002/adbi.202400386. Epub ahead of print. PMID: 39410831. **https://doi.org/10.1002/adbi.202400386**
- Jasbir Kour, Bashir Ahmad Lone, **Amit Kumar**, Bashir A. Ganai, **Govind Yadav**, Prasoon Gupta, Md.Niamat Ali, Seema Akbar,Bioassay-guided isolation and identification of antimutagenic compounds from *Morina coulteriana* and evaluation of its therapeutic potential., PhytomedicinePlus5(2025)100676, , https://doi.org/10.1016/j.phyplu.2024.100676.
- Hossain, M.M., **Khalid, A.,** Akhter, Z., Parveen, *S.,* Ayaz,M.O., Bhat,A.Q., Badesral,N., Showket,F., Dar,M.S.,Ahmed,F.,Dhiman,S.,Kumar,M.,Singh,U.,Hussain,R.,Keshari,P.,Ghulam,M.,Nargotra, A.,Taneja,N.,Gupta,S.,Mir,R.A.,Kshatri,A.S.,Nandi,U.,Khan,N.,Ramajayan,P.,**Yadav,G.,**Ahmed, Z.,Singh,P.P.,Dar,M.J. Discovery of a novel and highly selective JAK3 inhibitor as a potent hair growth promoter. *J Transl Med* **22**, 370 (2024). https://doi.org/10.1186/s12967-024-05144-4

2. Scientific work done:

Evaluation of Anti-Inflammatory and Immunosuppressant Potential of Isotelekin in Lipopolysaccharide (LPS) Stimulated Macrophage (RAW 264.7) and Sheep Red Blood Cells (SRBC) Sensitized Murine Models

The present study explored the natural compound Isotelekin isolated from Inula racemose against anti-inflammatory and immunomodulatory potential in LPS-induced RAW264.7 cell lines and immune-elevated SRBC-sensitized animal models. Isotelekin in in vitro studies, inhibited the production of Th-1 cytokines Interleukin-6 (IL-6), Tumour necrosis factor (TNF-α), and Interferon-gamma (INF-γ), and increased Th-2 cytokines Interleukin-10 (IL-10). Whereas it inhibited the nitrites and reactive oxygen species (ROS) production by mitigating the effect of LPS significantly. In vivo immunomodulatory activity in Delayed-type hypersensitivity (DTH) and Hemagglutinating antibody (HA), Isotelekin suppressed the cellular as well as humoral immunity in immune-affected and SRBC-sensitized mice. Isotelekin decreased the phagocytic responses against carbon particles and plaque-forming mainly IgG (Immunoglobulin G) production. Additionally, Isotelekin showed immunosuppressive potential through the evaluation of splenocytes, allograft acceptance, and haematological parameters. Molecular studies, including western blot analysis and immunocytochemistry, revealed that Isotelekin reduced the expression of iNOS (Inducible nitric oxide synthase), COX-2 (Cyclo-Oxygenase 2), and p-IkBα (Phospho I-kappa-B-alpha), and significantly inhibited the nuclear translocation of NF-κB/p65. Based on these results, Isotelekin at 10 µm in in vitro and at 30 mg kg^{-1} in in vivo demonstrated strong anti-inflammatory and immunosuppressive therapeutic potential.

Keywords: RAW 264.7 macrophages; allograft; anti-inflammatory; cell-mediated immunity; humoral immunity; isotelekin.



Clients Details: 2024-25

No. of client	Animals (IIIM-Pedigreed)	Amount
9	761	331200 (3.31Lakh)

Name of client	Institution	State
Deputy Director, RIUM, SRINAGAR	RRIUM, SRINAGAR	J&K
Prof (Dr.) SAMEENA	GMC, Srinagar	J&K
Dr. Khalid Z. Masoodi	SKUAST-K	J&K
Dr. Pawan Kumar Verma	SKUAST-J	J&K
Mr. Avinsh kumar, PhD, Prof.Saroj Arora	GNDU, Amritsar	Punjab
Monika attre c/o Prof. Pankaj	SKUAST-Jammu	J&K
Bhumika kapoor c/o Dr Pankaj	SKUAST -J	J&K
Dr. Showkeen	SKUAST-K	J&K
Dr. Tajpreet Kaur/ Principal Khalsa College, Amritsar	Khalsa college Amritsar	Punjab

Training Details: 2024-25

No. of Trainee	Training Area	Amount
8	Preclinical studies	230000 (2.30Lakh)

Name of Trainee	Institution/University	State	Period	Training Area
Nitika Chauhan	Bahra university	HP	6 Month	Antistress activity
Mahima Choudhary	Bahra university	HP	6 Month	Antimicrobial activity
Anchal choudhary	Bahra university	HP	6 Month	Immunomodulation
Sidhant Sharma	IEC UNIVERSITY BADDI	HP	4Month	Cardiotoxicity
Tanisha Khandelwal	Chandigarh University	Punjab	6 Month	Antistress Activity
Simran	Chandigarh University	Punjab	6 Month	Immunomodulation
Koka Sai Santosh Koushik	National Forensic Sc.	Gujrat	6 Month	Genotoxicity
Manshi Chandan	Baba Gulam Shah Badshah	J&K	6Month	Tissue repair

Clients and Training Details
2024-25

Name of client	Institution	State
Deputy Director, RIUM,SRINAGAR	RRIUM,SRINAGAR	J&K
Prof(Dr.) SAMEENA	GMC ,Srinagar	J&K
Dr.Khalid Z. Masoodi	SKUAST-K	J&K
Dr. Pawan Kumar Verma	SKUAST-J	J&K
Mr. Avinsh kumar,PhD, Prof.Saroj Arora	GNDU,Amritsar	Punjab
Monika attre c/o Prof. Pankaj	SKUAST-Jammu	J&K
Bhumika kapoor c/o Dr Pankaj	SKUAST -J	J&K
Dr. Showkeen	SKUAST-K	J&K
Dr. Tajpreet Kaur/ Principal Khalsa College,Amritsar	Khalsa college Amritsar	Punjab

No. of client	Animals (IIIM-Pedigreed)	Amount
9	761	331200 (3.31Lakh)

Over all Distribution of client in five years

Name of Trainee	Institution/University	State	Period	Training Area
Nitika Chauhan	Bahra university	HP	6 Month	Antistress activity
Mahima Choudhary	Bahra university	HP	6 Month	Antimicrobial activity
Anchal choudhary	Bahra university	HP	6 Month	Immunomodulation
Sidhant Sharma	IEC UNIVERSITY BADDI	HP	4Month	Cardiotoxicity
Tanisha Khandelwal	Chandigarh University	Punjab	6 Month	Antistress Activity
Simran	Chandigarh University	Punjab	6 Month	Immunomodulation
Koka Sai Santosh Koushik	National Forensic Sc.	Gujrat	6 Month	Genotoxicity
Manshi Chandan	Baba Gulam Shah Badshah	J&K	6Month	Tissue repair

No. of Trainee	Training Area	Amount
8	Preclinical studies	230000 (2.30Lakh)

RAMAJAYAN PANDIAN

Dr. Ramajayan Pandian (Senior Scientist) with his Research Group

1. Publications/Patents:

Publications:

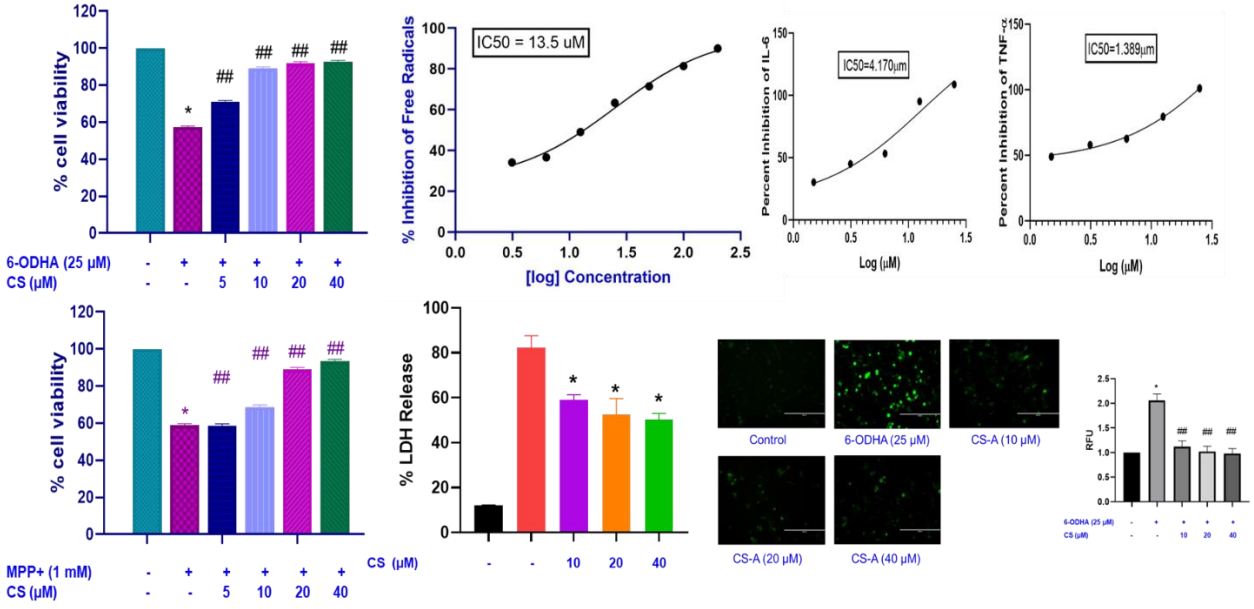
- Arti Rathore, Irshad Ahmad Zargar, Jyoti Kumari, Biplab Sarkar, Rakshit Manhas, Shifa Firdous, **Ramajayan Pandian**, Debaraj Mukherjee & Avisek Mahapa. Synthesis and antibacterial evaluation of trisindolines against methicillin-resistant *Staphylococcus aureus* targeting cell membrane. *npj Biofilms Microbiomes*, **11**, 184 (2025). https://doi.org/10.1038/s41522-025-00739-1.
- Sandha, Kamalpreet Kaur, Sukhleen Kaur, Kuhu Sharma, Syed Mudassir Ali, **Ramajayan Pandian**, Ajay Kumar, and Prem N. Gupta. Autophagy inhibition alleviates tumor desmoplasia and improves the efficacy of locally and systemically administered liposomal doxorubicin. Journal of Controlled Release. 2025, 378, 1030-1044. (https://doi.org/10.1016/j.jconrel.2024.12.078).
- Aalim Maqsood Bhat, Irshad Ahmad Bhat, Mushtaq Ahmad Malik, Peerzada Kaiser, **Ramajayan Pandian**, Sheikh R. Rayees, Zabeer Ahmed, and Sheikh Abdullah Tasduq. Inhibition of IKK complex by (2 methyl butyryl) Shikonin, a naturally occurring naphthoquinone, abrogates melanoma growth and progression via modulation of the IKK/NFκB/EMT signaling axis. International Immunopharmacology. 2025, 148:114026. (https://doi.org/10.1016/j.intimp.2025.114026).

