सीएसआईआर - भारतीय समवेत औषध संस्थान
CSIR-Indian Institute of Integrative Medicine
(Council of Scientific and Industrial Research)

वार्षिक प्रतिवेदन
ANNUAL REPORT
2018-19

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सीएसआईआर - भारतीय समवेत औषध संस्थान,
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JAMMU-180001 (INDIA)


IIIM

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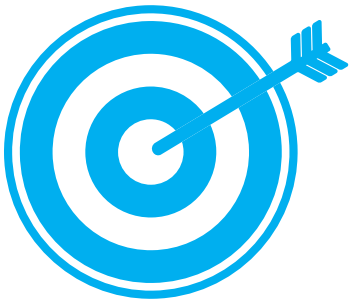
IIIM

OVERVIEW OF CSIR-IIIM

The Laboratory was established in 1941 as a research and production centre, known as Drug Research Laboratory of J&K State and was later taken over by Council of Scientific & Industrial Research (CSIR) of Govt. of India in December 1957 as Regional Research Laboratory, Jammu. In view of its core strength in natural products based drug discovery, the mandate of Institute was redefined in 2005 and its name changed to Indian Institute of Integrative Medicine (IIIM). The current mandate of IIIM is to discover new drugs and therapeutic approaches from Natural Products, both of plant and microbial origin, enabled by biotechnology, to develop technologies, drugs and products of high value for the national and international markets.



Mission

To become a Centre of Excellence in Natural Products chemistry and biotechnology driven drug discovery, integrating modern biology with chemistry

Vision

The vision of the Institute is to position IIIM as a International center of excellence for natural products chemistry, chemical biology, pharmacology and biotechnology to discover new chemical entities (NCEs) as drugs for unmet medical needs and provide scientific rationale and validity to various Indian systems of medicine. The institute aspires to achieve leadership position as a research Institute for creating a broad knowledge base, a work force of dedicated and trained scientists and a technology development center through scientific exploration of secondary metabolites from plants and microbial biodiversity, at the same time generating awareness for their conservation and protection.

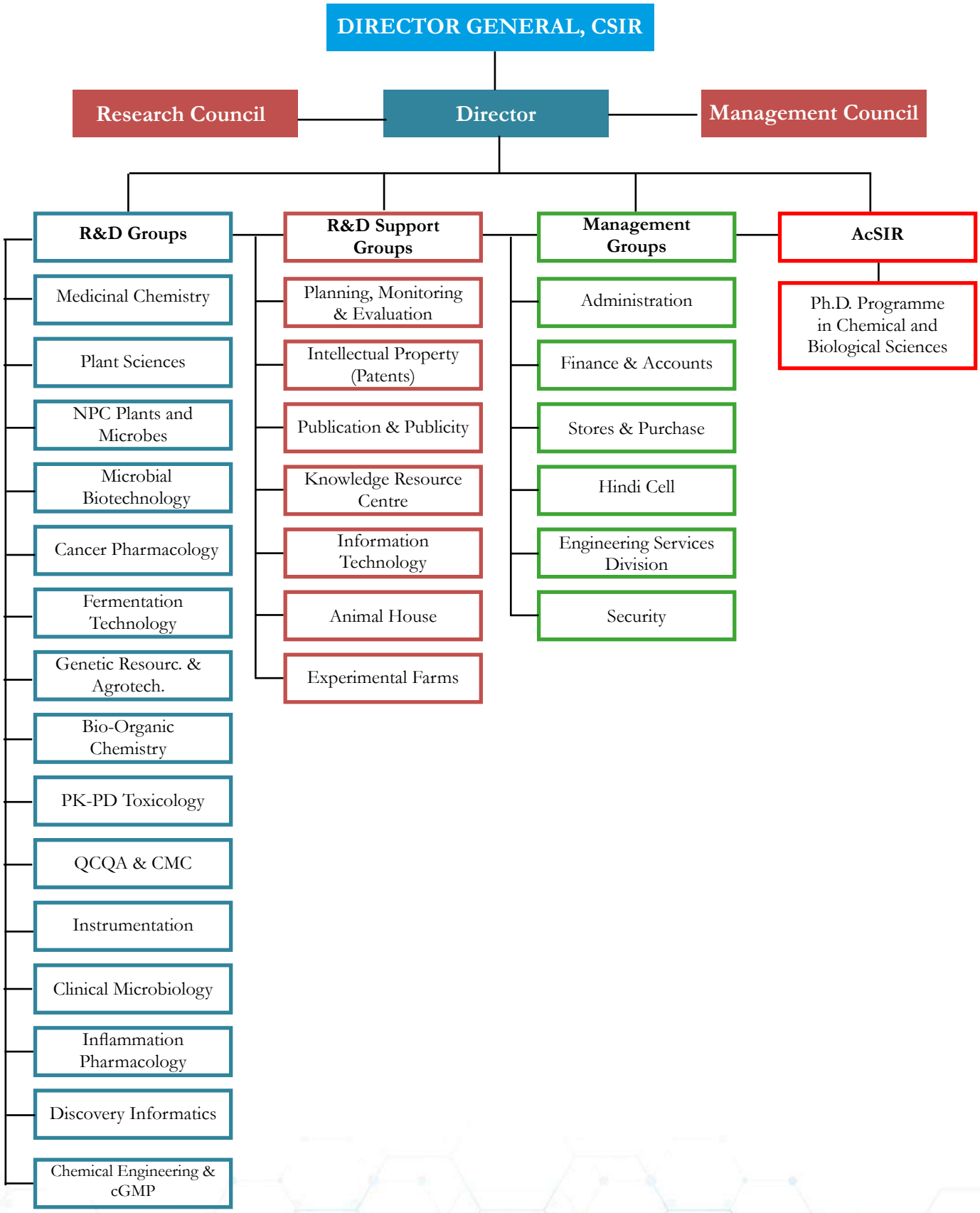
Mandate

The mandate of IIIM is to be an internationally competitive centre of excellence in all facets of natural products research and technology, including (a) discovery of novel pharmacologically active natural products from plants and microbial species and translating them into drug leads and candidates by medicinal chemistry, preclinical pharmacology and clinical development. This approach is pursued both in NCE as well as botanical herbal mode; (b) Preclinical and clinical validation and establishment of mechanism of action of drugs used in various Indian systems of Medicines (Ayurveda, Unani, Siddha and other Indigenous systems of medicine); (c) develop agro-technologies and commercial cultivation of high value medicinal and aromatic plants from Western Himalayas including Kashmir Valley and Laddkh for national and international markets; and (d) to work with Indian and global pharmaceutical industry to out-license new products and technologies.

Current Focus Areas:

- Medicinal Chemistry (Hit to pharmacokinetics, formulation and Preclinical development)
- Biotechnology of plants and microbial secondary metabolites
- Fermentation based technologies of Industrial products
- Phytopharmaceutical drug discovery (GAP,GLP,GMP,GCP)
- NABL accredited QC/QA of drugs, foods, essential oils etc.
- Pharmacology of Cancer, Inflammation, Infection (Clinical microbiology) and Neurodegenerative disorders
- Societal outreach programme in cultivation of Medicinal and Aromatic crops for better income and lively hood to rural poor and employment generation.

ORGANISATIONAL SETUP OF CSIR-IIIM, JAMMU



RESEARCH COUNCIL

1.	**Dr. Bipin Alreja**	Chairman	503, Marble Arch, 94, Pali Hill, Bandra, Mumbai
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10.	**Dr. Ram Vishwakarma** (Director, CSIR-IIIM)	Member	Director. CSIR- Indian Institute of Integrative Medicine, Canal Road, Jammu-180001
11.	DG CSIR or his nominee	Member	

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Sh. Satish Kumar **COFA / FAO** CSIR-Indian Institute of Integrative Medicine, Jammu	**Member**
Sh. Pankaj Bahadur **COA / AO** CSIR-Indian Institute of Integrative Medicine, Jammu	**Member Secretary**

From the Director's Desk

It gives me immense pleasure to present the annual report of CSIR-IIIM for the year 2018-19. This report summarizes the achievements in all facets of natural products research and technology including discovery of novel pharmacologically active natural products from plants and microbial species and translating them into drug leads, preclinical pharmacology and clinical development in both NCE as well as botanical herbal mode. Based on our research performance, innovation outputs and societal impact, CSIR-IIIM, Jammu has been ranked third within the country as the best government institutes as released by Scimago Institutions ranking-2018. CSIR-IIIM Jammu has been ranked second among CSIR laboratories, and ranked first within biology cluster of CSIR. CSIR-IIIM jumped 93 Places ahead in Global Scimago Ranking from 510th position in 2017 to 417th position in 2018. In particular, the innovation rank of CSIR-IIIM has improved from 292nd in 2017 to 193rd in 2018. We have filed 10 patent applications both in India and in foreign and 14 patents were granted to CSIR-IIIM. During this period, IIIM published a total of 105 scientific publications with an average impact factor of 3.0319.

Several important events took place during this year. Firstly, Hon'ble Vice President of India, Shri M. Venkaiah Naidu visited CSIR-IIIM Jammu on 28th May, 2018. He addressed the scientists, scholar, and technical staff of the Institute and eminent citizens of Jammu. Governor N N Vohra, Union Minister Dr Jitendra Singh, Deputy Chief Minister of J&K, Kavinder Gupta, Minister for Science and Technology, J&K, Sajad Gani Lone, Minister for Higher Education, J&K, Imran Raza Ansari and others were present on the occasion. Secondly, CSIR-Indian Institute of Integrative Medicine (IIIM) CSIR-IIIM, Jammu has licensed a technology on a Saffron based nutraceutical product for brain health to Pharmanza Herbal Pvt. Ltd., Gujarat for launching this product both in domestic and US market. Thirdly, CSIR-IIIM, Jammu has signed 19 MoUs with various parties.

CSIR-IIIM Aroma Mission team received the "Ultra International Team Award" at the International Congress & Expo-2018 organized by the Essential Oil Association of India, at Hotel Grand Sheraton, Bengaluru. The successful implementation of this mission is an impactful effort for enhancing the income of large number of farmers under the mission. CSIR-IIIM organized Public Outreach Programme as a part of the India International Science Festival (IISF-2018), which was jointly organised by Ministries of Science and Technology and Earth Sciences and Vijnana Bharati (VIBHA). CSIR-IIIM, Jammu actively participated in the mega exhibition on women empowerment. During the exhibition, CSIR-IIIM displayed various posters on Research & Development done in the institute such as Agrotechnology, Leather Technology, Fermentation Technology, Technology Business Incubators (TBI), Quality Control and Quality Assurance (QCQA), cGMP, HRD etc to encourage and motivate the gatherings. Apart from this, we also displayed herbal products from cGMP, Fermentation and sold essential oil kits of 3ml and 6 ml to the visitors. The motto of CSIR-IIIM was to attract as many as "*Women to Science*". National Conference-cum-Industry-Academia meet on "Opportunities and Challenges in Fermentation Based Industrial Processes" (IAMF-2018) organized by CSIR-Indian Institute of Integrative Medicine, Jammu (IIIM) concluded successfully on present state of knowledge and future of fermentation bas J&K state and India.

I wish to thank the Research and Management Council of CSIR-IIIM, for their constant support and cooperation. Lastly, I acknowledge the role of stakeholders, the scientists, staffs and the students of CSIR-IIIM who made possible this outstanding output for inclusion in this annual report.

(Ram A. Vishwakarma)

1.0 GENETIC RESOURCE AND AGROTECHNOLOGY

1.1. Targeting wastelands of India through extension of CSIR Agrotechnology of aromatic plants and their economic potentials

Rajendra Bhanwaria, Bikarma Singh, Ravi Shankar, Sabhajeet, V.P. Rahul, Rajendra Gochar, SR Meena, Mamta Gochar and K.K. Sharma

Barren lands are characterized by exposed rocky substratum, desert scarps, talus, slides and other accumulations of rock without any plant community. In other sense, such landscapes are called 'wastelands', and to work on those areas and to tackle the problem of degradation of lands, restoration of ecology and to meet the growing demands of fuel wood and fodder at the national level, CSIR under ministry of science and technology has developed agrotechnology of several aromatic crops which are suitable for such climate and lands. Overall, India shares 16% of the world population, while its land is only 2% of the total geographical area of the world. At present, approximately 68.35 million hectare area of the land is lying as wastelands, and around 50% lands are non-forest lands, which can be made fertile again if treated properly. Considering these in mind, several extension of aromatic plants have been carried out in India under Aroma Mission Project. Some of activities undertaken during 2018-2019 are given below in subheads:

1.1.1. Extension of Rosagrass [RRL (J) CN-5]

The aromatic crop, *Cymbopogon nardus*, called RRL(J)CN-5 was developed by IIIM, Jammu is commonly called 'Rosagrass' belong to the family Poaceae is suitable for rainfed tropical regions of India. This crop is rich in geraniol (45-60%), geranyl acetate (15-25%), CIS-ocimene (12-13%), which has high demand in industries looking for flavor and fragrance products. As far as cultivation and agrotechnology is concerned, a single plant slip is planted per hole at 40cm x 40cm inter and intra row spacing. At least 62,500 slips are required for planting in an area of one hectare. First year plantation gives 2-3 cuttings depending upon the period of planting, while four to five cuttings are taken in the second subsequent years .When the crop is planted in Feb-March, the first cutting is taken after 130-150 days after planting and thereafter crop is harvested at an interval of 55 to 65 days. First year plantation gives an average of 50-55 tones of fresh herbage. Second year plantation yields 65-72 tones/ha of fresh herbage. 200 to 220 kg oil/ha is obtained during 1st year, while in second and subsequent years 250 to 280 kg oil/ha is obtained. It has got net profit of Rs. 1,20,000 /-1st year and Rs. 2,80,000/- 2nd year onwards. It is depending on well management and following of scientific package and practices. Rajasthan is a 10% of the total geographic area of India and more than 60% of the desert lies in the state of Rajasthan. The types of soil available in Rajasthan are mostly sandy, saline, alkaline and chalky (calcareous). In Rajasthan, state this crop grows well on poor sub-marginal lands of shallow soils along eroded river banks and bunds of agricultural fields. The farmers have grown this verity successfully in such type of soil condition and getting more profited than other traditional crop. The Jodhpur district of Rajasthan is a major part of Thar Desert. For the first time, CN-5 is cultivated in 15 acres of waste lands nearby regions of Jodhpur district in Balesar Tehsil.

Figure 1.1.1. QPM uprooting and slips formation of RRL(J)CN-5 at Balesar (Jodhpur) Rajasthan

1.1.2. Extension of Himrosa [IIIM (J) CK-10]

IIIM(J)CK-10 (*Cymbopogon khasianus*) was developed by IIIM, Jammu is commonly called 'Himrosa' belong to the family Poaceae is an aromatic crop suitable for rainfed tropical regions of India. This crop is rich in geraniol (70-75%), CIS-ocimene (10-15%) and geranyl acetate (5-10%).

Figure 1.1.2. Field demonstration and planting material distribution of CK-10 at Balesar (Jodhpur) Rajasthan

This variety is hardy in nature, high drought tolerance capacity and easily cultivated in topical and sub tropical environment. It responds well under rainfed climatic condition and poor fertile soil condition. It grows in sandy to sandy loam soil having pH ranging from 5 to 9. The CK-10 was cultivated for the first time in Rajasthan in almost 50 acres of land in area of Balesar, Dechu in Jodhpur district. More Than 50 framers family getting benefits cultivation through this crop. When the crop is planted in Feb-March, first cutting is taken after 130-150 days after planting and thereafter crop is harvested at an interval of 55 to 65 days. The first year plantation gives an average of 50-55 tones of fresh herbage. Second year plantation yields 65-72 tones/ha of fresh herbage. Total 200 to 220 kg oil/ha is obtained during the 1st year, while in second and subsequent years 250 to 280 kg oil/ha is obtained. It has got net profit of Rs. 1,30,000 /- 1st year and Rs. 2,50,000/- 2nd year onwards.

1.1.3 Extension of *Tagetes minuta*

Tagetes minuta is commonly known as wild marigold belongs to family Asteraceae. This plant species is a 1-2 m tall annual herb, which are grown for essential oil production. The major essential oil components are (Z)-β-ocimene (35-39 %), dihydrotagetone (11-15%), (Z)-tagetone (6-9 %), (E) -ocimenone (12-16 %) and (Z)-ocimenone (8-10 %). The crop prefers slightly acidic soil to normal range pH (pH=5.5 to 8.5). A well-drained sandy loam to clay loam soil suitable for plant growth. It grows wild in Africa, South America, Australia Nigeria, Brazil, France and India. CSIR-IIIM Jammu has developed Agrotechnology of *T. minuta* and extended its know-how technology to Himachal Pradesh, J&K and hills of Uttaranchal, where this crop is growing as natural habitat. This species blooms in October-November. During the reporting period, approximately 100 acres of land was brought under cultivation of *T. minuta* in block of Lali and Panchari at Udhampur district of J&K state. More than 150 farmers families were cultivated this crop under rainfed condition in Jammu region. The yield obtained fresh flowers 20-25 tan and 40-50 kg essential oil/ha by distillation process. The crop gives 1.5 to 2.00 laks/ha/year net profit in well management condition.

Figure 1.13 Agrotechnology extension and seed production technology of *Tagetes minuta* in Udhampur

1.2 Farmers fair coupled with skill development and training programmes

Rajendra Bhanwaria, Bikarma Singh, Ravi Shankar, SR Meena, Rajendra Gochar and Chandra Pal

Under societal upliftment programmes as CSIR-IIIM activities, several farmers fair coupled with skill development and training programmes were organized in various parts of India. More than one thousand farmers were benefitted. These programmes were organized under various themes such as catalyzing rural employment through cultivation, processing, value addition and marketing of aromatics crops under CSIR-Aroma mission. Snapshorts of programmes undertaken at various places are given below in figures 1.2.1, 1.2.2 and 1.2.3:

Figure 1.2.1. Training programme organized at Balesar, Jodhpur in Rajasthan

Figure 1.2.2. Skill development cum training programme organized at Dechu (Lohawat), Jodhpur

Figure 1.2.3 Training programme conducted on aroma bearing crops at Ajoli mali (Uttrakhand).

1.3 Exploring commercial cultivation of tissue cultured raised Banana in Himalayan Shivalik range

Sabha Jeet, VP Rahul, Rajendra Bhanwaria, CP Singh, Rajendra Gochar, Amit Kumar, Kaushal Kumar, Jagannath Pal and Bikarma Singh

It is for the first time that agro-technology of banana (variety BHIM) has been introduced and developed through tissue culture technique for the commercial cultivation in Himalayan Shivalik range by CSIR-Indian Institute of Integrative Medicine Jammu. The basic aim was to study the potential of tissue culture (TC) banana production in a diverse environment of Shivalik range, to make the state self-sufficient in Banana production, employment generation and generate revenue for the farmers and to studies on the post harvest handling & marketing of TC Banana. Initially, the sapling of this high quality tissue culture variety {BHIM Grand naine (G-9)} Banana was brought from Agro-division of Cadilla pharmaceuticals limited Ahmadabad, Gujarat. The field experimental trial was conducted during, 20016-2017 at CSIR-IIIM research station, Chatha, Jammu. In which four treatment combination arranged in Randomized Complete Block Design (RCBD) replicated fifth times in which four date of planting, T^1 10th August, T^2 10th September, T^3 10th October and T^4 10th November. Significant differences were observed among the treatments for all the parameters studied. Among the date of planting, Banana planted at 10th August reported significantly highest pseudostem height (cm), pseudostem girth (cm), more average no. of leaves/plant, first flower emergence (days), first finger ripening (days), more no. of finger per hand, more no. of hand/ branch, higher weight of finger/hand (kg), higher weight of single finger (g), more finger diameter (cm), higher length of finger (cm), more weight of finger/ bunch (kg), more percentage of plant harvested at a time, higher yield (64.22 tonnes/ ha), gross return (Rs. 12,84,400/ha), net return (Rs. 9,58,730.5/ha) and B:C ratio (3.94) as compared to all other treatments. On an average the yield of per plant was 20-30 kg and an average yield 50- 64 tonnes per hectare. In terms of economy as per market analysis, price of Banana in Jammu is approximately Rs. 20 per kg. Thus, on an average it gave Rs. 250-300 per Banana plant. On the basis of market demand, approximately Rs 6.17- 9.50 lakh net return can be obtained by cultivation of one hectare of land which is alternative business for the farmers of the Jammu and Kashmir.

1.4 Demonstration of cultivation, processing and value addition of selected aromatic crops in rainfed/ rain-fed/waste land/ unutilized land of Bundelkhand region, U.P. & M.P., India

Sabha Jeet, Sumit Gandhi, Chandra Pal Singh and Sonali Bhagat

Bundelkhand is one of the least developed regions of the country consisting of 14 district (Niwari is additional district) located in the states of Uttar Pradesh and Madhya Pradesh. However, agriculture remains the backbone of the economy of this region, as over 75 percent of its population depends on agriculture and allied sectors. The food production in this region is considerably low this is because of scanty rainfall, poor water retaining capacity of soil, large scale damage of crop because of wild domestic animals (Anna Pratha). The major problem of Bundelkhand regions is small size land holdings and agriculture is completely depends on rainfall, 65-85% of the cultivable area is rain-fed. This region covering highest area of the rain-fed/waste land/ unutilized land which are not suitable for commercial cultivation of crops. In this regions farmers facing livelihood challenges due to continuous drought in past few years. The routine agricultural crops *viz.,* cereals, pulses etc. are not able to grow and produce satisfied yield due to water scarcity. Since, the cultivable area of India is limited and cannot be enhance. In diversification era of agriculture, growing of medicinal and aromatic plants in existing cropping systems to be more appropriate to boost up farmers income and full fill the Nations domestic and export demand. Introduction and demonstration of region specific superior genotypes of aromatic crops is most profitable crops, which have immense potential to enhance socio-economic status of marginal and small farmers. These crops because of their inherent capacity to survive and grow under stress condition, rainfed condition, grow very well in wasteland and marginal land with lowest cost of production. Essential oil of these aromatic crops has very high demands of National as well as International market. In order to determined and transmuting change in the economy of population living in rural areas, market dynamics and growth opportunity for utilization of these uncultivated, rainfed wasteland

of Bundelkhand region. Govt. of India, D.B.T. sponsored project for Bundelkhand region conceptualized. Under this project, CSIR-IIIM aims to introduce and demonstrate newly developed superior varieties of selected 3 high value aromatic plants *viz.,* Lemongrass, Rosagrass, and Jammu Monarda in the farmers fields under captive cultivation of 500 acres of area in 03 years in 8 district of Bundelkhand region of U.P. and M.P. We are targeting rain-fed and degraded wasteland and also infrastructure support for distillation units to farmers/growers, enabling effective buy-back mechanisms to assure remunerative prices to the farmers/ growers. CSIR-Indian Institute of Integrative Medicine, Jammu has been transferred CSIR technology from lab to land and distributed > 16 lakh slips/quality planting material (QPM) in free of cost and demonstrated aromatic plants Lemongrass (CKP 25) "Rosagrass" (CN-5 & CK- 10) and Jammu monarda at more than 90 farmers field in different villages of Jalaun, Mahoba, Lalitpur, Rath, Hamirpur and Jhansi district (U.P.) and Sagar, Datia and Tikamgarh district (M.P.) from June 2018 to March 2019. In this project we are also providing technical know through conducted "Awareness cum training programme" in whom 496 peoples were benefitted and also approaching to IT company for developing mobile app for digital registration of beneficiary farmers, recording of location through GPS coordinates, present picture of the farmer and their field, performance of crops on particular beneficiary farmers, reporting of Project/Field Assistant on their project site, record keeping, etc. This CSIR technology may help to farmers for doubling the income through growing of aromatic crops by utilizing the rainfed/wasteland of Bundelkhand region.

2.0 BIODIVERSITY AND APPLIED BOTANY

2.1. Collection and Certification of Plant Vouchers in Janaki Ammal Herbarium

Bikarma Singh

The proper authentication of raw material is critically important as far as safety and efficacy of herbal medicines are concerned. Plant authentication and identification services are provided to industries and growers by the scientific staff working in herbarium section. Janaki ammal Herbarium is recognized as a National Referral Centre for plant identification and authentication. The identities of these plants were confirmed by following SOP followed in Janaki Ammal Herbarium. During 2018-2019, many field tours for collection of plant materials were undertaken and plant vouchers were collected for studying plant diversity, ecology, genetic variability, DNA bar-coding, tissue culture, and for isolation of different markers and compounds from different bio-geographic regions of Himalaya.

Figure 2.1.1. Investigation of economic plants during field survey

- Kathua, J&K State: Field tour to Bani, Sarthal and adjoining areas on 3-7th April 2018 for survey and collection of plant samples for R&D
- Katra, J&K State: Field tour on 24/4/2018 for survey and collection of targeted plant samples, *Cannabis sativa* and *Cassia tora* for R&D
- Reasi, J&K State: Field tour on 25/04/2018 for collection of targeted plant, *Woodfordia fructicosa* and *Colebrookia oppositifolia*.
- Batote-Sanasar, J&K State: Field tour on 26/4/2018 for collection of targeted plant *Valeriana jatamansi, Rubia cordifolia* and *Cannabis sativa.*
- Amritsar, Punjab State: Three days field tours between 4-6th July 2018 were undertaken to Amritsar Punjab for purchase of bulk quality of Valeriana jatamansi for Phytopharmaceutical project for chemistry works of IIIM.
- Trikuta Hills, J&K State: Scientific expedition field tour on 5/8/2018 for exploring and discovering plant diversity of Trikuta Hills with specific site visit to Devi Pindiya.

2.2. Studies on Diversity, Composition and Structure of Vegetation in Forests of Sarthal Mountains in J&K Himalayas

Sumit Singh, Bikarma Singh, Rajendra Bhanwaria

Himalaya is a unique geographical entity, which occupies an important status in terms of promoting tourism in India. Having bestowed with natural beauty and climatic variations ranges from temperate to alpine, Sarthal Mountain in J&K State, located between 32°49'41.51'"-32°49'43.27' north latitude, 75°43'32.37"-75°43'27.80" east longitude, covering a total geographic area of 16,000 ha. The region abode in temperate and alpine vegetation mostly rich in conifers, whose elevation ranges from 2100m and 4500 m above sea level. Evergreen tall waiving deodar forests, crystal clear water, streams and brooks, snow clad mountains, and green pasture enhances the beauty to these mountain. There is peculiar association of *Rhododendron-Cedrus-Castanopsis-Zanthoxylum-Taxus*, which is very rare in other places. In Sarthal hills, common tree species are *Cedrus deodara*, *Pinus wallichiana*, *Alnus nitida*, *Juglans regia*, *Juniperus cumminus*, *Abies pindrow, Picea smithiana* etc. Among Shrub species, common species found are *Viburnum grandiflorum*, *Phlomis bracteosa*, *Isodon rugosus*, *Rubus idaeus* etc. Among herbaceous flora, *Bergenia ciliata*, *Thymus serpyllum*, *Origanum vulgare*, *Fragaria vesca*, *Primula denticulata, Viola canescens* etc were the common species growing in the study area. During preliminary investigation, total 80 plant species belonging to 21 families and 61 genera were documented from the Sarthal mountain, out of which 15 (16.25%) are tree species, 12 (15%) are shrubs, and 53 (66.25%) are herbs. While collecting data on ethnobotany, 11 species are recorded as wild edible and 16 plant species used for ethnomedicine. The phyto-sociological analysis of the forests was undertaken by randomly laying quadrats. Tree density recorded at the study area was 230 individuals per hectares, and *Pinus wallichiana* was the dominant species with around 60 individuals ha^{-1}, followed by *Abies pindrow* (45 individuals ha^{-1}), and *Cedrus deodara* (30 individuals ha^{-1}). The total basal areas of all tree species recorded were 151.8 (m^2ha^{-1}), and *Abies pindrow* has more basal area as compared to other tree species. The total abundance values of all recorded species were 13.0. In terms of importance value index (IVI), *Pinus wallichiana* was the dominant tree species (IVI=72.43) followed by *Abies pindrow* (IVI=62.43) and *Cedrus deodara* (IVI=57.17). Total volume of the entire tree species recorded was 27.83m^3, and *Cedrus deodara* has the highest value (10.29 m^3), followed by *Abies pindrow* (6.99 m^3). Among shrub community, the species such *Phlomis bracteosa*, *Berberis aristata* and *Isodon rugosus* shows the highest number of frequency in terms of percentage. The density of shrub species recorded was 250 individuals per hectares (ha^{-1}), and *Phlomis bracteosa* was the dominant species (60 individuals ha^{-1}), followed by *Isodon rugosus* (50 individuals ha^{-1}) and *Strobilanthes wallichii* (40 individuals ha^{-1}). The total abundance values of all species recorded was 11.8. In terms of importance value index (IVI), *Phlomis bracteosa* was the dominant shrub species (IVI=50.92) followed by *Isodon rugosus* (IVI=39.23). In herbaceous community, a total of 53 herb species were recorded from this study and *Eragrostis nigra*, *Ranunculus sceleratus* and *Isachne himalaica* shows highest number of frequency. The density of herb species recorded was 1,10,800 individuals per hectares (ha^{-1}), and *Ranunculus sceleratus* was the dominant species (12,500 individuals ha^{-1}), followed by *Isachne himalaica* (11,000 individuals ha^{-1}) and *Origanum vulgare* (10,000 individuals ha^{-1}). The total abundance values of all species recorded were 114.7. In terms of importance value index (IVI), *Ranunculus sceleratus* was the dominant herb species (IVI=19.35) followed by *Isachne himalaica* (IVI=16.38). This finding indicate that Sarthal occupy a luxuriant position in terms of biodiversity richness, and can serve as a model site for future research in terms of biodiversity conservation and future research of high altitude plants.

Figure 2.2.1. Natural growth of *Rhododendron arboreum* and *Valeriana jatamansi* in Sarthal

2.3. Indian Rhododendrons and their value addition: revision and review

Sumit Singh and Bikarma Singh (published in edited Book 'Plants of Commercial Value)

Evolution theory postulates that the collision between the Indian and the Eurasian plates in early Eocene and Miocene epoch leads to formation of the Himalayas, and currently recognized across the globe as repository of life. Some species of this regions categorized under endangered and endemic group. Rhododendrons placed under family Ericaceae is an important genus of flowering plants. It is one of the multiferous keystone member of plants, mostly endemic to south east Asia. Wide distribution of rhododendrons concentrated in Himalayas. The Eastern Himalaya, especially Arunachal Pradesh and Sikkim states of India is main centre of species distribution. Several species exhibits many nutritional, medicinal and aromatic properties as evident from tribal knowledge and published research sciences. Different parts of plant such as flowers and leaves used in folklore, herbal medicine and for preparation of local wines. Chemically, rhododendrons are repository of several bioactive molecules in the form of taraxerol, hyperoside, betulinic acid, quercitin, arbutin, rutin, coumaric acid, and several other fine molecules in minor quantities. In the present communication, the Indian rhododendrons revised and presented as a source of value added species for Indian economy.

Figure 2.3.1 A. Rhodendrons of Himalayas and Indo-Myanmar Hotspots in India

Figure 2.3.1B. Rhodendrons of Himalayas and Indo-Myanmar Hotspots in India

Scrutiny of herbarium and recent published literatures indicate 116 species under this valuable genus. Besides checklist, chemistry, traditional knowledge, ecological requirement, keystone taxa, potential value added products in future, threat and future perspective of rhododendrons for conservation also discussed and presented in different sub heads. First time checklist of all Indian rhododendrons are provided.

2.4. Cartographic representation on preliminary investigation of Woody Pure Strand Forest Vegetation around District Doda (J&K State) of Western Himalaya

Opender Surmal and Bikarma Singh

Doda district is in the eastern part of Jammu Division of Indian state of Jammu and Kashmir. The District consists of 8 Tehsils: Bhagwa, Assar, Doda, Gundana,Marmat, Bhaderwah, Gandoh (Bhallesa) and Thathri. The Doda District lies at 32° 53´ and 34°21´N latitude and 75°1´ and 76°47´E longitude. It has an average elevation of 1107 meters above from mean sea level. The climate of the district being sub tropical is hot and dry in summer and cold in winter. Due to its varying physical features, the District does not have a uniform climate. Average rainfall in District Doda has been recorded as 35.08 inches per year which is lowest as compared to other Districts of Jammu Division. Due to low average annual precipitation, the whole of the Doda District has been declared drought prone. A field tour was conducted in tha Gandoh (Bhallesa) Tehsil of district Doda w.e.f 29th march to 8th April 2019 total 80 plant species were collected from 3 different locations viz. Ghill kunan, Gandoh and Bani forest range having elevation range from 2000 metre to 2500 metre ASL. Some of the common tree species which are growing in the study areas are *Cedrus deodara* , *Pinus wallichiana*, *Rhododendron arboreum*, *Juglans regia*, *Quercus oblongata* ,*Pyrus malus* etc.Among common shrub species which were growing in the study area are Isodon *rugosus*, *Vibernum grandiflorum*., *Berberis lycium*, *Nepeta lamiaopsis* etc. Among herbaceous flora ,*Bergenia ciliata*, *Valeriana jatamansii*, *Vioala canesens*, *Pteris cretica, Ajuga bracteosa*, *Rumax nepalensis* etc. As per literature survey, the area is botanically very less explored. Hence more field trips and inventory work should be done in the study area to carry out more knowledge about biodiversity and endemic flora.

Figure 2.4.1. Topographical representation of forest vegetation in District Doda

2.5. Investigation of ethnobotanical knowledge in Uttarakhand Himalaya: Preliminary Review

Anjali Saini and Bikarma Singh

The Himalayan state, Uttarakhand state is a part of central Himalaya, and the region is rich in biodiversity. It is estimated that more 7,000 species of different higher plants in this state mostly distributed in hotspot sites such as in 7 wild life sanctuaries (Binsar WLS in Almora, Askot WLS in Pithoragarh, Kedarnath WLS in Rudraprayag, Govind Pashu Vihar WLS in Uttarkashi, Benog WLS in Dehradun, Jhilmil WLS in Haridwar, Asan WLS in Dehradun), 5 National Parks (Corbett NP in Nanital, Rajaji NP in Haridwar, Nanda Devi NP in Chamoli, Valley of Flower NP in Chamoli, Gangotri NP in Uttarkashi) and Nanda Devi Biosphere Reserve, which contribute to 31% of total flora diversity of India. As per reported records, 119 plant species are endemic to the state which encompasses 2.35% endemism richness at national level. There is of the record that 1127 flowering species belonging to 153

families are of medicinal values. Most of the medicinal plants are traditional used in folklore system of medicine by tribes inhabiting the state. These include Juonshari, Bhoxa, Bhoyta, Tharu and Raji, who mostly depends on wild plants for their food, shelter and medicine. An investigation has been initiated to documents different plants species growing in Uttarakhand Himalaya as ethnomedicine, and plants used as wild food.

2.6. Application of Mentha species in North-Western Himalaya: a case study of Mentha diversity in Uttarakhand State

Sneha and Bikarma Singh

The state of Uttarakhand (20°26′-31°38′ north latitude, 77°49′-80°59′ east longitude), known for Rishikesh as Hindu pilgrimage site and Jim Corbett National Park across the globe. It covers an area of 53,483 km2 encompasses with a wide spectrum of diverse ecosystem that include tropical rainforests, temperate forests, alpine vegetations and alpine meadows. The state is known for rich repository of medicinal and aromatic plants, and mints are an important house hold herbal medicinal plants for local people. Himalayas accounts for 18% of the total geographic area of India and represents approximately 31.05% of forest cover in the country. In this study, we collected data on mint species growing in Uttarakhand Himalayas, and reports four species of mints from the state, which are widely distributed in tropical to semi-temperate agro-climatic zones of the state. These include *Mentha arvensis*, *M. citrata, M. longifolia*, and *M. spicata* var. *viridis*. The spearmint called *M. spicata* var. *viridis* and bergamot mint (*M. citrata*) are cultivated to large extent in different regions of the state for their volatile oils, while, *M. arvenis* and *M. longifolia* grows as wild plants. There is report that *Mentha x piperita* is also cultivated in few pockets as introduced mint for essential oils. The wild mints usually grows in moist places and along the streams/rivers and road side. Literature revels that the diversity of mint mostly concentrated in Kumaon, Haridwar, U.S Nagar, Dehradun and Rishikesh area, as these regions climate favour the luxuriant growth of these species. The most of the mints species yield essential oils rich in compounds such as menthol, menthone, iso-menthone, menthofuran, carvone, linalool, linalyl acetate and piperitenone oxide. These volatile chemical constituents had wide applications in pharmaceutical, food, flavour, cosmetics, beverages and allied industries for value additions and product development. In India, *Mentha* species are being cultivated as spring-summer crop which act as an industrial crop for the production of their essential oils. The wild species needs conservation and R&D, where as promotion and cultivation of cultivated variety promotes industrialization for the state, which can earn economic for the country.

Figure 2.6.1. Habit of *Mentha arvensis* and *Mentha longifolia* in Uttarakhand Himalaya

2.7. Investigation of Medicinal Wealth of District Kupwara in Kashmir Himalaya, India

Mudasir Nazir Bhat and Bikarma Singh

Scientific exploration through resource mapping, documentation and plant introduction is one of the oldest activities of mankind. Since the dawn of human civilization, men have gathered many new and useful plants information from far-away places. In proportion to its area, Kashmir Himalaya in Jammu and Kashmir (J&K) State is floristically less explored due to international border problems especially in LoC regions of China and Pakistan. There is no doubt that Himalayan belts are rich resources of unique medicinal and otherwise economic valued plants, and more than 50% of India's documented plant diversity is from these regions. District Kupwara is one of the twenty-two districts of J&K located in the Northern most part of Kashmir Himalaya. Scrutiny of herbarium specimens at Janaki Ammal Herbarium in CSIR-IIIM Jammu indicate that this district is floristically unexplored as no evidence of plant collection deposited in RRLH, however, being a part of Himalaya, we can predict that this district is also a rich repository of wild plants, and harbor unique medicinal plants. While studying the plant composition of Kupwara, a list of 233 species of plants were prepared, which includes 24.46% trees, 16.74% shrubs, 44.21% herbs, 11.59% and 3.00% parasites. The dominant families include asteraceae, rosaceae, lamiaceae, ranunculaceae, poaceae, fabaceae and apiaceae. Reviews of literatures reveals that out of these documented species, 67% species have medicinal and therapeutic potentials, and more than 100 species used as ethnomedicine in local diseases. Some of the common medicinal valued plants are *Artemisia absinthum, Taraxacum officinale, Urtica dioca, Sinopodophyllum hexandum, Euphorbia wallichii, Saussurea costus, Rheum emodi*, and several other high altitude plants. These medicinal plants are used in treatment of obesity, liver infection, diabetes, intestinal infections, rheumatism, tumours, stomach-ache, insomonia, nerve troubles, skin infection, constipation, cough and asthma, migraine, paralysis, jaundice, cancer, swelling and inflammation. Majority of the plants are used as wild food, timber and for construction of houses.

2.8. Assessing ethnic traditional knowledge, biology and chemistry of *Lepidium didymum* L., lesser-known wild plants of Western Himalaya

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Bikarma Singh, Sumit Singh, Bishander Singh, Surinder Kitchlu and Vikash Babu

Tribal communities have a long history of association living in close contact with nature as herdsmen, and their mode of use of natural products as food and medicine dates reverse to ancient time. Usually, the folklore knowledge transfers from one generation to next generation by the way of living and the mode of usage of available resources. There is less known information on taxonomy, ethnic traditional knowledge, nutrient contents and chemistry of *Lepidium didymum* L., a leafy wild edible Himalayan culinary herb. The authors have documented such folklore knowledge for the first time from two Himalayan nomadic and pastoral communities-Gujjars and Bakarwals, from seven regions (Patnitop, Sanasar, Kud, Batote, Bani, Nathatop and Mantalai) of Jammu and Kashmir, India. Investigations were carried out using snowball technique from 167 people both the male and the female, aged 17–68 years. As per knowledge investigated, *L. didymum* is commonly used as seasonal cooked vegetable, local medicine, fodder for animals, salad, chapati making and traditional dish *Wazwan* preparation. The field data analysis shows high use value of this species. The plant prefers to grow in subtropical and temperate climate and has high nutritive values due to the presence of high glucose, unsaturated fatty acids, proteins, vitamins and minerals. This finding will lead to the formulation of new nutraceutical products as value addition from wild edible plants for people residing in the high-altitude regions of Jammu and Kashmir and elsewhere in the world.

2.8.1. Ethnobotanical data analysis of *Lepidium didymum*

Based on information provided by all the informants, the use value of *Lepidium didymum* were classified into five categories, *viz.,* cooked as vegetable, medicine, fodder, salad, chappati making and local spices in meat preparation. The details of investigation report are given in Table- 2.8.1.1 and Table 2.8.1.2.

Table–2.8.1.1. Characteristic of informants during the ethnobotanical surveys in Udhampur district, J&K state

District	Patnitop	Sanasar	Kud	Batote	Khooninala	Nathatop	Mantalai	Total
Total participants[a]	37	26	12	32	17	19	24	167
Total informants (N)[b]	26	20	9	28	10	19	24	136
Male (N)	16	14	7	9	7	8	13	74
Female (N)	21	12	5	23	10	11	11	93
Age range	24-67	17-68	40-60	30-60	26-60	19-65	27-55	-
Median Age	45.5	42.5	50	45	43	42	41	-
Year of the survey	April (2015)	September (2014)	July (2016)	March (2016)	June (2015)	November (2014)	October (2016)	-

[a]People participated during the investigation at different study areas in Udhampur district

[b]People in Gujjar and Bakarwal community having knowledge on traditional uses of *L. didymum* as food or as medicine.

Table–2.8.1.2. Traditional use categories of *Lepidium didymum* based on Gujjars and Bakarwal folkare information

Use category	Usage mode
Cooked vegetable	Edible as wild vegetables after boiling the young aerial parts, and consumed as local *Saag*. Leaves contribute in flavoring, and therefore, used in decorating cooked food items.
Medicine	Whole plants can be used to treat human or animal diseases. Bakarwals traditionally used it as ethno-veterinary medicine against insects and used to kill body louse and ticks. The whole plant valued as local medicine in treatment of human allergies and wounds. Boiled water of root drunk to cure headache, constipation and fever.
Fodder	Used as animal foods (sheeps, goats). This plant is given to buffaloes and cows whose milk smells.
Salad	Young twigs along with oxalis leaves cut into pieces and used with local tomatoes and wild garlic as salads.
Chappati making	Cut pieces of dried leaves are used in making chappati in the form of local parantha.
Meat preparation	Used in preparation of a local Kashmiri dish called *Wazwan*. It is an indigenous method of cooking meat of goat and sheep.

The analysis of data on traditional knowledge collected from Gujjars and Bakarwals shows a strong association with nature and their use varies (Table-2.8.1.3). Investigation data on UV reveals that 32.13% prefer to eat *L. didymum* as cooked vegetable, 17.12% people relish the dried leaves in chapatti or/in local traditional way of paratha preparation, 13.81% people used in local dish called '*Wazwan*' and remaining 36.94 % UV indicate its use in medicine, fodder and salad.

Table–2.8.1.3. Use Value (UV) and use category of *Lepidium didymum* based on Gujjars and Bakarwal folkare information

Use category	Use Value (UV)	% of UV
Cooked vegetable	107	32.13
Medicine	54	16.22
Fodder	53	15.92
Chappati	57	17.12
Salad	16	4.80
Meat preparation	46	13.81
Total	333	100.00

2.8.2 Nutrient content and nutraceutical potentials

Lepidium plants were source of glucosinolates (sulfur containing glycosides), linolenic acid (polyunsaturated fatty acids), glucose, crude protein, vitamins and minerals. Glucosinolates on hydrolysis produce isothiocyanates and anticarcinogenic bioactive compounds. Alpha-linolenic acid is one of the two essential fatty acid (other being Linolenic acid) necessary for human and animal health, and cannot be produced within the body, and need to be fulfilled from the outside source. Various vitamin components found in *Lepidium* includes vitamin A, vitamin B2, B9, B6, vitamin C and vitamin K. Reported minerals in *Lepidium* were Mn, Cu, Fe, K and P. The nutraceutical properties of *Lepidium* were determined by evaluating total phenolic content (TPC), flavonoid and tannin contents[26]. Analysis of *Lepidium didymum* shows high content of glucosinolates, linolenic acid, glucose, vitamins and minerals. Further studies on their nutraceutical potentials activities are under study as shown below 2.8.2.1.

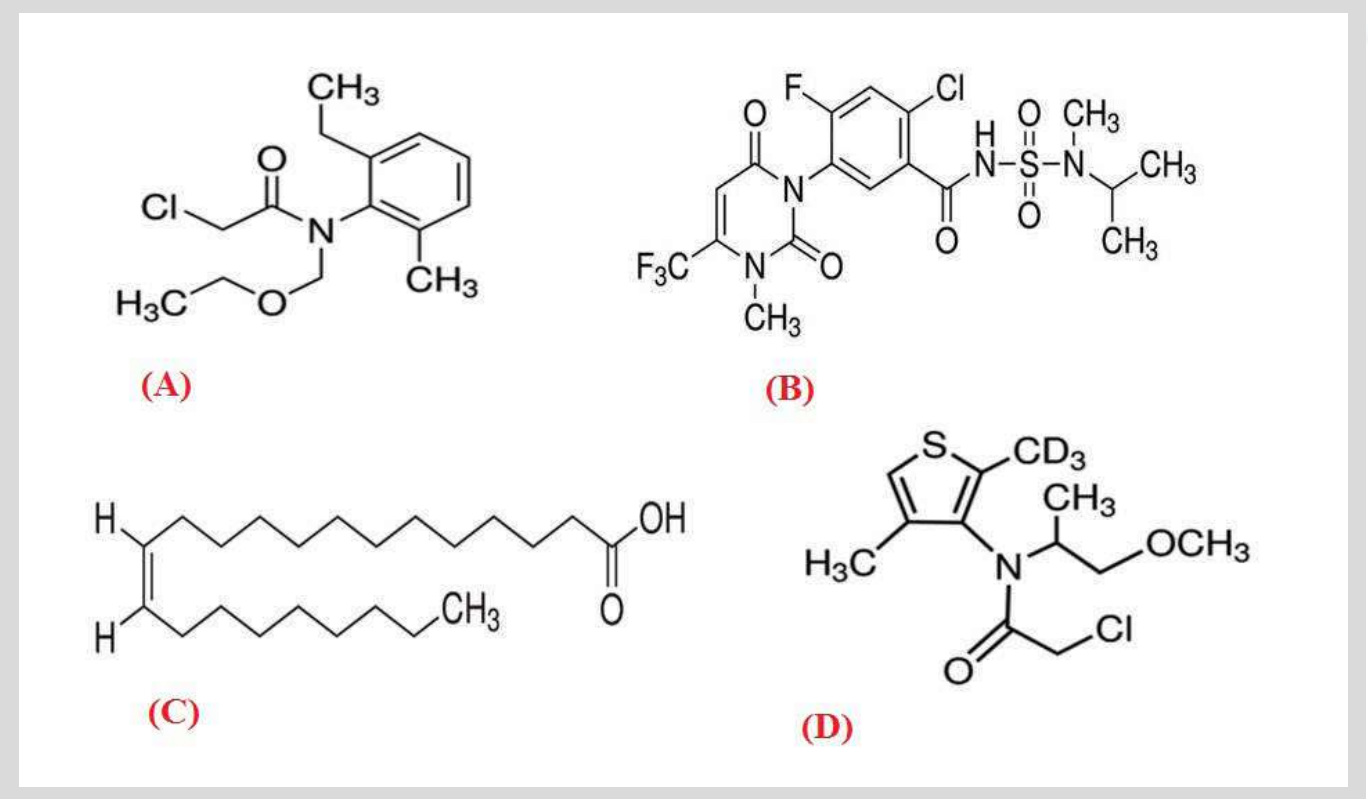

Figure 2.8.2.1. Major herbicides prepared from organic chemical constituents of Lepidium didymum (A: acetochlor, B: Dimethenamid, C: Erucic acid, D: Saflufenacil)

2.9. New distribution records of the leopard plants *Ligularia amplexicaulis* DC. and *Ligularia sibirica* (L.) Cass. (Asteraceae) in the Indian Himalaya

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Bikarma Singh, Sumit Singh and Bishander Singh

Two leopard plant taxa, *Ligularia amplexicaulis* DC. and *L. sibirica* (L.) Cass., are reported for the first time from Bandipora District of Jammu & Kashmir in India and are taxonomically enumerated. *Ligularia amplexicaulis* is a new record for the district Bandipora of the Kashmir Himalaya, which was previously reported in the elevation range of 2700–4800 m from the states of Himachal Pradesh, West Bengal, and Sikkim in India. The specimens from Bandipora extends the geographic distribution of L. *amplexicaulis* in Jammu & Kashmir State, from Paddar Valley of district Kishtwar to the extreme northern range of the western Himalaya.

Ligularia sibirica is reported for the first time from the Kashmir Himalaya of India and its known distribution extended to southeastern Asia. The specimens from Lidder Valley represents the first report of *L. sibirica* from the Kashmir Himalaya and extends its distribution range from Europe, Russia, and China to northern India. The present paper deals with the taxonomic description, phenology, ecological notes, associated vegetation components, and a note on the history of species discovery of these two leopard plant taxa. This finding also presents an updated distribution map of these two Indian species in the western Himalaya as per figure 2.9.1.

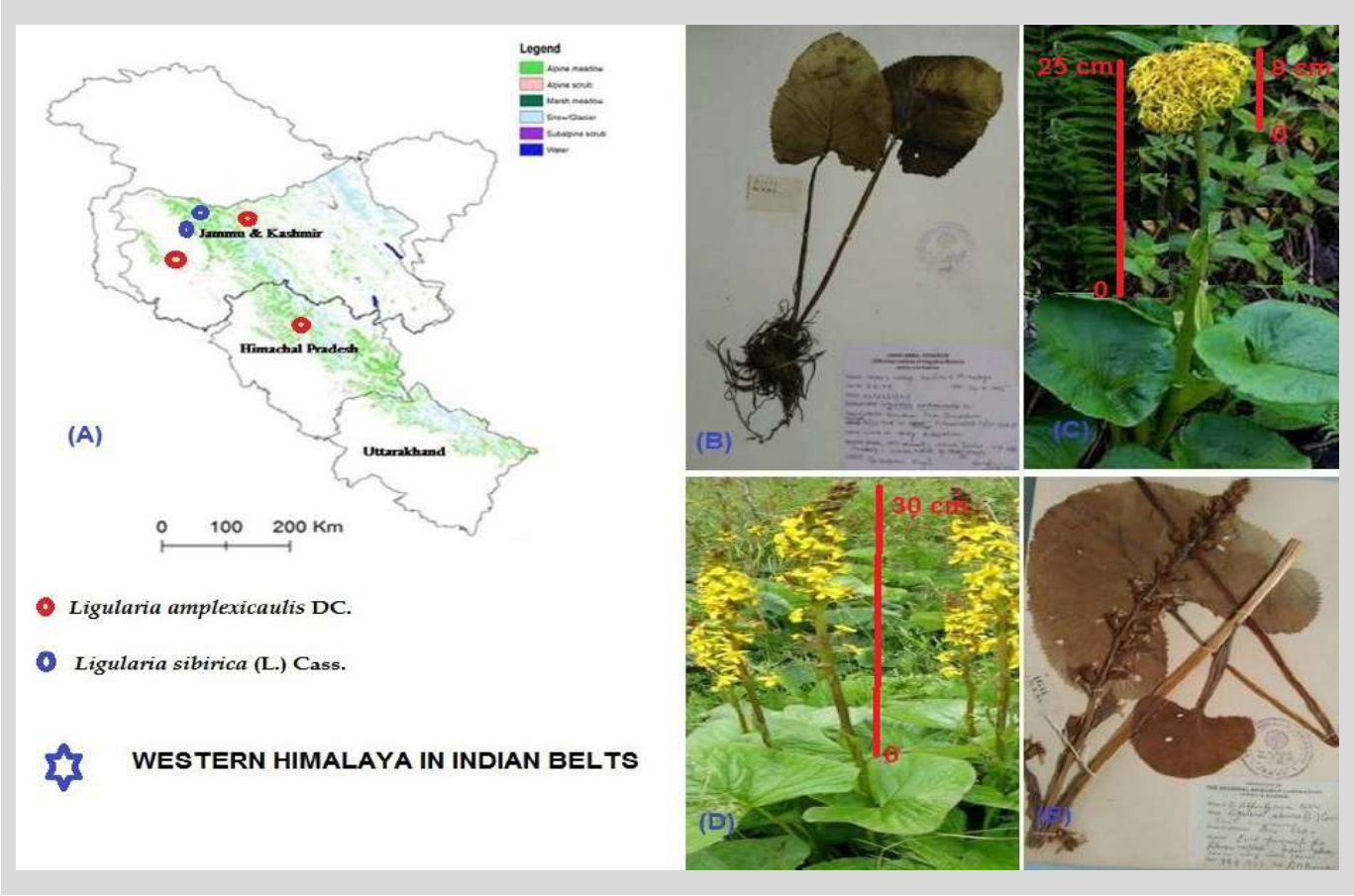


Figure.2.9.1. Location map and morphological habit of *Ligularia siberica* and *Ligularia amplexicaulis* in Western Himalaya, (A)-Mapped distributional record, (B-C) Herbarium voucher and wild habit of *L. amplexicaulis,* (D-E) Wild habit and herbarium of *L. siberica.*

Taxonomic accounts

I. Ligularia sibirica (L.) Cass., Dict. Sci. Nat. 26: 402. 1823.

= *Othonna sibirica* L., Sp. Pl. 2: 924. 1753. *Cineraria sibirica* (L.) L., Sp. Pl. (ed.2): 1243. 1763. *Hoppea sibirica* (L.) Rchb., Flora 7(1): 245. 1824. *Senecio cacaliifolius* Sch. Bip., Flora 28: 50. 1845. *Senecillis sibirica* (L.) Simonkai, Enum. Fl. Transsilv. 143. 1886. *Ligularia bucovinensis* Nakai, J. Jap. Bot. 20: 185. 1944. *Ligularia ucrainica* Minderova, J. Bot. Acad. Sci. Ukraine 14(2): 46. 1957. *Ligularia arctica* Pojark., Fl. URSS 26: 817, 891. 1961. *Ligularia longipes* Pojark., Fl. URSS 26: 816. 1961. *Ligularia pojarkovana* S.W. Liu & T.N. Ho, Acta Phytotax. Sin. 39(6): 560. 2001.

Perennial herbaceous plants, 50-150 cm tall; stems erect, 0.3-0.8 cm diam. at base, glabrous, yellowish brown, pubescent; rootstocks fibrous; rhizomes aromatic, with minute root hairs. Leaves basal ones petiolate; petioles 14-39 cm, glabrous, base sheathed; leaf blades ovate-cordate or broadly cordate, 3.5-32 cm long, 4.5-29 cm broad, glabrous base cordate, apex rounded or obtuse, margin regularly dentate; veins raised, prominent; sinus 1/4-1/3 as long as leaf blade, basal lobes sub-orbicular; petioles slightly pubescent when young, 3-14 cm long; sheaths enlarged, 3-6 cm long. Bracts leaf-like, ovate-lanceolate, 0.2-0.3 cm long, 0.1-0.2 cm broad, margin entire or denticulate, herbaceous. Inflorescence racemose-type, 10-30 cm long; involucre purplish red, broadly campanulate or campanulate-turbinate, 0.7-1 cm long, 0.6-1 cm broad, base rounded; phyllaries 7-12, in 2 rows, lanceolate or oblong, 0.7-1 cm long, margin membranous, apex acute. Ray florets numerous, usually 5-9, yellow; laminas oblanceolate or oblong, 1-2.2 cm long, 0.3-0.5 cm broad, apex obtuse; tubes 0.5-0.8 cm diam. Disc florets numerous, 0.6-1.2 cm long; tubes 0.4-0.5 cm diam. Achenes brown, cylindric, 0.4-0.6 cm long, 0.2-0.3 cm broad. Pappus yellow, 0.4-0.8 cm long, pubescent.

Phenology: The flowering starts in the month of May and can be seen till the first week of September. Fruits start appearing in the middle month of September, usually matured in October and even dried fruits attached with inflorescence can be noticed till November in temperate belts of Himalaya.

***Cytology*:** The chromosome numbers reported in *L. sibirica* varies. Liu (2004) recorded chromosome number is 58 (2n = 58), while studies by Malla et al. (1981) reported the sporophytic chromosome counts in *L. sibirica* as 60 (2*n* = 60).

Habitat and ecology: The plant prefers swamps habitat. It grows well in sparse temperate forests or along slope side on forest margins at altitudes of 1800-3500 m above mean sea level. Single inflorescence arise at tip of the plant, and usually all flowers are hermaphrodite, i.e. both male and female organs are on the same plant. As observed in field, insects are main pollinators. Soils are characterized as sandy, and loamy, and prefers moist soil environment.

***Associated taxa*:** Species of the genus *Iris* L., *Ranunculus* L., *Aconitum* L., *Nepeta* L., *Primula* L., *Caltha* L. and some temperate grasses found to be growing in meadows along with *L. sibirica* in Western Himalaya.

Distribution: China, Tibet Province, Europe, India (Aru in Jammu & Kashmir state), Mongolia, Russia and Siberia.

Voucher examined: India-Western Himalaya, Jammu & Kashmir State, District Ladakh, Aru Valley, 34°32.748N, 74°37.908E, elevation 2400 m ASL, 29 July 1977, BM Sharma 16241 (RRLH!).

***II. Ligularia amplexicaulis* DC.,** Prodr. 6: 314. 1838.

= *Ligularia corymbosa* DC., Prodr 6: 314. 1838. *Senecio amplexicaulis* (DC.) Wall. ex C.B.Clarke, Compos. Ind. 204. 1876. *Senecio yakla* C.B.Clarke, Compos. Ind. 204. 1876.

Perennial herbaceous robust plants, 30-70 cm tall; stems slightly erect, 0.2.-0.5 cm diam. depending on habit, young ones light green, old dark brown, slightly grooved, glabrous at base, slightly pubescent near flowering inflorescence; rootstocks fibrous; fresh rhizomes aromatic. Leaves petiolated; leaf blades orbicular to reniform, 8-15 cm long, 7-12 cm broad, cordate at base, acute at apex, irregularly toothed, glabrous bothside; sinus 1/4-1/3 or as long as leaf blades; veins raised, prominent, reticulate; petioles 8-20 cm long, slighly pubescent, with interruptedly winged. Bracts leaf-like, ovate-lanceolate, 0.5-0.6 cm long, 0.2-0.3 cm broad, margin entire, rarely dentate, connate below. Inflorescences radiate, corymbose, 3-8 cm long, 0.6-1.7

cm diam.; involucres campanulate, distantly pubescent; phyllaries 6-10 in rows, lanceolate, 0.5-0.7 cm long. Ray florets linear, 1-1.5 cm long; rays oblanceolate, 0.4-0.6 cm long, apex obtuse; tubes 0.4-0.8 cm long. Disc florets numerous, 0.4- 0.7 cm long; limbs 0.1-0.3 cm long, 5-lobed; tubes 0.3-0.4 cm long. Achenes slightly pale brown, oblong, minute, 0.1-0.2 cm long, oblong, slightly ribbed. Pappus pale-brown, 0.5-0.6 cm long, pubescent.

***Phenology*:** Plants flowers between July and October. Fruiting starts in the month of September and matured green fruits can be seen till the end of October in Kashmir, Ladakh and Himachal Pradesh.

***Habitat and ecology*:** The plant prefers meadow grasslands and rocky ledges are the habitat of this taxa. It grows well in open areas or sometimes along mountain slopes on forest margins at altitudes of 1200-2000 m above mean sea level. Usually flowers are hermaphrodite, and insects are main pollinators. Soils are characterized as sandy, and clay.

***Associated taxa*:** Species of the genus *Ranunculus* L., *Fragaria* L., *Potentilla* L., *Nepeta* L., *Caltha* L. and some subtropical and temperate grasses such as *Carex* L., *Eragrostis* Wolf., etc. found to be growing along with *L. amplexicaulis* in the study area.

***Distribution*:** Bhutan, India (Paddar valley, Kishtwar and Razdhan Pass in Jammu & Kashmir, Uttar Pradesh, Sikkim and West Bengal).

Voucher examined: India-Western Himalaya, Jammu & Kashmir State, District Bandipora, Razdhan Pass, 34°32.748N, 74°37.908E, elevation 3492 m ASL, 26 August 2015, *B Singh* 53138 (RRLH!).

Economic importance: Leaves edible by goats and sheeps. Stems, leaves and flowers are used in Tibetan system of medicine in case of vomiting from indigestion.

2.10. Preliminary investigation of ethnobotanical plants of district Poonch (J&K)

Abhishek Dutta, Bikarma Singh and Yash Pal Sharma

The term 'Ethnobotany' was introduced by Harshberger in 1896 and is defined as the study of traditional and indigenous knowledge about overall relationship of plants with man since ancient times. Ethnobotanical knowledge (EK) is the wisdom evolved and developed by human society over generations for proper utilization and conservation of the plant wealth. In India, the pioneer work on ethnobotany was initiated in the year 1956 by Dr. E.K. Janaki Ammal and its growth and development owes much to the painstaking work done by eminent scientist Dr. S.K. Jain, also known as "Father of Indian Ethnobotany". Plants have been regarded as an indispensable part of life in several indigenous communities since time immemorial. All cultures of the world have shown dependency on plants and their products for food, shelter, fodder, medicine, clothing, dyes, ornamentations and religious ceremonies. Further, the healing power of plants is an ancient idea which finds its mention in historic scripts. The sacred Vedas also referred many medicinal plants (3500 B.C. and 800 B.C.). In Rig Veda (2000 B.C.), there is mention of *Cinnamomum verum* J.Presl, *Zingiber officinale* Roscoe, and *Santalum album* L. as medicinal plants. Thus, the magical power of these green edibles to heal ailments has prompted mankind to explore his natural surroundings. Poonch, one of the districts of Jammu province, is situated in the western part of Jammu and Kashmir and is bounded by the Pir Panjal Himalayan range (which separates it from Baramulla, Budgam, and Shopian districts of Kashmir province) in the North and East, Rajouri district in the South, and Pakistan occupied Kashmir (PoK) in the West. It has an altitudinal range of 800-4,750 masl, lies between 73° 58´- 74° 35´ E and 33° 25´- 34° 01´ N and is divided into 6 tehsils namely Haveli, Mandi, Mendhar, Surankote, Balakote and Mankote. The total geographical area of the district is about 114387 ha out of which 951 sq km comes under forest cover. A systematic and extensive ethnobotanical survey was carried out in four villages of the district during April 2018 to March 2019 for collection of information on ethnomedicinal plant species being used by the locals in the study area. Information was gathered from the informants on the indigenous uses of plant species as medicine by using questionnaire. All the informants were from the rural regions of the district having agriculture and animal keeping as the main occupations. The information collected included common conditions or ailments or diseases occurring in humans and animals which are curable by plants, local name of plant species, habit, wild/cultivated, flowering time, plant part used, ethnomedicinal use, method of crude drug preparation, drug given individually or in combination, mode of administration, dosage. During the reporting year, ethnomedicinal information of 32 plants was documented by interviewing informants using questionnaire. These 32 species belonging to 24 families and

30 genera were collected possessing ethnomedicinal importance for the treatment of multiple ailments of both humans and livestock. Out of 32 plants, 13 plants were found to be commonly used against human ailments, 13 plants were having ethnoveterinary importance and 06 were found to be effective against ailments of both humans as well as animals. In addition, a total of 46 formulations prepared from these plants were recorded for 37 diseases with respect to their medicinal properties. Specifically, 19 species with 26 formulations used against 16 diseases were recorded to be of ethno-veterinary importance.

Figure2.10.1. Investigation of ethnobotanically important plants of District Poonch

3.0 PLANT BIOTECHNOLOGY

3.1 Development of an elite somaclonal variety of Rose-scented geranium (PG-IIIM-101) through biotechnological interventions (National Registration No. INGR17054, ICAR-NBPGR)

Surrinder K. Lattoo, Qazi Parvaiz Hassan, Shabnam Khan, Mahendra K. Verma

Pelargonium graveolens L'Hér. (Rose-scented geranium PG-IIIM-101):

A high yielding variety of Rose-scented geranium (*Pelargonium graveolens* L'Hér.) suitable for temperate and sub-tropical climates has been developed through biotechnological interventions. The variety developed (PG-IIIM-101) is superior to parental genetic stock 'Bourbon' in terms of oil content (0.14-0.16%), essential oil profile (citronellol: 36.9-42.5%, linalool: 14.4-16.7%, geraniol:15.6-19.9%, geranyl formate: 5.6-7.8%, γ-eudesmol: 1.3-1.9%) and fresh herb yield (1170-1430 g/plant). It has been registered as a national variety (INGR17054) with ICAR-NBPGR (Indian Council of Agricultural Research-National Bureau of Plant Genetic Resources).

Table 3.1.1.: Comparative multilocational evaluation of yield and yield components of Rose-scented geranium (PG-IIIM-101) in comparison to parental genetic stock*

Location/ Coordinates	Plant height (cm)	Plant spread (cm)	No. of branches/ plant	Herbage yield/ plant (g)	Oil content (%)	Herbage yield/ha (Tonne)	Oil yield/ ha (kg)
CSIR-IIIM (Jammu) 32. 44° N, 74. 55' E, 304 m asl	120-150 x̄ 135.70; SD ±18.38 *105-125 x̄ 118.18; SD ±11.31	95-105 x̄ 100.30; SD 6.36 87-100 x̄ 98.80; SD 4.94	31-39 x̄ 36.60; SD ±2.83 24-33 x̄ 28.09; SD ±5.65	1170-1430 x̄ 1320.57; SD ±77.66 1120-1280 x̄ 1183.18; SD ±48.08	0.14-0.18 x̄ 0.15; SD ±0.015 0.10-0.12 x̄ 0.11; SD ±0.009	35-36 (31-32)	40-42 (28-30)
Pulwama (Kashmir) 33.87° N, 74.89° E, 1650 m asl	107-142 x̄ 126.50; SD ±14.85 98-118 x̄ 108.00; SD 9.19	92-100 x̄ 96.40; SD 4.24 89-104 x̄ 94.70; SD 4.23	32-36 x̄ 33.80; SD ±0.70 31-35 x̄ 33.10; SD ±0.69	1130-1340 x̄ 1234.00; SD ±74.44 1110-1220 x̄ 1158.20; SD ±378.96	0.14-0.16 x̄ 0.15; SD ±0.009 0.10-0.12 x̄ 0.11; SD ±0.007	33-34 (31-32)	39-40 (32-33)
Bhaderwah 32.98° N, 75.71° E, 3110 m asl	93-122 x̄ 108.60; SD 14.85 85-112 x̄ 109.00; SD 12.72	80-98 x̄ 94.00; SD 9.19 76-93 x̄ 84.00; SD 4.24	31-35 x̄ 33.40; SD ±1.41 26-32 x̄ 28.60; SD ±2.12	1045-1260 x̄ 11769.50; SD ±80.84 980-1120 x̄ 1049.30; SD ±40.69	0.13-0.18 x̄ 0.15; SD ±0.017 0.10-0.12 x̄ 0.11; SD ±0.008	31-32 (28-29)	38-39 (25-26)
**BGSBU Campus (Rajouri) 33.37° N, 74.31° E, 940 m asl	63-78 x̄ 71.20; SD 8.48 60-72 x̄ 67.20; SD 3.53	72-83 x̄ 79.30; SD 5.65 65-76 x̄ 69.80; SD 6.36	18-25 x̄ 22.10; SD ±4.24 18-23 x̄ 19.71; SD ±0.71	690-810 x̄ 748.00; SD ±41.85 540-780 x̄ 649.00; SD ±74.94	0.08-0.10 x̄ 0.09; SD ±0.008 0.07-0.09 x̄ 0.08; SD ±0.007	20-21 (17-18)	14-15 (11-12)

*Data shown for parental genetic stock 'Bourbon' as control.

**BGSBU Campus, Rajouri is not recommended for commercial cutivation of Rose-scented geranium (PG-IIIM-101) due to its poor performance.

Table 3.1.2. Average leaf biomass and percentage composition of major constituents of oil at different ontogenetic stages of elite variety of Rose-scented geranium (PG-IIIM-101) to determine the optimum stage of harvest in relation to biomass production, essential oil content and quality. The stage of harvest is coincident with flower/anthesis to obtain best yields.

Ontogenetic phase	Average leaf biomass (g)	Oil conc. (%)	Oil composition (%)						
			Linalool	Geraniol	Isomenthone	Citronellyl formate	Geranyl formate	Citrollenol	ϒ- eudesmol
Vegetative (I)	700 750	0.10 0.11	14.34 14.45	9.90 7.71	5.97 5.25	11.82 11.90	0.60 0.55	34.01 34.25	0.55 0.62
Flower bud initiation (II)	840 892	0.12 0.12	13.78 13.82	11.55 13.50	6.86 6.89	11.62 11.59	2.80 3.76	32.62 32.55	0.57 0.56
Flowering/ anthesis (III)	1330 1170	0.16 0.16	19.79 19.52	17.77 15.58	6.26 6.32	12.11 12.09	7.78 6.95	36.91 34.57	1.83 1.52
Over-maturation (IV)	1323 1153	0.09 0.10	8.12 8.10	10.14 12.11	8.03 8.09	12.00 11.89	1.60 1.49	25.47 26.50	1.21 1.18

Values are given as means of three replicates ± SD (below 10% in all the cases)

Rose-scented geranium (PG-IIIM-101) depicting characteristic features of habit and morphology from juvenile to mature stages

Figure 3.1.1. Morpho-agronomic traits of elite variety of Rose-scented geranium (PG-IIIM-101) under cultivation conditions at CSIR-IIIM, Jammu: Juvenile plant with multiple branches bearing broad lobed dentate leaves (**a**), plant bearing light to dark pink coloured flowers with reddish purple markings on petals (**b**), mature plants in full bloom ready to be harvested at Jammu (**c**) and Pulwama, Srinagar (**d**).

Scientific methodology used in the development of an elite variety of Rose-scented geranium (PG-IIIM-101)

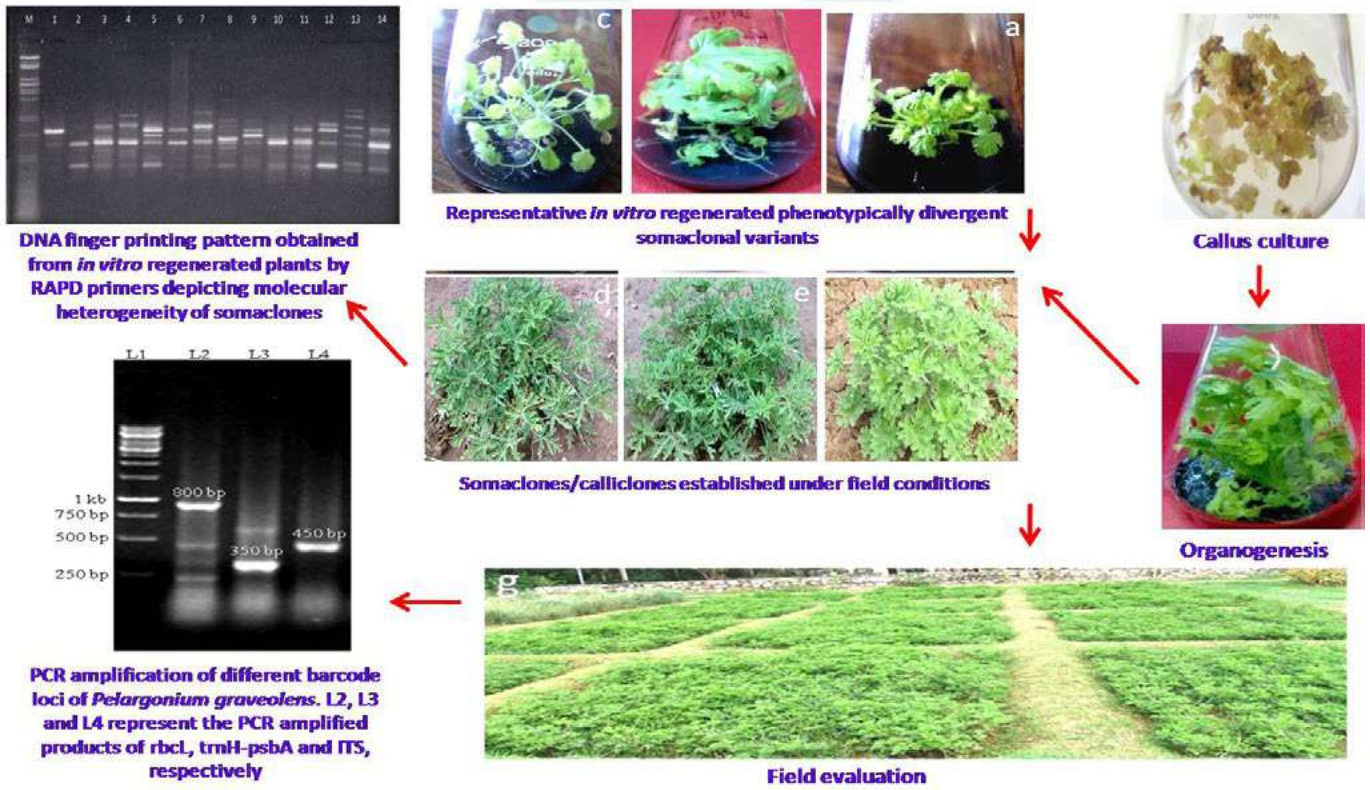


Figure 3.1.2.