- Sapna Saini, G Lakshma Reddy, Anjali Gangwar, Harpreet Kour, Gajanan G Nadre, **Ramajayan Pandian**, Sunny Pal, Utpal Nandi, Rashmi Sharma, and Sanghapal D Sawant. Discovery and biological evaluation of nitrofuranyl–pyrazolopyrimidine hybrid conjugates as potent antimicrobial agents targeting Staphylococcus aureus and methicillin-resistant S.aureus. RSC Medicinal Chemistry. 2025, 16, 1304-1328. (https://doi.org/10.1039/D4MD00826J).

2. Scientific work done:

Insights into non-cannabinoids (Spiro-indanes) in the modifications of Parkinson's Disease

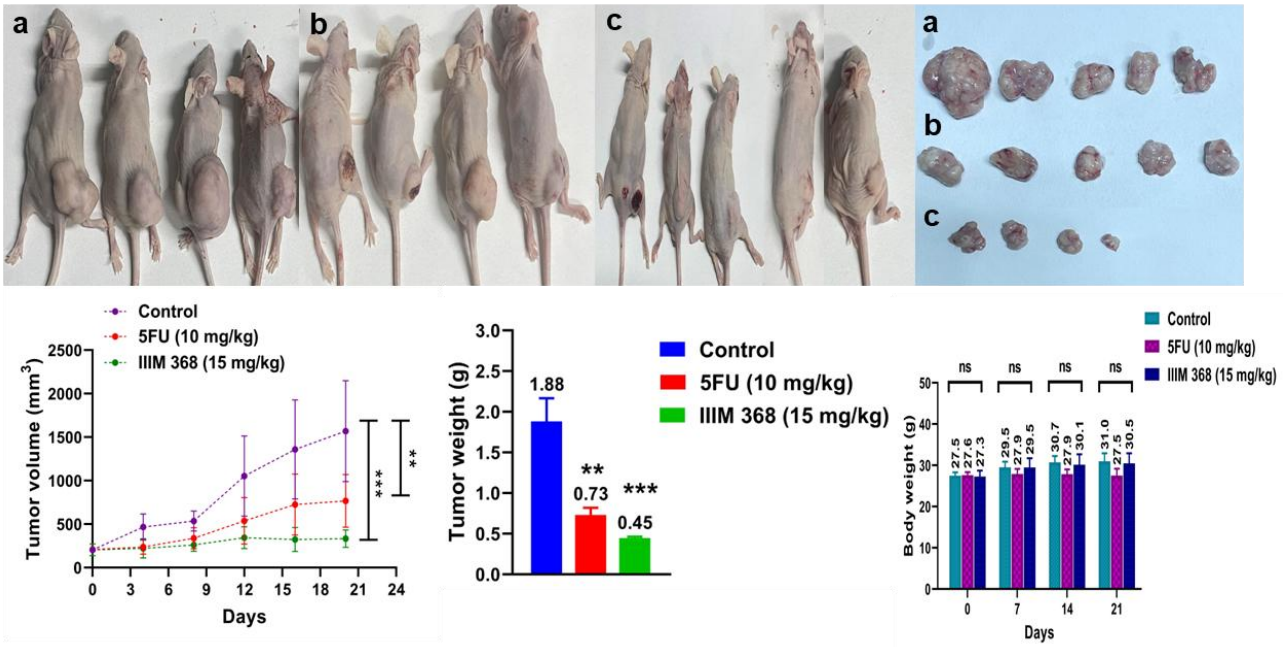
Parkinson's Disease (PD) is the second common neurodegenerative disease with the selective degeneration of midbrain dopaminergic (DA) neurons in the substantia nigra region of the brain, leading to changes in the neurotransmission of basal ganglia motor function. Oxidative stress, mitochondrial dysfunction, neuroinflammation, dysregulation of protein degradation through autophagy, and gut dysbiosis are the common identified mechanisms of PD, which impose great challenges in targeted drug development. CBD has been explored for its neuroprotective effect through autophagy-mediated clearance of alpha-synuclein and inhibition of the NLRP3 inflammasome. However, non-cannabinoid constituents were still not explored for their activities. In our research work, we explored the neuroprotective effects of cannabis spiro-indanes in an MPP+ induced Parkinson's model using BE(2)-M17 cells. The extract demonstrated high cell viability, contrasting with MPP+ induced neurotoxicity, and exhibited effective antioxidant and anti-inflammatory activities in BE(2)-M17 and J774a.1 cells.



Development of Xenograft models in Athymic nude mice for cancer research

The xenograft model was developed using HTC 116, OVCAR-8, A549 cell lines, etc., in athymic nude mice (NU/J Foxn1nu https://www.jax.org/strain/002019) maintained at the Animal House Facility. The mice were housed in individually ventilated cages (IVCs) under controlled environmental conditions,

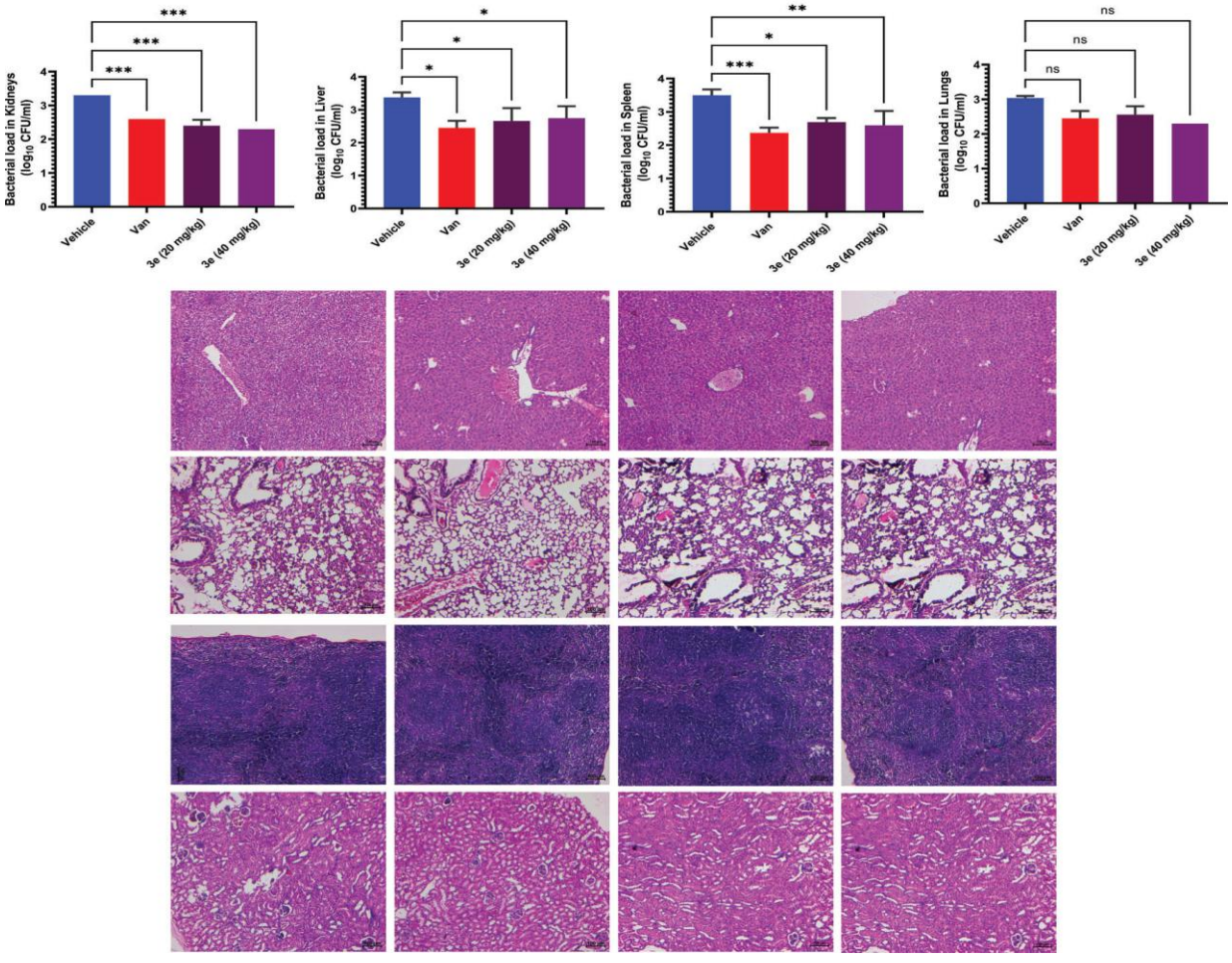
with a temperature of 25 ± 2 °C, a Relative Humidity of 50-60%, and a 12-hour light/dark cycle. Gamma irradiated feed and autoclaved RO water were provided *ad libitum* to all experimental animals. The cells were cultured in DMEM media with 10% FBS (Fetal Bovine Serum) and harvested by trypsinization. The cell pellets were resuspended in sterile PBS at 5 x 10^6 cells/100 µL. To develop a xenograft model in athymic nude mice, the cell suspension was mixed with Matrigel at a 1:1 ratio and injected subcutaneously in the right flank region of each mouse. The tumor volume was calculated using the formula: TV (mm3) = (L x W2)/2, where L is the length (largest reading) and W is the Width (shortest reading). When the tumor volume reached around 150-200 mm3, the mice will be randomized for the experiments. After experiments, the animals were humanely euthanized by CO2 asphyxiation, and tumors were excised and weighed using a calibrated analytic balance. The experimental data were analyzed by one-way ANOVA using GraphPad Prism 8.0. Dunnett's t-test was used as *post hoc* to measure the significance between the control and other groups at $P<0.05$.