Pelargonium graveolens L'Hér. (Rose-scented geranium; Family-Geraniaceae) is a high value aromatic crop which is cultivated for its essential oil obtained from distillation of above ground freshly harvested shoot/leaf biomass. The oil finds extensive use in aromatherapy, flavour and fragrance industry besides being used for the production of a commercial aroma chemical- rhodinol (a mixture of citronellol, geraniol and linalool) which has a wider use in fine grade perfumes. Rose-scented geranium is a sexually sterile crop due to genome complexity (2n=7x=77). Reproductive failure restricts its genetic improvement through conventional breeding methods. In absence of sexuality, we resorted to biotechnological interventions through tissue culture. We employed 'Bourbon' cultivar as a parental genetic stock for its improvement. Young leaf tissues of 'Bourbon' were used to induce callus formation and subsequently using appropriate plant growth regulators and cultural conditions, totipotentiality of dividing cells was used to regenerate complete plants. Since callus represents mass of proliferating cells which lose control over their growth and as a consequence genetic anomalies creep into the dividing cells. The whole process resulted in the development of deviant *in vitro* phenotypes which were successfully transferred under the field conditions for evaluation of different growth parameters, essential oil content and quality (GC-MS profiling). Among 176 somaclonal regenerants, the variety designated as PG-IIIM-101 was selected on the basis of higher oil content and quality essential oil profile. It was further evaluated at four muilti-locational sites for its stability and quality profile for two growing seasons.

Cultivation and evaluation of Rose-scented geranium (PG-IIIM-101)

Figure 3.1.3. Muilti-locational cultivation and evaluation of Rose-scented geranium (PG-IIIM-101): Raising of geranium nursery through vegetative ramets (**a,b,c**), experimental plantation at CSIR-IIIM, Srinagar, Pulwama experimental farm (33.87° N, 74.89° E,1650 m asl) (**d,e**), mature crop at CSIR-IIIM campus, Jammu (32°44' N, 74° 55' E, 304 m asl) (**f**), geranium plantation at Bhaderwah (32.98° N, 75.71° E, 3110 m asl) (**g**), and at BGSBU campus, Rajouri (33.37° N, 74.31° E, 940 m asl) (**h**).

Additionally, production dynamics of essential oil at different ontogenic stages was also studied in relation to optimum stage of harvest in terms of quality and quantity of essential oil. Ontogenic turnover rates of essential oil and its constituents were further corroborated with the glandular ontogeny. The investigation of morphologically identical or distinct clones was confirmed at the molecular level using RAPD markers. Furthermore, three different universal bar-code loci as identified by the Plant Working Group of the Consortium for the Barcode of Life (CBOL-PWG) were used to validate the identity of *P. graveolens*. The molecular barcode generated can be effectively utilized for Intellectual Property Right (IPR) protection of Pelargonium varieties and used as a standard reference system for varietal identification.

Table 3.1.3 Sequences of the DNA bar-code loci amplified from genomic DNA of elite variety of Rose-scented geranium submitted to NCBI (National Centre for Biotechnology Information) data base.

DNA bar-code	Sequence (5-3) along with title and Accession Number
ITS (Accession No. KF871281.1)	*Pelargonium graveolens* 5.8S ribosomal RNA gene, partial sequence; internal transcribed spacer 2, complete sequence; and 28S ribosomal RNA gene, partial sequence GGTACAGTTTGACGCAGTTGCGCCCGAGCCATTAGGCCGAGGGCACGCCTGCCTGGGCGTCACGCGCTCT GTCGCTCCTCCTGCCACCGAATGCCAATTTGGCATTTCGGGGCACGGCGGCGCGGAGATTGGTCTCCCGT GCGCTATCGCTCGCGGTTGGCCTAAAAACGAGTCCAAGGCGTGCGCGCCGCGGTCGACGGTGGTTGAGAA GCCTTCGACAAACAGCCGCGGCTGCGCTCCCTCGAAACGGACCCTACGACCCGCGCGCGTCTCCCCCTCC TCCTCGCGGGGGCGGGGAGGTCGCTCCATCCTGCGACCCCAGGTCAGGCGGGGCTACCCGCTGAGTTTAA GCATATCAAAAGGCCGAAGG
rbcL (Accession No. KF894699.1)	*Pelargonium graveolens* ribulose-1,5-bisphosphate carboxylase/oxygenase large subunit (rbcL) gene, partial cds; chloroplast ATAGAGTGTGAAGATTATAAATTGACTTATTATACTCCTGATTATGAAACCAAAGATACTGATATCTTGG CAGCATTCCGAGTAACTCCTCAACCTGGAGTTCCACCTGAGGAAGCGGGGGCCGCGGTAGCTGCTGAATC CTCTACTGGTACATGGACAACCGTGTGGACCGATGGGCTTACCAGCCTTGATCGTTACAAAGGACGATGC TATCACATCGAGCCCGTTGCTGGAGAAGAAAATCAATATATTGCTTATGTAGCTTACCCTTTAGACCTCT TTGAAGAAGGTTCCGTTACTAATATGTTTACTTCCATCGTGGGTAATGTATTTGGGTTCAAAGCCCTTCG CGCTCTGCGTCTCGAGGATCTGCGAATCCCTCCTGCTTATGTTAAAACCTTCCAAGGCCCGCCGCATGGC ATCCAAGTTGAGAGAGATAAATTGAACAAGTATGGACGTCCCTTATTGGGATGTACTATTAAACCTAAAT TGGGATTATCCGCTAAGAACTACGGTAGAGCAGTTTATGAATGTCTTCGTGGTGGACTTGATTTTACCAA AGATGATGAAAACGTGAACTCCCAACCTTTTATGCGTTGGAGAGACCGTTTCTTATTTTGTGCCGAAGCA ATTTATAAAGCGCAGGCCGAAACAGGTGAAATCAAGGGGCATTACTTGAATGCTACTGAG
psbA-trnH (Accession No. KF923979.1)	*Pelargonium graveolens* psbA-trnH intergenic spacer, partial sequence; chloroplast CGCTGTCGAGCCCATCTACAAATGGATAAGATTTGGGTTGGGTCTGAGTGTATACGAGGTTTTGAAATTG AAAGTAAAGGAGCAATACTAACCCTCTTTCTTGCTAGAACAAGAAGTTGGTTACTGCTCCTTTTTCAATT AGAAGCCTTTTCCTTACATACATCCGTTTTTTTCCTTCAACATAAGAAAAAAGATTCTATTCTTCTTTTT TTTTTTATTTTGAATAGCCGAGGGGCGGATGTAGCCAAGTGGATCAAGGCAGTGGATTGTGAATCCACCC ATGCGCG

Rose-scented geranium (PG-IIIM-101) - ultra-structure of essential oil secretary glands:

The volatile essential oils are secreted by structurally and functionally specialised structures known as trichomes in *Pelargonium graveolens*. Glandular trichomes contribute in a significant portion to plant chemistry.

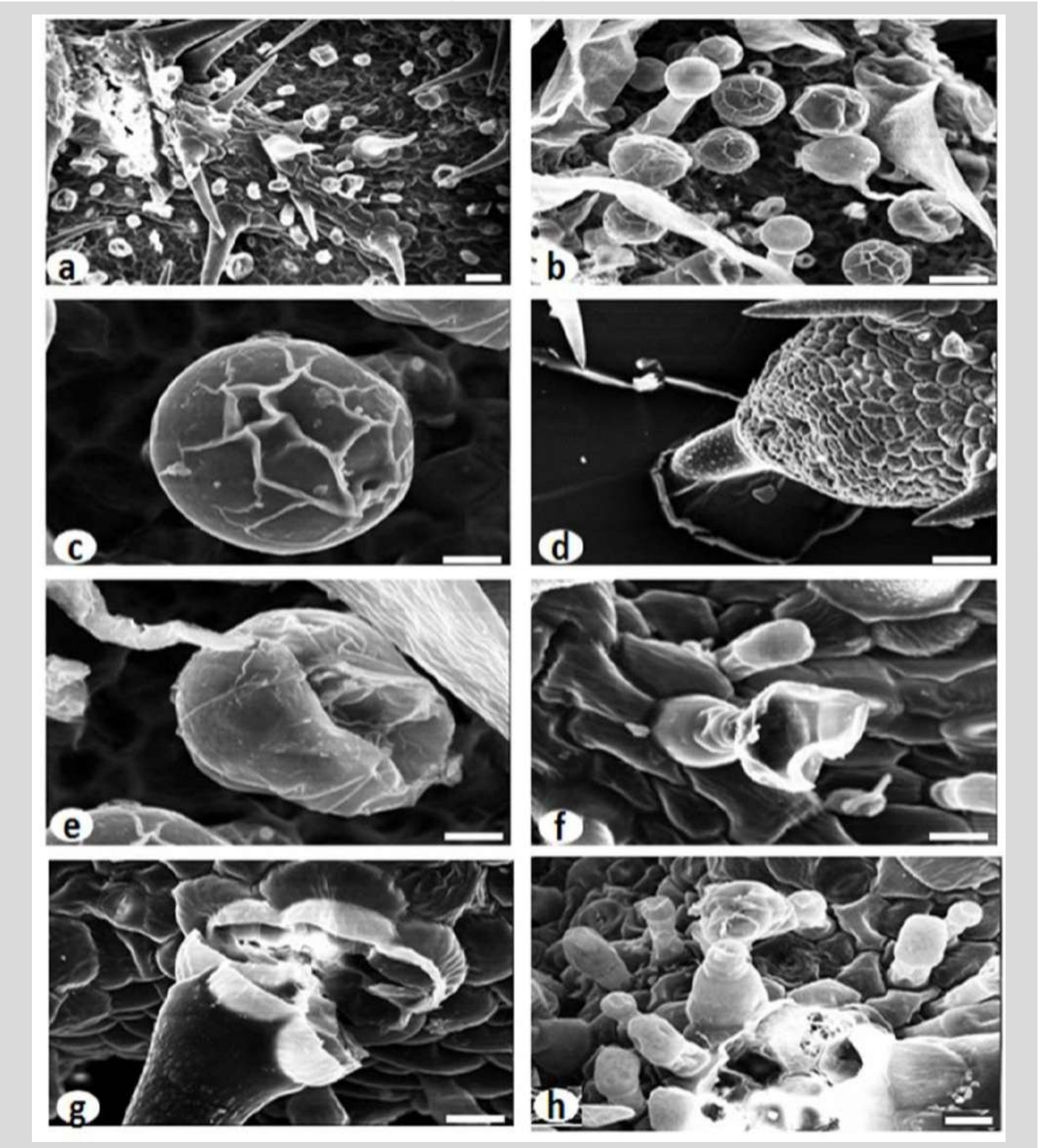


Figure 3.1. 4. Trichome diversity and changes in glandular morphology observed by SEM from leaf samples at different phenophases of elite variety of Rose-scented geranium (PG-IIIM-101): (**a**) The landscape of a young leaf showing distribution of glandular and non-glandular trichomes, (**b**) A close-up view of the portion of leaf showing peltate oil glands (neogenic) at stage 1, (**c**) Fully filled capitate and (**d**) peltate glands at stage 3, (**e-h**) Wrinkled, senescing oil glands at stage 4 (over maturity). Scale bars: 100 µm (a, h), 50 µm (b, c, d, e, f, g).

Morpho-agronomic Characteristics:

Rose-scented geranium is a multi-branched crop that grows 1-1.5 m in height and has a spread of about 1m. Its foliage is fragrant with broad lobed leaves. The lobes are dentate, pubescent with acute apices. The texture of leaves is shinny with cuticular wax. The variety developed (PG-IIIM-101) was evaluated at four locations namely Jammu (32.44° N, 74.55° E, 304 m asl), Pulwama, Kashmir (33.87° N, 74.89° E, 1650 m asl), Bhaderwah (32.98° N, 75.71° E, 3110 m asl) and Rajouri (33.37° N, 74.31° E, 940 m asl) (J & K state) over two years. The comparative data of yields at different locations is provided in table 3.1.1.

Associated Characters and Cultivated Practices:

The variety developed (PG-IIIM-101) is superior to parental genetic stock 'Bourbon' in terms of oil content (0.14-0.16%), essential oil profile (citronellol: 36.9-42.5%, linalool: 14.4-16.7%, geraniol:15.6-19.9%, geranyl formate: 5.6-7.8%, γ-eudesmol: 1.3-1.9%) and fresh herb yield (1170-1430 g/plant). It shows wider range of adaptability as it can be grown as a short duration winter crop under sub-tropical Jammu conditions (November-April) and as a summer crop under temperate conditions of Kashmir and Bhaderwah (April-September). During cultivation experiments and muilti-locational trials, there was no incidence of any disease or insect-pest infestation. It grows in well drained, light to medium textured sandy loam soils having pH 5.0 – 8.5. It is cultivated vegetatively through terminal cuttings of 10-15cm long. A light irrigation at the time of planting is necessary for the establishment of cuttings. The crop is planted with inter-row spacing of 60 cm and intra row spacing of 70 cm. Decomposed farm yard manure (FYM) at the rate of 7-8 tonnes/ha is recommended before planting the crop. During growing season 2-3 irrigations are required. The crop matures in 160-170 days and the optimum stage of harvest in relation to essential oil quality and quantity is coincident with flowering stage. Fresh biomass is steam distilled for 2-3 hours using 1-2 kg/cm^2 steam pressure. The oil is stored in air tight aluminium or amber-coloured glass containers, capped tightly and kept in cool and dark place.

3.2 Gene silencing and over-expression studies in concurrence with promoter specific elicitations reveal the central role of WsCYP85A69 in biosyntheses of triterpenoids in *Withania somnifera* (L.) Dunal

Arti Sharma, Gulzar A. Rather, Prashant Misra and Surrinder K. Lattoo

Brassinosteroids (BRs) are naturally occurring polyhydroxylated steroids which are involved in growth-promoting activities. They regulate plant growth and developmental processes involving germination, cell elongation, photo-morphogenesis etc and also play a significant role in combating stress related conditions. Reduction in the content of BRs lead to altered leaf morphology, extreme dwarfism, delayed flowering and senescence, abnormal vascular development and reduced male fertility. Therefore, regulation and maintenance of BR levels in plants are crucial for various biological functions. The biosynthetic pathway of BL from campesterol has been elucidated in suspension cell cultures of *Catharanthus roseus* using isotope-labeling of intermediates and their identification via gas chromatography-mass spectrometry (GC-MS) Such studies using these mutants have revealed that cytochrome P450s monooxygenases (P450s) oxidize C-2, C-3, C-6, C-22, C-23, and C-26 of brassinosteroids shown in Figure 3.2.1. Against the backdrop, we have successfully isolated, cloned and characterized *CYP85A69*, from *Withania somnifera*.

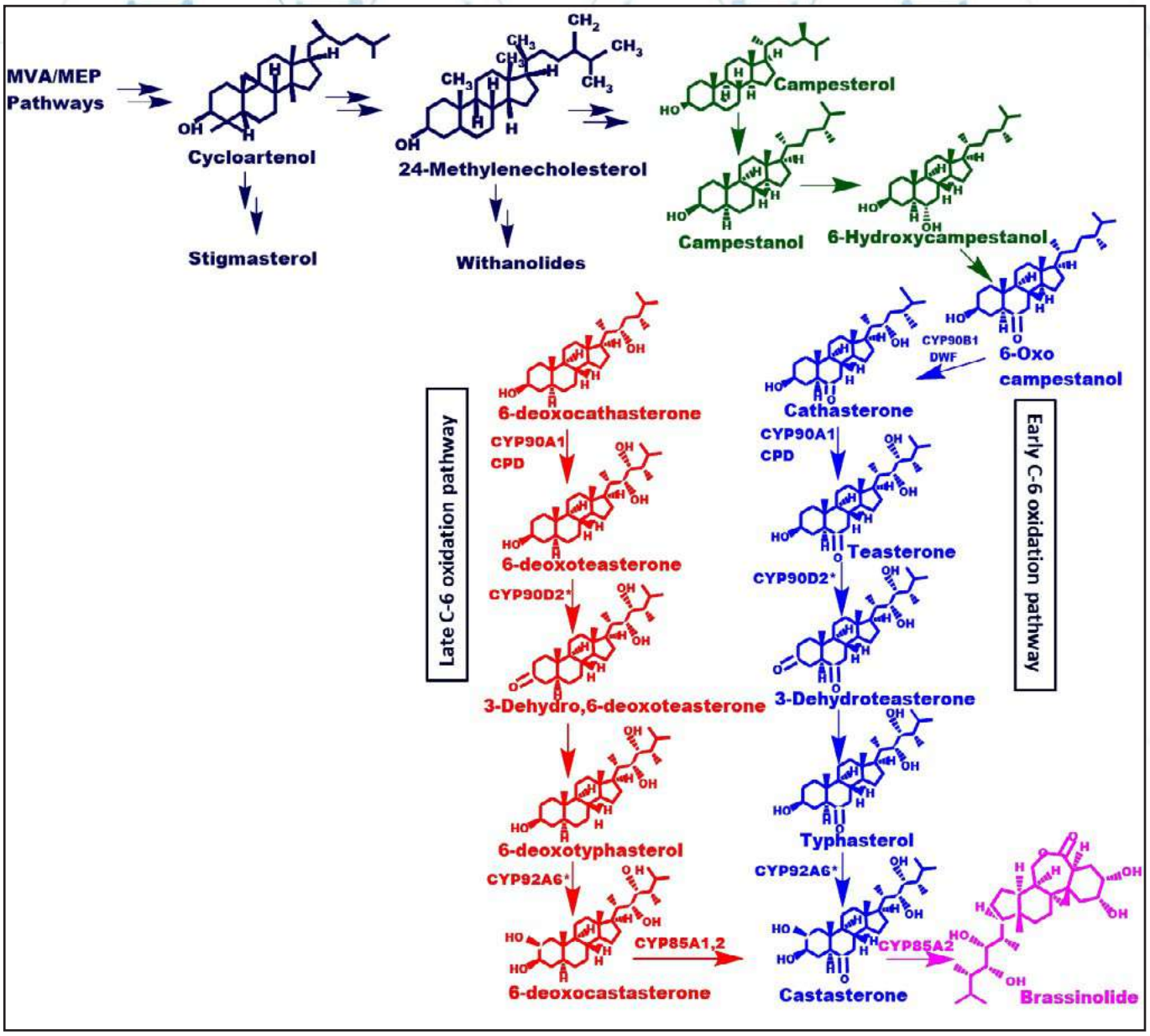


Figure 3.2.1. Putative brassinosteroids biosynthetic pathway: Schematic representation of brassinosteroids biosynthetic pathway showing early and late C-6 oxidation pathways.

Full length open reading frame of *WsCYP85A69* (MK410296) gene included 1,413 bp nucleotides that codes for a protein of 470 amino acids. Furthermore, the secondary structure of *WsCYP85A69* was predicted by using Self-Optimized Prediction Method with Alignment (SOPMA) online tool (Figure 3.2.2A). Active residues in ligand binding sites were predicted using GALAXY web server and displayed I^{112}, H^{120}, M^{244}, T^{269}, L^{270}, S^{273}, T^{277}, E^{340}, V^{344}, R^{346}, L^{403}, F^{404}, R^{409}, C^{411}, P^{412}, G^{413}, L^{416}, G^{417} (Figure 3.2.2B). These entire features substantiate that *WsCYP85A69* belongs to the cytochrome P450 superfamily that mediate the biosynthesis of various secondary metabolites.

Phylogenetic analysis of *WsCYP85A69* was performed with characterised

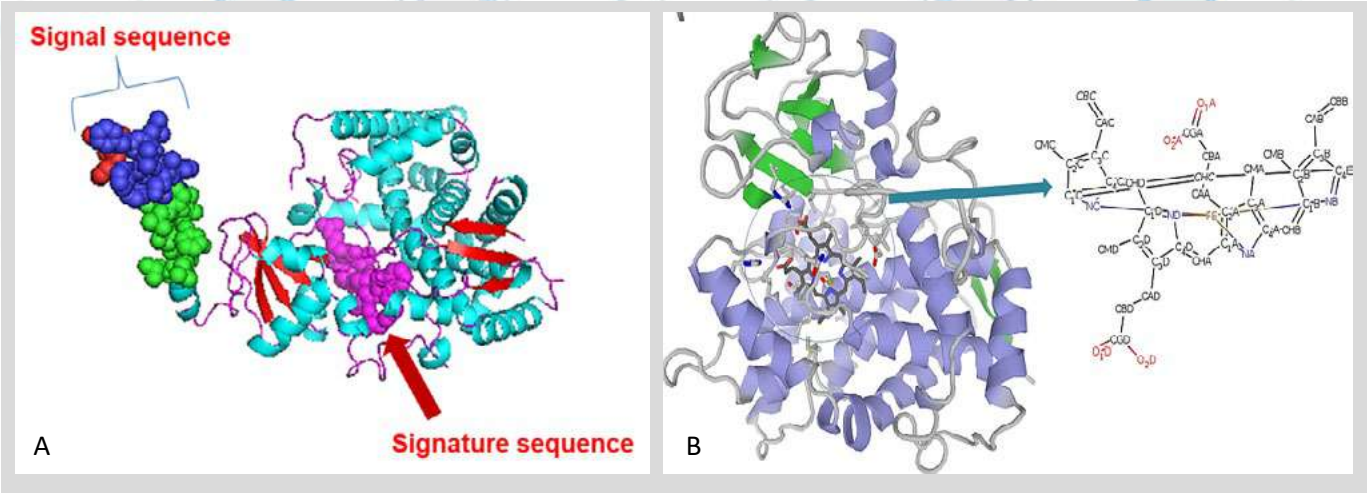


Figure 3.2.2. Three-dimensional model and ligand-binding site prediction for *WsCYP85A69*: A- Display of ribbon model of three-dimensional structure of *WsCYP85A69* predicted via Phyre2 web server **B-** Ligand-binding sites (zoom view) as predicted by GALAXY web server displays the presence of heme-binding site and presence of I^{112}, H^{120}, M^{244}, T^{269}, L^{270}, S^{273}, T^{277}, E^{340}, V^{344}, R^{346}, L^{403}, F^{404}, R^{409}, C^{411}, P^{412}, G^{413}, L^{416}, G^{417} residues in its ligand binding sites.

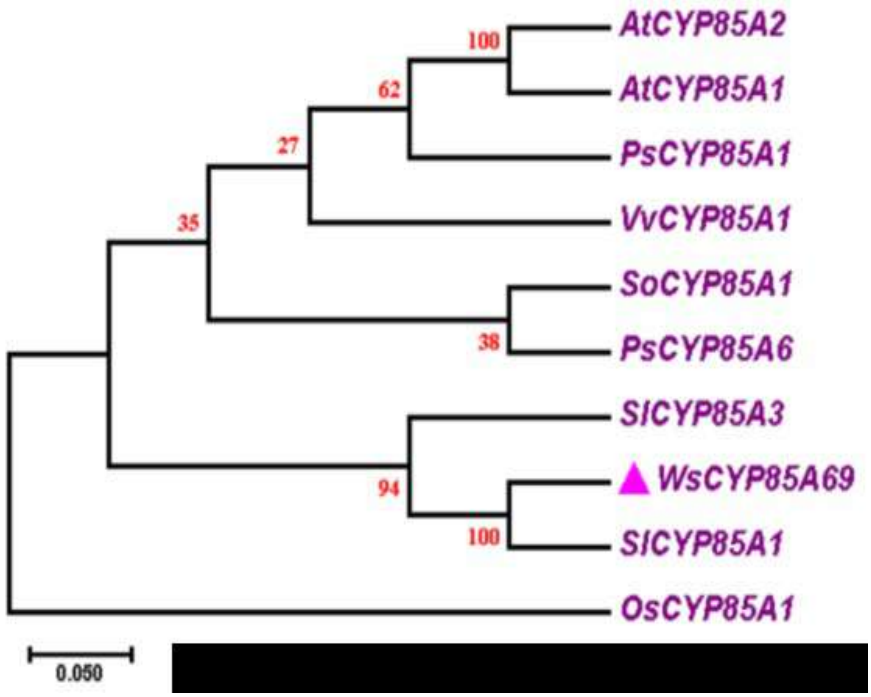


Figure 3.2.3. Phylogenetic tree of WsCYP85A69**:** The phylogenetic analysis was executed using the ClustalW program as well as MEGA7 software. The numbers on the nodes indicate the bootstrap values after 100 replicates. The bar represents an evolutionary distance of 0.05%. Poisson correction method was used to compute the evolutionary distances. The analysis was performed by aligning *CYP85A* amino acid sequences chosen by available data related to characterized *CYP85A* gene from different plant species from NCBI database.

CYP85A from other plant species to elucidate the degree of evolutionary relatedness. The phylogenetic tree displayed that *CYP85A69* of *W. somnifera* falls in same clade with *CYP85A1* of *Solanum lycopersicum* revealing their orthologous nature (Figure 3.2.3).

Further, *WsCYP85A69* gene was investigated at the transcription level to determine its role in the differential accumulation of brassinosteroids (castasterone). It revealed that juvenile leaf showed the highest expression level of *WsCYP85A69* followed by stem and roots while berries and inflorescence exhibited the least expression (Figure 3.2.4A). In addition to this, phytochemical analysis revealed that young leaves accumulated highest amount of castasterone as compared to stem and roots, whereas inflorescence and berries showed the least levels (Figure 3.2.4B).

To investigate the catalytic function of *WsCYP85A69*, enzymatic assay was performed. LC-MS analysis of reaction product showed the presence of castasterone which was eluted at retention time of 22.19 min with calculated mass of 506 $[M+ACN]^+$ (Figure 3.2.5C, 3.2.5D). These results functionally validate the C-6 oxidase activity of *WsCYP85A69* as it efficiently converted 6-deoxocastasterone (substrate) to castasterone (product). However, no activity was observed in yeast transformed with empty vector as control (Figure 3.2.5A, 3.2.5B).

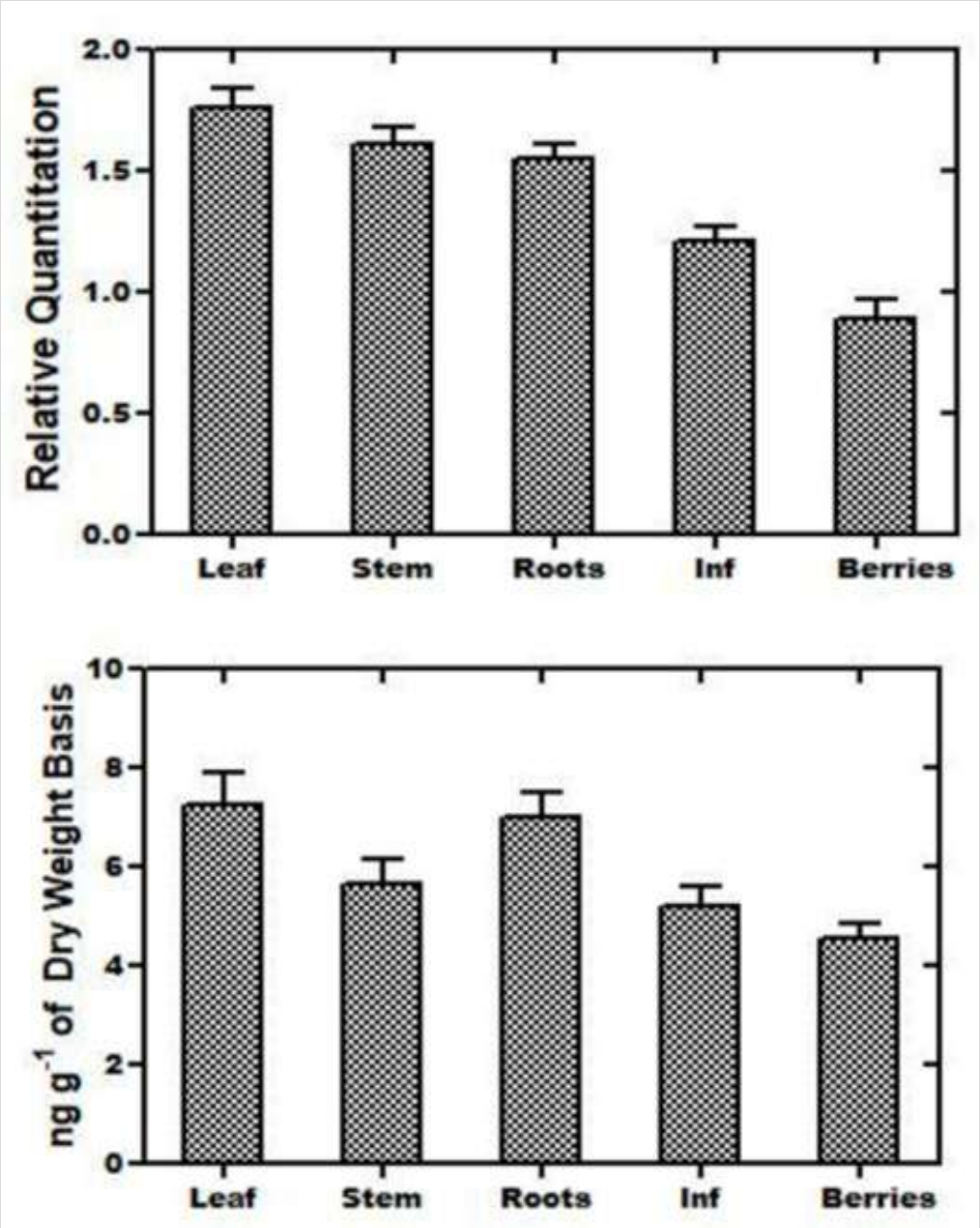


Figure 3.2.4: Tissue-specific real-time expression analysis and HPLC analysis of castasterone: (a) Quantitative assessment of the expression levels of *WsCYP85A69* in different plant parts of *W. somnifera* viz. leaf, stalk, roots, inflorescence (abbreviated as Inf) and berries were performed using quantitative real-time PCR. (b) HPLC analysis of castasterone production in different parts of *W. somnifera* plants viz. leaves, stem, roots, inflorescence and berries. Its contents were higher in young leaves followed by stem and roots whereas berries and inflorescence showed lower production.

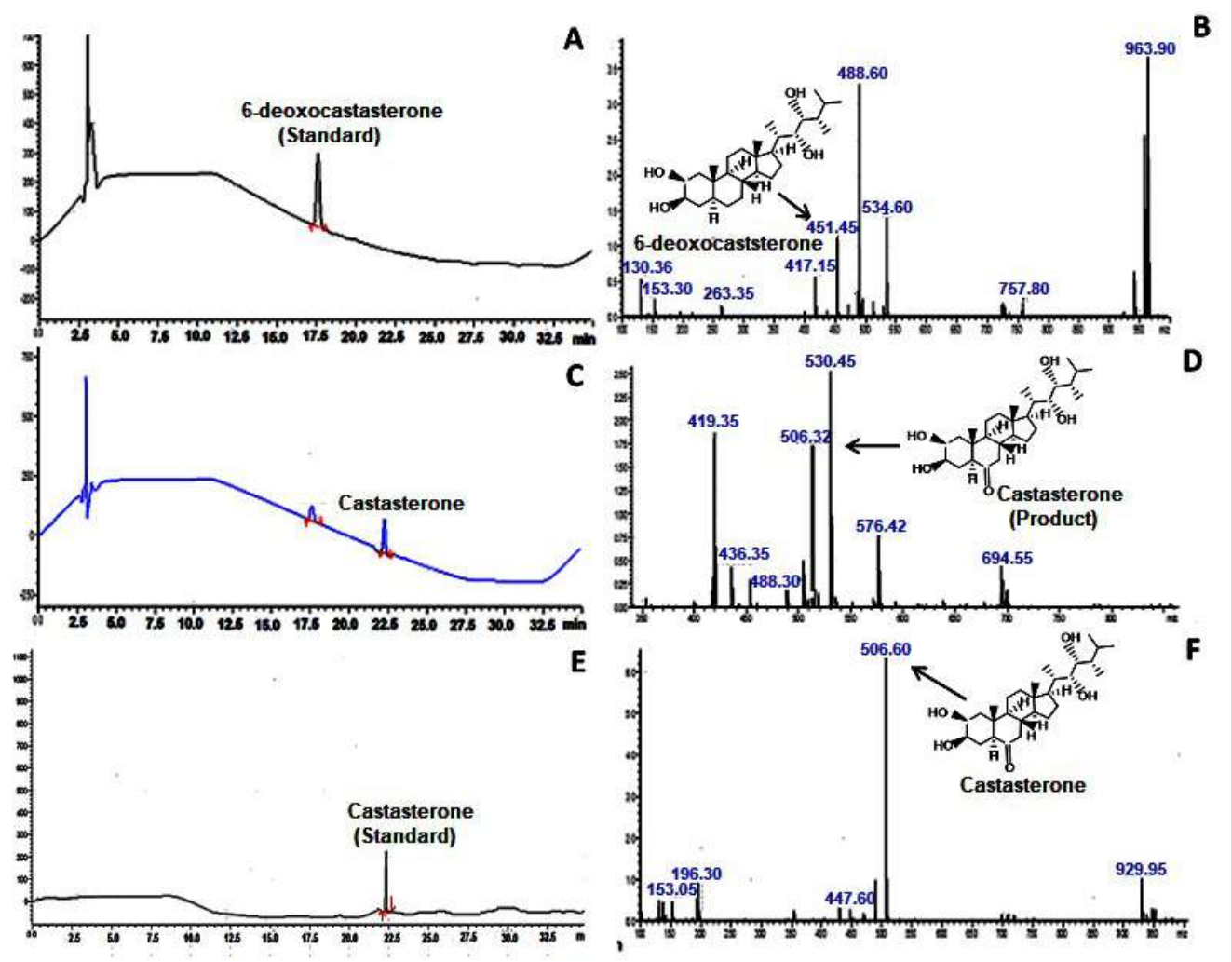


Figure 3.2.5. LC-PDA-MS analysis of *in vitro* conversion of 6-deoxocastasterone into castasterone: Liquid chromatography equipped with photo-diode array detection (LC-PDA) chromatogram and mass spectrometry spectra of authentic standard 6-deoxocastasterone which was eluted at retention time of 17.61 min with mass m/z 451.45 (A,B); LC-PDA and mass spectrometry spectra of reaction product castasterone which was eluted at retention time of 22.1 with mass m/z 506 (C,D) LC-PDA chromatogram and mass spectra of authentic standard castasterone eluted at retention time of 22.17 with mass m/z 506 (E,F).

Transient over-expression assay was performed to investigate the role of *WsCYP85A69* in the biosynthesis of steroids and withanolides. After 3rd day of post-infiltration, transformed leaf samples were harvested for GFP detection, quantitative RT-PCR (Figure 3.2.7A) and phytochemical analysis (Figure 3.2.7B, 3.2.7C). Expression of *WsCYP85A69*-GFP in infiltered leaves was confirmed by fluorescent microscopy (Figure 3.2.6A-I).