Development of infectious mice model for anti-microbial activities

The systemic infection model was developed in Balb/c mice bred and maintained at the Animal House Facility of CSIR-Indian Institute of Integrative Medicine. The procedure for systemic mice infection was approved by the Institutional Animal Ethics Committee (IAEC), CSIR-IIIM (IAEC No.: 406/84/8/2024), adhering to the guidelines of the Committee for Control and Supervision of Experiments on Animals (CCSEA). A total of 24 MRSA free (uninfected) female Balb/c mice (25–30 g) were involved in this study. The mice were housed in IVC's (Individually Ventilated Cages) under controlled environment conditions with temperature 25 ± 2 °C, Relative Humidity of 50–60% and a light cycle of 12 h light/dark. Autoclaved rodent feed and RO water were provided ad libitum to all experimental animals. The mice were acclimatized to experimental condition for 5 days prior to inoculation. Based on the body weight, the mice were randomized to four groups (n=6mice/group). Group I—Vehicle control, Group

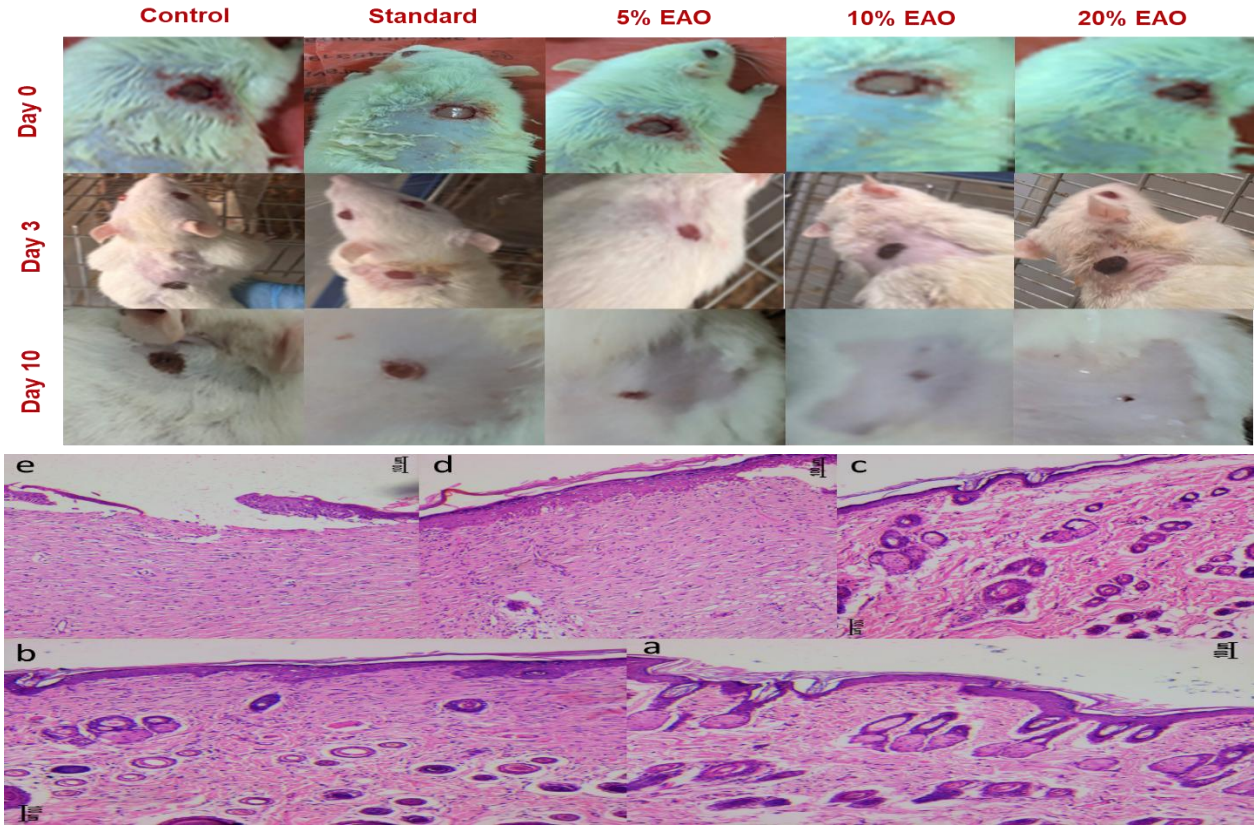
II—Standard control (Vancomycin), Group III and IV—Two different concentrations of compound 3e. The mice systemic infection experimental model was developed according to the described protocol with slight modifications. Mice were first infected with 100 µL MRSA suspension (106 cells/100 µL) via intraperitoneal injection. After 12 hours of incubation, two doses of treatment were administered intraperitoneally with a 4-hour interval. Group III and IV mice were treated with the compound at the designated dose concentrations of 20 mg/Kg and 40 mg/Kg body weight (b.w.), respectively. Group II mice were administered standard antibiotic vancomycin at 20 mg/Kg b.w., whereas Group I was injected with vehicle (5% DMSO, 30% PEG 200 and 2% Tween 20) in distilled water. Around 4 h of final treatment, all animals were humanely euthanized by cervical dislocation and samples of organs such as liver, lungs, spleen and kidneys were collected to examine the MRSA load via colony plating method. The organs, including the liver, lungs, spleen, and kidneys, were collected in 10% neutral buffered formalin for histopathological examination. The tissue sections (10 µm) were stained with hematoxylin and eosin (H&E) and viewed at 10x and 40x magnifications using the light microscope (Leica, DM750) for histopathological analysis.



Sponsored Studies Conducted at Animal House Facility

Evaluation of wound healing activity of *Eupatorium adenophorum* Essential Oil in Wistar rats

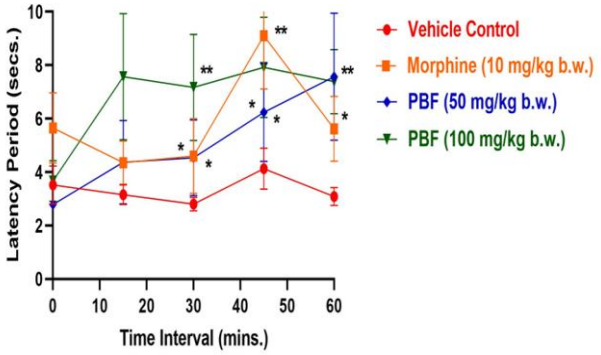
The study was conducted to evaluate the wound-healing activity of *Eupatorium adenophorum* essential oil (EAO) using a surgical excision wound model in Wistar rats. *Eupatorium adenophorum* essential oil was prepared at concentrations of 5%, 10%, and 20% in distilled water and applied topically at a dose volume of 0.5 mL per animal daily for 14 days. The wound contraction area was recorded using a vernier calliper on days 0, 2, 5, 7, 10, and 14, respectively. EAO at 10% and 15% concentrations demonstrated significant wound closure from day 5 to day 10 compared to the control group, indicating its rapid wound-healing activity. Similarly, there was a gradual and significant increase in the percentage of wound closure in 10% and 15% EAO groups compared to the control up to day 10. The histopathological examination of the EAO groups revealed re-epithelialization with intact skin morphology, including epidermis, dermis, and hair follicles. From these findings, it can be concluded that *Eupatorium adenophorum* essential oil, at concentrations of 10% and 15%, exhibits better wound-healing activity in Wistar rats than the control and standards.

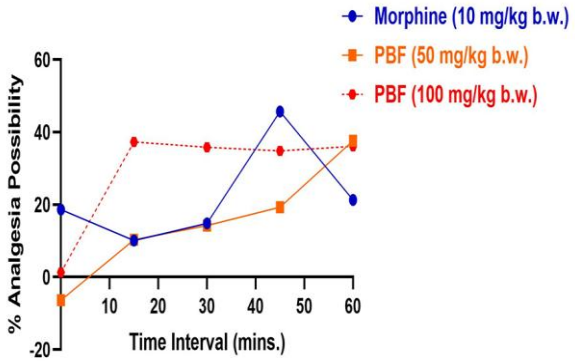


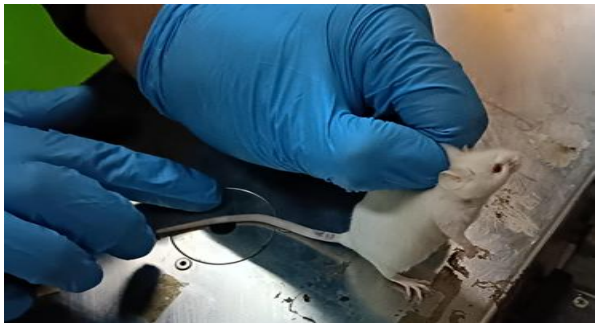
Evaluating the analgesic activity of furanoeudesma-1,3-diene (pbf) by tail flick test in Balb/c mice

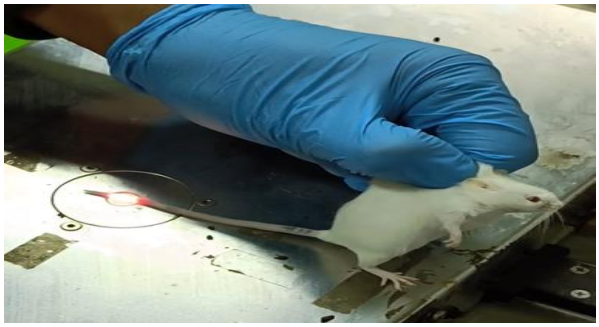
The study aims to evaluate the analgesic activity of Furanoeudesma-1,3-diene (PBF) in Balb/c mice by tail flick test using an analgesia meter. PBF was administered orally at the dose of 50 mg/kg and 100 mg/kg body weight (b.w.), while the standard morphine was dosed at 10 mg/kg b.w. The dose formulation was prepared using PEG 200 (Polyethylene Glycol 200) as the vehicle for all the treatment

groups, whereas the control animals received only PEG at 10 ml/kg b.w. *Per os*. The analgesic effect was measured by an analgesia meter (Tail Flick 602000 series, TSE Systems), and the percentage of maximum possible analgesia (MPA) was calculated using the standard formula. PBF at both doses exhibited a significant analgesic effect at different time intervals than the control groups. PBF showed an MPA of 36.1 – 37.6 %, equivalent to morphine (45.7%). From the study findings, it can be concluded that PBF, when administered orally in Balb/c mice, possessed significant analgesic (antinociceptive) activity in the tail flick test.









SABHA JEET

Dr. Sabha Jeet (Principal Scientist) with his Research Group

1. Publications/Patents:

Publications

- Yadav, G.K., Baligah, Syed Hujjat Ul, Jeet, S., Kumar, V. and Bhanwaria, R. 2024. Therapeutic potential and chemo-morphological characterization of silver nanoparticles synthesized using aqueous extracts of Monarda citriodora Cerv. Ex Lag., Biocatalysis and Agricultural Biotechnology, Volume 57: pages 103076, Publisher: Elsevier, DOI: https://doi.org/10.1016/j.bcab.2024.103076, (I.F. 3.40).
- Jeet, S., Verma, R., Yadav, G.K., Bhagat, S., Tabassum, S., Kumar, K., and Bhanwaria, R. 2024. Morphological and phenological characteristic, oil yield, quality and economics of Lemon bee balm (Monarda citriodora Cerv. ex-Lag) at diverse environment condition, India. The

Institutional number of this manuscript is CSIR-IIIM/IPR/00536 dated 02/24/2023, Journal of Essential oil Bearing plants, Publisher Taylor & Francis, https://doi.org/10.1080/0972060X.2024.2387653, (I.F. 2.10).

- Jeet, S., Verma, R., Bhagat, S., Bhanwaria, R., Tabassum, S. and Yadav, G.K. 2025. Physicochemical Properties of Soil and Plant Geometry in Oil Yield, Quality and Economics of Lemongrass in Rainfed Bundelkhand Region, India. (The Institutional number of this manuscript is CSIR-IIIM/IPR/00707 dated 04/02/2024), *Journal of Scientific & Industrial Research ,* Vol. *84, February 2025, pp. 136-147,* DOI: 10.56042/jsir.v84i02.9598, (I.F. 0.70).
- Chopra C, Jeet, S., Bhagat, S., Tabassum, S., Bhanwaria, R. 2025. Morphological and phytochemical characteristics of Cymbopogon flexuosus (Nees ex Steud.) W.Watson cultivars at different harvest intervals in the Western Himalayas, India, *Journal of the Science Food and Agriculture,* Published by Wiley Online Library, DOI 10.1002/jsfa.14354, (I.F. 3.30).

2. Scientific work done:

Effect of Organic-Based Biochar on Yield and Quality of Lemongrass (*Cymbopogon flexuosus*)
Sonali Bhagat and Sabha Jeet

Introduction

Biochar, a carbon-rich product produced through the pyrolysis of organic waste, has emerged as a promising soil amendment for sustainable agriculture. It improves soil structure, nutrient availability, microbial activity, and water retention. In aromatic and medicinal plants like lemongrass (*Cymbopogon citratus*), biochar may not only enhance biomass yield but also influence the quantity and quality of essential oil, particularly citral, the major compound responsible for its fragrance and therapeutic value.

Experimental Methods

A field experiment was conducted at the IIIM Field Station, Chatha, Jammu, using a Randomized Block Design (RBD) with three replications. The study evaluated the effects of varying application rates of lemongrass waste-derived biochar 2.5, 5.0, 7.5, 10.0, 12.5, 15.0, 17.5, and 20.0 tons per hectare alongside a control treatment (0 t/ha). The objective was to assess the influence of these biochar levels on the growth, yield, and essential oil composition of lemongrass, with particular emphasis on citral content and other key oil constituents.

Biochar | **Weighing of biochar as per treatment** | **Incorporation of biochar into the pots**

Extraction/ processing of lemongrass through the Clevenger appratus

Results

The application of biochar had a noticeable influence on the agronomic performance of lemongrass. Moderate Doses (7.5, 10.0, and 12.5 t/ha) showed a significant improvement in plant height, tiller number, biomass production and essential oil yield. The 10.0 and 12.5 t/ha treatments recorded the highest biomass (35-40 t/ha and 45- 50 t/ha) and oil yields (230- 235 kg/ha and 240- 245 kg/ha), with better root development and chlorophyll content due to improved nutrient uptake. High Doses (15.0, 17.5, 20.0 t/ha): Although soil carbon content and moisture retention were high, plant performance plateaued or declined slightly. Signs of nutrient imbalance or pH-induced stress (e.g., nitrogen lock-up) were suspected. The highest citral content was observed in the 10.0 and 12.5 t/ha treatments. Citral levels were 10–15% higher than the control and lower-dose treatments. Over-application (15.0 t/ha and above) did not further improve citral content and in some cases slightly reduced it, likely due to plant stress. Geraniol, Linalool, and Myrcene were also enhanced at moderate biochar doses. The 10.0 t/ha treatment showed the best balance of oil yield and desirable compound concentration. High doses led to an increase in some undesirable or minor compounds, possibly due to altered soil microbial communities or physiological stress.

Conclusion

This field experiment confirms that biochar application can significantly enhance both the quantity and quality of lemongrass production. The optimal range for maximizing biomass yield, oil yield, and citral concentration lies between 10.0 and 12.5 tons per hectare. Application beyond this range may not offer additional benefits and could adversely affect oil composition due to nutrient lock-up or pH imbalance.

Therefore, for sustainable cultivation of lemongrass with enhanced essential oil quality (especially citral), a biochar dose of 10 to 12.5 t/ha is recommended. These findings support the use of lemongrass waste-derived biochar as an effective and eco-friendly amendment in aromatic crop production systems.

Science to Society/ Societal upliftment:

Popularization of cultivation and processing of aroma crops suitable for underutilized lands and providing higher income to the farmers.

Sonali Bhagat, Subhas Chandra Bos and Sabha Jeet

A significant opportunity has been created for farmers in Jharkhand, Uttar Pradesh, Madhya Pradesh, Jammu & Kashmir and the Bundelkhand region through the promotion of cultivation, processing, and marketing of medicinal and aromatic plants such as Lemongrass (CKP-25) and Himrosa (IIIM (J) CK-10). These crops are being promoted under various agro-climatic conditions, including irrigated, rainfed, dryland, and wasteland areas. In these regions, particularly in Bundelkhand, over 65% of agricultural land is rainfed and unirrigated, making traditional farming difficult and economically unsustainable due to frequent droughts and moisture stress. As a result, conventional agriculture has low productivity, pushing farmers into economic hardship. To address this, the cultivation of aromatic crops using CSIR agrotechnologies has been encouraged as a means of utilizing wasteland and developing alternate land use systems. Under the CSIR-Aroma Mission-III, these aromatic crops have been successfully demonstrated and cultivated across 172.80 acres — including 90 acres of Lemongrass and 82.50 acres of Himrosa. A total of 28.80 lakh plant slips were distributed free of cost to farmers as a token support, benefitting 104 growers across various villages and regions. Furthermore, as part of the Lavender Procurement & Transportation Committee, 7.90 lakh Lavender plants were procured from Bhadarwah in the Doda District and distributed across multiple locations: to Poonch (30,000 plants), Rajouri (20,000 plants), Ramban (80,000 plants), Srinagar (3,00,000 plants), Ramnagar & Basantgarh (10,000 plants), Udhampur (10,000 plants), North east, Meghalaya & Assam (50,000 plants) and Uttarakhand (3,00,000 plants). These plants have been allocated for cultivation over 100 acres as part of the CSIR-Aroma Mission-III, further promoting sustainable agriculture and alternative livelihoods in challenging agro-climatic zones.

Glimpses of activity of QPM distribution (Himrosa & Lemongrass) in U.P., Jharkhand & M.P.

Capacity Building and Outreach Activities under CSIR-Aroma Mission-III

Sonali Bhagat, Subhas Chandra Bos and Sabha Jeet

As part of our commitment to promoting the cultivation and utilization of Medicinal and Aromatic Plants (MAPs), we successfully organized a series of awareness camps and training programs across Jammu & Kashmir and other states in India. These initiatives aimed to educate farmers, entrepreneurs, and other stakeholders on the economic and therapeutic potential of MAPs, while also encouraging sustainable practices in their cultivation and harvesting.

A total of 15 training-cum-awareness programs were conducted, engaging 1,089 participants from diverse backgrounds. These included progressive farmers, self-help groups, women entrepreneurs, students, and rural youth. Each session was carefully designed to cover critical aspects such as identification of commercially viable MAP species, cultivation techniques, value addition, processing, marketing strategies, and the importance of conservation.

These training programs significantly contributed to raising awareness about MAPs and building the capacity of local communities to explore alternative and sustainable livelihood options. Participant feedback reflected high levels of satisfaction and motivation to adopt MAP-related activities. The

initiative also served as a platform to link growers with buyers and policy makers, fostering a more integrated MAP value chain across the participating regions.

S.No.	State	District	Village Name/ Location	Date	Type of Program	Total Participants	Women Participants
1	Bihar	Motihari	KVK Piprakothi	29.07.2024	One days	60	5
2	Bihar	Lakhisarai	KVK, Halsi	31.07.2024	One days	105	5
3	Bihar	Rohtas	KVK Bikramganj	01-02.08.2024	Two days	85	10
4	U.P.	Jhansi	Birguan	05.08.2024	One days	78	20
5	U.P.	Jhansi	Pahadi Chirgaon	06.08.2024	One days	90	0
6	U.P.	Jhansi	Gursarai, Atarsua	07.08.2024	One days	95	3
7	M.P.	Datia	Lakhanpur	08.08.2024	One days	83	7
8	U.P.	Lalitpur	Pawa	09.08.2024	One days	102	11
9	M.P.	Niwari	Niwari	10.08.2024	One days	84	9
10	U.P.	Jhansi	Bonda, Bangra	11.08.2024	One days	88	0
11	U.P.	Jhansi	Behata	12.08.2024	One days	102	14
12	M.P.	Tikamgarh	KVK	13-14.08.2024	Two days	60	6
13	U.P.	Sultanpur	Meerpur Sarriya	10.11.2024	One days	15	3
14	U.P.	Ayodhya	Sindhaura, Haringtonfanj	12.11.2024	One days	24	1
15	M.P.	Tikamgarh	Kantikhas	16.11.2024	One days	18	4
		Total				**1089**	**98**

Glympses of Awareness cum training cum skill development activities

KVK., Piprakothi, Motihari, Bihar (29.07.2024)

KVK., Halsi, Lakhisarai, Bihar (31.07.2024)

KVK., Bikramganj, Rohtas, Bihar (01-02.08.2024)

Vill., Birguan, Jhansi, U.P. (05.08.2024)

Vill., Pahadi Chirgaon, Jhansi, U.P. (06.08.2024)

Vill., Gursarai, Tarsua, Jhansi, U.P. (07.08.2024)

Vill., Lakhanpur, Datia, M.P. (08.08.2024)

Vill., Pawa, Lalitpur, U.P. (09.08.2024)

Niwari, M.P. (10.08.2024)

Media Coverages


औषधिय एवं सुगंधित फसलों की एक दिवसीय प्रशिक्षण


कृषि विज्ञान केन्द्र में एक दिवसीय प्रशिक्षण का आयोजन


हिन्दुस्तान

सुगंधित फसलों की खेती के बारे में दी गई जानकारी

■ औषधीय फसलों पर जागरूकता कार्यक्रम
■ कृषि विज्ञान केन्द्र परिसर में कार्यक्रम का आयोजन


दैनिक भास्कर सासाराम / कैमूर भास्कर 02-08-2024

रोहतास में औषधीय एवं सुगंधित फसलों की वैज्ञानिक खेती, प्रसंस्करण, मूल्य संवर्धन पर प्रशिक्षण शिविर

औषधीय और सुगंधित पौधों की खेती उपयोगी


प्रभात खबर

औषधि फसलों को लेकर प्रशिक्षण आयोजित


दैनिक भास्कर टीकमगढ़ भास्कर 15-08-2024

भास्कर खास • कृषि विज्ञान केंद्र में सुगंधित पौधों की खेती, मूल्य संवर्धन और विपणन पर दिया प्रशिक्षण

जम्मू में होने वाले नींबू और गुलाब घास को टीकमगढ़ में लगवाया, यहां आकर जम्मू के वरिष्ठ वैज्ञानिक ने किसानों से चर्चा की

टीकमगढ़ जिले में 25 किसानों ने शुरू की खेती

वैज्ञानिक ने पौधे लगाने के किसानों को तरीके बताए


औषधि की खेती किसानों के लिए फायदेमंद : डॉ. सभाजीत

केविके में दी गई सुगंधित फसलों की खेती, प्रसंस्करण, मूल्यसंवर्धन व विपणन की जानकारी