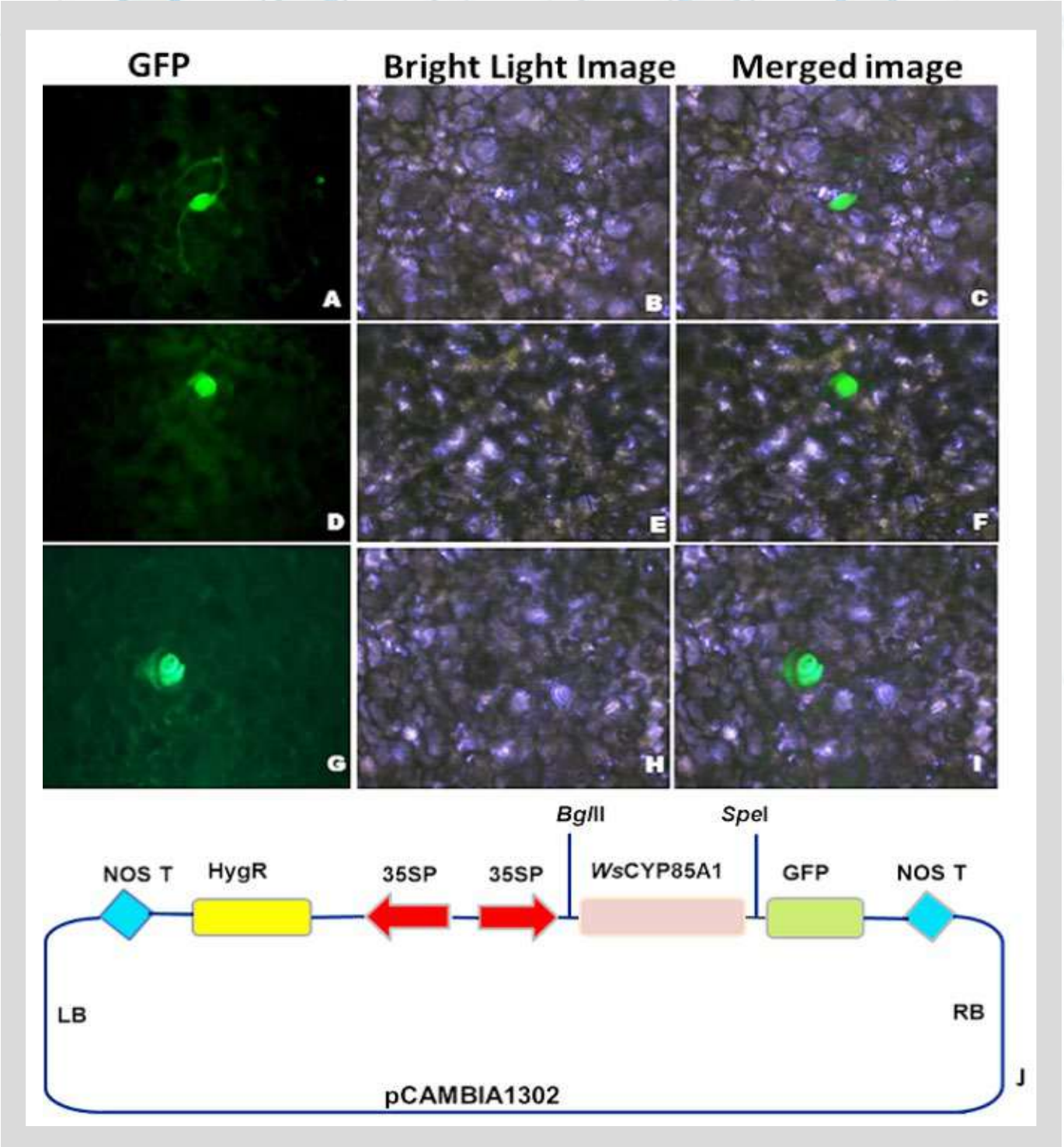


Figure 3.2.6. Analysis of Green Fluorescent protein in infiltered leaves: (A- I) Green Fluorescent Protein detection in infiltered leaves of *W. somnifera* performed using fluorescent microscope. *WsCYP85A69* is fused with N-terminal fragment of GFP in pCAMBIA1302. Construct was infiltrated into leaves of *W. somnifera*. GFP fluorescence was detected 3 d post infiltration. (J) Vector map citing the position of *WsCYP85A69* in pCAMBIA1302.

Further, aMIR mediated silencing of *WsCYP85A69* was also performed to confirm its functional role in triterpenoids biosynthesis. It showed suppression of CYP85A69 transcript levels along with reduced castasterone, withanolides and stigmasterol accumulation.

In order to study the transcriptional regulation of *WsCYP85A69*, its 5′ upstream flanking region of 610 bp (GenBank accession no. MK611931) was isolated using genome walking approach. *In silico* investigation of the promoter region was performed by using PLACE and PlantCare databases which revealed the presence of several significant *cis*-acting regulatory components (Figure 3.2.9).

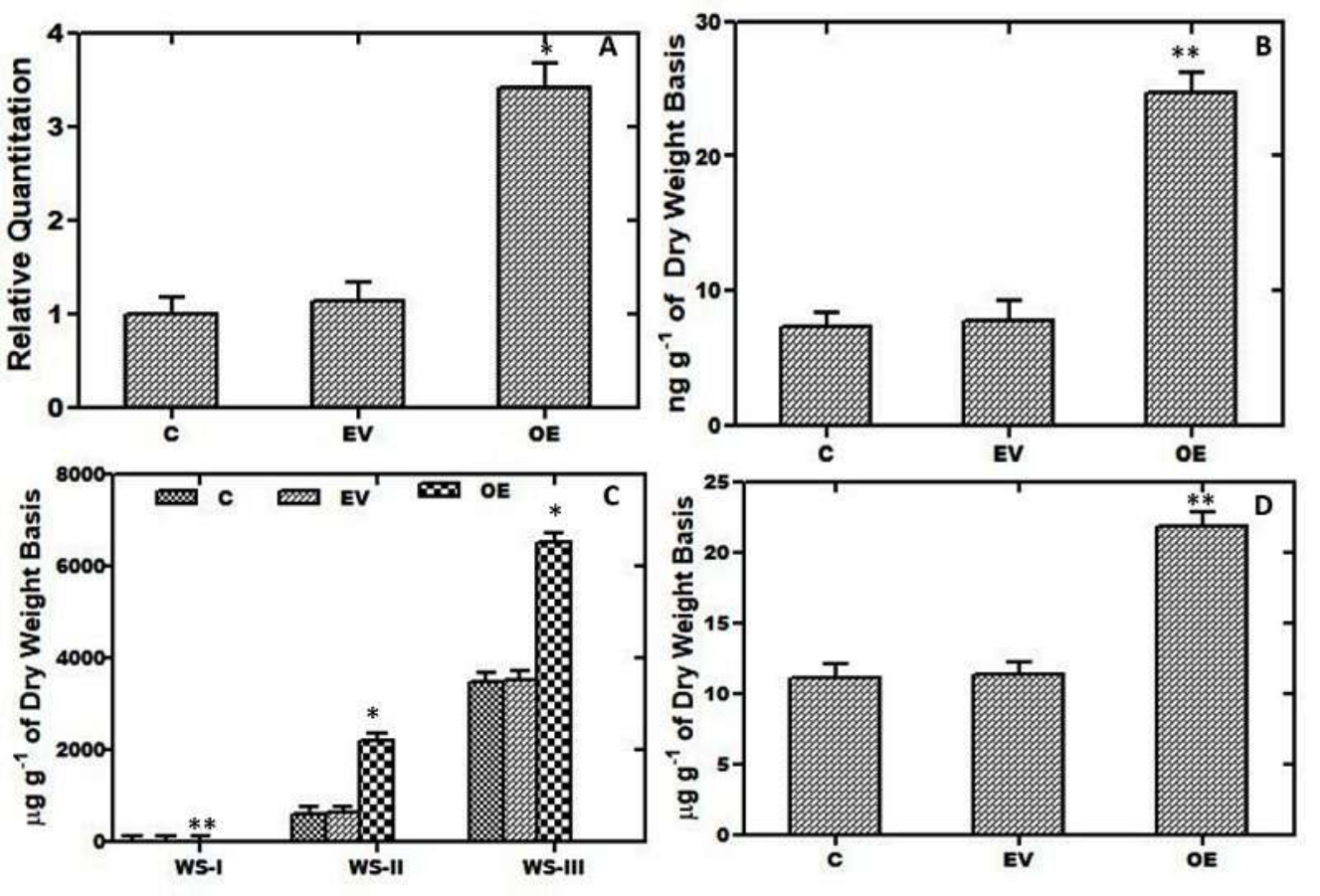


Figure 3.2.7. Transient over-expression assay of WsCYP85A69**:** A) Quantitative real-time expression of *WsCYP85A69* gene showing enhanced transcript levels of *WsCYP85A69* in infiltered leaves compared to control. B) HPLC analysis of castasterone in leaves infiltered with *WsCYP85A69*-pCAMBIA1302 showing increased castasterone content compared to control. (C and D) HPLC analysis of transformed leaves for elevated levels of withanolides and stigmasterol respectively.

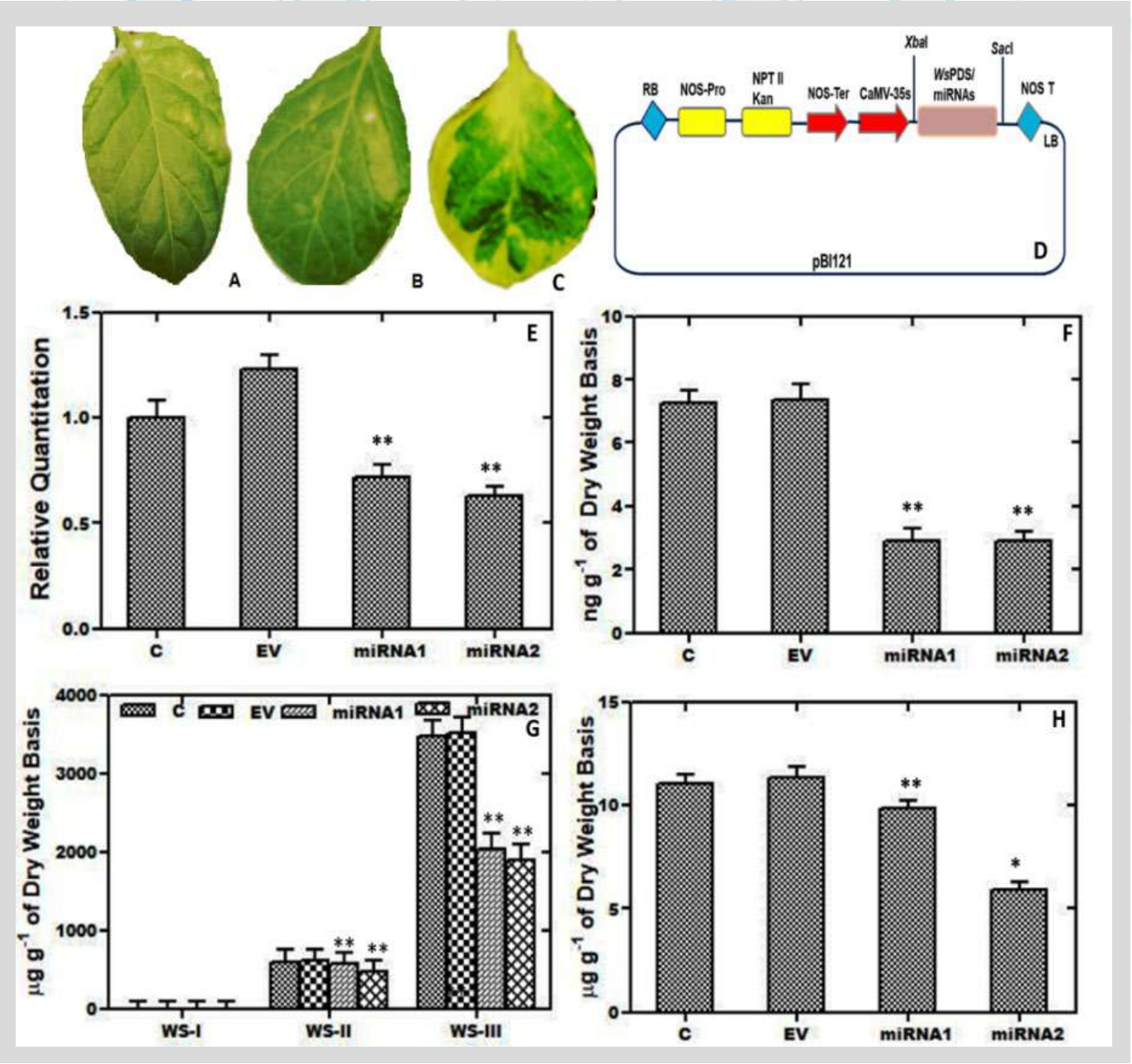


Figure 3.2.8. Artificial micro-RNA mediated silencing of WsCYP85A69**:** (A,B,C) Phytoene desaturase was used as marker whose silencing resulted in white spots on infiltered leaves. (D) Vector map showing PDS-pBI121/aMIR-pBI121 (E) aMIR1-*WsCYP85A69* and aMIR2-*WsCYP85A69* constructs infiltered in leaves illustrating reduced expression levels of *WsCYP85A69* compared to control after 3rd day of post-agroinfiltration. (F) HPLC analysis of castasterone levels in agro-infiltered leaves showed decrease in its content compared to control. (G) Phytochemical analysis of reduced levels of withanolides in transformed leaves via HPLC showed on 3rd day (H) HPLC analysis of stigmasterol levels in infiltered leaves also showed decreased stigmasterol content compared to control.

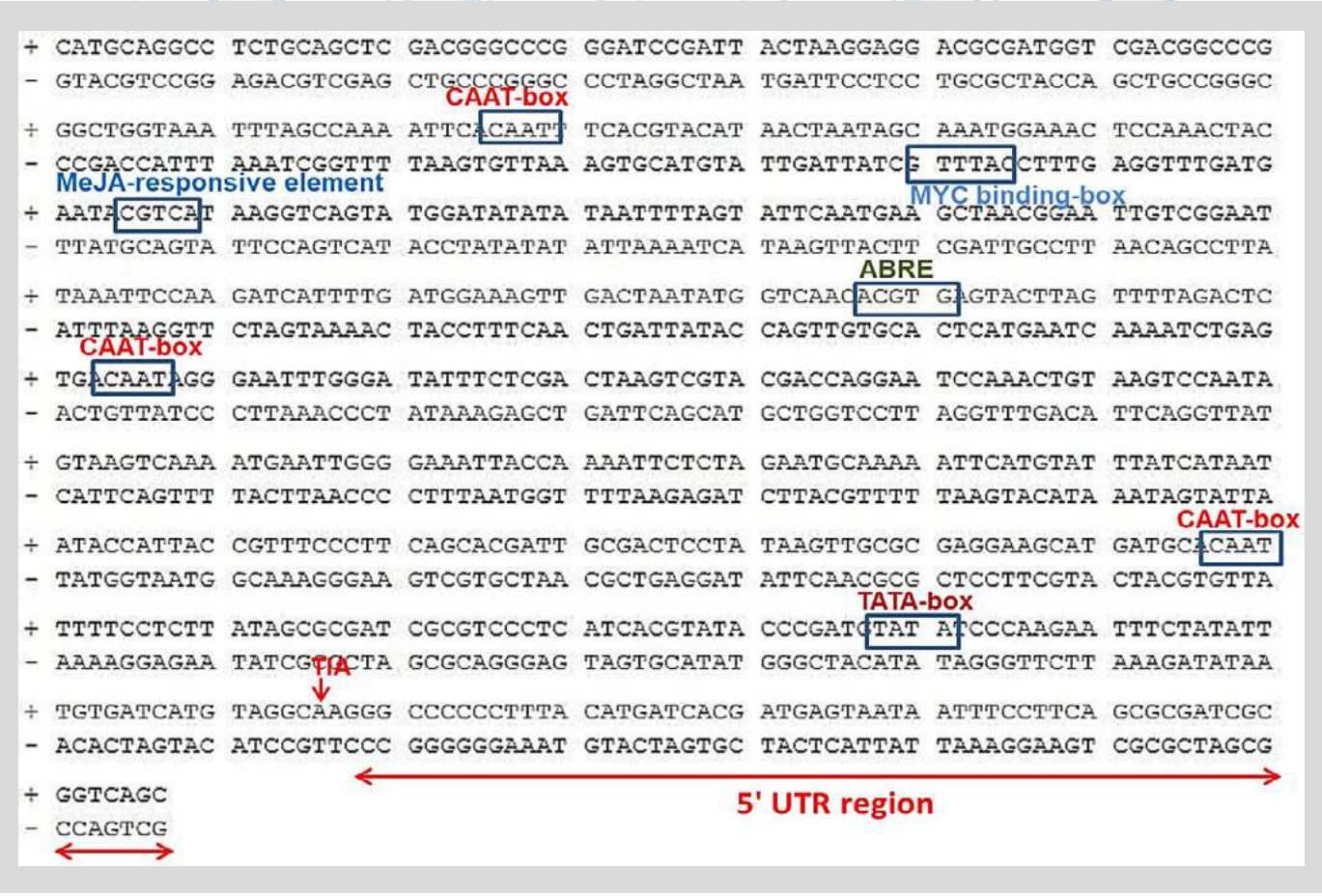


Figure 3.2.9. Analysis of promoter region: Isolation of promoter region of *WsCYP85A69* was performed using genome walker kit and analysis was performed using PlantCare and PLACE server tools to reveal the presence of various putative *cis*-acting regulatory elements

Further, to elucidate the inducible/repressible nature of *WsCYP85A69* promoter, various *cis*-regulatory elements were analysed and subsequently used to assay the modulation in relative transcript levels of *WsCYP85A69* along with change in metabolic flux. Elicitation studies revealed MeJA is a potent inducer of *CYP85A69* expression leading to 2.3 fold increase in its relative mRNA levels which corroborated well with the increased metabolic levels.

In conclusion, key pathway gene of brassinosteroids, *WsCYP85A69*, from *W. somnifera* has been isolated and functionally validated in *S. cerevisiae* WAT11 strain. Moreover, its oxidative functionality as well as catalytic potential has been confirmed using LC-PDA-MS and further corroborated by bio-informatic analysis. These findings have implications to increase the metabolite levels, in *W. somnifera*. Thus, molecular and functional characterization of *WsCYP85A69* provides a fresh prospective for manipulation/modulation of increased production of metabolites in *W. somnifera*.

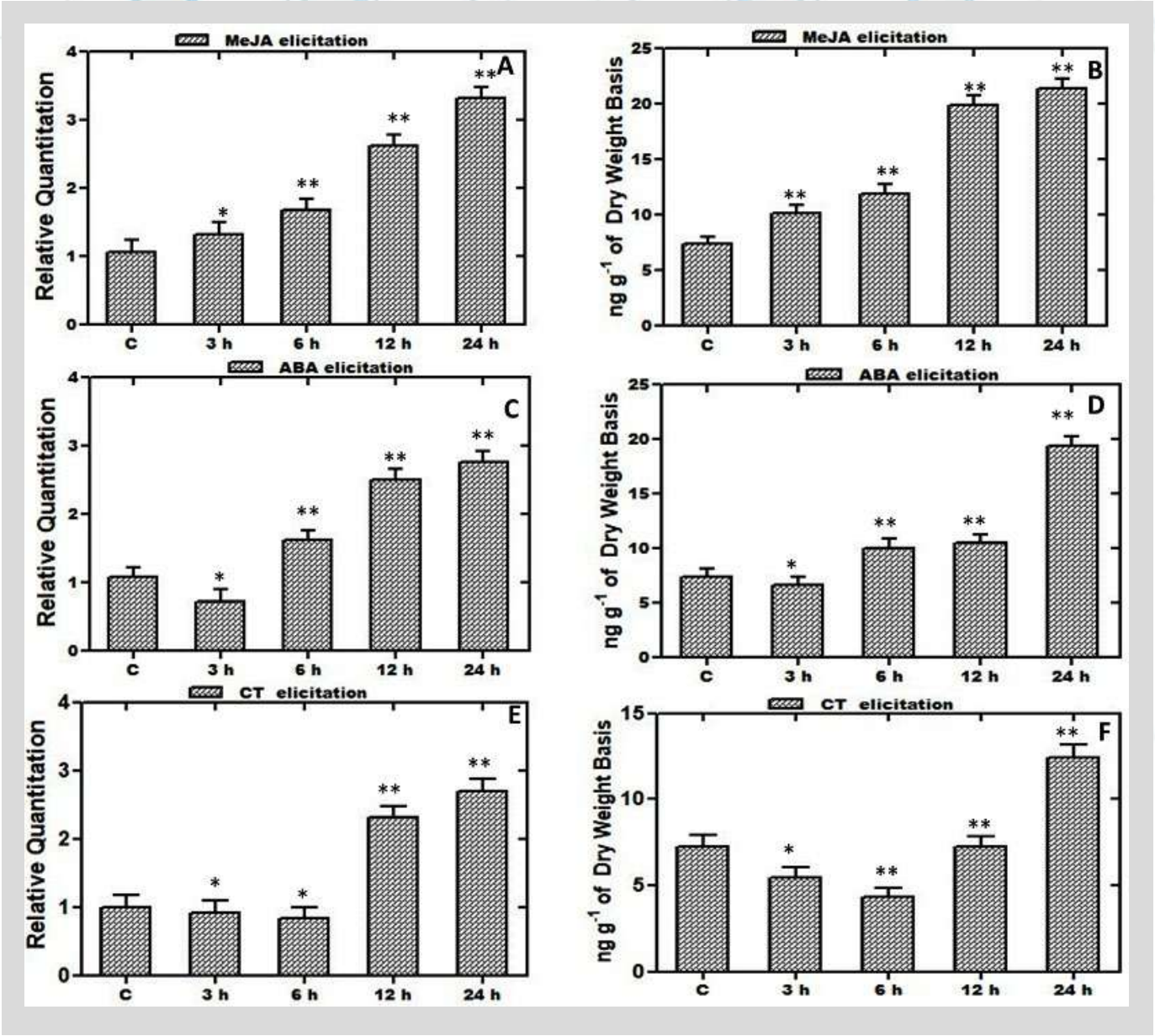


Figure 3.2.10. Effect of elicitor treatments on transcript profiles of WsCYP85A69 **and castasterone accumulation at different time intervals.** Effect of (A) 0.1 mM MeJa, (C) 0.1 mM ABA and (E) cold treatment was studied on the transcript levels of *WsCYP85A69* and on accumulation pattern of castasterone (B, D, F) in green house grown *W. somnifera* plants. Samples were harvested after 3, 6, 12, 24 h and processed for qRT-PCR and HPLC analysis. For cold treatment, untreated plants were kept as control and for MeJA and ABA elicitation plant treated with equal amount of ethanol were treated as control.

3.3 Functional characterization and overexpression of secologanin synthase; a penultimate enzyme of seco-iridoid pathway from *Nothapodytes nimmoniana*

Gulzar A. Rather, Arti Sharma, Utpal Nandi, Prashant Misra and Surrinder K. Lattoo

Monoterpene indole alkaloids (MIAs) represent one of the largest and biologically most active class of alkaloids having diverse structural complexities and pharmacological activities. This important category of metabolites is often produced *via* complex and highly regulated seco-iridoid pathway under the influence of different enzymatic reactions. Camptothecin (CPT) one of the important MIA having anti-tumor, anti-cancerous, anti-viral and anti-fungal properties. CPT is produced in many taxonomically unrelated species among them *Nothapodytes nimmoniana* is the richest source. Chemical synthesis of CPT remains a daunting challenge at the industrial level and biotechnological interventions in homologous/ heterologous hosts has been greatly mired by poor understanding of its biosynthetic and regulatory mechanisms. Moreover, metabolic analysis of different CPT producing species showed the presence of different intermediates involved in CPT biosynthesis.

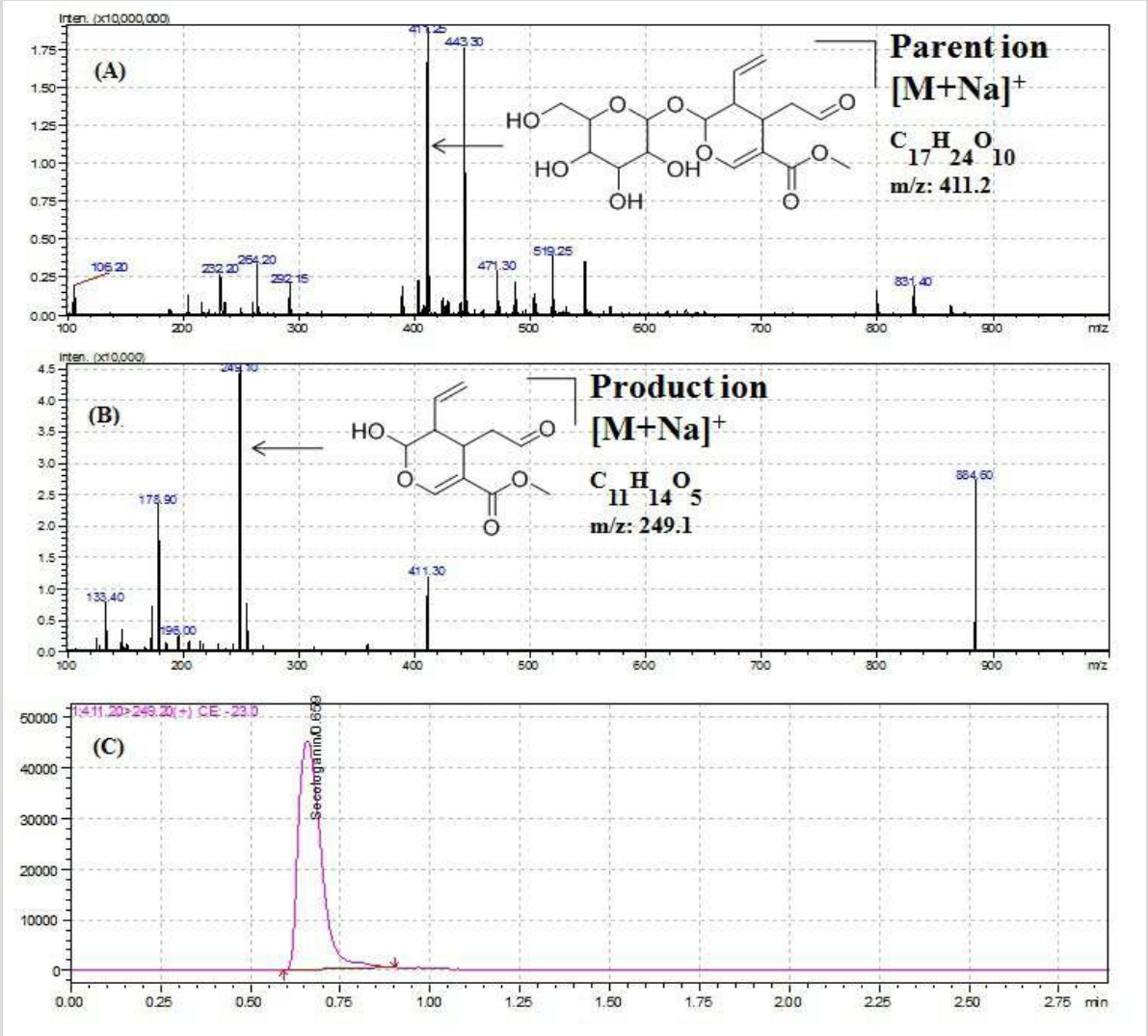


Figure 3.3.1. LC-MS/MS mass spectra of secologanin with parent ion at m/z 411.2 (A); tandem mass spectra of secologanin with product ion at m/z 249.2 (B); MRM chromatogram for LC-MS/MS analysis of secologanin (C).

To resolve the key intermediate of seco-iridoid pathway in *N. nimmoniana*, LC-MS/MS analysis of root and leaf tissues were performed (Figure 3.3.1). The mass spectra data showed the presence of secologanin as a central compound of MIA pathway. The secologanin was eluted at the retention time of 0.7 min and its mass was monitored with precursor to product ion transition at m/z 411.2 to 249.2. Moreover, at molecular level, full length secologanin synthase (*Nn*CYP72A1) gene of 1566 bp in length was isolated and confirmed by sequencing. *In vitro* enzymatic assay of *Nn*CYP72A1 was performed using highly efficient yeast expression system. Microsomes isolated from transformed yeast containing *Nn*CYP72A1 were used for carrying out enzymatic reactions. LC-MS/MS analysis of enzymatic reaction products revealed the presence of secologanin confirmed by mass spectrometry and fragmentation patterns (Figure 3.3.2).

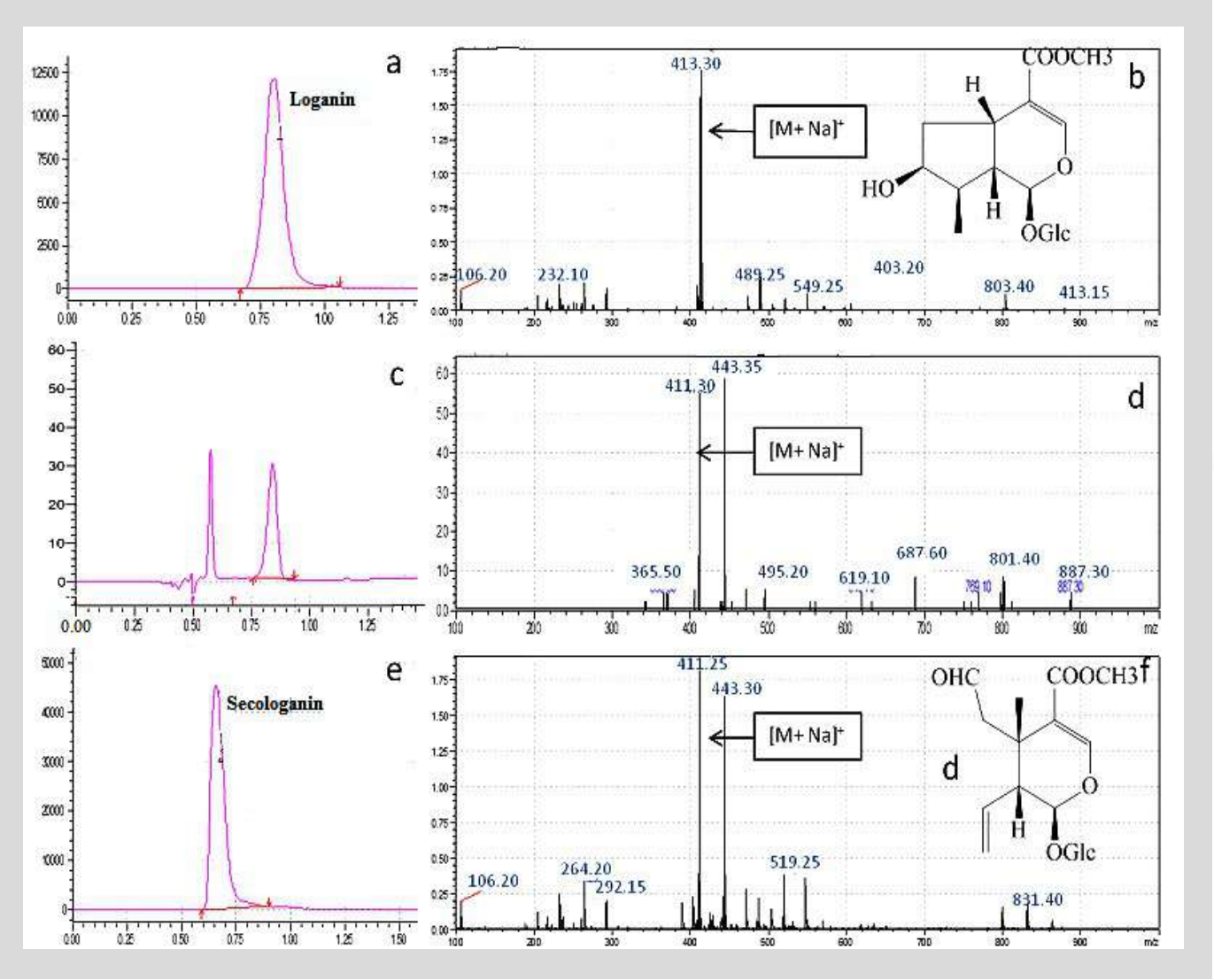


Figure 3.2.2. LC-MS/MS analysis of in vitro **conversion of loganin to secologanin by the reaction of microsomes from yeast expressing** Nn**CYP72A1.** Multiple reaction monitoring (MRM) chromatograms and mass spectrometry spectra of substrate loganin which was eluted at about the retention time of 0.8 min with transition masses of m/z 413.0/219.3 (a, b); MRM and mass spectrometry spectra of reaction product secologanin which was eluted at about the retention time of 0.65 with transition mass of m/z 411.2/249.2 (c, d) Chromatogram and mass spectra of authentic standard secologanin (e, f).

Using transient expression system, *Nn*CYP72A1 was overexpressed in leaves of *N. nimmoniana* to predict its role in CPT biosynthesis. The fusion construct of *Nn*CYP72A1was prepared in pCAMBIA1302 plant expression vector at the 5'-terminal end of the green fluorescent protein (GFP) gene under the control of CaMV 35S promoter (Figure 3.3.3a). The construct of *Nn*CYP72A1-pCAMBIA 1302 and empty vector (control) were transformed into host plant via agroinfiltration and expression was confirmed via green fluorescent microscopy (Figure 3.3.3 b-g). Samples were harvested after 3rd and 6th day of post agroinfiltration and investigated at molecular level for gene modulation as well as at metabolic level by quantifying secologanin and CPT content. qRT-PCR analysis of *Nn*CYP76B6 in transformed leaves showed 4.21 fold increase in transcript levels on 3rd day and 2.73 fold increase in transcript levels on 6th day in comparison to non-transformed control (Figure 3.3.3 h). A slight increase of *Nn*CYP72A1 expression was also observed in leaves transformed with empty vector. Interestingly, phytochemical analysis of transformed leaf showed 1.13 and 1.43 fold increase in secologanin accumulation on 3rd and 6th day respectively (Figure 3.3.3 i), while CPT content was increased to 2.86 and 2.02 fold on 3rd and 6th day respectively (Figure 3.3.3 j). Overall, metabolic analysis of N. *nimmoniana* root and leaf tissues identified secologanin as central intermediates of CPT biosynthetic pathway. Further, functional characterization of secologanin synthase in *S. cereviceae* confirms its catalytic activity. Moreover, overexpression of *Nn*CYP72A1 enhances secologanin and CPT accumulation which confirmed its potential role in CPT biosynthesis. These findings may plausibly serve as prognostic tool for metabolic engineering of CPT biosynthesis.

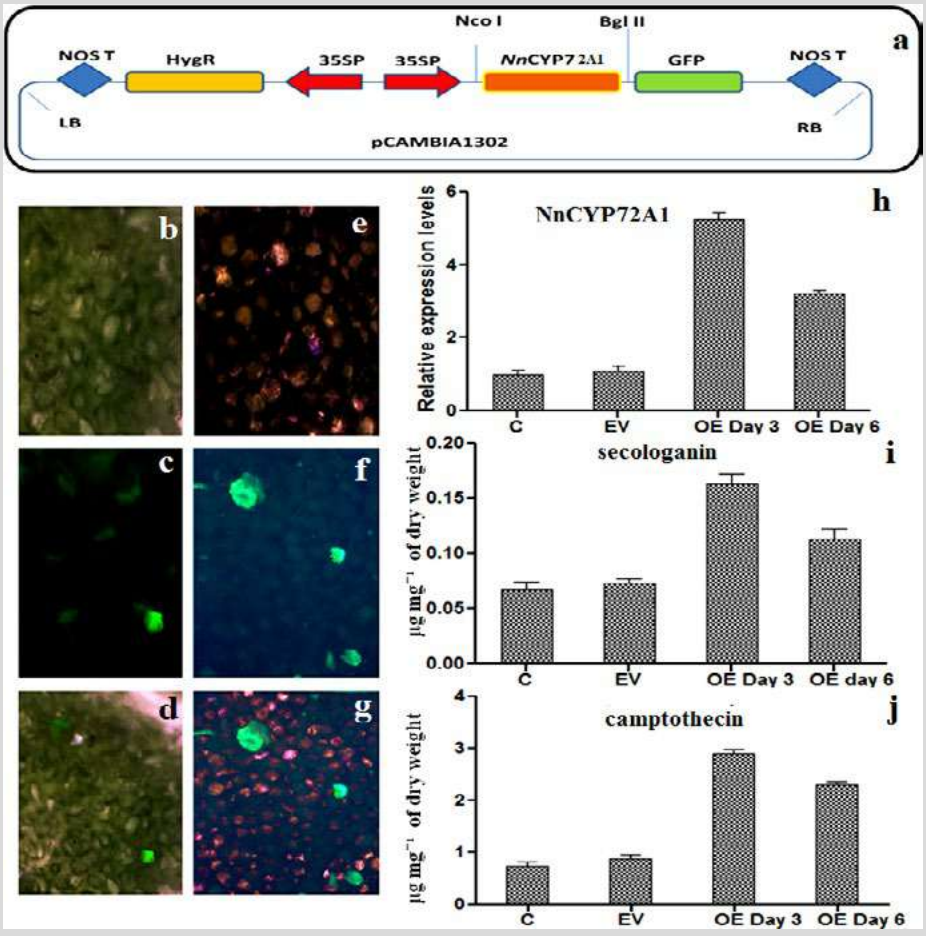


Figure 3.3.3. Overexpression of Nn**CYP72A1.** Construct of *Nn*CYP72A1 in pCAMBIA1302 vector at the 5'-terminal end of the green fluorescent protein (GFP) gene under the control of CaMV 35S promoter (a); expression analysis of transformed leaves under normal light (b,e); transformed leaves under green fluorescence (c,f); merged image of b and c (d); and merged image of e and f (g); qRT-PCR analysis of *Nn*CYP72A1 in control and transformed leaves on day 3rd and 6th of postagroinfiltration (h); determination of secologanin and camptothecin accumulation in transformed leaves in comparison to control (i, j). Values are expressed as means ±SD representing three independent biological samples, each with three technical replicates.

3.4 Mining transcriptome of medicinally important *Plantago* species for terpenoid biosynthetic pathway genes

Suruchi Gupta, Gulzar A. Rather, Arti Sharma, Surrinder K Lattoo

Genus *Plantago* of family Plantaginaceae has more than 200 species, which exist as weeds, except *Plantago ovata*. It is cultivated for the production of psyllium (isabgol). India holds monopoly in the world trade of Isabgol and earns sizeable foreign exchange through exports. Isabgol is not only a highly effective laxative but also finds application in pharmaceutical, food and cosmetic industries. Another species, *P. major,* has a long history of use in traditional medicine. *Plantago* species contain several phytochemicals like flavonoids, iridoid glycosides, polysaccharides and polyphenols, tannins, phenylpropanoid glycosides, triterpenes, saponins, sterols, etc. Terpenes are the largest and most diverse class of secondary metabolites produced by plants. So far, the terpenoid biosynthetic pathway has not been elucidated at molecular level in *Plantago sp*. Therefore, the present study was aimed at unravelling the terpenoid biosynthetic pathway in wild and cultivated species of *Plantago* using subtractive transcriptomic approach. Transcriptome analysis of *P. ovata* and *P. major* leaf tissues was performed using Illumina Hiseq 2500 platform to identify genes involved in terpenoid biosynthetic pathway. A total of 29,279,384 and 29,904,920 pair end raw sequence reads were generated from *P. major* and *P. ovata* leaf tissues, respectively. Sequenced transcripts of both the plants accounted for approximately 6.5 GB data. Raw data was subjected to quality control screening to remove low quality/short reads, adapter sequences, and primer sequences using Adapter Removal 2. After pre-processing of raw reads, a total of 58,558,768 and 59,809,840 high quality (HQ) reads from *P. major* and *P. ovata* were obtained, respectively. These HQ reads were then assembled using Trinity software with default options. Trimmed reads were aligned to the assembled unigenes using Bowtie 2 programme. Of all the filtered reads 96.54% from both the plants were aligned to assembled unigenes. GC content of all the assembled transcripts were in the range of 42-50%. The results of transcriptome assembly are summarized in table 3.4.1.

Table 3.4.1. Summary of raw data and assembled contigs.

	Plantago major	*Plantago ovata*
Number of raw reads	65,155,132	65,593,284
Number of filtered reads	58,558,768	59,809,840
Total pair end reads	29,279,384	29,904,920
% Alignment	97.11%	95.53%
Unigenes above FPKM≥1	48,128	42,848
Assembled transcripts	2,76,581	
Assembled Unigenes	2,09,432	
Longest read length	15,007	
Mean GC% of transcripts	42.37%	
Mean GC% of unigenes	42.16%	

117,172 assembled transcripts with >= 200 bp were considered for expression estimation and annotations. The assembled unigenes were compared with uniprot plant database using BLAST X programme. Matches with E-value cut-off of 10^{-5} and percent identity of 40% were retained for annotations. Overall, 41120 unigenes were assembled having at least one significant hit in uniprot plant database. The predicted proteins from BLASTX were annotated against NCBI, UniProt, Pathway and other databases (Table 3.4.2). The top BLASTX hit of each unigenes were analysed and names of the prominent organisms showing maximum homology with *P. ovata* were extorted. The largest number of *P. ovata* unigenes showed significant similarity with *Erythranthe guttata* (7184 unigenes) followed by *Nicotiana tabacum* (1462 unigenes).

Table 3.4.2. Unigene annotation summary

Number of Unigenes with no BLASTX Hit	16,080
Number of Unigenes with a significant BLASTX hit and UniProt information	41,120
Number of Unigenes with significant BLASTX hit with PMN	11,300

Gene ontology (GO) analysis was carried out to decipher the functional aspects of genes. Biological process, cellular components and molecular functions are the three broad ontological domains in which genes were classified. Among the annotated genes, 17,883 unigenes were categorized into 2608 GO functional groups. The molecular functions category possessed the maximum number of unigenes among the three categories followed by cellular components and biological process (Table 3.4.3).

Table 3.4.3. Gene Ontology terms and unigenes identified in each category

Ontological category	GO terms	Number of unigenes
Molecular functions	1154	14,868
Biological process	1102	7905
Cellular components	352	8490

Within molecular functions, ATP binding have the highest number of unigenes while integral component of membrane were enriched in the cellular components category. Translation and transcription classes constituted the largest proportion in biological process category. Top 15 classes from each domain are depicted in figure 3.4.1.

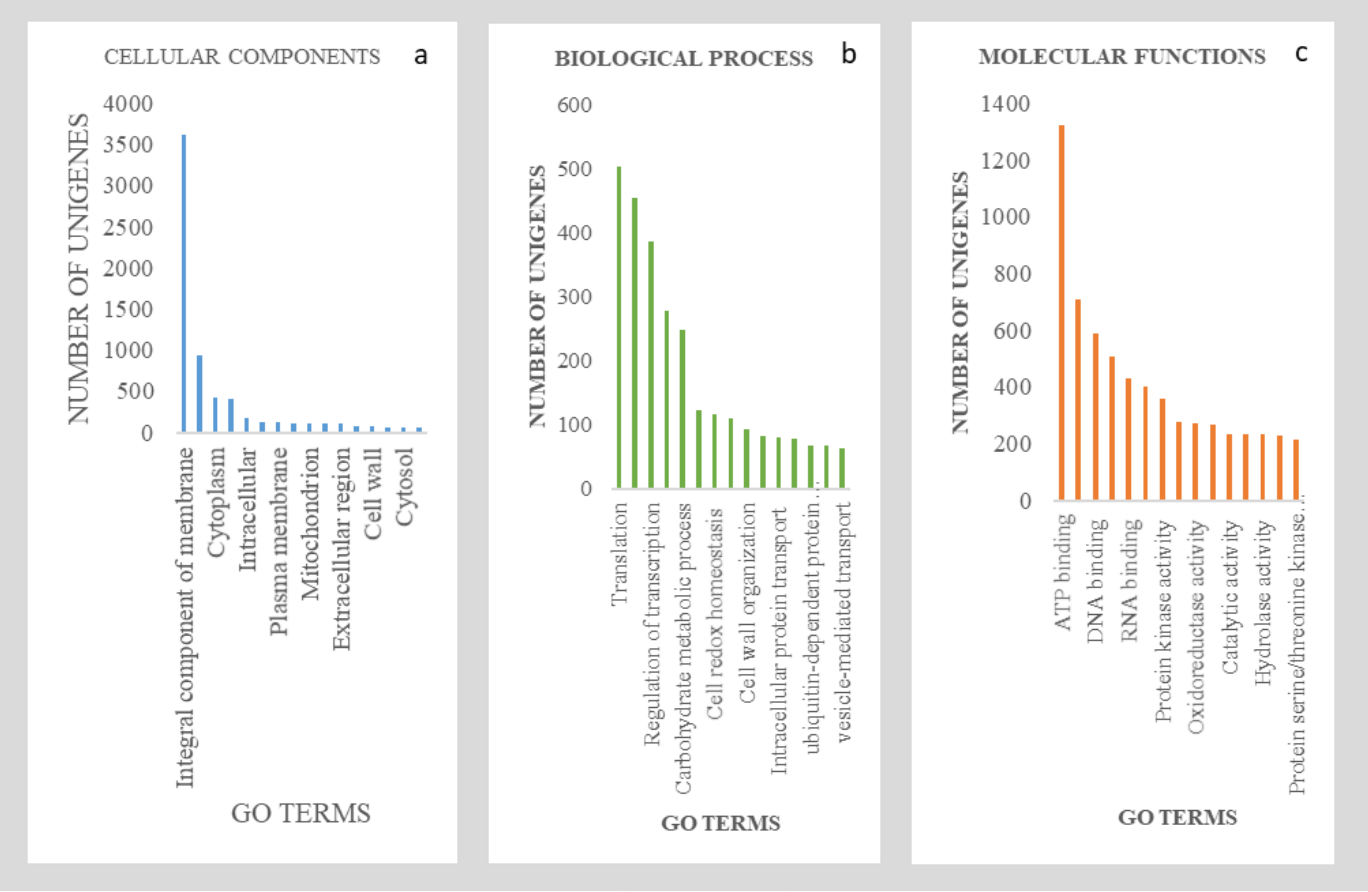


Figure 3.4.1. Gene ontology (GO) classification. Bar chart representing functional categorization of unigenes annotated from RNA-Seq data of *Plantago ovata*. The results are summarized in three categories Cellular components (a), Biological process (b), and Molecular functions (c)

Thirty one genes related to three pathways namely MVA, MEP and iridoid were identified from the assembled data. Each gene had more than one transcript. Their contig IDs, contig length, read count and FPKM are summarized in table 3.4.4. In addition, two crucial genes involved in urosolic acid and catalpol biosynthesis were taken for further characterization and functional validation in heterologous host.

Table 3.4.4. Identified genes involved in terpenoid biosynthesis along with their Fragments Per kilobase of transcript per million mapped reads (FPKM) values

S.no	Annotations	Contig id	Contig length	Plantago major Read count	Plantago major FPKM	Plantago ovata Read count	Plantago ovata FPKM
1.	Acetyl CoA- acetyltransferase	DN28842_c1_g1_i9	1741	310	6.0813	164	3.1499
2.	HMG CoA synthase	DN27975_c1_g1_i15	1998	385	6.58117	1	0.01673
3	HMG CoA reductase	DN28943_c0_g3_i3	3144	38	0.412799	241	2.563255
4.	Mevalonate Kinase	DN26820_c1_g1_i13	1591	0	0	1325	27.848
5.	5-Phosphomevalonate kinase	DN29352_c1_g1_i7	3090	120	1.3263	1004	10.865
6.	2-C-methyl-D-erythritol-2,4-cyclodiphosphate synthase (MDC)	DN25821_c0_g5_i5	1590	102	2.1909	1552	32.640
7.	Farnesyl diphosphate synthase (FDS)	DN24876_c0_g2_i8	1536	304	6.759591	113	2.460054
8.	Geraniol 10- Hydroxy dehydrogenase	DN24472_c2_g2_i2	1716	1623	32.30274	9	0.175381
9.	Beta amyrin synthase	DN23898_c0_g1_i13	2581	1	0.013233	127	1.645406
10.	CYP76A26	DN25556_c1_g1_i2	1959	4	0.069737	54449	929.4217
11.	Geraniol 10-Hydroxylase	DN26801_c2_g2_i2	1861	7917	145.2956	67	1.203887
12.	Geraniol synthase	DN29836_c2_g2_i12	2638	1702	22.0355	32	0.405632
13.	Geranyl diphosphate synthase(GDS)	DN21483_c0_g1_i2	1633	0	0	1119	22.914
14.	Iridoid synthase	DN21576_c1_g1_i4	2208	10	0.1546	414	6.2698
15.	Squalene epoxidase	DN28437_c0_g1_i3	2367	3	0.043287	344	4.85979
16.	Isopentenyl diphosphate isomerase or Isopentenyl pyrophosphate isomerase (IDI)	DN27359_c0_g1_i11	1458	934	21.879	246	5.642024
17.	1-deoxy-D-xylulose-5-phosphate synthase (DXS)	DN30823_c0_g1_i14	3306	32	0.330587	487	4.925876
18.	1-deoxy-D-xylulose-5-phosphate synthase (DXR)	DN29142_c0_g1_i15	2199	712	11.05841	717	10.90313
19.	2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase(MCT)	DN27734_c3_g1_i13	1382	50	1.235663	58	1.403387
20.	2-C-methyl-D-erythritol 4-phosphate cytidylyltransferase(MCS)	DN25821_c0_g5_i5	1590	102	2.190994	1552	32.64014
21.	Geranylgeranyl diphosphate synthase (GGDS)	DN26390_c1_g1_i8	1769	7	0.135148	1544	29.18615

S.no	Annotations	Contig id	Contig length	Plantago major Read count	Plantago major FPKM	Plantago ovata Read count	Plantago ovata FPKM
22.	4-hydroxy-3-methylbut-2-enyl diphosphate synthase (HDS)	DN30679_c0_g1_i10	2914	11626	136.2633	4691	53.8311
23.	Squalene synthase (Farnesyl diphosphate farnesyl transferase)	DN27279_c0_g1_i27	1786	278	5.316201	410	7.676438
24.	Alpha amyrin synthase	DN12295_c0_g1_i2	2086	183	2.996	0	0
25.	Cytochrome P450 CYP72A219	DN30674_c1_g1_i20	1968	9	0.156191	789	13.40631
26.	Uridine diphosphate glycosyltransferase (UGT)	DN30987_c3_g1_i15	2449	160	2.231358	1	0.013654
27.	Aldehyde dehydrogenase(ALD)	DN17992_c0_g1_i5	1598	69	1.474723	2	0.041851
28.	Flavonol synthase or Flavanone 3- dioxygenase	DN27979_c0_g1_i12	3182	1142	1	335	5.76
29.	2-hydroxyisoflavanone dehydratase	DN27979_c0_g1_i10	3562	136	1.304016	153	1.436
30.	Uroporphyrinogen decarboxylase	DN29005_c1_g3_i6	2640	1	0.012937	166	2.102624
31.	Squalene monooxygenase	DN28437_c0_g1_i2	2096	100	1.629472	745	11.88563

Transcription factors (TFs), are key regulatory factors that bind to specific DNA sequences and are involved in regulation of gene expression. BLASTX and UniProt database were used to screen the transcripts for the presence of TFs. The results revealed presence of 609 TFs distributed in 29 families including MYB, WRKY, bHLH, GATA among others. MYB family of TFs was found to be the most abundant followed by WRKY (Figure 3.4.2).

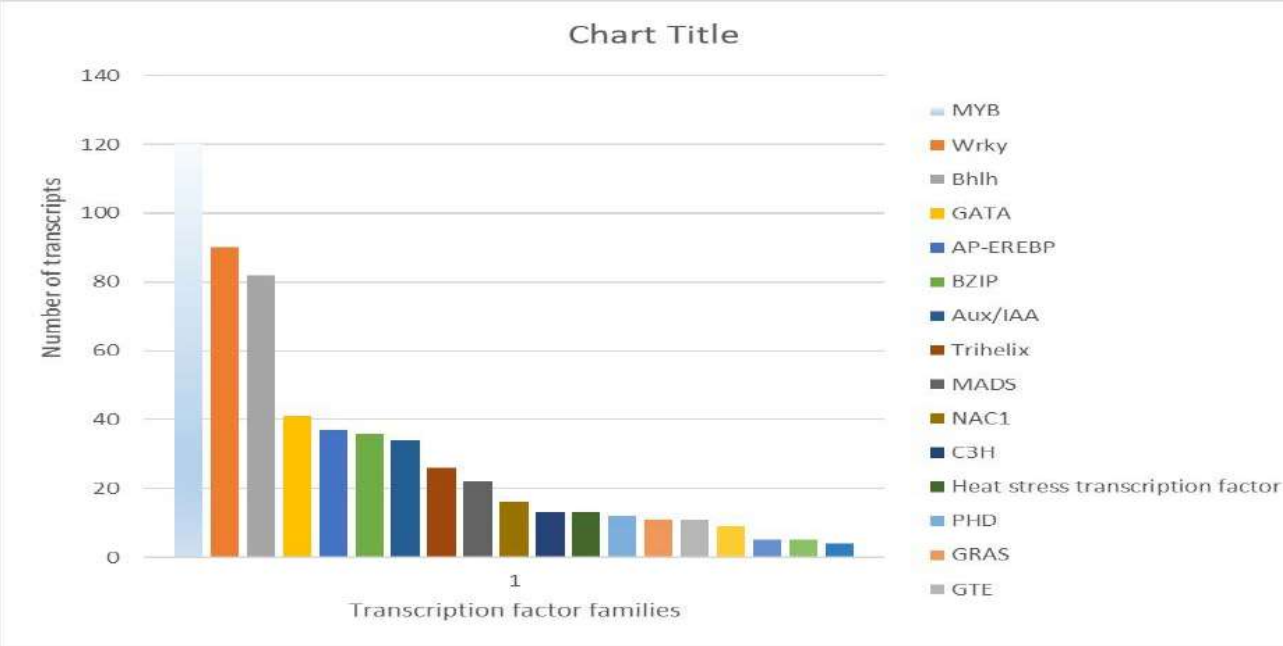


Figure 3.4.2. Distribution of *Plantago ovata* transcripts in different transcription factor (TFs) families.

3.5 Analysis of chemotypic diversity in relation to ploidy in various populations of *Inula royleana* C.B. Clarke from Kashmir Himalayas

Syed Mudassir Jeelani, Ajai Prakash Gupta, Surrinder K. Lattoo

Inula royleana of the family Asteraceae is a critically endangered species with its populations witnessing a speedy decline in the entire north-western Himalayan range at different altitudes (2000-3500 m). The species is popularly called as 'Poshkarmool' bearing diverse active components that have been utilized for therapeutics both in organized (Ayurveda, Unani) and unorganized (folk, tribal, native) systems of medicine from ancient times. It is used for the treatment of asthma, chronic bronchitis, hypotension, pulmonary disorders, tuberculosis, skin diseases, cardiac disorders, obesity, diabetes, lung cancer, spasm etc. It also acts as an expectorant. Especially the roots of the species possess hypoglycemic, hypocholesterolemic and hypolipidemic properties and are also used as cardioprotective tonic. It is being prescribed as a medicine for precordial chest pain, cough and dyspnoea, both singly and as poly-herbal preprations. The medicinal value of this plant is recognized mainly due to the presence of significant percentage of eudesmanolide group of sesquiterpene lactones such as isoalantolactone and alantolactone. The present study was undertaken to examine the diversity in concentration of major chemical/bioactive constituents of different populations/ cytotypes of the species collected from various geographic areas of Kashmir Himalayas. To have an insight into the chemical diversity in relation to genome organisation of different populations/cytotypes of the species, the cytogenetic studies were also corroborated with relative chemo-profiling. In the present study, six populations of *I. royleana* growing at different localities from Kashmir Himalayas were cytologically worked out (Table 3.5.1). The broad investigation of these populations reveal incidence of various chromosomal races including n = 10, 20 (Fig. 3.5.1a,b). The chromosome number n = 20 adds a new tetraploid cytotype for the species. The existence of intraspecific polyploids in the species is important to increase the adaptive and survival rate under diverse ecological niches of Himalayas. This further reveals that genome of such species is still in constant flux. The morphological comparison of diploid and tetraploid cytotypes of *I. royleana* at intraspecific level revealed variations in the quantitative and qualitative characters (Table 3.5.2). Generally, it was observed that the tetraploids mostly inhabit higher altitudes with stunted growth, fewer leaves and more flowers which are much brighter than the populations collected at lower altitudes. Additionally, the number of seeds was more in tetraploids than diploids. Such trends were also observed in dry weight of roots. The stomatal and pollen grain size in tetraploid cytotypes were more conspicuous as compared to diploid cytotypes.

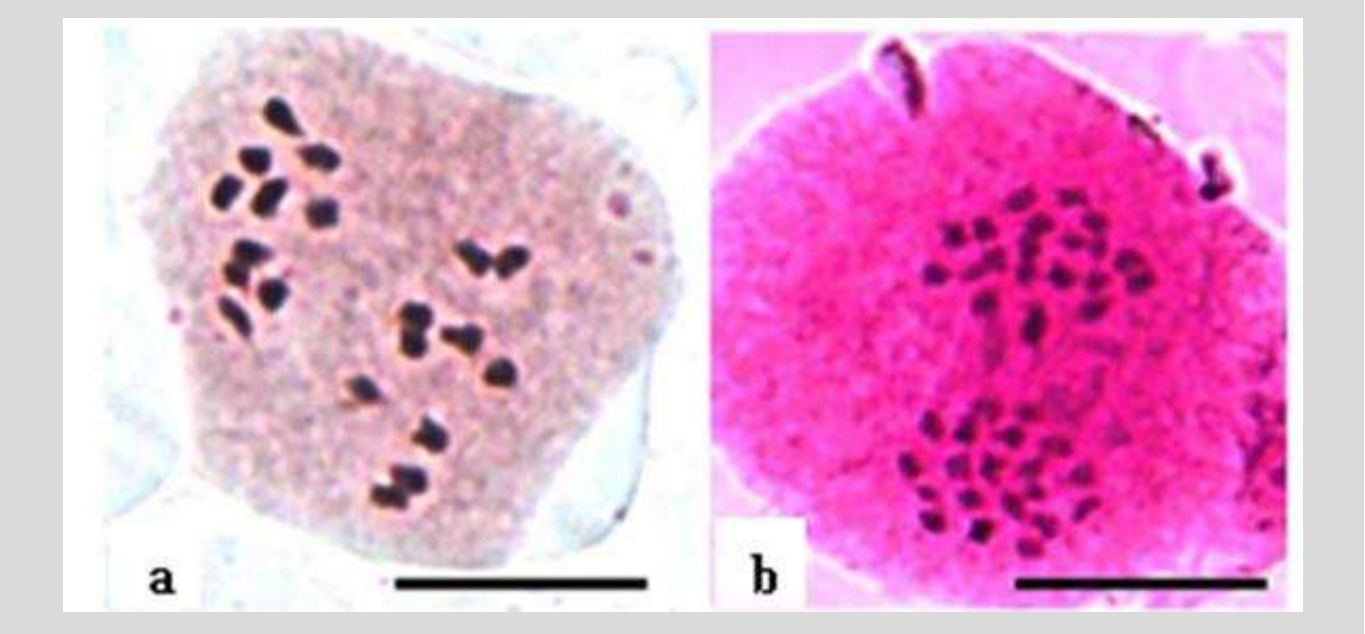


Figure 3.5.1. Meiotic chromosome numbers in different populations of *Inula royleana*: a) PMC at anaphase-I showing ten chromosomes (2n = 2x = 20); b) PMC at anaphase-I showing twenty chromosomes (2n = 2x = 40). Scale bar= 10 µm.

Table 3.5.1. Data on chromosome number, ploidy status and place of collection in different populations of *Inula royleana* C.B. Clarke from Kashmir Himalayas

S. no.	Observed chromosome number ('n')	Ploidy status	Place of collection & voucher number
IR1	10	Diploid (2n = 2x = 20)	Patalwan (34°35′N, 74◦52′E; 2700 m)/ 52401
IR2	10	Diploid (2n = 2x = 20)	Tulial (34°37′N, 74°59′E; 2600 m)/
IR3	10	Diploid (2n = 2x = 20)	Izmarg (31°20′ N, 78°20′E; 2600 m)/
IR4	10	Diploid (2n = 2x = 20)	Aru (34°05′ N, 75°15′E; 2800 m)/
IR5	20	Tetraploid (2n = 4x = 40)	Chumnai (34°04′N, 75°19′E; 3200 m)/52403
IR6	20	Tetraploid (2n = 4x = 40)	Razdan (34°34′N, 75°43′E; 3500 m)/52402

Table 3.5.2. Quantitative morphological comparison of different cytotypes in *Inula royleana*

S. no.	Characters	Diploid cytotypes (2n = 2x = 20)	Tetraploid cytotypes (2n = 4x = 40)
1.	Plant height (cm)	171-182	160-167
2.	No. of stems	2-3	4-5
3.	Leaf length (cm)	35-43	45-52
	Breadth (cm)	12-16	18-24
6.	Stomatal size (µm)		
	(a) Upper surface	32.23 × 22.20 -	34.15 × 24.34 -
		33.12 × 23.34	35.32 × 25.12
	(b) Lower surface	30.45 × 21.10 -	32.32 × 22.44 -
		31.85 × 22.50	33.12 × 23.24
4.	Flower heads per plant	8-12	14-17
5.	Primary root length (cm)	14-20	22-26
6.	Fresh root weight (g)	255-300	310-340
7.	Pollen grain size (µm)	19.50 × 18.10-	22.34 × 21.50-
		21.56 × 20.11	24.45 × 23.78
8.	Fresh seed weight (g)	1-1.5	2-2.4

In order evaluate the concentration of major bioactive compounds viz. isoalantolactone and alantolactone, these populations were examined phytochemically through standard LC-E-MS/MS technique (Fig. 3.5.2a,b). The relative concentration of alantolactone was more than isoalantolactone in the investigated populations/ cytotypes (Table 3.5.3). Similarly, the tissue-specific chemo-profiling revealed trend of maximum accumulation of isoalantolactone and alantolactone in roots followed by leaves and stem. However, the tendency of highest concentration in roots was not only persistent in polyploids but for diploids too. The results also revealed some remarkable changes in the content of chemical constituents against a specific ploidy level. An increasing trend in the concentration of isoalantolactone and alantolactone was recorded from lower to higher ploidy levels along the altitudinal gradient. Therefore, tetraploid cytotypes exhibited maximum accumulation of these secondary metabolites.

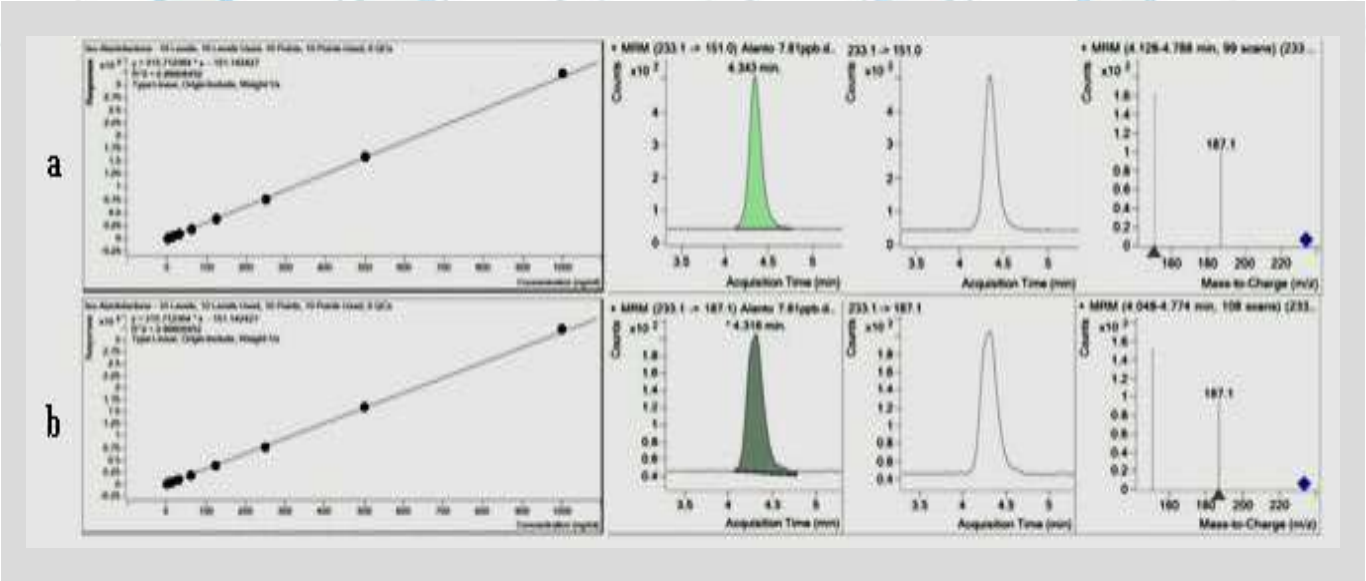


Figure 3.5.2. Multiple ion monitoring (MIM), calibration and fragmentation curve graphs of investigated compounds (a) isoalantolactone (b) alantolactone.

Table 3.5.3. Concentrations on dry weight basis (ng/mg) of major bioactive compounds in different populations/cytotypes *Inula royleana*

S. no.	Ploidy status & collection site	Plant part	Isoalantolactone	Alantolactone
IR1	Diploid, Patalwan,	Root	274.249 ± 1.125	604.105 ± 0.580
	34°35′N, 74◦52′E;	Leaf	27.790 ± 2.312	58.733 ± 1.123
	2700 m	Stem	6.234 ± 0.499	13.077 ± 0.566
IR2	Diploid, Tulial	Root	114.389 ± 0.918	216.234 ± 1.076
	34°37′N, 74°59′E;	Leaf	26.160 ± 0.588	33.724 ± 0.285
	2600 m	Stem	1.540 ± 0.063	3.140 ± 0.011
IR3	Diploid, Izmarg	Root	234.043 ± 0.583	480.580 ± 1.732
	31°20′ N, 78°20′E;	Leaf	20.148 ± 0.606	44.119 ± 0.513
	2600 m	Stem	5.299 ± 0.398	10.506 ± 0.575
IR4	Diploid, Aru,	Root	371.356 ± 1.85	750.866 ± 2.878
	34°05′ N, 75°15′E;	Leaf	60.049 ± 1.223	117.296 ± 1.154
	2800 m	Stem	7.7146 ±1.153	16.296 ±1.119
IR5	Tetraploid, Chumnai,	Root	525.363 ± 2.068	1103.851 ± 4.59
	34°04′N, 75°19′E;	Leaf	62.877 ± 1.721	65.160 ± 1.125
	3200 m	Stem	15.359 ± 1.27	17.279 ± 1.1951
IR6	Tetraploid, Razdan,	Root	529.382± 3.238	1413.592 ± 4.968
	34°34′N, 75°43′E;	Leaf	70.2142 ± 2.185	149.382 ± 2.319
	3500 m	Stem	17.697 ± 1.317	33.572 ± 1.191

Taken together, comparative transcriptome analysis of *P. ovata* and *P.major* resulted in the identification of putative pathway genes of triterpenoids and secoiridoid which may plausibly be helpful for genetic and biotechnological interventions for pathway intensification.

3.6 Transcriptome analysis provides detailed insights into gene expression and regulation in trichomes of *Nicotiana tabcaum*

Abhishek Nautiyal, Umar Gani, Maridul Kundan, Priyanka Sharma, Surrinder K. Lattoo, Ram A. Vishwakarma and Prashant Misra

Glandular trichomes of *N. tabacum* harbor impressively active machinery for the biosynthesis of secondary metabolites, particularly of diterpenoid backbone. For obvious reasons, *N. tabacum* trichomes can be suitable model system to understand molecular basis of regulation of secondary metabolism. In addition, through strategic genetic engineering and genome editing, tobacco glandular trichomes could be developed as platform for production of economically important plant secondary metabolites. However, very little is known about mechanism of gene regulation in connection to secondary metabolism in glandular trichomes of *N. tabacum*. In order to gain comprehensive knowledge about genes expressing in trichomes, we have carried out next-generation transcriptome sequencing of tobacco trichomes (T) and trichome-less leaf (TL) using illumina platform. The alignment of clean illumina reads to the publically available *N. tabacum* reference genome revealed that a total of 37290 and 37383 genes express in TL and T samples, respectively at a FPKM cutoff of ≥1. The top 5000 most highly expressing genes in the two samples were classified in different functionally annotated groups such as "Protein synthesis, modification' and degradation 'RNA, transcription and processing', 'Photosynthesis', 'Transport,' 'Signaling', 'Enzymes', 'Stress', 'Secondary metabolism', 'Redox', "Lipid Metabolism 'Major and minor carbohydrate metabolism (CHO) 'Amino acid metabolism' etc. (Figure 3.6.1). The number of genes within the categories 'Lipid Metabolism' and 'Secondary Metabolism' were higher in T as compared to TL sample. Out of the top 5000 highly expressing genes, certain genes remain un-annotated and without an assigned functional group. Further, the differential expression analysis led to the identification of 1671 and 2226 genes, as up and down-regulated in T as compared to TL sample with a cutoff of ≥log2 fold change 2 at p-value less than 0.05. The differentially regulated genes were classified in different functional groups based on MapMan ontologies. Gene set over-representation analysis clearly suggested that the functional categories like 'secondary metabolism', 'fatty acid synthesis and elongation' were overrepresented within the list of up-regulated genes in T as compared to TL. We reported over-representation of C2C2 Zn Finger CO Like, MYB and TCP family transcription factor genes within the category of up -regulated genes in T samples. Among the up-regulated genes, as expected, genes involved in the biosynthesis of diterpenoid class of secondary metabolites were up-regulated. Additionally, the expression of genes involved in the biosynthesis of flavonols was also reported to be significantly higher in T as compared to TL.

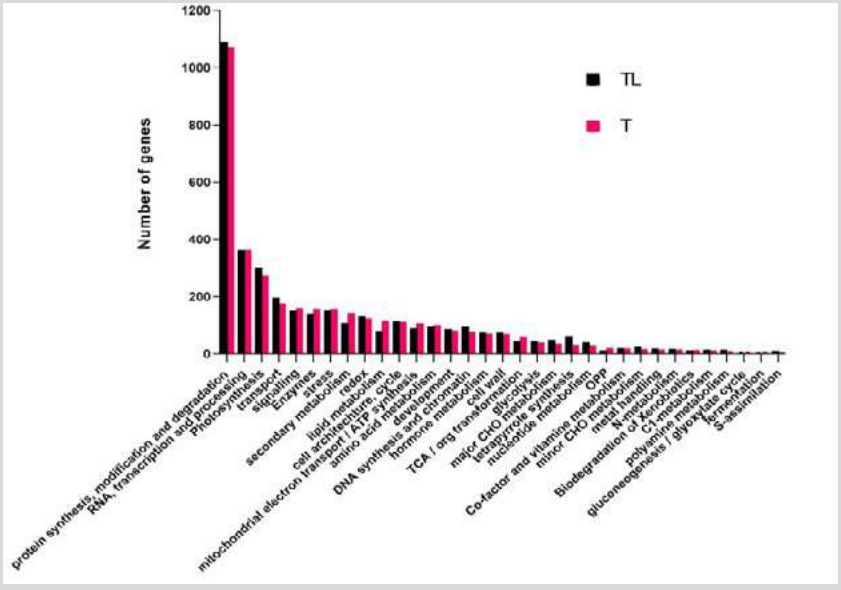


Figure: 3.6.1. Classification of top 5000 highly expressing genes in different functional classes

The annotation of genes was carried out using Mercator tool. Only annotated genes and with assigned group were used for the analysis. TL, trichome-less (leaves after removing trichomes), T, Trichomes (Scratched trichomes from leaf surface)

In an attempt towards elucidation of metabolic networks supporting excessive production of secondary metabolites in trichomes, we analyzed the gene expression data using MapMan tool (Figure 3.6.3). The analysis indicated that apart from secondary metabolism, pathways related with primary metabolism, for example, photosynthesis, amino acid biosynthesis, pentose phosphate pathway, sucrose metabolism, lipid metabolism etc. were modulated in trichomes. Taken together, a comprehensive resource of genes expressing in tobacco trichomes has been developed and currently, functional studies on some of the genes, including transcription factors are underway.