पीपराकोठी/पू.च/सं। स्थानीय कृषि विज्ञान केंद्र परिसर स्थित सरदार वल्लभ भाई पटेल सहकारिता संस्थान के सभागार में सोमवार को एसआईआर भारतीय समवेत औषद्य संस्थान, जम्मू की ओर से औषधि फसलों को लेकर जागरूकता सह प्रशिक्षण कार्यक्रम का आयोजन किया गया। जिसमें किसानों को सुगंधित फसलों की खेती, प्रसंस्करण, मूल्यसंवर्धन व विपणन की जानकारी दी गई। कार्यक्रम का उद्घाटन केविके प्रमुख व वरीय वैज्ञानिक डॉ. अरविंद कुमार सिंह व भारतीय समवेत औषद्य संस्थान के डॉ. सभाजीत सिंह ने संयुक्त रूप से दीप प्रज्जवलित कर किया। भारतीय समवेत औषद्य संस्थान के डॉ. सभाजीत सिंह ने इस प्रशिक्षण में किसानों को सुगंधित फसलों के बारे जानकारी देते हुए कहा कि औषधि खेती से जंगली जानवरों द्वारा खेती को नुकसान, पानी की कमी तथा पलायन को इससे काफी हद तक कम किया जा सकता है। फसलों में यह क्षमताएं हैं कि, इसमें जानवर नहीं आते है, तथा इन्हें सिंचाई की बहुत कम आवश्यकता होती है।


सुगंधित पौधे की खेती प्रसंस्करण एवं विपणन विषय पर हुआ प्रशिक्षण

• गौरव खरे पत्रकार

निवाड़ी । नगर में सीएसआईआर- भारतीय समवेत औषध संस्थान, जम्मू द्वारा आयोजित औषधीय एवं सुगंधित पौधे की खेती प्रसंस्करण, मूल्य संवर्धन एवं विपणन विषय पर प्रशिक्षण का आयोजन किया गया। इस अवसर पर एफ.पी.ओ. प्रधान रविकान्त चतुर्वेदी के द्वारा इस कार्यक्रम का उद्घाटन किया गया। उन्होंने किसानों को औषधीय एवं सुगंधित पौधों की खेती कर कमाई का एक नया साधन बनाने को प्रेरित किया साथ ही किसानों को कहा गया कि आप औषधीय एवं सुगंधित पौधों की खेती से अपनी आमदनी को दोगुना कर सकते हैं ।इस अवसर पर सीएसआईआर से वरिष्ठ वैज्ञानिक डॉक्टर सभाजीत ने किसानों को लेमन ग्रास ग्रास रोजाग्रास, मिंट एवं अन्य औषधीय एवं सुगंधित पौधों की बारे में विस्तार पूर्वक बताया गयो उन्होंने कहा लेमन ग्रास की खेती करके किसान प्रतिवर्ष में प्रति एकड़ लगभग 1.0- 1.5 लाख रुपये तक की आमदनी कर सकते हैं।इस अवसर पर उन्होंने किसानों को उपयुक्त लक्षित वाणिज्य फसलों के परियोजना पैकेज अरोमा मिशन के तहत पूर्ण जानकारी दी।इस अवसर पर अखिलेश कुमार, मुकेश यादव, मनीष पटेरिया, एफ पी ओ डायरेक्टर राकेश गुप्ता , अंकित पुरोहित, श्रीमति हेमलता, श्रीमति ऊषा कुम्हार ,चंद्रशेखर, गौरव तिवारी,ब्रजेश यादव, मिथलेश खरे इत्यादि प्रमुख उपस्थित रहे।


केवीके में सुगंधित पौधों की खेती, प्रसंस्करण, मूल्य संवर्धन और विपणन पर 2 दिवसीय प्रशिक्षण आयोजित

निकरा परियोजना के तहत कांटी गांव के 25 किसानों ने शुरू की खेती

BHAHWAL ALI SHAH

Dr. Bhahwal Ali Shah (Sr. Principal Scientist) with his Research Group

1. Publications/Patents:

Publications:

- Kumar, S.; Choudhary, R.; Khanum , G.; Ansari, S.M.; Ali, S.M.; Kour, G.; Javed, S.; Ahmed, Z.; **Shah, B.A*.** Anti-Inflammatory Properties of Allylic Sulfone Derivative: In Vitro and In Silico Investigations using DFT and Molecular Dynamics. *J. Mol. Struct.,***2025,** *1339*, 142429
- Khanum, G.; Ansari, S.M.; Choudhary, R.; Kour, G.; Gupta, V.; Javed, S.; Ahmed, Z.; **Shah B.A.***Computational and biological evaluation of naphthofuran-based scaffold as an anti-inflammatory agent. *J. Mol. Struct.,***2025,** *1321*, 139989.
- Fayaz, F.; Ganie, M.A.; Kumar, S.; Raheem, S.; Rizvi, M.A.; **Shah, B.A.***Modular access to sulfur substituted analogues of isocytosine via photoredox catalysis. *Chem. Commun.,* **2024**, 60, 8256-8259.
- Kumar, S.; **Shah, B.A**.* Synthesis of Diverse Allylic Sulfone Derivatives via Sequential Hydroalkoxylation of 1,3-Enynes. *Chem. Eur. J.* **2024**, *30*, e202401049.

2. Scientific work done:

Our lab specializes in the field of photo-redox chemistry, focusing on harnessing the power of light to drive redox reactions for organic synthesis. Utilizing state-of-the-art photo-reactors and a range of

photocatalysts, we explore new methodologies to facilitate challenging chemical transformations that are otherwise difficult to happen under normal circumstances. Primarily, we investigate the reactive behavior of vinyl radicals produced by the photoredox reaction of alkynes/alkenes. Also, we intend to explore the possibility of using these radicals for late-stage functionalizations of bioactive molecules. Our research includes developing novel systems that operate under visible light, aiming to improve reaction efficiency, selectivity, and sustainability. We employ a variety of analytical techniques, such as NMR, mass spectrometry, and X-ray crystallography, to characterize reaction intermediates and products. Collaborating with computational and electrochemists, we also delve into the mechanistic aspects of these processes, seeking to understand the fundamental principles governing these reactions. By integrating experimental and theoretical approaches, our lab aims to advance the application of photo-redox chemistry in pharmaceuticals, materials science, and drug development.

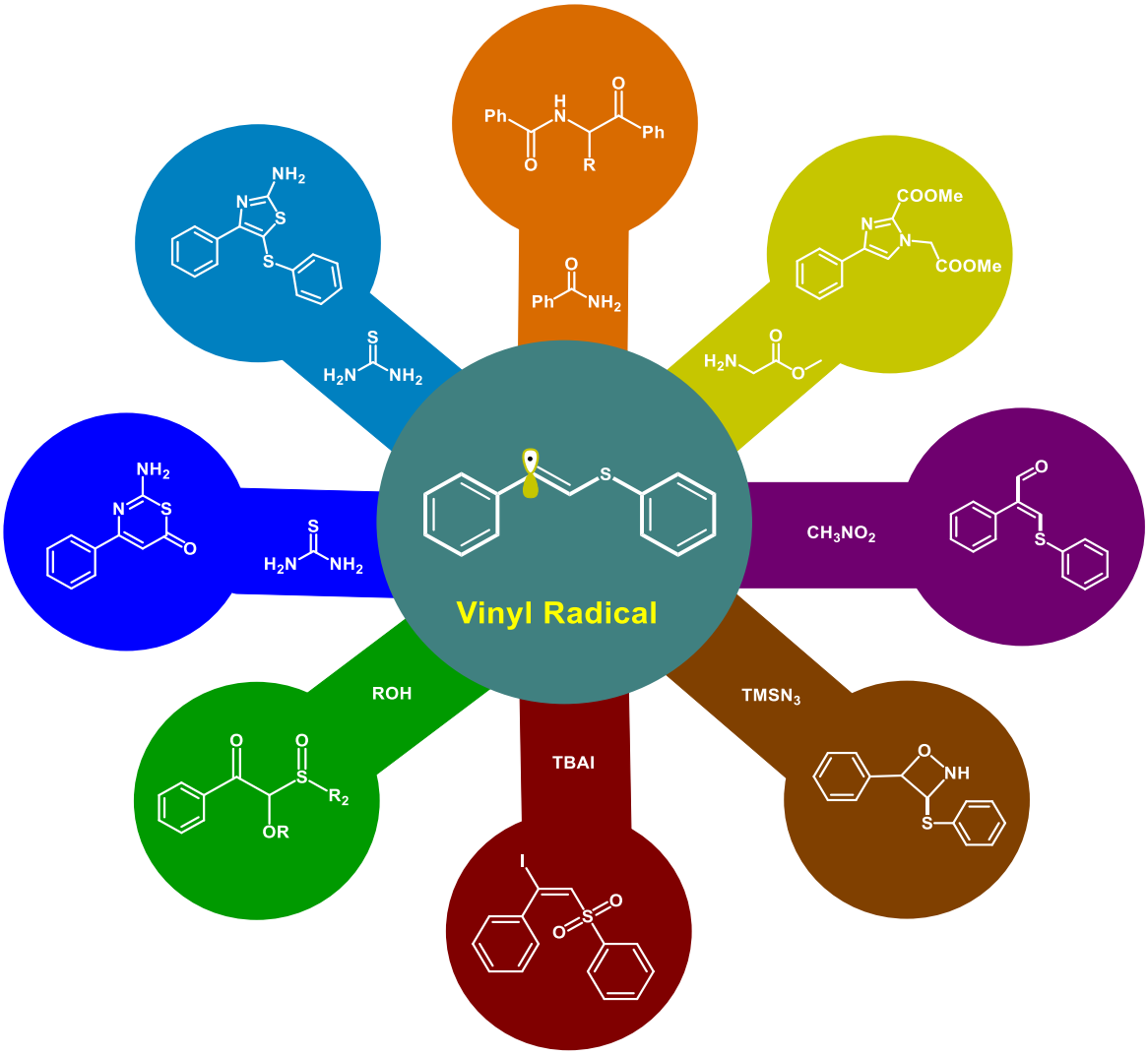


Figure 1: Our work around vinyl radical via photo-redox catalysis.

CSIR-INTEGRATED SKILL INITIATIVE

SKILL DEVELOPMENT PROGRAMMES

CSIR-IIIM Jammu this year has successfully trained **748** participants in campus which involved capacity building, Workshops in thrust areas as well as Skill Development Cum Entrepreneurship programs. Several Programs were tailor made to suit corresponding skills of participants and the SDP's ranged from different fields of Microbiology, Industrial Microbiology, Health care including Phytopharma Drug Development, Floriculture through Cultivation of High value Aromatic plants, Entrepreneurship of women through Lavender and Rose production & processing and Rosemary & Clatystsage production & processing.