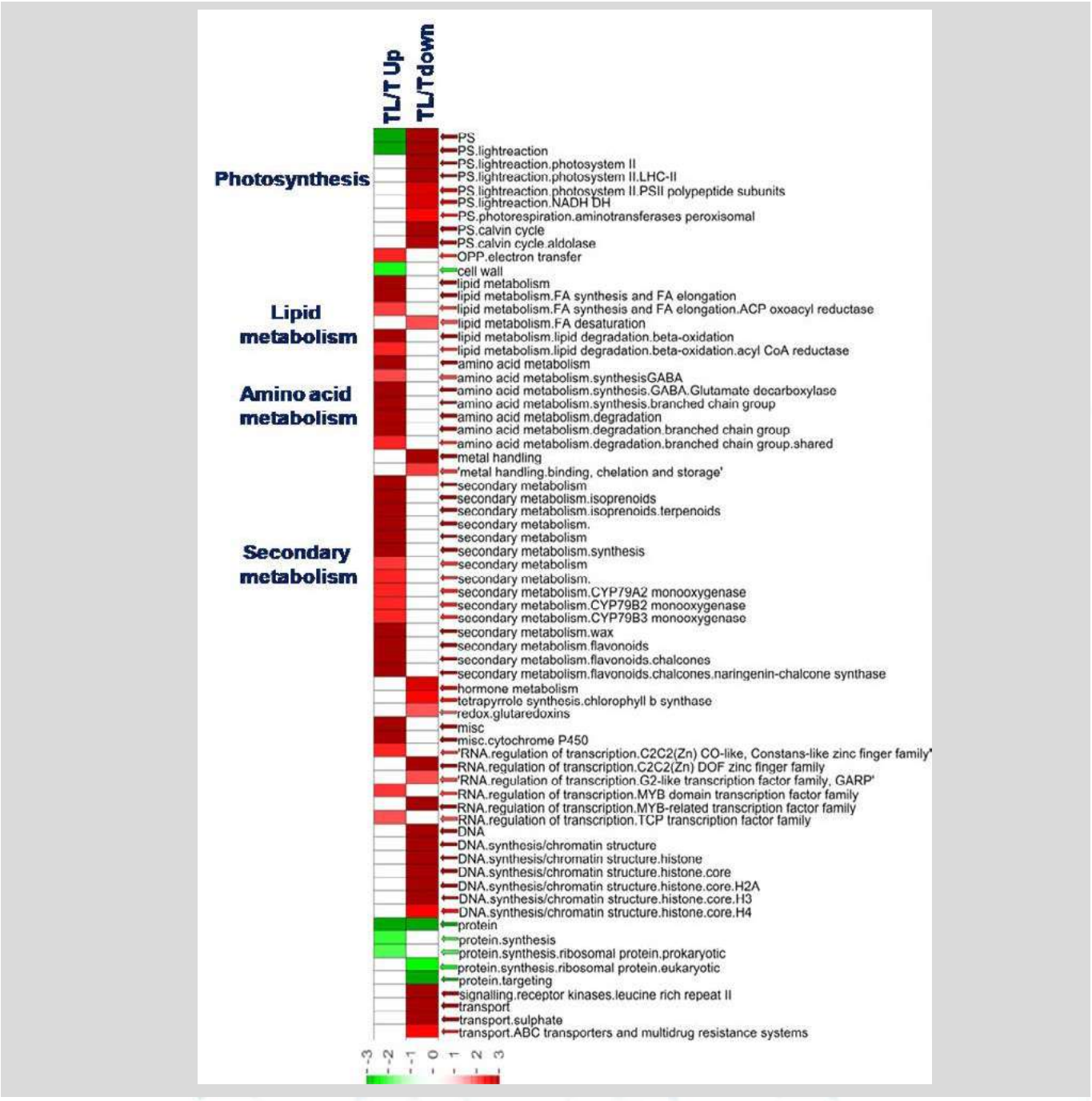


Figure 3.6.2. Over- and under-representation analysis of differentially regulated genes

The differentially regulated genes were annotated using Mercator tool and analyzed through PageMan tool for over-presentation. Red color and green color represent significant over and –under-representation, respectively. (T, trichome and TL, trichome-less sample).

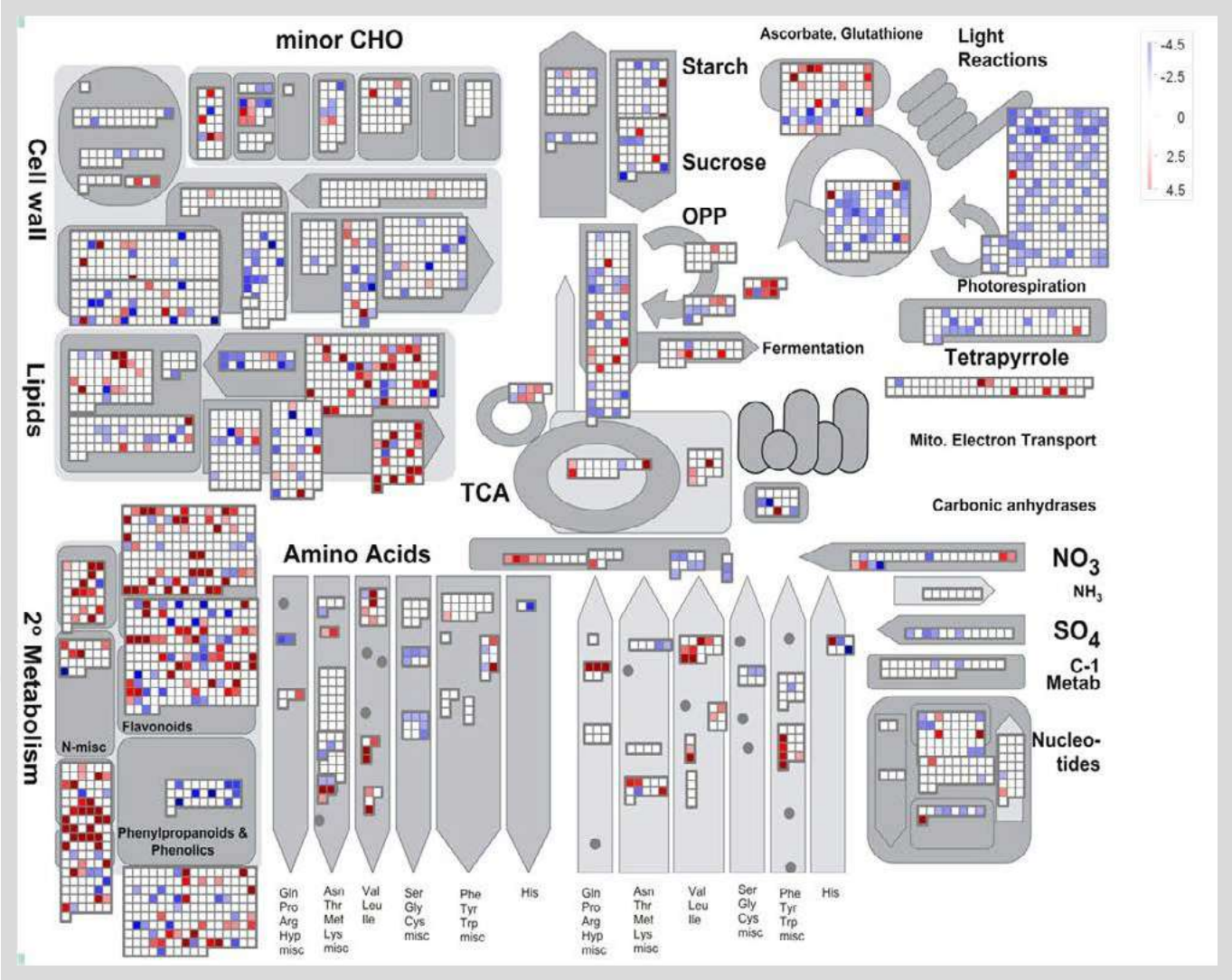


Figure 3.6.3. Overview of metabolic pathways modulated in trichomes based on expression on differentially expressed genes in trichomes as compared to trichome free leaf

Red and blue color represent up- and down-regulation, respectively in trichome as compared to trichome-less sample. The analysis was carried out using MapMan tool. (TCA, tricarboxylic acid, CHO, carbohydrate metabolism, OPP, oxidative pentose phosphate pathway)

3.7 Functional characterization of MATE family transporters in *Nicotiana tabacum*

Umar Gani, Abhishek Nautiyal, Ram A. Vishwakarma and Prashant Misra

Multidrug and toxic compound extrusion (MATE) family, displaying remarkable expansion in higher plants has been implicated in transport of a range of molecules including secondary metabolites in plants. We identified two highly homologous genes putatively encoding MATE family transporters in a transcriptome resource of *N. tabacum* glandular trichomes. The *in silico* expression analysis suggested that these MATE genes, named hereafter as *NtFT1* and *NtFT2*, were up-regulated in trichomes as compared to trichome-less tobacco leaf. The phylogenetic analysis grouped NtFT1 and NtFT2 with MATE family transporters, which are involved in transport of secondary metabolites, particularly flavonoids (Figure 3.7.1). The expression analysis using semi-quantitative and real time PCR indicated that *NtFT1* and *NtFT2*, express primarily in flower and trichome of tobacco (Figure 3.7.2). Further, the expression of *NtFT1* and *NtFT2* was reported to be up-regulated by several folds in flavonol rich tobacco transgenic lines as compared to wild type tobacco and empty vector control tobacco lines (Figure 3.7.3). These results led us to speculate that *NtFT1* and *NtFT2* could be involved in transportation of flavonoids. In our venture towards functional characterization of *NtFT1* and *NtFT2* genes, the corresponding coding regions of approximately 1.5 Kb were cloned. The sequence analysis revealed that coding regions of *NtFT1* and *NtFT2* genes display 99% identity at nucleotide and protein level and are homeologous. The Phobius prediction program for transmembrane regions (http://phobius.sbc.su.se/) suggested that NtFT1 and NtFT2 protein contains 12 transmembrane helices, with a topology representative of MATE transporters. The constructs for overexpression and silencing of *NtFT1* and *NtFT2* genes in tobacco were developed in pBI121 vector. For, silencing of *NtFT1* and *NtFT2* genes, artificial microRNA approach was adapted. Two artificial microRNAs (aMIRs) targeting both the genes were screened and their functionality was tested through transient expression system in *N. tabacum*. The transient expression of aMIR overexpression construct led to significant suppression of the expression of *NtFT1* and *NtFT2* genes (Figure 3.7.4). Further, stable transgenic lines for overexpression of aMIRs and *NtFT1* and *NtFT2* genes have been developed and their analysis is currently underway.

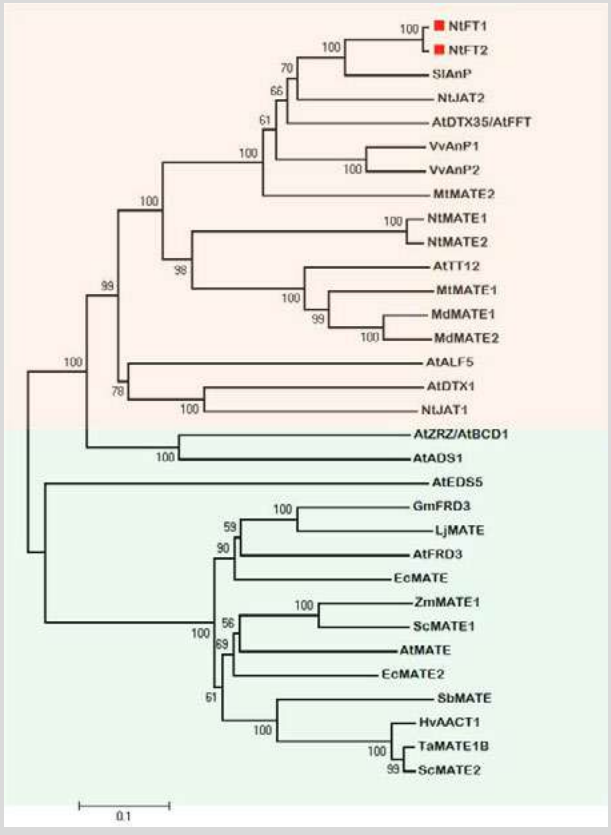


Figure 3.7.1. Phylogenetic analysis of MATE transporter genes

The phylogenetic analysis was carried out using the neighbor-joining method following CLUSTAL W alignment of known MATE proteins with deduced amino acid sequences corresponding to *NtFT1* and *NtFT2*. The phylogenetic tree was constructed and visualized by MEGA6 software.

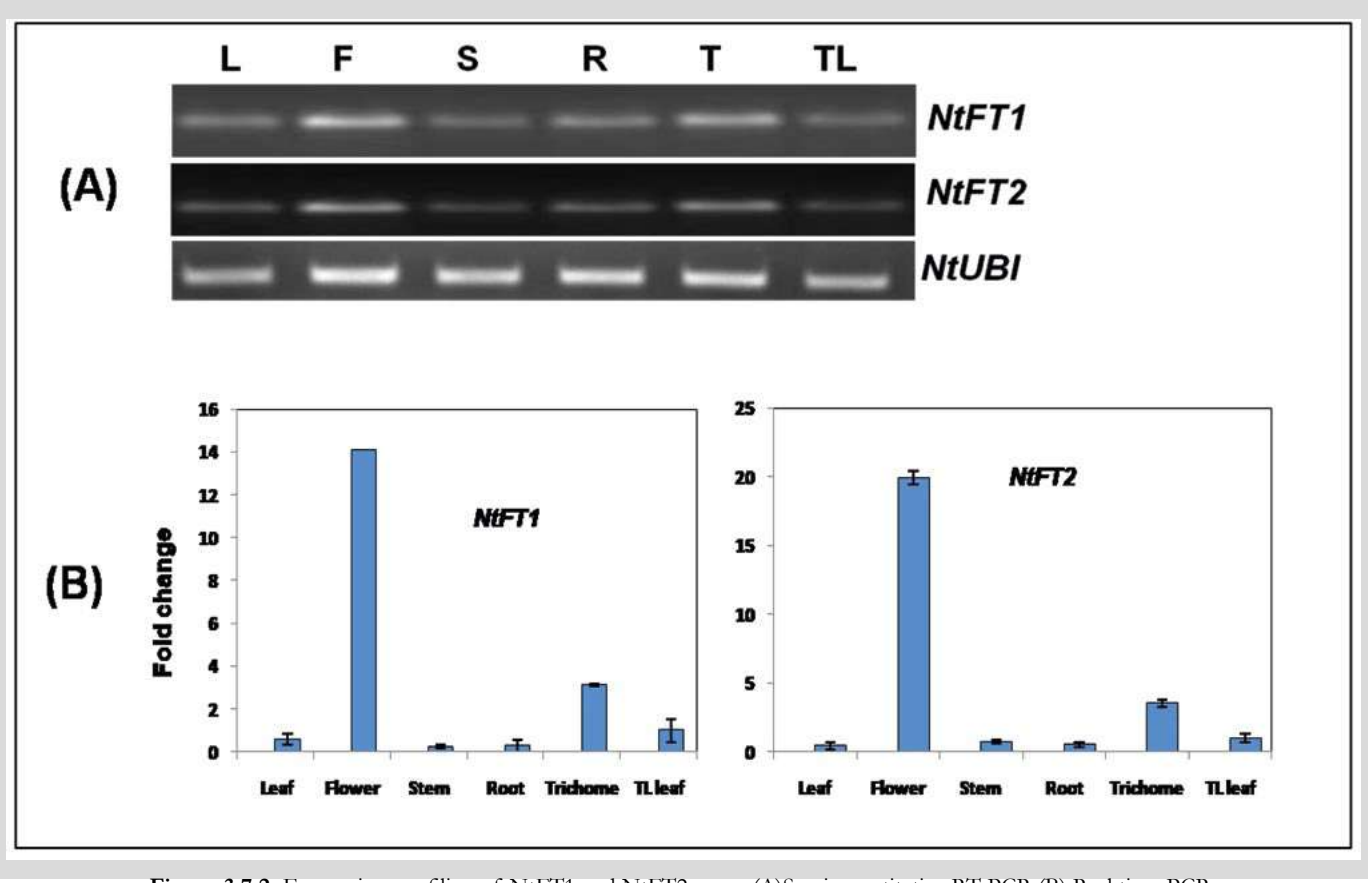


Figure 3.7.2. Expression profiling of NtFT1 and NtFT2 genes (A)Semi-quantitative RT-PCR (B) Real time PCR

N. tabacum ubiquitin (*NtUBI*) was taken as internal control for normalization. L, leaf, F, flower, R, Root, S, stem, T, trichome, TL, trichome-less leaf

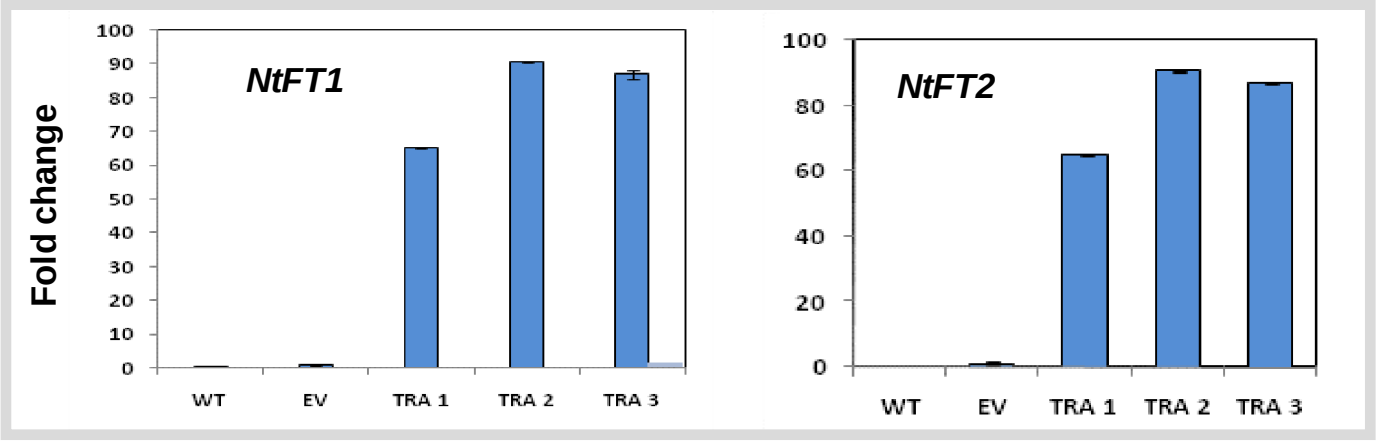


Figure 3.7.3. Expression of *NtFT1* and *NtFT2* genes in flavonol over-producing transgenic tobacco

WT, wild type tobacco, EV, empty vector transformed tobacco

TRA1, TRA2 and TRA3 are AtMYB12 expressing transgenic tobacco lines.

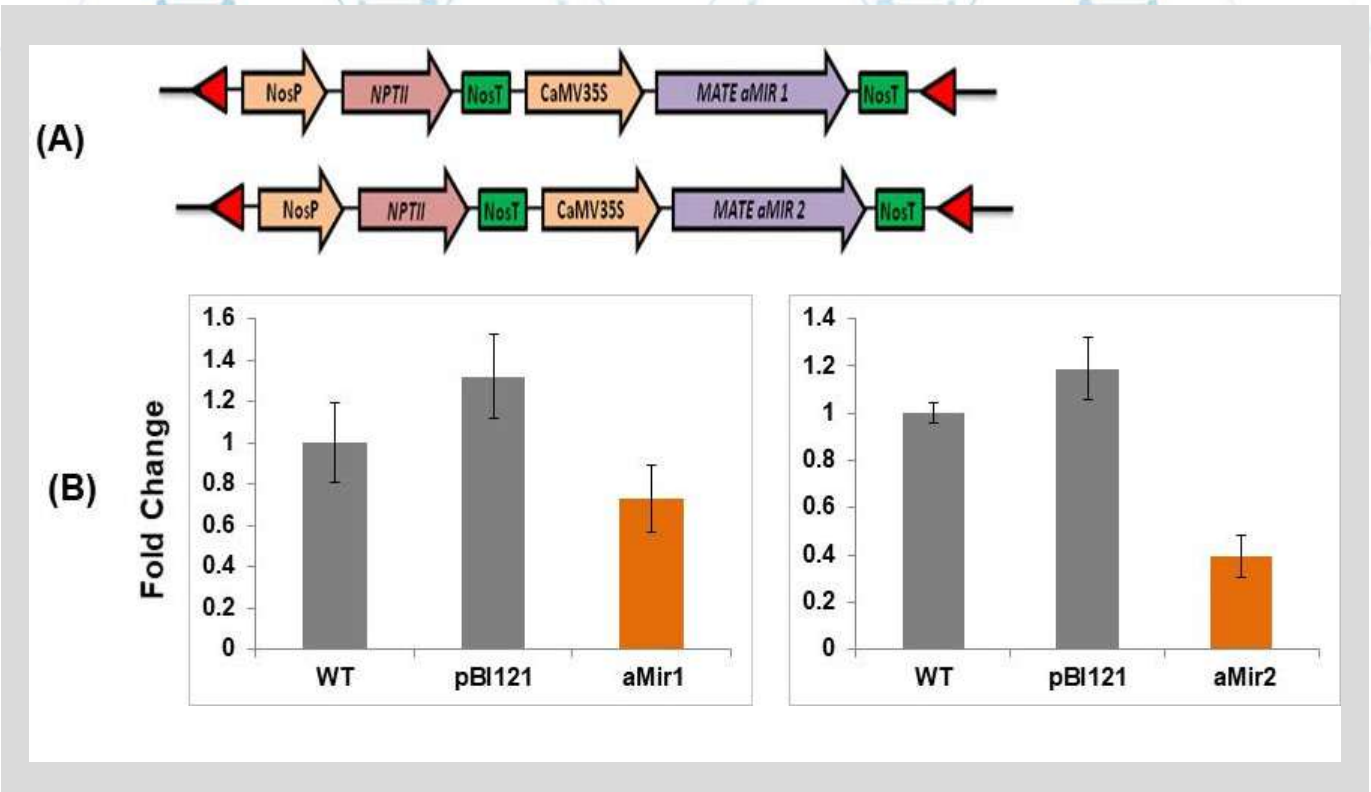


Figure 3.7.4. Artificial microRNA mediated suppression of *NtFT1* and *NtFT2* (A) Schematic representation of T-DNA regions of plant expression constructs for over-expression of artificial microRNAs (MATE aMIR1 and MATE aMIR2) intended to target *NtFT1* and *NtFT2* genes. **(B)** Real time PCR based expression profiling of *NtFT1* and *NtFT2* genes following agro-infiltration of tobacco leaves to transiently expression aMIR1 and aMIR2 plant expression constructs

In order to ascertain sub-cellular localization of *NtFT1* and *NtFT2*, GFP fusion constructs were developed and transiently expressed in protoplasts derived from BY2 cell lines. The confocal imaging indicated that *NtFT1* and *NtFT2* localize on plasma-membrane (Figure 3.7.5). In order to understand the regulation of *NtFT1* and *NtFT2* genes, corresponding upstream regions (1500 bps upstream to the start codon) were cloned. The *in silico* analysis of the promoter regions indicated presence of several *cis*-acting elements including putative binding sites for transcription factors such as MYB, MYC etc. The promoter regions were cloned upstream to the GFP and GUS gene in destination vector pKGWFS7 through Gateway cloning. The fusion constructs, thus developed were transformed in tobacco through *Agrobacterium* mediated transformation. Our preliminary analysis of primary transformats suggested that GFP expression was localized in trichomes only, and no detectable expression of GFP was evident in other cells of leaves. These results confirm that in leaf tissue, *NtFT1* and *NtFT2* primarily express in trichomes. Detailed study of the promoter-GFP/GUS fusion transgenic lines is underway.

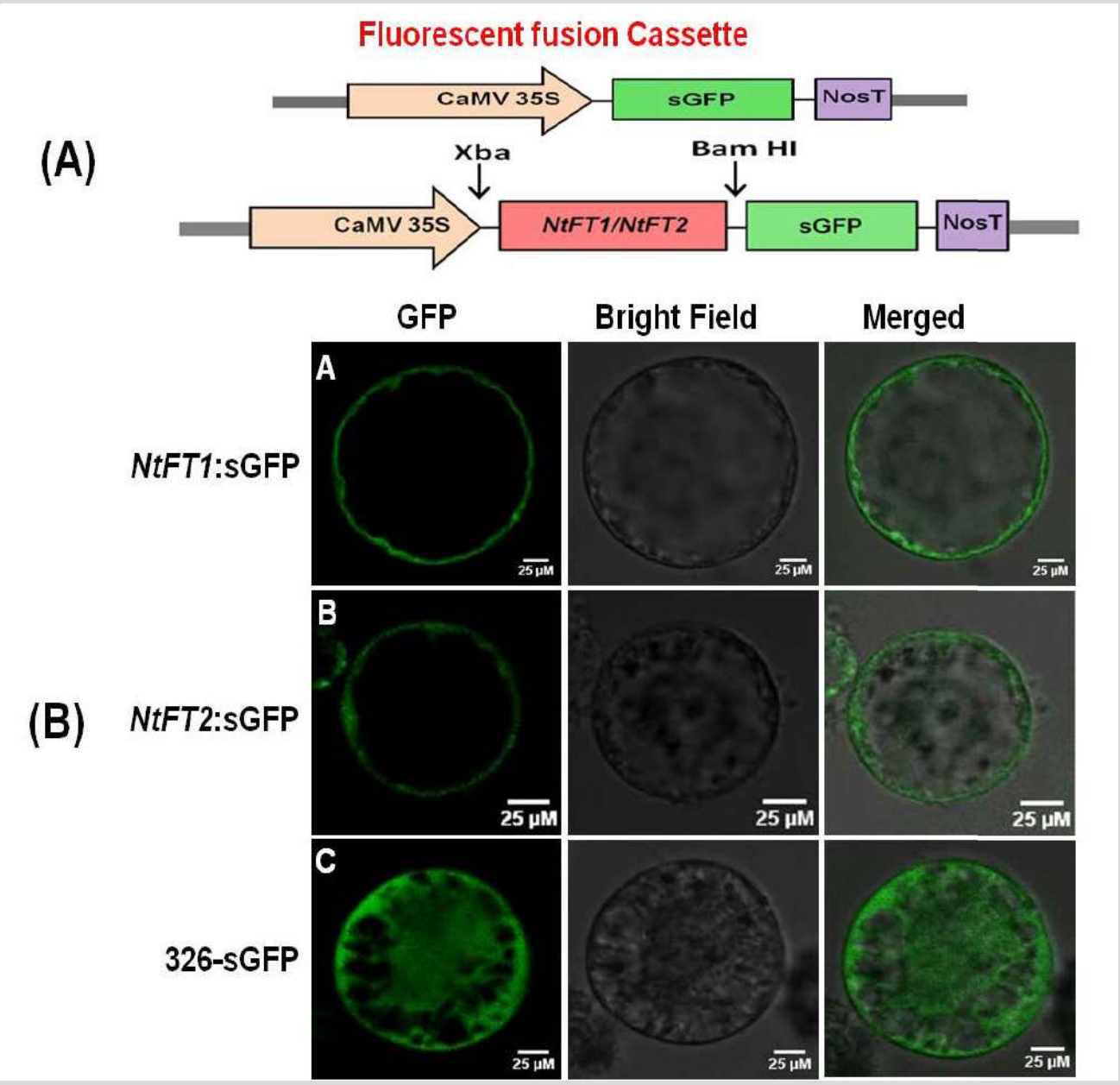


Figure 3.7.5. Localization of *NtFT1* and *NtFT2* in protoplasts of BY2 cell line. (A) Schematic representation of constructs for expression of *NtFT1* and *NtFT2* in translational fusion with GFP. **(B)** Confocal imaging of transfected protoplasts derived from tobacco BY2 cell line The translational fusion constructs of *NtFT1* and *NtFT2* with sGFP were developed in 326-sGFP vector. The expression constructs were transfected in protoplasts followed by confocal imaging.

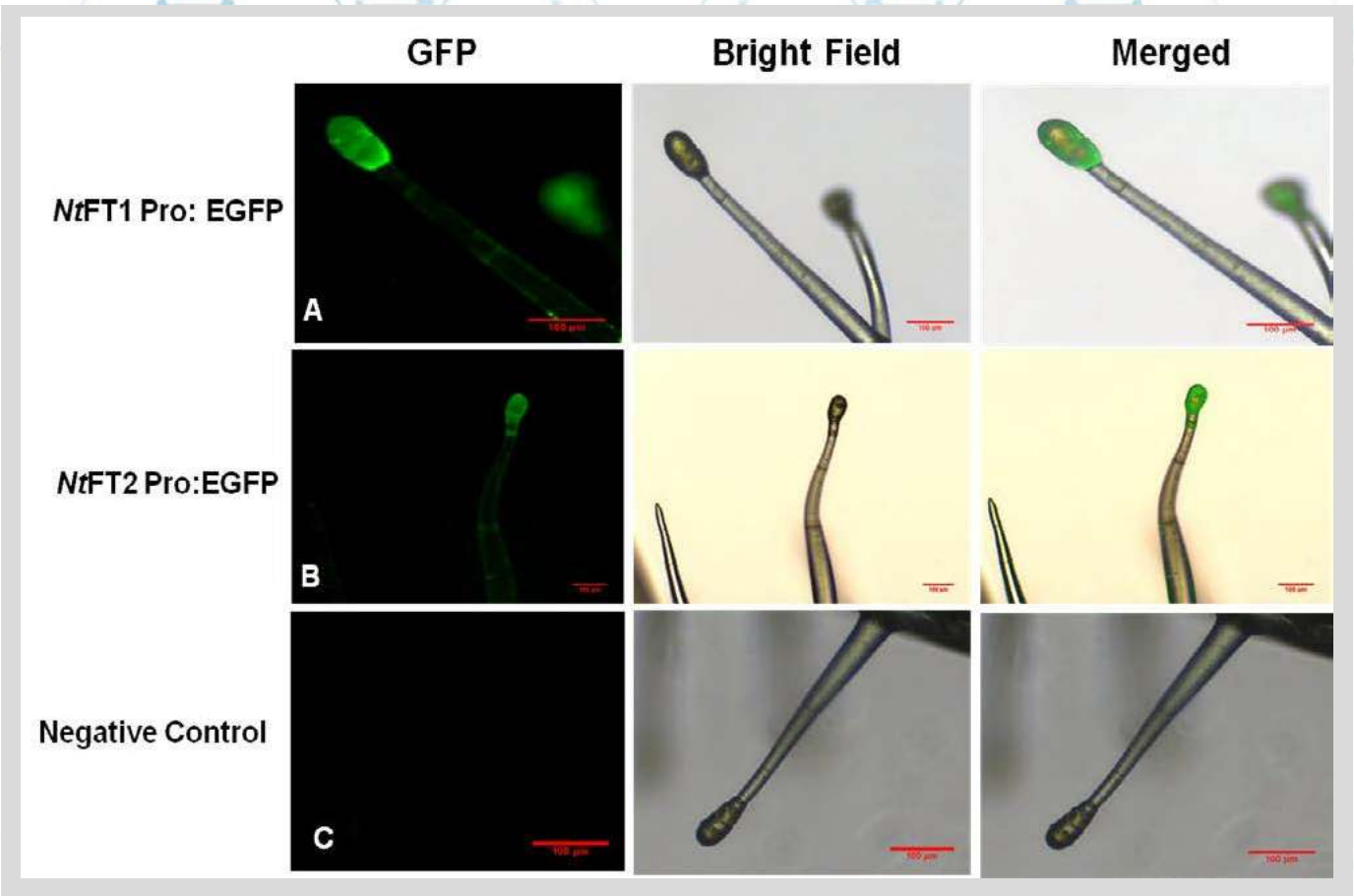


Figure 3.6.6. Fluorescent microscopic images of tobacco trichomes. (A) NtFT1 Pro: EGFP and (B) NtFT2 Pro: EGFP fusion constructs showing the GFP signal localized to the glandular trichomes only (C) Negative Control (Tobacco WT).scale bars = 100µm

3.8 Functional characterization and hetrologous expression of Squalene epoxidase Promoter and Gene from *Glycyrrhiza glabra*

Malik Muzafar Manzoor, Pooja Goyal, Pankaj Pandotra, Prashant Misra, Ajai P Gupta, Ram A Vishwakarma and Suphla Gupta

Squalene, the starting material for the tri-terpenoid saponins in plants, is synthesized by the mevalonate (MVA) pathway in the cytoplasm and 2-C-methyl-D-erythritol 4-phosphate (MEP) pathway in plastids, through well-understood steps. It is acted upon by squalene epoxidase (SE) which catalyzes the first oxygenation and rate-limiting step, converting squalene into oxido-squalene. The product, oxido-squalene is subsequently catalyzed and cyclized by several tri-terpene synthases to generate almost eighty different tri-terpene skeletons. These skeletons in turn act as precursors for all the known angiospermic cyclic triterpenoids including membrane sterols, brassinosteroid phytohormones, and non-steroidal triterpenoids, in the biosynthetic pathway of triterpenoid and phytosterol class of compounds. Literature reveals several plants are having multiple squalene epoxidase. Multiple predicted squalene epoxidase (SE) enzymes had been biochemically characterized in *Medicago truncatula Brassica napus*, *Populus trichocarpa* and *Oryza sativa* genomes each. Multiple copy number of the enzyme probably underlines its significant and unique regulation in plant system. The literature cites six putative *Arabidopsis* SE enzymes heterologously expressed in *Saccharomyces cerevisiae,* lacking squalene epoxidase for functional characterization.Three squalene epoxidase genes were cloned and characterized from *Panax vietnamensis*. However, there are no reports on cloning and characterization of squalene epoxidase gene from *Glycyrrhiza* species of the Fabaceae family. The squalene epoxidase gene codes for a noncytochrome-P450 type monooxygenase that participate to form a hydroxyl group characteristic of sterols and terpenoids class of compounds which are the important plant secondary metabolites. The enzyme has been known to function as a rate-limiting step in secondary products of several biosynthetic pathways. Cloning and characterization of the gene encoding the enzyme in *G glabra* will impart important information in the biosynthesis of the largest class of natural plant products, in general, and glycyrrhizin in particular. Glycyrrhizin, an oleanane-type triterpenoid saponin, is obtained from the dried roots (stolons) of *Glycyrrhiza species (G uralensis*, *G. glabra*, and *G. inflate*) which is widely recognized as a crude drug, a natural sweetener and a flavoring agent in Japan, China and Indian system of medicines. The demand for the roots is high and largely met from wild resources, with predicted annual global market growth of 4%, between 2017 and 2025. It is the major bioactive ingredient of several herbals possessing immuno-modulatory, antiulcer, anti-allergic and antiviral activities including HIV and severe acute respiratory syndrome (SARS)-associated *coronavirus.* Literature refers more than 20 triterpenoids being isolated from liquorice species synthesized via the cytosolic mevalonic acid pathway, for the production of 2,3-oxidosqualene which is subsequently cyclized to β-amyrin by β-amyrin synthase (bAS), the first committed step for glycyrrhizin biosynthesis. Recent excellent work including draft genome sequencing and further wet-lab experiments have created substantial knowledge base of genes involved in glycyrrhizin biosynthesis. Overall, two synthases (squalene synthase & β-amyrin synthase), two cytochrome-P450s (CYP88D6 & CYP72A154) and one UGT (GgUGT) have been identified from Glycyrrhiza species. However, complete understanding of the sequential steps of the pathway is still largely unknown. Also, SE gene from Glycyrrhiza species is yet to be cloned and characterized. Literature cites diverse non-natural plant products in *N. benthamiana* using transient expression technology including glucosinolates, cyanogens, phytoalexins, the etoposide aglycone , strictosidine, artemisinin , triterpenes and betalains . The study will help in understanding the regulatory role of squalene epoxidase in glycyrrhizin (triterpenoid) biosynthesis and provide an insight of molecular basis of metabolic regulation of triterpenoid saponins and sterols biosynthesis. The study will be useful for gene function discovery, pathway reconstitution and metabolic engineering of glycyrrhizin biosynthesis pathway related genes. The enzyme Squalene epoxidase (SE) is a crucial regulatory enzyme catalyzing the first step of several important bioactives of the isoprenoid pathway by stereo-specific conversion of squalene to (3S)-2,3- oxidosqualene in the presence of molecular oxygen (Figure 3.8. 1).

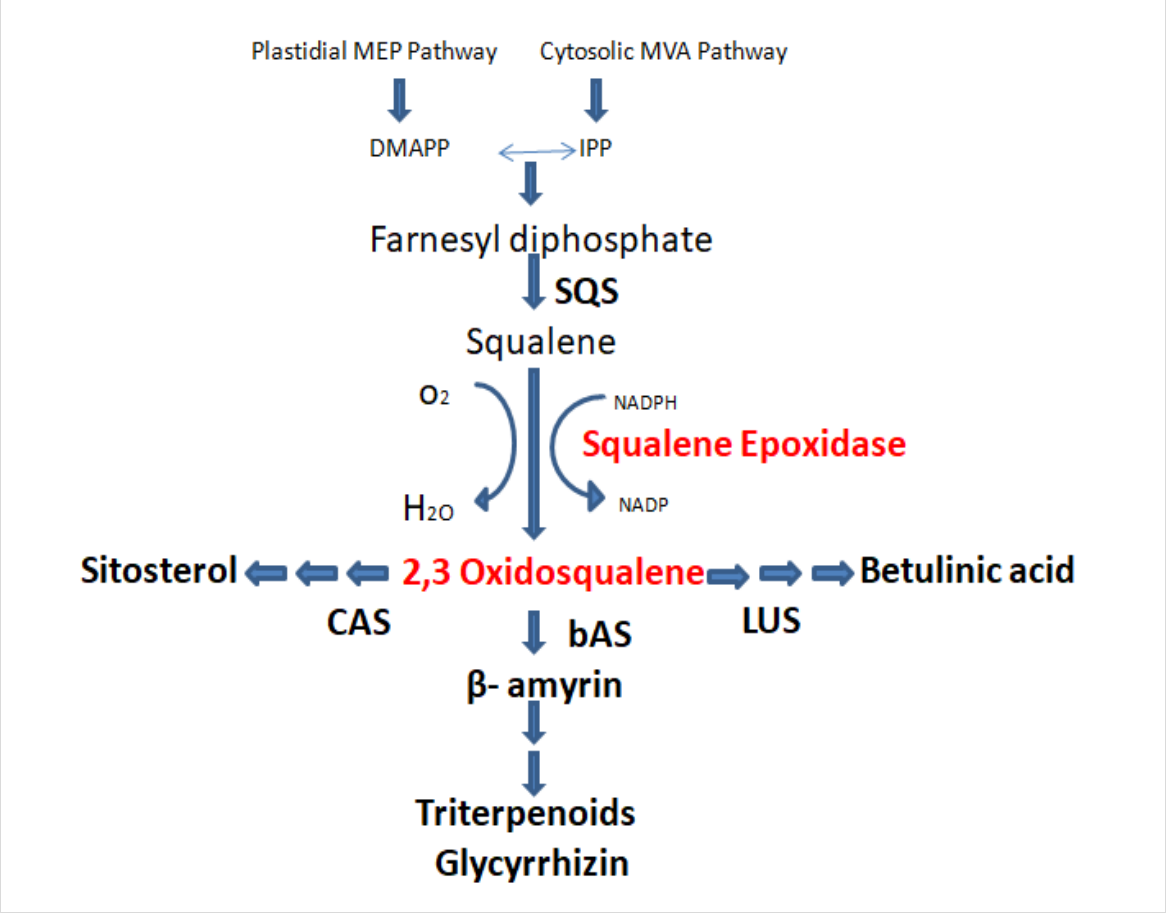


Figure 3.8.1

In the present study, we describe isolation, characterization and expression of the squalene epoxidase gene (GgSE) from *Glycyrrhiza glabra* and its expression in hetrologous plant host. The full-length open reading frame of *GgSE* gene was sequenced to be 1590 bp (Fig 3.8.2A) encoding 529 amino-acid residues with a molecular mass of approximately 57 kd and theoretical pI of 8.35 (Fig. 3.8.2 D,E).

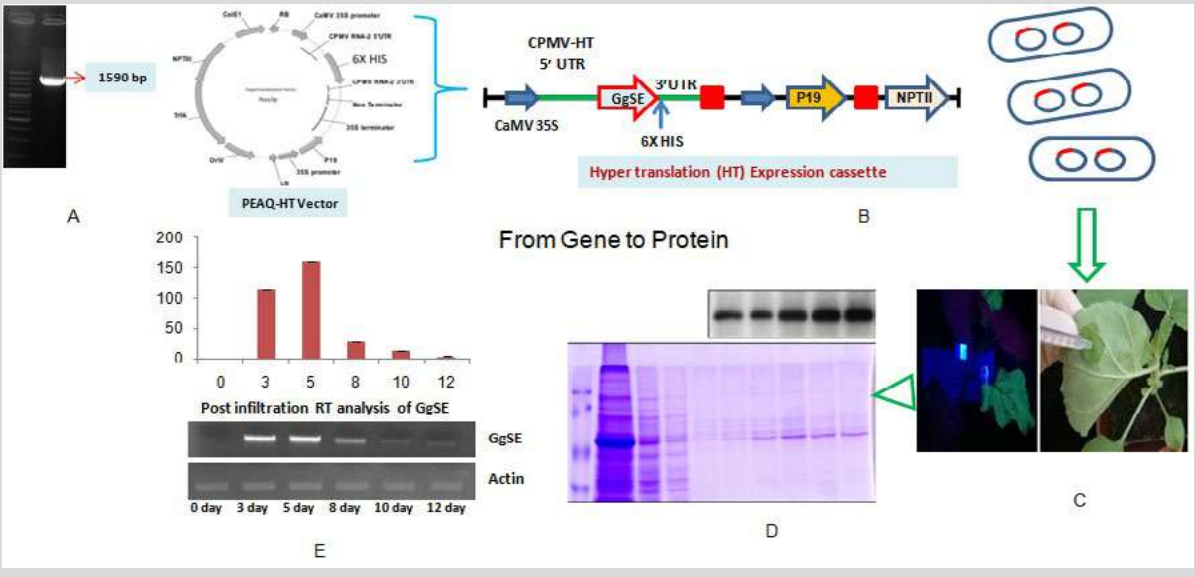


Figure 3.8.2.

The deduced gene sequences are submitted to NCBI (MG763680). Protein sequence alignment and phylogenetic analysis showed maximum sequence homology (91%) with *Astragalus membranaceus* (KJ010819.1) and *Medicago sativa* (KX034105.1) squalene epoxidase1 gene (89%) (Fig 3.8.3A). *In-silico* analysis predicted a U shaped trans-membrane protein with N-terminal signal peptide and α helix and β sheets (Fig 3.8.3B).

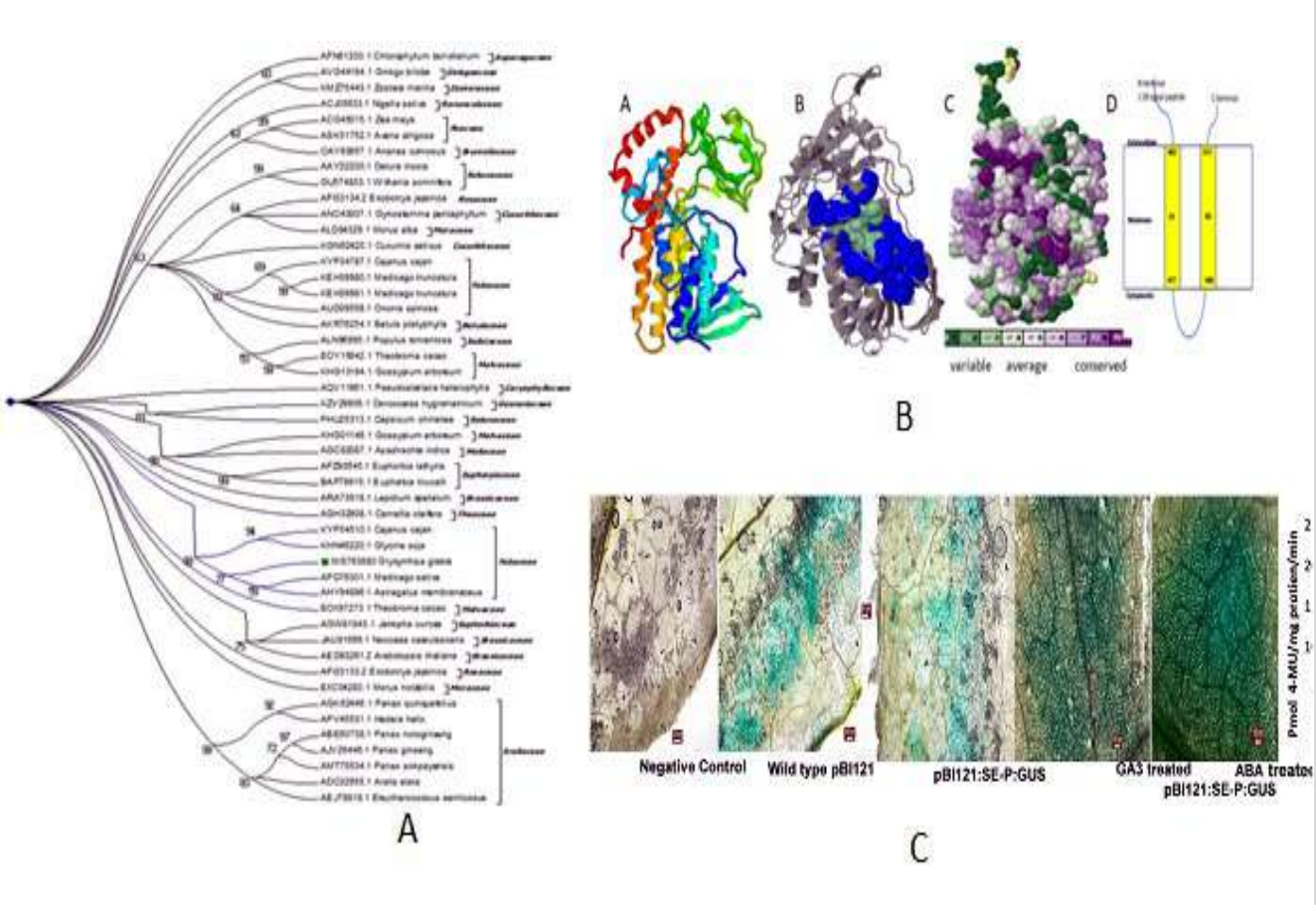


Figure 3.8.3

Spatial (leaf, stem and root) quantitative RT-PCR expression profile showed its wide expression in leaves, stem and root tissues with slightly higher accumulation in stem tissues (1.7) as compared to root (1.3) and leaves (1.0). Month-wise expression profile revealed highest transcript levels (6.3) in 10 month old root tissues however it was evenly expressed in shoot system (0.8 to 1.2) in all the months studied. Elicitation with methyl jasmonate (0.1mM) resulted in higher up-regulation in shoots (11.5) as compared to roots (4.5) tissues, after 8 hours of treatment (Fig 3.8.4A). The promoter region of the GgSE gene was also cloned and transiently expressed in plant system. The promoter showed enhanced GUS activity under ABA & GA treatment, when transiently expressed in the heterologos plant system (Fig 3.8.4B).

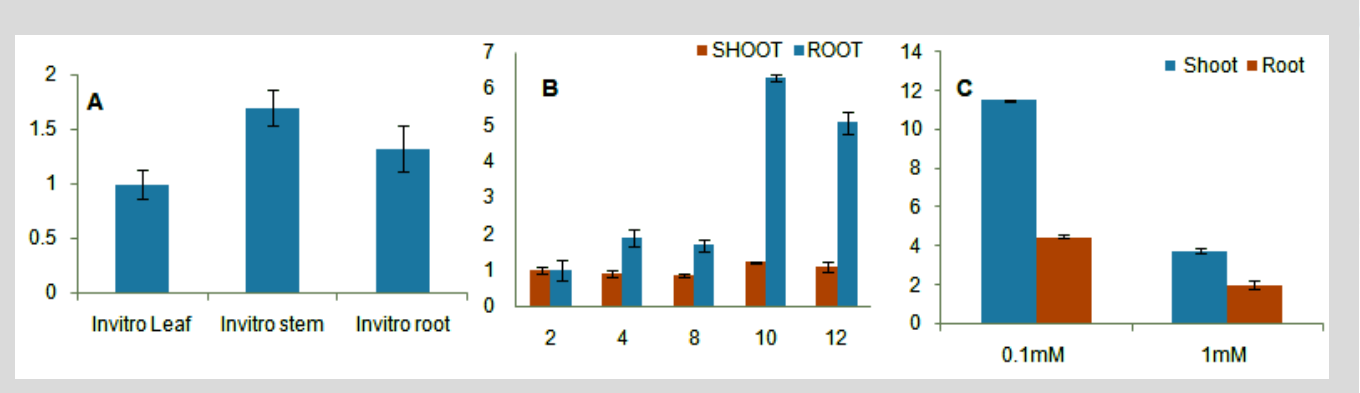


Figure 3.8.4

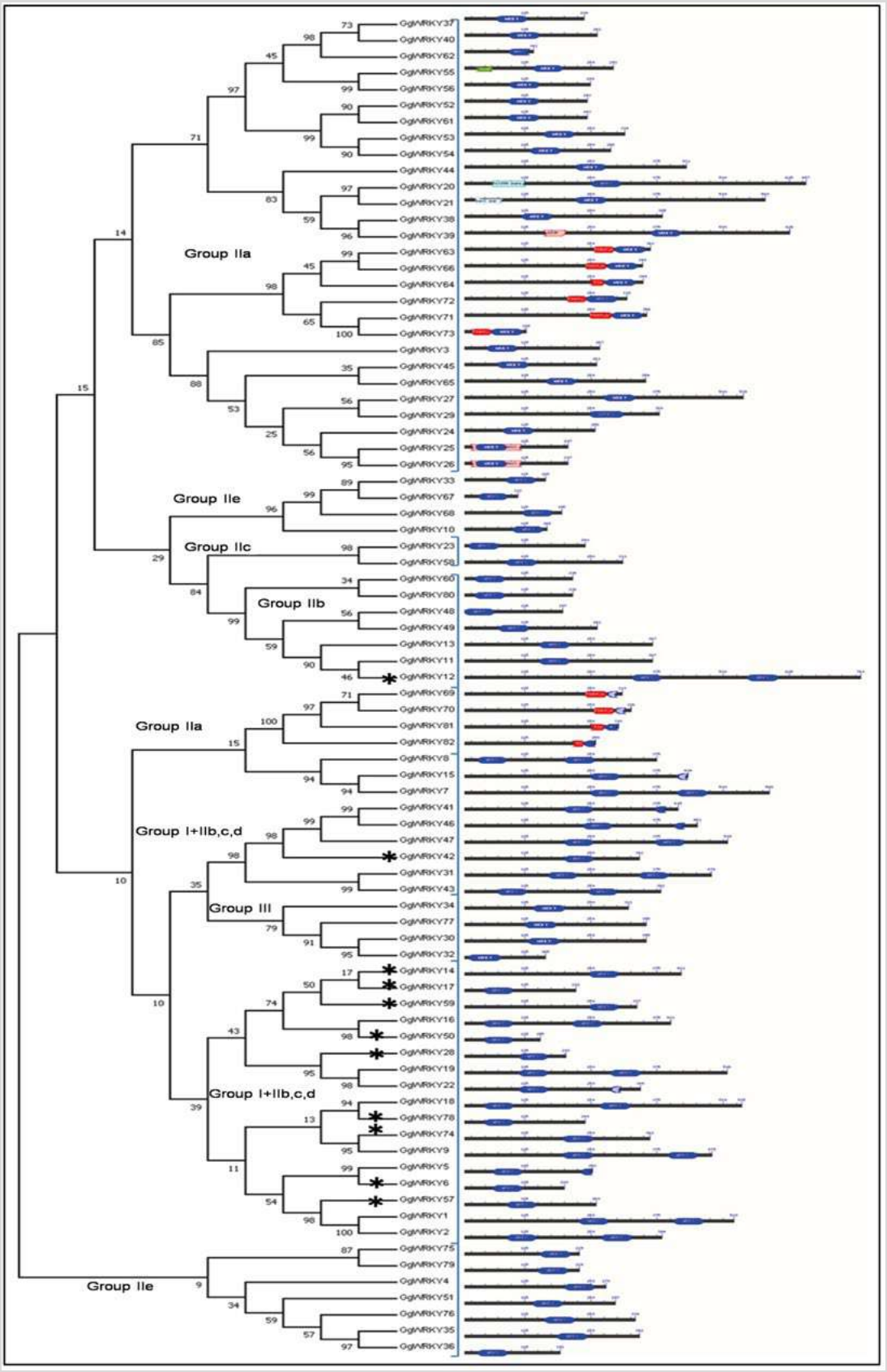
Further, the transiently expressed recombinant protein, in *Nicotiana bethamiana*, was purified and confirmed by western blot analysis. This is the first report of cloning and characterization of squalene epoxidase gene from *Glycyrrhiza* species (Fig 3.8.2B,C). Since it is a key regulatory gene in terpenoid and sterol biosynthetic pathways, the study will have significance in understanding the largely unknown regulation of glycyrrhizin biosynthesis, accumulation and cross-talk between other related pathways of *Glycyrrhiza* plant.

3.9 A Comprehensive Transcriptome-Wide Identification of WRKY Gene Family from *Glycyrrhiza glabra*

Pooja Goyal, Malik Muzafar Manzoor, Ajai P Gupta, Ram A Vishwakarma & Suphla Gupta

Transcription factors (TFs) are the regulatory proteins that control the related gene expression thereby modulating the pathway(s). The complexity in plant cell organization can be directly related to intricate inter-connections between genes and regulatory network inside the cell. The WRKYs are among the ten largest families of transcription factors (TFs) in higher plants. TFs identified in 17 plant species having varying number of WRKY genes. For example, the WRKY gene members in *Arabidopsis thaliana* and *Oryza sativa* are 88 and 129, respectively (http://plntfdb.bio.uni-potsdam.de/v3.0/). WRKY proteins are characterized by one or two highly conserved WRKY domain (WRKYGQK), with one or two zinc-finger-like motifs which possess the DNA-binding domain that is responsible for the recognition of the W-box sequence, (C/T)TGAC(T/C). Based on these two factors the WRKY proteins have been classified into three main groups (I, II and III). Further, group II is sub-divided into five subgroups (IIa, IIb, IIc, IId, and IIe). Group I has two WRKY domain, while II and III WRKY proteins contain a single WRKY domain. They differ in having different type/pattern of the zinc-finger motif.

Numerous WRKY genes have been cloned and characterized in several plant species. Since the first WRKY identified from *Ipomea batata*, several WRKYs are reported from plants such as *Triticum aestivum, Glycine max*, rice and even, *Dendrobium officinale*, an orchid. Genome-wide identification of WRKY family members has also been reported from *Arabidopsis thaliana*, rice, Cucumis, among various other species of plant. The 60 amino-acid characteristics conserved sequence of WRKY transcription factor (TFs) are most commonly identified by specific hepta-nucleotide signature sequence (WRKYGQK), the W-Box, which binds to the promoter sequence of the target gene(s) modulating its activity. Studies have shown WRKY binding motifs (W-boxes) are present in multiple numbers in WRKY responsive gene promoters. The promoters of 83% genes of the 72 WRKYs in *Arabidopsis* contain at least two perfect W-boxes (TTGACC/T), and 58% had four or more core element sequence (TTGAC). They have been found to regulate several target genes in response to stress and secondary metabolite biosynthesis. However, under normal growth conditions also, WRKY proteins have demonstrated broad-spectrum regulatory role as reported


GglMRKY37
GglMRKY40
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GglMRKY44
GglMRKY20
GglMRKY21
GglMRKY38
GglMRKY39
Group IIa
GglMRKY63
GglMRKY66
GglMRKY64
GglMRKY72
GglMRKY71
GglMRKY73
GglMRKY3
GglMRKY45
GglMRKY65
GglMRKY27
GglMRKY29
GglMRKY24
GglMRKY25
GglMRKY26
GglMRKY33
Group IIe
GglMRKY67
GglMRKY68
GglMRKY10
Group IIc
GglMRKY23
GglMRKY58
GglMRKY60
GglMRKY80
Group IIb
GglMRKY48
GglMRKY49
GglMRKY13
GglMRKY11
GglMRKY12
GglMRKY69
GglMRKY70
GglMRKY81
Group IIa
GglMRKY82
GglMRKY8
GglMRKY15
GglMRKY7
GglMRKY41
GglMRKY46
Group I+IIb,c,d
GglMRKY47
GglMRKY42
GglMRKY31
GglMRKY43
GglMRKY34
Group III
GglMRKY77
GglMRKY30
GglMRKY32
GglMRKY14
GglMRKY17
GglMRKY59
GglMRKY16
GglMRKY50
GglMRKY28
GglMRKY19
GglMRKY22
Group I+IIb,c,d
GglMRKY18
GglMRKY78
GglMRKY74
GglMRKY9
GglMRKY5
GglMRKY6
GglMRKY57
GglMRKY1
GglMRKY2
GglMRKY75
GglMRKY79
Group IIe
GglMRKY4
GglMRKY51
GglMRKY76
GglMRKY35
GglMRKY36

Figure 3.9.1

in morphogenesis and development of trichomes embryo development, senescence, dormancy, plant growth, immunity, systematic acquired resistant and metabolic pathways. Here we have studied transcriptome-wide identification and characterization of WRKY TFs in *G glabra*. We have identified and characterized 87 WRKY genes from *G glabra*, categorized them into different structural groups based on their conserved motif composition and predicted functions. All the identified gene sequences were deposited in public database, NCBI. Subsequently, their expression profiles were investigated under various stress conditions in the aerial tissues of the *in vitro* cultured plant. The study also reports additional motifs DivIVA (GgWRKY20), SerS Superfamily (GgWRKY21), bZIP (GgWRKY39) and Coat family motifs (GgWRKY55) in 16 GgWRKY proteins. Nine GgWRKYs63,64, GgWRKY66, GgWRKYs69-73, and GgWRKY86, had Plant Zn cluster super-family domain ranging between 26 aa to 40aa residues (Fig 3.9.1). Based on sequence alignment and phylogenesis, the study identified a new subgroup-IIf, having novel zinc finger pattern (C-X_4-CX_{22}-HXH) and GgWRKY62 with different Zn finger pattern (C-X_5-C-X_{13}-HN) (Fig 3.9.1). The study identified auxin-responsive GgWRKYs55 & GgWRKY38, GA_3 responsive GgWRKYs15&59 in roots and GgWRKYs8,20,38,57 &58 in the shoots of treated plant. Several GgWRKYs were identified to be involved in various stresses like cold (GgWRKY33), senescence (GgWRKY4), salinity (GgWRKYs2, 28 & 33) and wounding (GgWRKY40). Overall, 23 GgWRKYs responded to abiotic stress and 17 were induced by hormonal signals, while 13 WRKYs responded to both suggesting inter-connection between hormone signaling and stress response (Fig 3.9.2). The present study will help in understanding the transcriptional reprogramming, protein-protein interaction and cross-regulation during stress and other physiological processes in the plant.

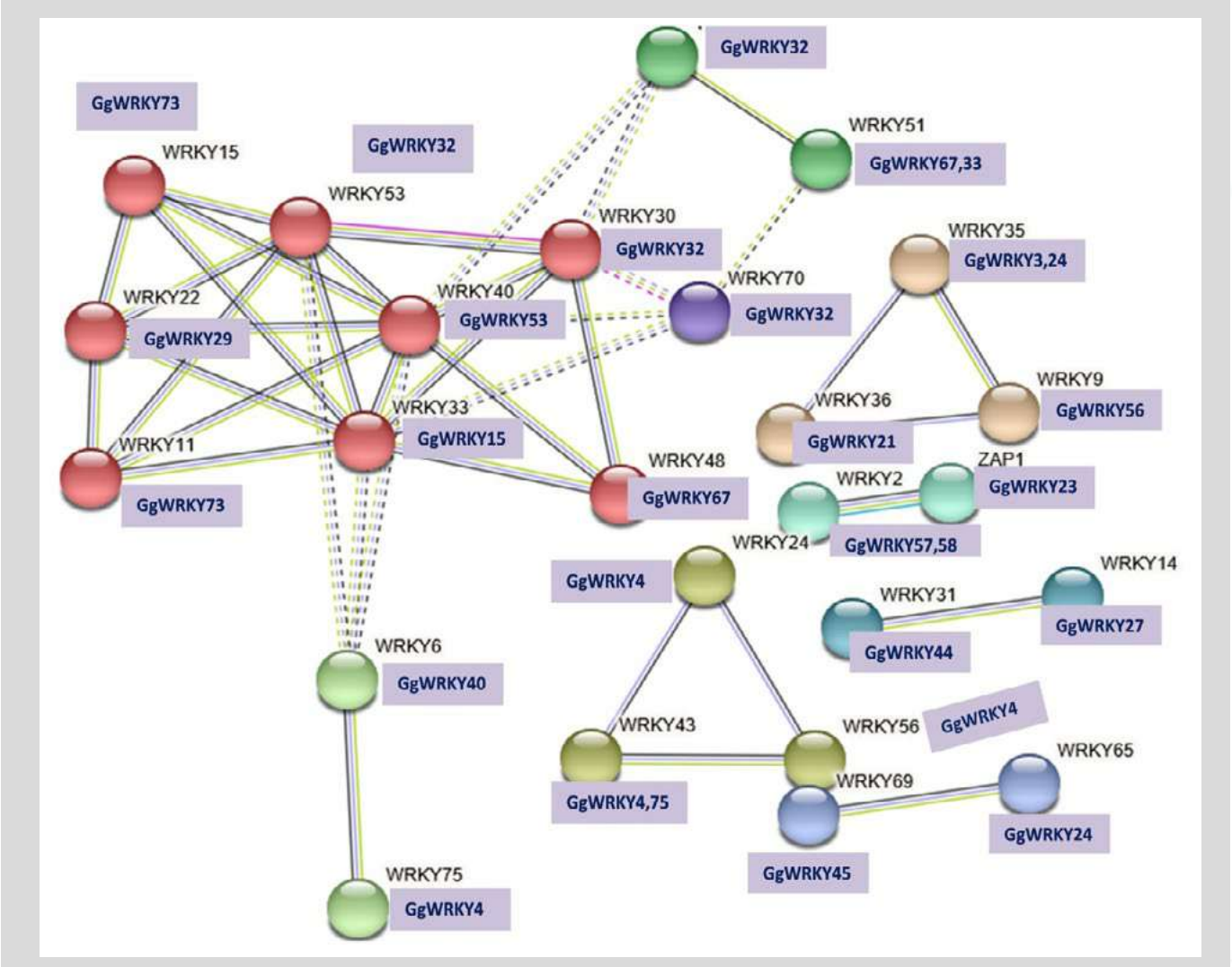


Figure 3.9.2.

3.10 Establishment of DNA Barcodes and tissue culture regeneration protocol for mass multiplication of *Crepedium acuminatum*

Yadunandan Sen, Vijay Lakshmi Jamwal, Natish Kumar, Sumeet Gairola, Rekha Sapru Dhar and Sumit G. Gandhi

Crepedium acuminatum D. Don (Orchidaceae), a terrestrial orchid species, commonly called as 'Rishbhak'. It is known for its therapeutic importance as its dried pseudobulbs are an important ingredient of 'Ashtavarga' (a group of eight drugs, namely *Jivak, Rishbhak, Mahameda, Meda, Kakoli, Kshirkakoli, Ridhi* and *Bridhi*) drugs used in the preparation of an ayurvedic medicine 'Chyavanprash' which is one of the most widely used Ayurvedic preparations for promoting human health and preventing disease. *Crepedium acuminatum* is small, medium-sized orchid, up to 30 cm in height, with pseudo-bulbs at the base, and fibrous roots. The plant was earlier also known as *Malaxis acuminata*. In India, it dwells in the Himalayan, Khasia and Jaintia, and peninsular (Western Ghats, Nilgiris) hills on the mainland and Andaman hills offshore. This medicinally important orchid is faced with extensive collections and habitat destruction pressures which far exceeds its natural regeneration. As a result the species has become rare in its natural habitats. Tissue culture provides an alternate method for large scale propagation of threatened and endangered plants, including orchid micropropagation using various explants. Murashige and Skoog medium supplemented with thidiazuron (TDZ) induced shoot induction from protocorms (Fig 3.10.1 a-c). Shoot multiplication and elongation was observed on Knudson C orchid medium (Fig 3.10.1 d-f) and rooting was found on MS supplemented with IAA. Further, DNA Barcoding of authentic samples was also carried out using the four standard plant DNA Barcoding markers (h). The DNA Barcodes were sequenced and the obtained sequences were clustered with homologous sequences from closely related species (i). The DNA Barcodes will help to assist in correct identification of plants at any stage or in any form.

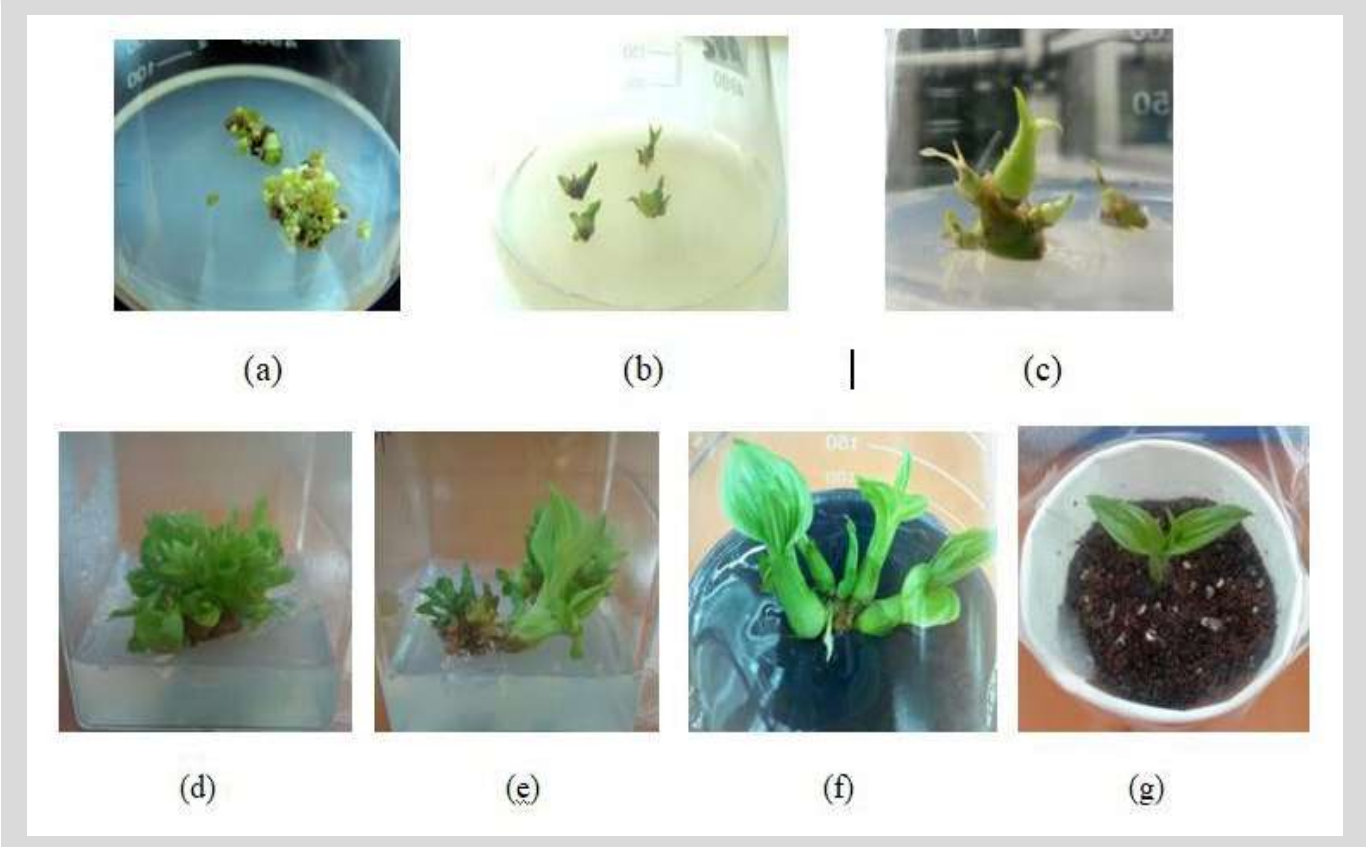


Figure 3.10.1 (a-c) Induction and regeneration of protocorms, (d-e) shoot multiplication and elongation, (f-g) rooting and hardening

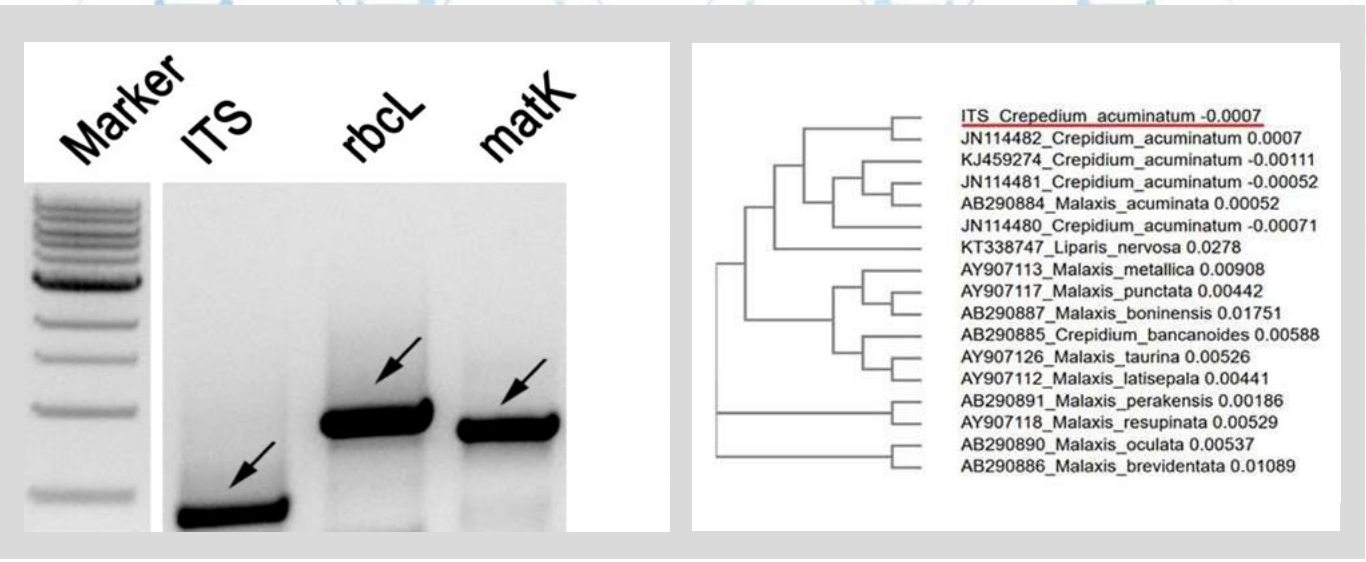


Figure 3.10.1. (h) **Figure 3.10.1. (i)**

3.11 Development of in vitro shoot induction and multiplication protocol for *Colebrookea oppositifolia* Smith

Yadunandan Sen, SR Meena, Rekha Sapru Dhar and Sumit G. Gandhi

Colebrookea oppositifolia Smith is a monotypic genus of Lamiaceae (Labiatae) mostly distributed in the hilly parts of India and also found in Burma, Bhutan, China, Nepal, Myanmar and Thailand. *Colebrookea* is a densely woolly shrub growing up to 1-3 m tall commonly known as Indian Squirrel Tail (English), Binda (Hindi), Pansara (Bengali). In folk medicine, the roots are used for epilepsy and the leaves are applied for wounds and bruises. Some other traditional uses are: the decoction of its roots is given as an abortifacient; the juice of the leaves is used to stop bleeding and as an eye and ear drop; and the paste of the leaves is applied to toothaches and mouth and tongue sores. Different extracts of this shrub are reported to exhibit antibacterial, antimyco -bacterial, antioxidant, and antifertility activities. *Colebrookea* seeds have poor germination and the plant also grows slowly. Tissue culture technique can overcome this problem and there are no reports available in the literature concerning tissue culture of *Colebrookea*. Therefore, our aim is to develop *in vitro* protocol for its optimum growth. Different media with different combinations of growth hormones were tried. MS basal medium supplemented with 6-Benzyl aminopurine (BAP) at optimum concentration induced shoot induction from nodal segments (Fig 3.11.1a) and shoot multiplication was found on MS medium supplemented with BAP and TDZ (Fig 3.11.1b,c). Rooting was observed in MS medium supplemented with IAA (Fig 3.11.1 d).