S.No.	Date(s)	Title of SDP	Total Number of Trainees
1.	April-June 2024	Research & Training Program - Phase 1	47
2.	October- December 2024	Research & Training Program - Phase 2	49
3.	Jan- March 2025	Research & Training Program - Phase 3	42
4.	20 Jan-22 Jan 2025	Hands on training program on cgmp pilot plant for the extraction of traditional (ism) herbal medicinal plants	18
5.	31 Jan 2025	Research methodology, science communication & ipr-a futurist perspective	223
6.	03-05 Feb 2025	Hands-on training on synthesis of key intermediates and active pharmaceutical ingredients (APIS)	33

7.	10th Feb - 14th Feb, 2025	Hands on training on upstream & downstream processing of industrially important products	18
8.	18th Feb - 20th Feb, 2025	Hands on training program on plant tissue culture techniques	16
9.	18th Feb - 20th Feb, 2025	Hands on training on advanced techniques in industrial microbiology	17
10.	19-21 Feb 2025	Hands-on training on advanced techniques in natural products and medicinal chemistry	15
11.	15th March-21st March, 2025	Crop Diversification through Medicinal & Aromatic Plants in Rainfed Areas for Doubling of Farmers Income	24
12.	18 Jan 2025	Capacity Building Of Integral University Speakers	181
13.	October 2025	Sdp For Value Added Products From Essential Oils	15
14.	25 March 2025	Capacity Building Of Ayurveda Students & Tree Talk	50
		Total Participants = 748	

SOME GLIMPSES OF SKILL DEVELOPMENT PROGRAMMES

Skill Development Program Training Program On cGMP Pilot Plant for the Extraction Of Traditional (ISM) Herbal Medicinal Plants at CSIR-IIIM Jammu, January 2025

Skill Development Training Program on Research Methodology, Science Communication & Ipr-A Futurist Perspective at CSIR-IIIM Jammu, January 2025.

Skill Development Training Program on Upstream & Downstream Processing of Industrially Important Products at CSIR-IIIM Jammu, February, 2025

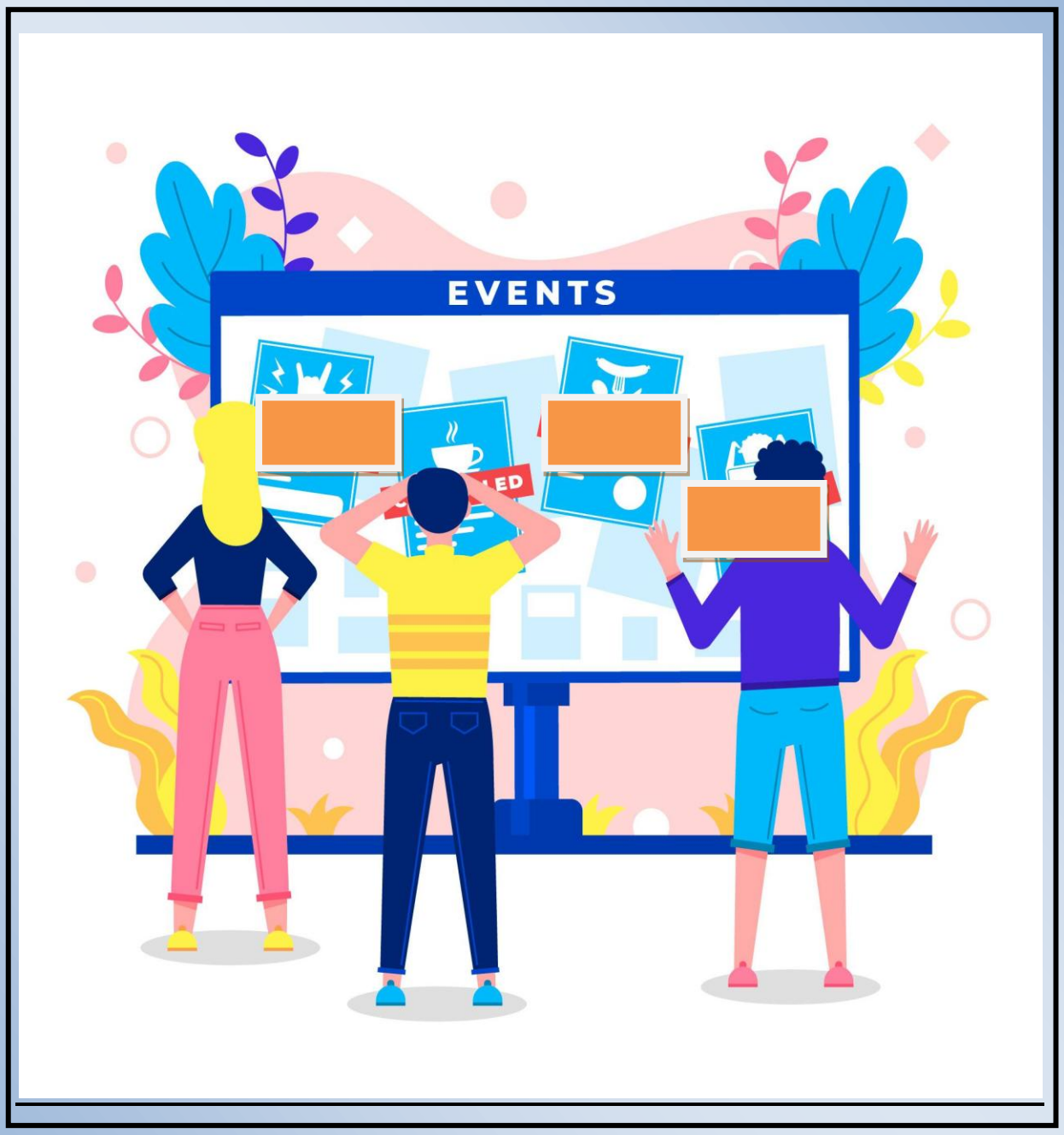
Skill Development Training Program On Synthesis Of Key Intermediates And Active Pharmaceutical Ingredients (APIs) at CSIR-IIIM Jammu, February, 2025

Skill Development Training Program on Plant Tissue Culture Techniques at CSIR-IIIM Jammu, February 2025

Skill Development Training Program on Advanced Techniques in Industrial Microbiology at CSIR-IIIM Srinagar Branch, February 2025

Skill Development Training Program on Advanced Techniques in Natural Products and Medicinal Chemistry at CSIR-IIIM Srinagar Branch, February 2025

A-ESDP on Crop Diversification through Medicinal & Aromatic Plants in Rainfed Areas for Doubling of Farmers Income at CSIR-IIIM, Srinagar Branch, March 2025



MAJOR EVENTS

Event Managed/Coordinated in the Financial Year of 2024-2025

S.No.	Date/Month	Name of Event
1	14th April 2024	CSIR-IIIM in collaboration with NHAI kickstarted the "Lavender Hub Project" aimed at beautifying the National Highway44 and fostering sustainable development near Navyug Tunnel, Banihal, J&K
1	2-3 May, 2024.	CSIR–IIIM in collaboration with Roy Society Chemistry organized 2 days workshop for capacity building
3	11th May 2024.	Coordinated National Technology Day. Schools, Colleges, Universities, Industries and Startups were invited to participate.
4	9th May 2024	Coordinated Rashtriya Boudhik Sampada Mahotsav with a series of lectures arranged on Patent Prosecution, Search, and Ensuring Patentability
5	1-15 May 2024	Conducted Swachhata Pakhwada. During the fortnight the staff & students were involved in cleaning various respective sections. Essay & painting competition for the staff & students was also conducted.
6	5th June 2024	organized one day workshop on "Intellectual Property Rights (IPR), Entrepreneurship & Startup Ecosystem"
7	10th June 2024	Organized Summer Science Camp.
8	1st July 2024	Organized a workshop was designed to impart technical training to the 25 faculty members from 13 different colleges of Kashmir and focused on the Application of Real-Time PCR and High Performance Liquid Chromatography
9	28 -29 June, 2024.	Coordinated a two days training program for women researchers.
10	7 July 2024	Coordinated visit of Hon'ble Union Minister and Vice President CSIR Dr Jitindera Singh who launched the "Ek Ped Maa Ke Naam" plantation drive at CSIR-IIIM jammu
11	6th August 2024	Organized Indian Organ Donation Day
12	6th January 2025	Organized the capacity building program for researchers of universities of J&K.

13	22nd January 2025	Organized a Two Days Awareness, Training & Quality Seed Distribution Program on Production and Crop Management of Marigold.
14	29th- 30th January 2025	Organized a 2 days' workshop for science teachers
15	11th March 2025	Coordinated Tree Talk.
16	2nd March 2025	Organized the Brush and Paint Floral Drawing and Painting Competition for school children
17	6th March 2025	Organized Nationwide Roadshow to showcase the newly developed E-Tractor & E-Tiller by CSIR-CMERI
18	8th March 2025	Organized Flori Tech Startup Conclave.
19	9th March 2025	Organized Annual Flower Show 2025
20	24th March 2025	Coordinated visit of Dr. Serge Mignani's. Lecture on Targeted Protein Degradation

RESEARCH OUTPUTS

Patent Applications Filed In India

S. No	Nfno	Country	Lab	Title	Inventors	Prov. Filing Date	Comp. Filing Date	Application No.	Status	Grant Date	Patent No
1	0105nf2023/In	In	Iiim	Spiro-Isoxazolines Of 14-Deoxy-11,12-Didehydroandrographolide As Anti-Cancer Agents And Process For Preparation	Gulshan Kumar, Misbah Tabassum, Bhupesh Kumar Sharma, Sanket Kumar Shukla, Ravi Shankar, Zabeer Ahmed	25-Aug-23	**01-Jul-24**	202311057433	Pp	---	---
2	0034nf2023/In	In	Iiim	Fermented Composition With Anti-Inflammation And Wound Healing Properties	Zabeer Ahmed, Vinod Kumar, Anu Radha, Varsha Sharma, Saurabh Saran, Mahendra Kumar Verma, Nalli Yedukondalu, Boobalan Gopu, Sanket Kumar Shukla, Deepika Singh, Diljeet Kumar, Rajendra Bhanwaria, Jasha Momo Hmsunghel, Sumeet Gairola, Rajendra Gochar	16-Oct-23	**15-Oct-24**	202311070419	Pp	---	---
3	0106nf2023/In	In	Iiim	A Process For The Biotransformation Of Geraniol To Geranic Acid	Vikash Babu, Prasoon Gupta, Sumeet Gairola, Haseena Shafeeq, Bashir Ahmad Lone, Ananta Ganjoo, Nargis Ayoub Bhat, Amit Kumar, Zabeer Ahmed	30-Oct-23	**29-Oct-24**	202311074007	Pp	---	---
4	0246nf2023/In	In	Iiim	A Nutraceutical Formulation For Improving Qualitative And Quantitative Sleep	Dhiraj Vyas, Dinesh Kumar, Damanpreet Singh, Premnarayan Gupta, Sumeet Gairola	08-Feb-24	**30-Jul-24**	202411008806	Pp	---	---
5	0233nf2023/In	In	Iiim	Pyranose Based 2-Deoxy -2-Iodo Nucleoside As Anti-Viral Agent	Norein Sakander, K M Archana, Ajaz Ahmed, Shriyanshi Mishra, Raj Kamal Tripathi, Qazi Naveed Ahmed, Debaraj	22-Mar-24	**12-Mar-25**	202411022366	Pp	---	---

					Mukherjee, Zabeer Ahmed						
6	0087nf2024/In	In	Iiim	Synergistic Composition Of Cdk Inhibitor And Cytotoxic Agent In The Treatment Of Lung Cancer	Rafia Basit, Ajeet Singh, Tenzen Yodun, Ghulam Mustafa, Ramajayan Pandian, Umed Singh, Parvinder Pal Singh, Gousia Chashoo, Shashank Kumar Singh, Zabeer Ahmed	---	**28-Jun-24**	202411050124	Pp	---	---
7	0008nf2024/In	In	Iiim	Functionalized Triazines As Anti-Cancer Agents And Process For The Preparation Thereof	Riyaz Ahmed, Mehedi Hossain, Zaheen Akhter, Ria Gupta, Pankaj Singh Cham, Muzamil Samad, Sumit Dhiman, Mohmmad Saleem Dar, Rayees Ahmad Naikoo, Mir Owais Ayaz, Ghulam Mustafa, Ashiya Jamwal, Ramajayan Pandian, Utpal Nandi, Zabeer Ahmed, Mohd Jamal Dar, Parvinder Pal Singh	---	**11-Jul-24**	202411053209	Pp	---	---
8	0114nf2024/In	In	Iiim	Hybrid Peptide As Anticancer Agent	Rubina Chowdhary, Aminur Rahman Sarkar, Manzoor Ahmed, Ghulam Mustafa, Diljeet Kumar, Ramajayan Pandian, Sanket Kumar Shukla, Zabeer Ahmed, Rajkishor Rai	---	**23-Aug-24**	202411064499	Pp	---	---
9	0248nf2024/In	In	Iiim	C-17 Substituted 14-Deoxy-11,12-Didehydroandrographolide Compound As A Potential Anti-Viral Agent And Process For Preparation Thereof	Gulshan Kumar, Shazia Choudhary, Bhupesh Kumar Sharma, Alna Kuriyickal Martin, Yogesh Sardana, Renuga Devi,	---	**19-Nov-24**	202411089701	Pp	---	---

					Bokara Kiran Kumar, Manzoor Ahmed, Sanket Kumar Shukla, Qazi Naveed Ahmed, Ravi Shankar, Zaheer Ahmed						
10	0190nf2024/In	In	Iiim	N-Substituted-2h-Chromene-3-Carboxamides As Potent Inhibitor Of Mycobacterium Tuberculosis And Process For Preparation Thereof	Summaya Perveen, Anjali Negi, Atul Chopra, Zabeer Ahmed, Rashmi Sharma, Parvinder Pal Singh	10-Dec-24	---	202411098131	Pp	---	---
11	0237nf2024/In	In	Iiim	(E)-5-Alkoxy-1-Phenylpentan-1-One O-(2-(N,N-Disubstitutedamino) Ethyl) Oximes And Their Therapeutic Use For Covid-19 Disease	Muneer-Ul-Shafi Bhat, Danish Mushtaq, Rayees Ahmad Naikoo, Faheem Fayaz, Ghazala Khanum, Sourav Kumar, Riyaz Ahmed, Alna Kuriyickal Martin, Yogesh Sardana, Renuga Devi, Bokara Kiran Kumar, Qazi Naveed Ahmed, Parvinder Pal Singh, Zabeer Ahmed, Bhahwal Ali Shah	---	**10-Dec-24**	202411098140	Pp	---	---
12	0121nf2024/In	In	Iiim	An Alginate Based Coating Composition Comprising Trans-Cinnamaldehyde For The Management Of Postharvest Rot Of Apples	Meenu Katoch, Pragya Rani, Mohini Sharma, Zabeer Ahmed	---	**11-Dec-24**	202411098113	Pp	---	---
13	0189nf2024/In	In	Iiim	A Process For The Preparation Of Lenalidomide And Intermediates Thereof	Amol Babasaheb Gade, Ahemad Mahebubsab Pathan, Raj Sunil Wandre, Zabeer Ahmed	---	**18-Dec-24**	202411100693	Pp	---	---
14	0187nf2024/In	In	Iiim	Pyridine-3-Yl Quinolin-2(1h)-One Derivatives As Anti-Viral Agent	Maryam Nabi, Raj Sunil Wandre, Yogesh Sardana, Alna Kuriyickal Martin, Gunjan Lakhanpal,	20-Dec-24	---	202411101808	Pp	---	---

					Bokara Kiran Kumar, Amit Nargotra, Qazi Naveed Ahmed, Amol Babasaheb Gade, Zabeer Ahmed						
15	0259nf2024/In	In	Iiim	Piperazine Adducts Of Dehydrocostuslactone And Costunolide As Antileishmanial Agent And Process For The Preparation Thereof	Prasoon Kumar Gupta, Kuljit Singh, Anil Bhushan, Diksha Kumari, Zabeer Ahmed	---	**13-Feb-25**	202511012500	Pp	---	---

MEMORANDUM OF UNDERSTANDINGS, AGREEMENTS & SERVICES

CDA, MOU and Agreements from 2024 to 2025

1.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and National Dope Testing Laboratory (NDTL) office at East Gate No. 10, Jawahar Lal Nehru stadium Complex, Lodhi Road, New Delhi-110003	11th January, 2024
2.	Semi Executed Agreements between CSIR-IIIM and NBA. (i) 3202304865 (ii) 3202304866 (iii) 3202304867 (iv) 3202304870 (v) 3202304835	06th February, 2024
3.	CDA Between CSIR-IIIM, Canal Road Jammu and Knowledgepie Pvt. Ltd., in the state of Assam, Nehru Park, New Colony, Samannypur path, Jorhat-785001.	29th February, 2024
4.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and President of India, acting through Dr. Amit Kr. Tripathi, Department of Biotechnology, Ministry of Science and Technology, Govt. of India, New Delhi.	11th March, 2024
5.	CDA Between CSIR-IIIM, Canal Road Jammu and Anphar Laboratories Pvt. Ltd., Industrial Extn. Area, Phase-III, Gangyal, Jammu (J&K), India.	16th March, 2024
6.	CDA Between CSIR-IIIM, Canal Road Jammu and Himalayan Essential Oils Producer Co. Ltd., C/o Munish Thakkar, Startupians CSC Bhalla, Doda, Jammu and Kashmir.	16th March, 2024
7.	CDA Between CSIR-IIIM, Canal Road Jammu and J K Aroma Bhaderwah Office at Jai Road, Bhaderwah, District Doda, Jammu	16th March, 2024
8.	CDA Between CSIR-IIIM, Canal Road Jammu and President of Union of India acting through Patnala Siva Sankar, Regional Officer, Regional office Jammu H.No. 315/1, Channi Himmat, Jammu.	16th March, 2024
9.	CDA Between CSIR-IIIM, Canal Road Jammu and Naval AIDS Research Center Namakkal Tamil Nadu, India (H&V Cure).	25th April, 2024
10.	CDA Between CSIR-IIIM, Canal Road Jammu and Development of the Banihal-Ramban Highway stretch, J&K as a “Hub of lavender cultivation jointly by CSIR-IIIM and NHAI, Ministry of Road Transport and Highways, India.	29th April, 2024

11.	MOA Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Aromatic and Allied Chemicals Pvt. Ltd., at B-8, Industrial Estate, C.B. Ganj, Bareilly, UP-243502.	14th June, 2024
12.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Jammu Institute of Ayurveda and Research College (JIAR), Nardani, Raipur, Bantalab Road, Jammu	06th July, 2024
13.	CDA Between CSIR-IIIM, Canal Road Jammu and HAUCH Ecovations Pvt. Ltd., Sector-329, Chandigarh Road, Ludhiyana Punjab	22nd August, 2024
14.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and President of India, acting through Secretary, Department of Biotechnology, Ministry of Science and Technology, Govt. of India, New Delhi (DBI)	13th September, 2024
15.	CDA Between CSIR-IIIM, Canal Road Jammu and M/s Agrovoltic Power Solutions Pvt., Ltd., 31, Dimri Niwas, Picture Palace Mussorie, Dehradun, Uttarakhand	19th September, 2024
16.	CDA Between CSIR-IIIM, Canal Road Jammu and Hapico Industries Pvt. Ltd., IGC, Lassipora, Pulwama, J&K	11th October, 2024
17.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Vishvakenah Herbs and Aromatic Pvt. Ltd., office at 671/201, Shalimar Garden, Ext-1, Sahibabad, Ghaziabad, UP, India	6th November, 2024
18.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Central Council for Research in Unani Medicine (CCRUM) situated at 61-65, Institutional Area, Opposite D-Block, Janakpuri, New Delhi-110058	22nd February, 2025
19.	CDA Between CSIR-IIIM, Canal Road Jammu and Hapico Industries Pvt. Ltd., IGC, Lassipora, Pulwama, J&K-192305	20th March, 2025
20.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Pharmanza Herbal Pvt. Ltd., #214, Borsad Tarapur Road, Kaniya Dharmaz-388430, Gujrat. (Haak Plant Collard Green).	27th March, 2025
21.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Pharmanza Herbal Pvt. Ltd., #214, Borsad Tarapur Road, Kaniya Dharmaz-388430, Gujrat. (Boswellia serrata-Phytopharmaceutical Lead).	27th March, 2025
22.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Pankajakasthuri Herbals	09th April, 2025

	India (P) Ltd., having its registered office at Poovachal Trivandrum, Kerala.	
23.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Indian Institute of Management, Jammu office at campus Jagti, Nagrota, Jammu-181221	12TH April, 2025
24.	MOU Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and Mehta Ayurvedic Sansthan, Indore, M.P.	14th August, 2025
25.	CDA Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and IIBAT-International Institute of Biotechnology and Toxicology, Padappai, Tamil Nadu	21st August, 2025
26.	CDA Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and SarvATGC Technologies Private Ltd., Whitefield, Bangalore.	13th September, 2025
27.	CDA Between CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu and FERMLAND BIO, The Probiotic Company near Indian Institute of Management, Indore, M.P. (India).	15th September, 2025

HUMAN RESOURCES

LIST OF STAFF

S.No.	Name
Director Pay Level - 15	
1	Dr. Zabeer Ahmed
Scientist-G/Chief Scientist Pay Level -14	
1	Er. Abdul Rahim
Scientist-F/Sr. Pr. Sci. Pay Level-13-A	
1.	Dr. Fayaz Ahmed Malik
2.	Dr. (Ms.) Asha Chaubey
3.	Dr. Shashank Kr. Singh
4.	Dr. Sheikh Tasduq Abdullah
5.	Dr. Dhiraj Kumar Vyas
6.	Dr. P.N. Gupta
7.	Dr. Sumit G. Gandhi
8.	Dr. Zahoor Ahmad Parry
9.	Dr. Qazi Parvaiz Hassan
10.	Dr. Syed Riyaz- Ul Hassan
11.	Dr. (Mrs.) Suphla Gupta
12.	Dr. Amit Nargotra
13.	Dr. Mohd. Jamal Dar
14.	Dr. Qazi Naveed Ahmed
15.	Dr. Khursheed A. Bhat
16.	Dr. Prasoon K. Gupta
17.	Dr. Parvinder Pal Singh
18.	Dr. Bhahwal Ali Shah
19	Dr. Syed Sajad Hussain
20.	Sh. Anil Kumar Katare
21.	Dr. Govind Yadav
22.	Dr. Saurabh Saran
23.	Dr. Sundeep Jaglan
Scientist-E II/Pr. Sci. Pay Level-13	
1	Dr. Muzamil Ahmad
2	Dr. (Mrs.) Nasheeman Ashraf
3	Dr. Bilal Ahmad Bhat
4	Dr. Prashant Misra
5	Dr. Ajay Kumar
6	Sh. Shaghaf Mobin Ansari
7	Dr. Vikash Babu

8	Dr. Ravi Shankar
9	Dr. (Ms.) Nazia Abbas
10	Dr. Shahid Rasool
11	Dr. Nasir Ul Rasheed Rather
12	Dr. V. P. Rahul
13	Dr. Sabha Jeet
14	Dr. Rajendra Bhanwaria
15	Dr. Sreedhar Madishetti
16	Dr. Ravail Singh
17	Dr. Avisek Mahapa
Scientist-E I/Sr. Scientist Pay Level-12	
1	Dr. Rajkishore Rai
2	Dr. (Mrs.) Meenu Katoch
3	Dr. Kancherla Prasad
4	Dr. Kanhaiya Kumar
5	Dr. Showkat Rashid
6	Dr. Maqsood Ahmed
7	Dr. Firdoous A. Mir
8	Dr. Love Sharma
9	Dr. Syed Khalid Yousuf
10	Dr. J.S. Momo Hmungshel Anal
11	Dr. Bharitkar Yogesh Pandharinath
12	Dr. Ramajayan P.
13	Dr. Boobalan G
14	Dr. (Ms.) Rashmi Sharma
15	Sh. Kuljit Singh
16	Dr. Vinod Kumar
17	Dr. Srinivas Kota
Scientist-C/ Scientist Pay Level – 11	
1	Dr. Jatinder Kumar
2	Dr. (Ms.) Padma Lay
3	Dr. Yedukondallu Nalli
4	Dr. (Mrs.) Manu Khajuria
5	Dr. (Mrs.) Gurleen Kour
6	Dr. Mir Mahmood Asrar
7	Dr. Amol Babasaheb Gade
8	Dr. Nagaraju Nekkala
9	Dr. Ravinder Suresh Phatake
10	Dr. (Ms.) Farina Sultan

LIST OF GROUP III (TECHNICAL) EMPLOYEES

S.No.	Name
Pr. Tech. Officer Level-13	
1	Dr. A.P. Gupta (on Deputation)
2	Dr. Amit Sharma (Medical Officer)
3	Dr. Mrs. Anju Gupta (Medical Officer)
4	Mrs. Asha Bhagat
5	Sh. Rajinder Kumar
6	Dr. Budh Singh
7	Sh. Ashwani Chopra (S.E. Electrical)
8	Dr. Siya Ram Meena
9	Dr. Phalisteen Sultan
Sr. Technical Officer (3) Level -12	
1	Sh. Sanjay Sharma
2	Dr. Sanket Shukla
3	Dr. Varun Partap Singh
4	Sh. Vikas C Rai
Sr. Technical Officer(2) Level -11	
1	Dr. Mahendra Kumar Verma
Sr.Technical Officer (1) Level-10	
1	Mrs. Bhavna Vij
2	Sh. Gourav Sharma
3	Sh. Manish Kumar
4	Sh. Ubair Nazir Wani (Civil Engg)
5	Sh. Jai Sharma (Civil Engg)
6	Sh. Mukesh Jhangra
7	Sh. Sumit Kumar
8	Sh. Arvind Kumar Yadav
9	Ms. Monika Gupta
10	Sh. Bikram Singh
11	Sh. Ashok Kumar Bhargava
Technical Officer Level-7	
1	Sh. Uma Shankar
2	Mrs. Priya Wajir
3	Sh. Narinder Kumar
4	Sh. Sumit Roy
5	Sh. Habibullah
6	Sh. Yadunandan Sen
Technical Assistant Level- 6	

1	Sh. Zabir Ahmad
2	Sh. Rajinder Kr. Shukla
3	Sh. Akash Verma
4	Sh. Ankit Bhagat
5	Sh. Keshav
6	Sh. Suman Kumar Singh

LIST OF GROUP II (TECHNICAL) EMPLOYEES

S.No.	Name
Sr.Technicain (2) Level-7	
1.	Sh. P.R. Mehta
2.	Mrs. Kiran Koul
3.	Sh. Satya Bhushan
4.	Sh. Vijay Kumar
5.	Mrs. Anjum Vashist
6.	Sh. Rajesh K.Sehdev
Technician (1) Level-5	
1.	Sh. Asad Ullah
2.	Sh. Rahul Kalgotra
3.	Sh. Kirshan Kumar

LIST OF GROUP I (TECHNICAL) EMPLOYEES

S.No.	Name
Laboratory Assistant Level-05	
01	Sh. Neel Kamal
02	Sh. Balwinder Singh
03	Sh. Manoj Kumar
04	Ajit Ram
Laboratory Attendant Level-02	
1.	Sh. Ashok Kumar
2.	Sh. Kuldeep Kumar

LIST OF MTS EMPLOYEES

S.No.	Name
MTS Level-04	
1.	Sh. Mohd Farooq Bhat
2.	Sh. Ashok Kumar
3	Sh. Pawan Kumar
4.	Sh. Rajesh Tandon
5.	Sh. Moses Tegi

6.	Sh. Subash Chander
7.	Sh. Sham Lal
8.	Sh. Bua Ditta
9.	Sh. Ashok Kumar S/o Sh. Gharoo Ram
10.	Sh. Dev Raj
11	Sh. Kali Dass
12	Sh. Ashok Kumar S/o Sh. Daya Ram
13.	Sh. Surinder Kumar
14	Sh. Bachan Lal
15	Sh. Karnail Chand
16	Sh. Daleep Raj
17	Mrs. Kirti
18	Sh. Ashwani Kumar

LIST OF ADMINISTRATION STAFF

S.No	Name
Sr. Controller of Administration 1	
Controller of Finance Accounts 1	
1	Sh. Ajay Kumar, CoFA
Finance & Accounts Officer **1 Vacant**	
Administrative Officer	
2	Sh. Rajesh Gupta AO
Store & Purchase Officer 1	
-	-
Pr. Private Secretary 1 Vacant	
Pr. Private Secretary 3 (3 Vacant)	
Section Officer- 5 (1 Vacant)	
3	Sh. Romesh K. Mottan
4	Sh. Manoj Kumar
5	Sh. Ashok Kumar
6	Mrs. Nisha Vij
7	Dr. Rekha Kumari
Section Officer(F&A)-2 (1 Vacant)	
8	Sh. Vikas Patiaya
Section Officer(S&P)-2 (1 Vacant)	

9	Mrs. Rajni Kumari
10.	Ms. Durga
Assistant Section Officer (Gen)	
11.	Sh. Rajinder Singh
12.	Mrs. Rekha Gupta
13.	Sh. Mohd. Ayub
14.	Sh. Rishu Sharma
15.	Sh. Kartik Kapoor
16.	Ms. Preeti
17.	Mr. Devvart Verma
18.	Mrs. Priyanka
19.	Mr. Rahul
20.	Mr. Rahul
Assistant Section Officer (F&A)-	
21.	Mr. Ravinder Kr. Sharma
22.	Mrs. Lovely Ganjoo
23.	Mr. Akhil Kumar
24.	Ms. Priya Badyal
Assistant Section Officer (S&P)- 01 (02 Vacant)	
25.	Ms. Jyoti Kumari
Sr. Secretariat Assistant (S&P)-01(02 Vacant)	
26.	Sh. Rakesh Choudhary
27.	Sh. Parshotam Kumar
Sr. Stenographer 04	
28.	Sh Abhishek Gupta
29.	Sh. Satish Kumar
30.	Sh. Sahil Salotra
31.	Mrs. Jyoti Devi
Jr. Stenographer	
32.	Ms. Nidhi Choudhary
Sr. Secretariat Assistant	
33.	Sh. Tarsem Kumar
34.	Sh. Rankush Pandita
35.	Sh. Ishan Dogra
36.	Sh. Krishan Mamwal

Jr. Secretariat Assistant 07 (1 Vacant)	
37.	Sh. Akhil Verma
38.	Ms. Kajal Sharma
39.	Sh. Ehtisam Hameed
40.	Sh. Vishal Kunyal
41.	Sh. Kannav Gautam
42.	Sh. Akshay
43.	Sh. Mohd. Abu Sufian Raza
44.	Ms. Pooja Bhawaria
45.	Sh. Ankit
Sr. Secretariat Assistant (F&A) 2 (0 Vacant)	
46.	Sh. Sanchit Sharma
Jr. Secretariat Assistant (F&A) 3 (02 Vacant)	
47.	Sh. Rahul Sharma
48.	Sh. Mohd Suhail Dar
49.	Ms. Radhika Sharma
50.	Ms. Sneha Dhar
51.	Sh. Vijayinder Kumar
Jr. Secretariat Assistant (S&P) 2 (0 Vacant)	
52.	Mrs. Nichal Raina
53.	Sh. Vineet Sharma
Security Assistant 03(1 Vacant)	
54	Sh. Balkrishan
Receptionist 01(0 Vacant)	
55.	Mrs. Jyoti Prabha
Jr. Hindi Translator	
56.	Sh. Mayank Mishra
Driver	
57.	Sh. Mohit Kumar
58.	Sh. Tarun Kashayp
59.	Sh. Rajat Kumar

वार्षिक प्रतिवेदन 2024–25

ANNUAL REPORT 2024-25

सीएसआईआर-भारतीय समवेत औषध संस्थान, जम्मू - 180001

CSIR-Indian Institute of Integrative Medicine, Jammu - 180001

CSIR-IIIM (Indian Institute of Integrative Medicine) focuses on drug discovery from natural products, leveraging plants and microbes for new therapies, developing agro-technologies for medicinal plants, and validating Indian traditional medicines (Ayurveda, Unani) using modern science, aiming to create high-value products for national and global markets through strong R&D, biotechnology, and industrial collaborations.