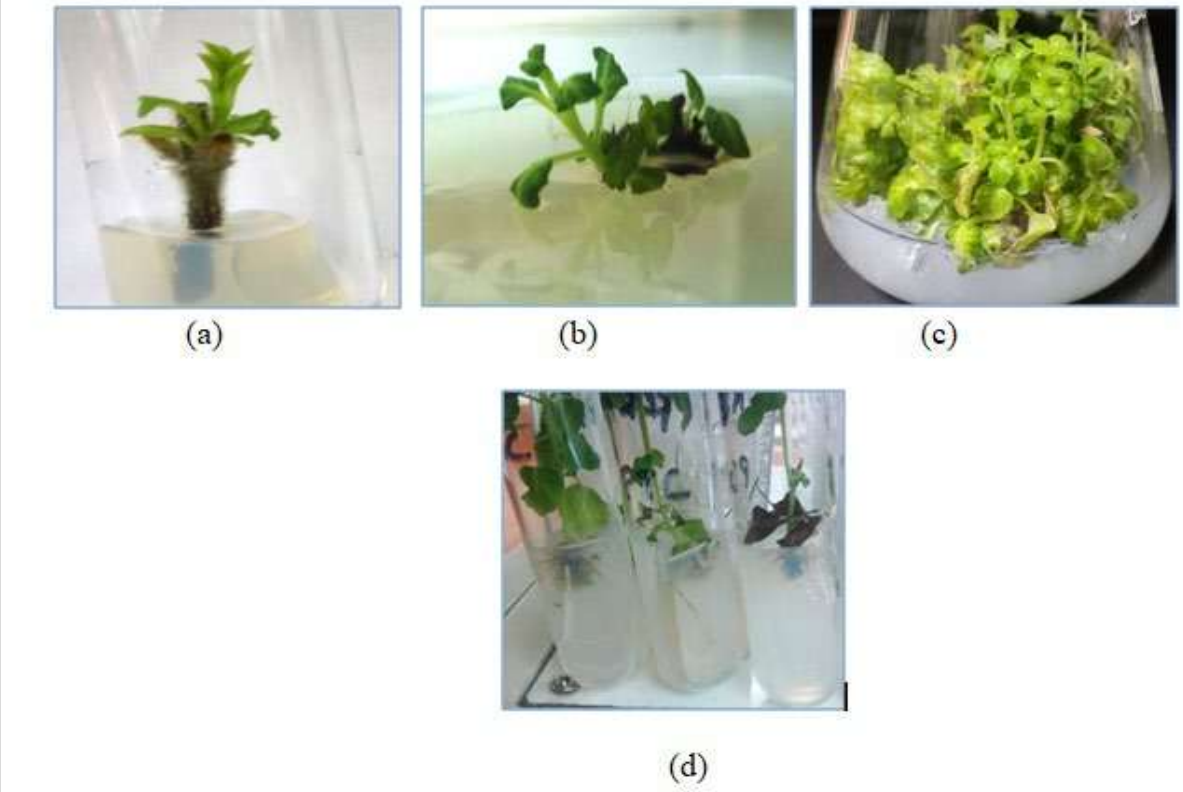


Figure 3.11.1. (a) shoot induction from nodal explants of *C. Oppositifolia*, (b,c) shoot multiplication, (d) rooting

3.12 Establishment of callus culture and development of transformation protocol in *Cannabis sativa*

Rekha Chouhan, Yadunandan Sen, and Sumit G. Gandhi

Cannabis sativa is an annual herb belonging to Cannabinaceae family. The plant, indigenous to eastern Asia, is now distributed worldwide. *Cannabis* was an important component of apothecaries for many uses, particular in the treatment of pain with various causes – muscle and joint pain due to rheumatic illnesses, to migraines and cramp-like pains connected with menses. More recently, the possible applications of cannabinoids in inflammation, diabetes, cancer, affective and neurodegenerative diseases have been worked on. However due to its abuse as a narcotic, the therapeutic potencies of *Cannabis* were neglected. At present, attempts have been made to differentiate between the intoxicating and medicinal effects more clearly. The well-known psychotropic effects of D9- tetrahydrocannabinol (THC) mediated by activation of brain CB1 receptors, have greatly restricted its clinical use. However, the plant *Cannabis* contains many cannabinoids with weak or no psychoactivity while therapeutically they might be more promising than THC. It includes mainly the cannabidiol (CBD) component of *Cannabis*. In an effort to raise plants or cell lines with significantly higher CBD:THC ratio, so far we have established callus culture and suspension culture protocols and have carried out *Agrobacterium tumefaciens* mediated transformation in *C. sativa* cell lines.

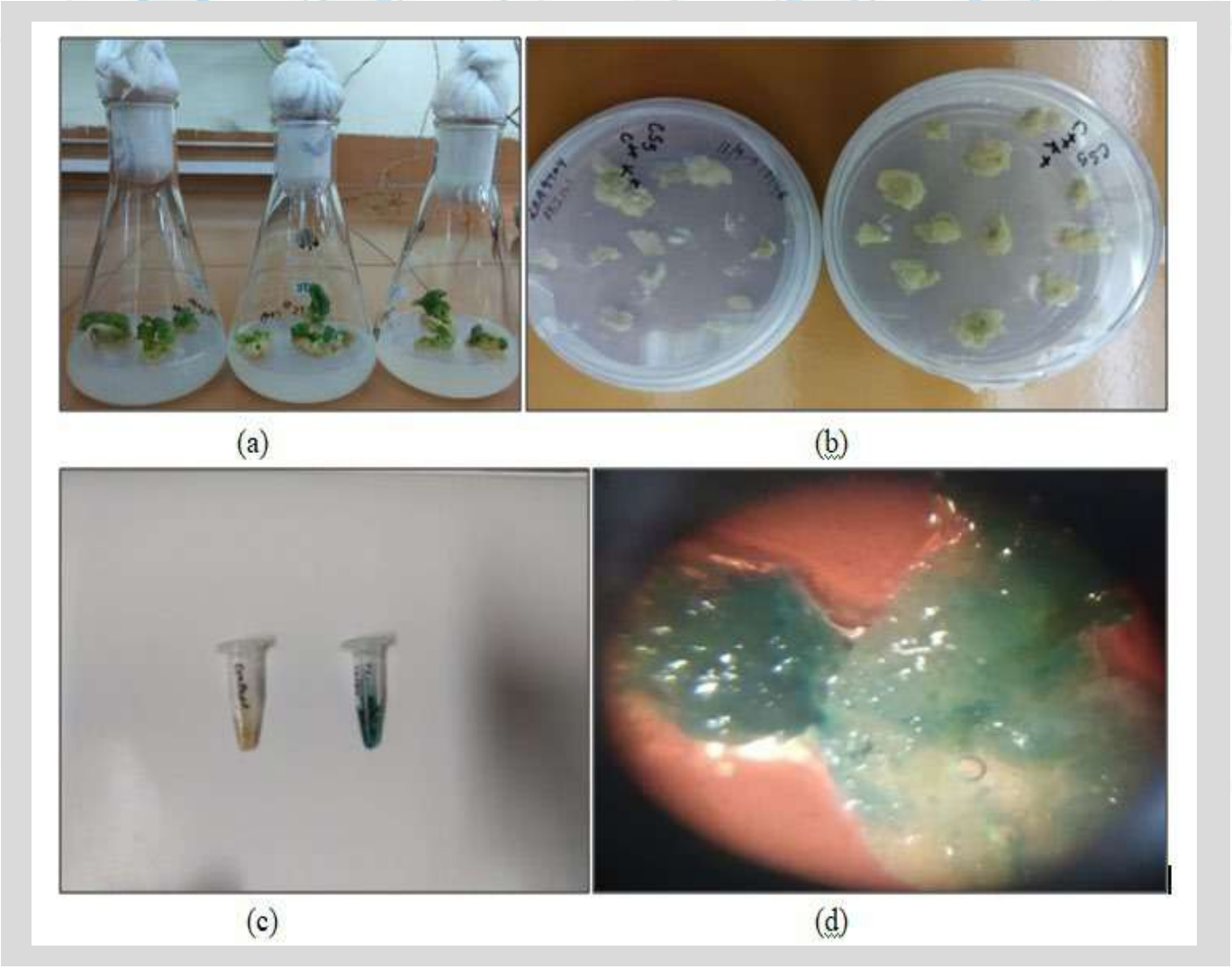
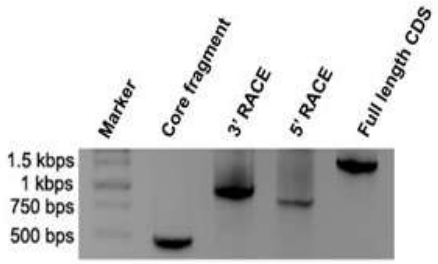


Figure 3.12.1. Transformation of *Cannabis* callus using *Agrobacterium tumefaciens* LBA4404 and confirmation of transformants using GUS staining in control and transformed callus (vector pBI121 carrying GUS expression cassette).

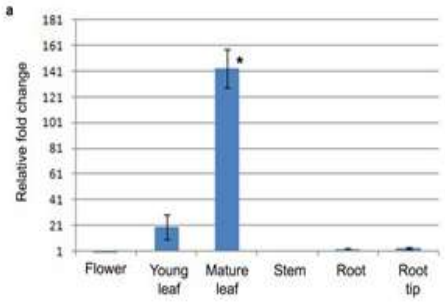
3.13 Characterization of the gene encoding 4-coumarate:CoA ligase in *Coleus forskohlii*

Praveen Awasthi , Vijay Lakshmi Jamwal, Nitika Kapoor, Yashbir S. Bedi and Sumit G. Gandhi

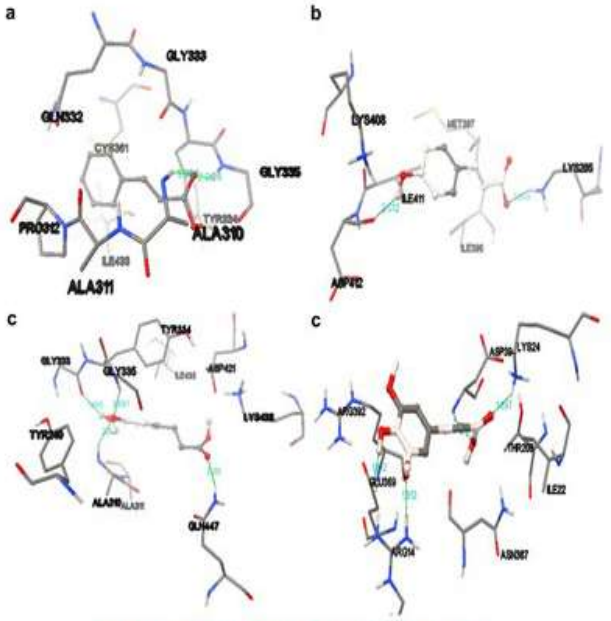
4-coumarate:coenzyme A ligase (4CL) converts 4-coumaric acid and its hydroxylated derivatives into the CoA thiol esters, directing carbon flux into various end-products of phenylpropanoid metabolism, such as flavonoids and lignins. In this study, full-length cDNA showing homology with plant *4CL* genes was cloned from *Coleus forskohlii* and was designated as *Cf4CL* (Accession No. KF643242). *Cf4CL* was found to contain an ORF of 1626 bps. The computational translation of *Cf4CL* encoded a protein of 542 amino acids. Theoretical isoelectric point and molecular weight of Cf4CL were calculated to be 5.55 and 58.77 kDa, respectively. Phylogenetic tree clustered *Cf4CL* with the class I 4CLs (involved in lignin biosynthesis). Spatial distribution of *Cf4CL* in different tissues and its expression in response to various stresses was carried out through qPCR. Abscisic acid (ABA) treatment strongly induced the expression of *Cf4CL*. Homology modeling and docking studies further ascertain the role of *Cf4CL* gene in lignin biosynthesis. *In silico* prediction suggested that that *Cf4CL* may be post-transcriptionally regulated by microRNAs. Decreased expression of miR1886 in response to ABA treatment was associated with an increase in *Cf4CL* transcripts and lignin content, thus suggesting a possible role of miR1886 in regulating lignin biosynthesis in *C. forskohlii*.



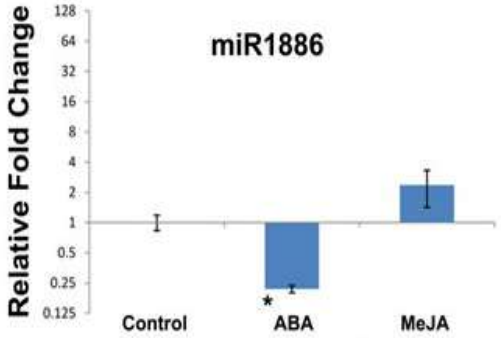
Full length Cloning of 4CL



Expression Analysis of 4CL



Homology modeling and docking of 4CL

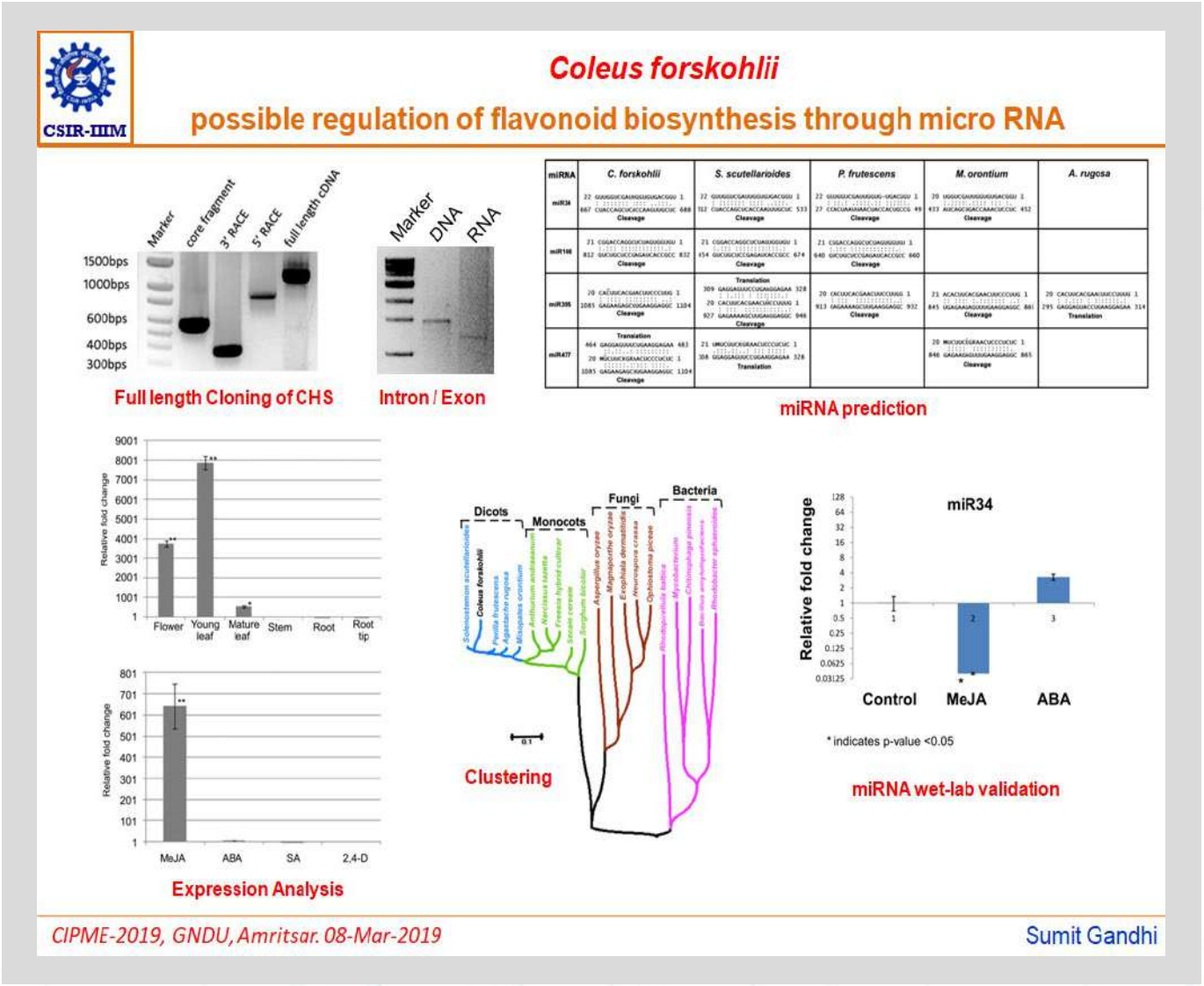


miRNA expression analysis

3.14 Cloning and Expression analysis of chalcone synthase gene from *Coleus forskohlii*

Praveen Awasthi, Vijay Lakshmi Jamwal, Vidushi Mahajan, Nitika Kapoor, Yashbir S. Bedi and Sumit G. Gandhi

Flavonoids are an important class of secondary metabolites that play various roles in plants such as mediating defense, floral pigmentation and plant-microbe interaction. Flavonoids are also known to posses antioxidant and antimicrobial activities. *Coleus forskohlii* (Willd.) Briq. (Lamiaceae) is an important medicinal herb with a diverse metabolic profile, including production of a flavonoid, genkwanin. However, components of the flavonoid pathway have not yet been studied in this plant. Chalcone synthase (CHS) catalyses the first committed step of flavonoid biosynthetic pathway. Full length cDNA, showing homology with plant chalcone synthase gene, was isolated from leaves of *Coleus forskohlii* and named *CfCHS* (GenBank accession no. KF643243). Theoretical translation of *CfCHS* nucleotide sequence shows that it encodes a protein of 392 amino acids having molecular weight 45.28 kDa and pI 5.36. Expression analysis of *CfCHS* in different tissues and elicitor treatments showed that methyl jasmonate (MeJA) strongly induced its expression. Total flavonoids content and antioxidant activity of *C. forskohlii* also got enhanced in response to MeJA, which correlated with increased *CfCHS* expression. Induction of *CfCHS* by MeJA suggests its involvement in production of flavonoids providing protection from microbes during herbivory or mechanical wounding. Further, our *in silico* predictions and experimental data suggested that *CfCHS* may be post transcriptionally regulated by miR34.



3.15 Development of micropropagation protocol of *Swertia chirata* through nodal explant

Yadunandan Sen, Natish Kumar, Manju Sambyal, Rekha Sapru Dhar and Sumit G. Gandhi

Swertia chirata a medicinal herb belongs to Gentianaceae family and commonly known as chirayita in India. It is distributed in the temperate region of Himalayas from Kashmir to Bhutan. *S. chirata* is used for a range of health ailments including liver disorders, malaria, gastrointestinal infections and diabetes. The extracts prepared from the plants consist of a variety of bioactive phytochemicals that have been unswervingly used for various health benefits such as amarogentin, mangiferin, xanthones and iridoid glycosides. *S. chirata* has been designated as critically endangered plant, due to the excessive exploitation through over- harvesting, for habitat, etc. Conventional approaches of germplasm preservation cannot give assurance for the reestablishment and recovery of this critically endangered plant species in their natural habitat. Thus, the application of alternative reproducible micropropagation strategies through plant biotechnological methods has become inevitable for the germplasm preservation and sustainable utilization of this age-old medicinal plant. Different media with different combinations of growth hormones were tried. MS basal medium supplemented with 6-Benzyl aminopurine (BAP) at optimum concentration induced shoot induction and shoot multiplication (Fig 3.15.1 a-b). Rooting was observed in MS medium supplemented with IAA (Fig 3.15.1 c-d). Hardening was done on vermiculite and soilrite in the ratio 1:1(Fig 3.15.1 e).

Figure 3.15.1.

4.1 Molecular modeling studies for developing an in silico protocol for the identification of MurA inhibitors

Harshita Tiwari, Amit Nargotra, Diksha Raina, Inshad Ali Khan

In continuation to our earlier work on MurA, ligand based and structure based models were developed for screening the compound repository against this target. As shown in figure 4.1.1, MurA exists in open and closed forms, based on the conformation of the surface loop (Pro112-Pro121 *E. coli* numbering).

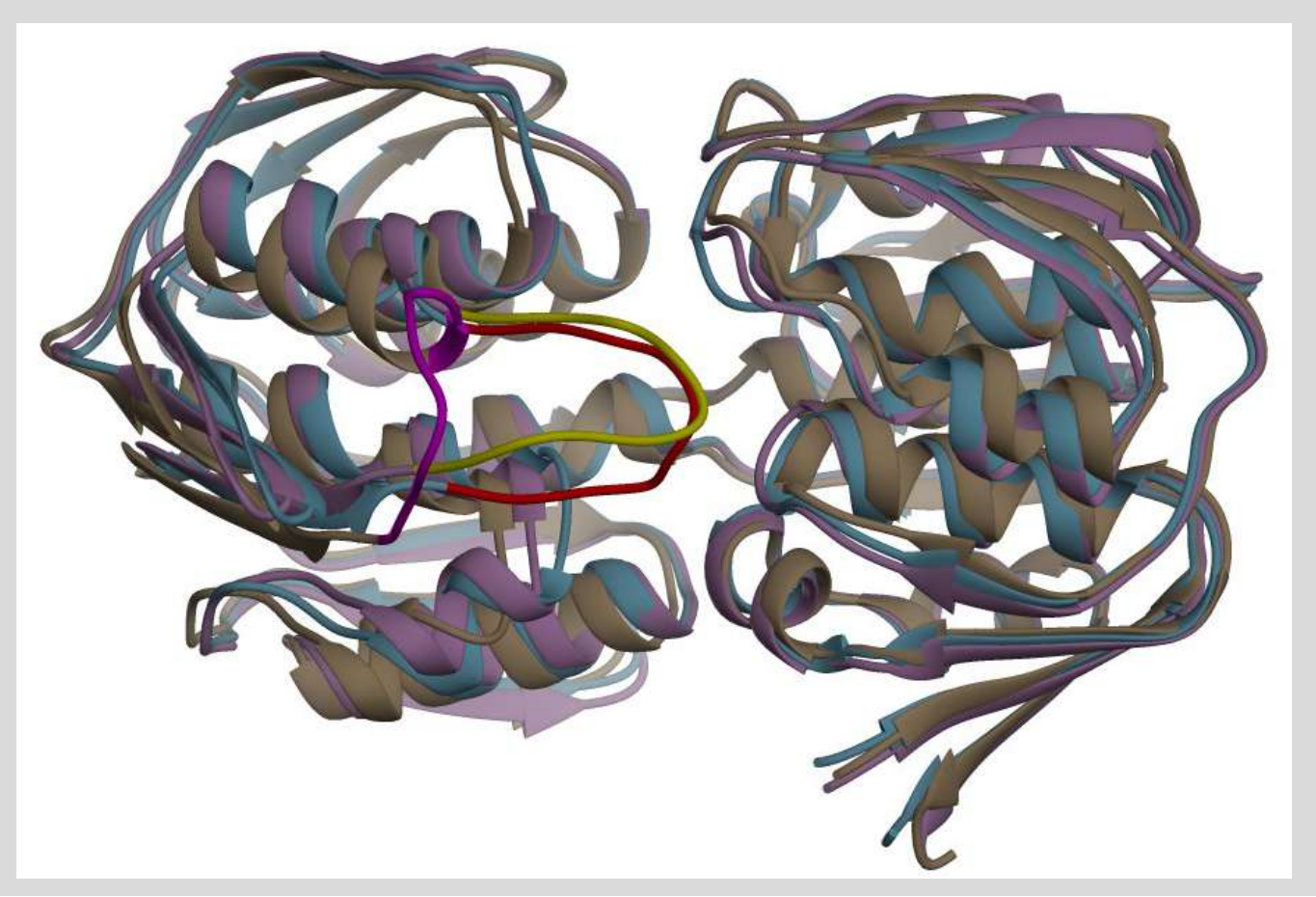


Figure 4.1.1. 3-D structure of MurA depicting the changing conformation of the surface loop.

Both the open and closed conformation of the enzyme was taken into consideration while developing the structure based models. Following strategies were adopted based on the literature report of the target:

I. Ligand based

- Pharmacophore and 3-D QSAR model development
- Similarity search with most active inhibitor at the threshold of >0.5 ChemAxon

II. Structure based

- Covalent docking and Induced Fit docking model based on the inhibitors acting on closed conformation of enzyme.
- SP docking (Glide module) based on the inhibitors acting on open conformation of enzyme.

Three hits were identified after wet lab validation studies of the same. Further work on the elucidation of the mode of inhibition of several in-house MurA inhibitors is under process.

4.2 Development and regular updation of Sickle Cell database

Rakhi Talwar, Harshita Tiwari, Manas Ranjan, Amit Nargotra, Ram Vishwakarma

This database has been developed to provide comprehensive information useful for the management of sickle cell disease and can be utilized by researchers to get information about different aspect of disease at one platform. The database is being updated regularly.

Statistically, the database had comprehensive information related to:

- 32 Therapeutic targets.
- 158 Plants used in the management of disease.
- 295 clinical trials collected from https://clinicaltrials.gov/ site.
- Publications since 2008 and news related to Sickle Cell Anaemia.

The database has been updated with the following information:

1. Two new fields have been added to the database which provide information related to:
    - The details about the new potential plants viz. Sea buckthorn and cabbage. (Figure 4.2.2).
    - The clinical trials related to sickle cell anaemia taking place in India collected from Clinical Trials Registry- India (CTRI).
2. Detailed information about plants such family, synonyms, phytoconstituents and related references have been added (figure 4.2.3).
3. New Publications and news related to Sickle Cell Anaemia were also added.

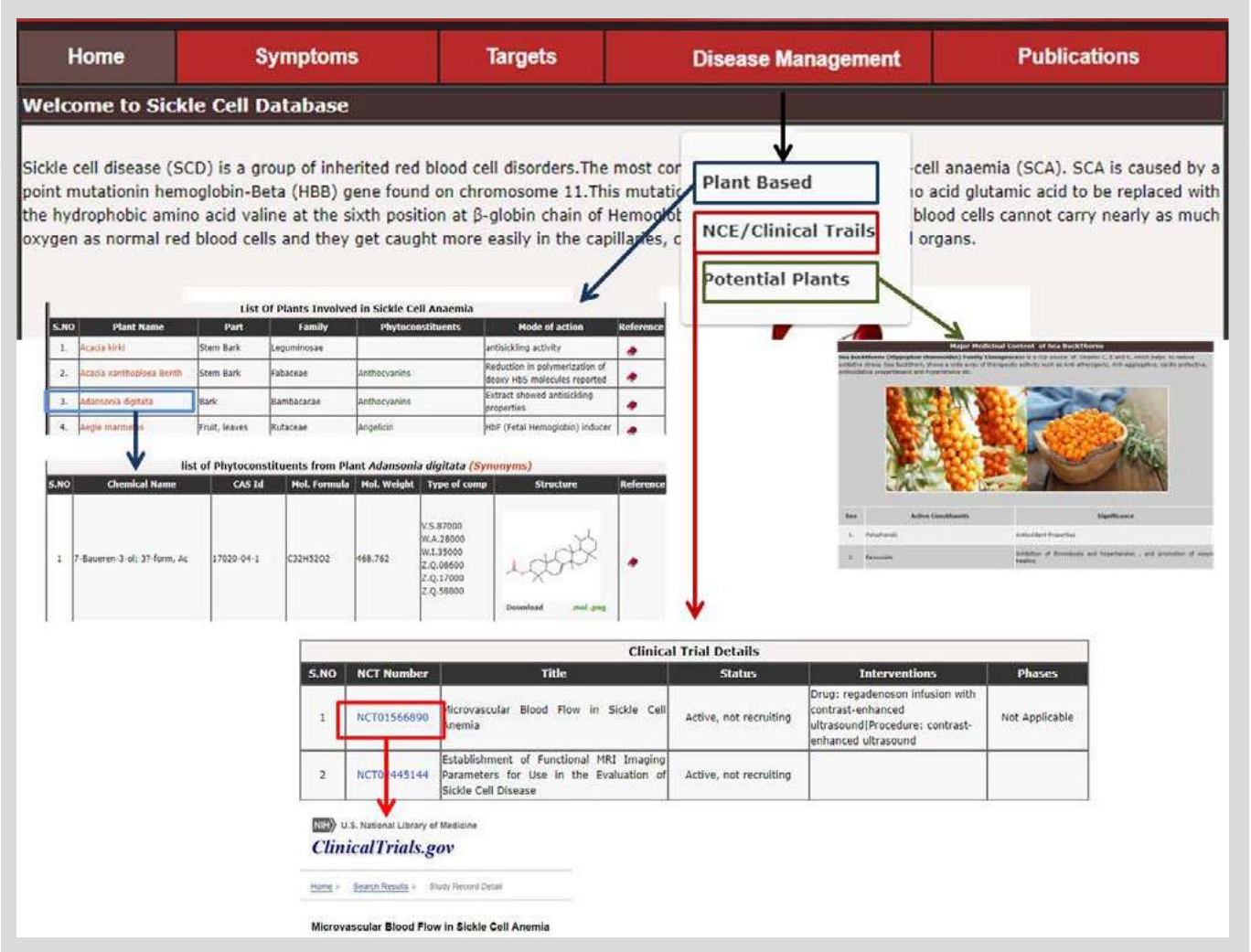
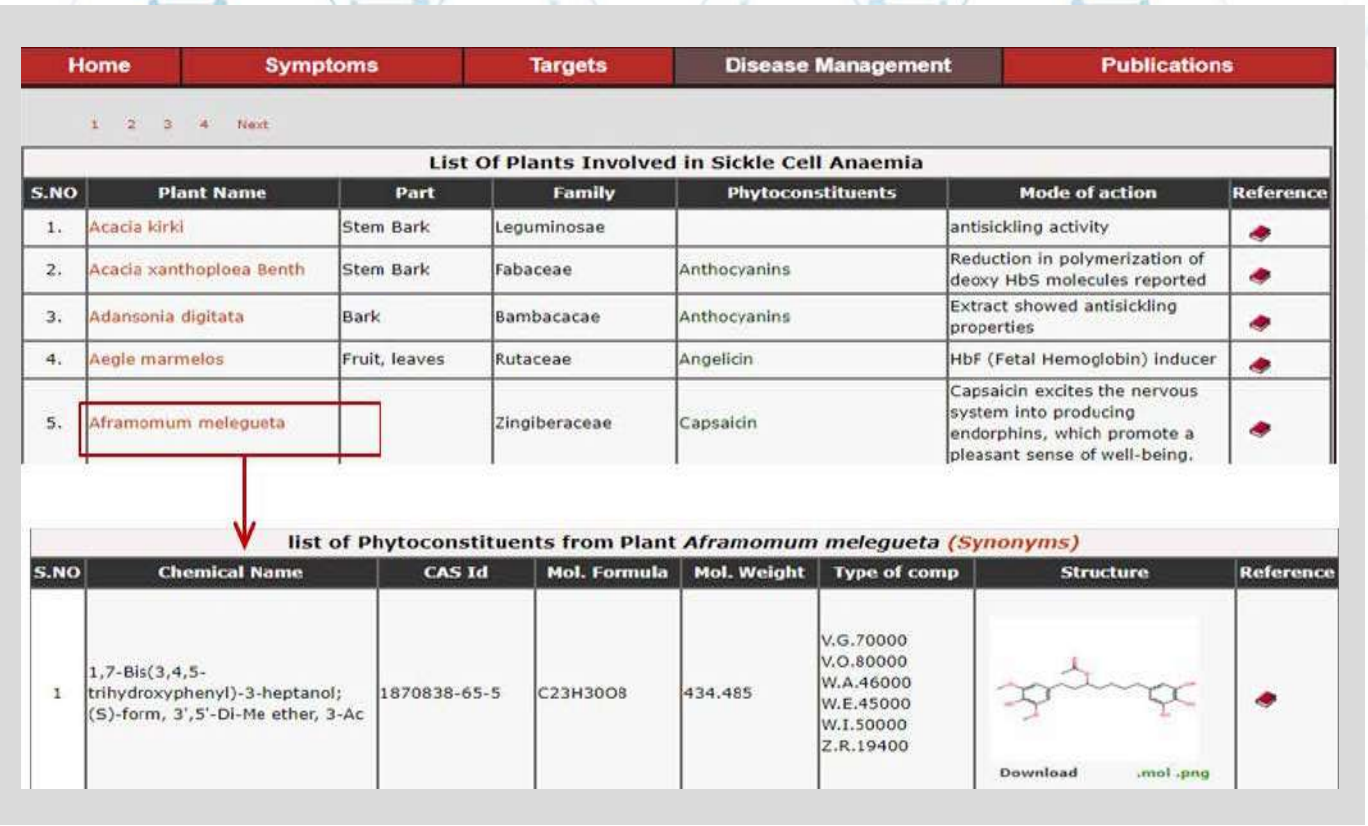


Figure 4.2.2. Potential plants tab under the Disease management Tab



Home | Symptoms | Targets | Disease Management | Publications

1 2 3 4 Next

List Of Plants Involved in Sickle Cell Anaemia

S.NO	Plant Name	Part	Family	Phytoconstituents	Mode of action	Reference
1.	Acacia kirki	Stem Bark	Leguminosae		antisickling activity	
2.	Acacia xanthoploea Benth	Stem Bark	Fabaceae	Anthocyanins	Reduction in polymerization of deoxy HbS molecules reported	
3.	Adansonia digitata	Bark	Bambacacae	Anthocyanins	Extract showed antisickling properties	
4.	Aegle marmelos	Fruit, leaves	Rutaceae	Angelicin	HbF (Fetal Hemoglobin) inducer	
5.	Aframomum melegueta		Zingiberaceae	Capsaicin	Capsaicin excites the nervous system into producing endorphins, which promote a pleasant sense of well-being.	

list of Phytoconstituents from Plant *Aframomum melegueta* (Synonyms)

S.NO	Chemical Name	CAS Id	Mol. Formula	Mol. Weight	Type of comp	Structure	Reference
1	1,7-Bis(3,4,5-trihydroxyphenyl)-3-heptanol; (S)-form, 3',5'-Di-Me ether, 3-Ac	1870838-65-5	C23H30O8	434.485	V.G.70000 V.O.80000 W.A.46000 W.E.45000 W.I.50000 Z.R.19400	Download .mol .png	

Figure 4.2.3. Tab showing detailed description of phytoconstituents of plants used in the management of Sickle Cell Anaemia

4.3 Insilico studies towards the management of sickle cell anaemia

Harshita Tiwari, Amit Nargotra

There are several approaches reported to manage Sickle Cell Anaemia (SCA) such as fetal haemoglobin induction (HbF, inhibits the polymerization of sickle haemoglobin), anti-polymerization of sickled RBCs and reduction of oxidative stress etc. In the present study, we attempted to contribute towards the management of SCA through in silico approach. A library of about 90,000 compounds comprising of procured drug like molecules and in-house library of natural and synthetic compounds, was screened for potential lead molecules for the treatment of SCA by using a combination of ligand based and structure based molecular modeling approaches. Following were the objectives of the study:

- To identify anti-sickling compounds by similarity search at Threshold of 0.6 Tanimoto similarities with reported anti-sickling compounds.
- Target based screening for selected targets (PDE9A, HDAC, HMT and DNMT) involved in SCA by similarity search at Threshold of 0.5 Tanimoto similarity.
- To identify compounds this can inhibit polymerization of HbS by targeting hemoglobin subunit α with in-silico molecular modeling studies.

A total of 343 compounds were identified based on similarity search with 37 known anti-sickling compounds, and were submitted for biological evaluation. Three compounds showed potent anti-sickling properties in-vitro assays. Further, 192, 200, 215 and 255 compounds were obtained from the repository for DNMT, HDAC, PDE9A and HMT respectively. These compounds have been submitted for their biological evaluation. Besides, in continuation to our earlier work on the target based studies on HbS, 192 compounds have been identified from the repository, and have to be submitted for biological evaluation.

4.4 Development of CSIR-Phytopharmaceutical mission portal

Monika Gupta, Manas Ranjan, Rakhi Talwar, Harshita Tiwari, Amit Nargotra, Inshad Khan, Ram Vishwakarma

A comprehensive Phytopharmaceutical mission portal have been developed which contains the entire mission project details at one place defining its objectives and participants roles. In addition to this, it also helps in keeping track of the progress of the project by capturing several activity indicators. It also contains the database of the compound repository and the extract repository of the Phytopharma mission. Besides, it contains all the presentations made and minutes of meetings during the project tenure. This database has been developed based on the Phytopharmaceutical mission project document. All the verticals, as well as the respective objectives of each participating Institute have been mapped. Activities under each vertical, as well as each plant have been mapped to the respective Institute. The regular updating of the database is carried out based on the work done by each Institute, which thereby, helps in monitoring the overall progress of the project i) Plant wise, ii) Institute wise and iii) Vertical wise.

The main page of the Institute contains the following tabs/information (as shown in figure 4.4.1:

i. About the Mission
ii. Vertical wise details of the project
iii. Activities assigned and carried out
iv. Mission progress
v. Compound repository details along with structures, CoA and purity profile.
vi. GMP extracts submission details along with report.
vii. Meeting details and minutes of each meeting.
viii. All the presentations in password protected pdf.

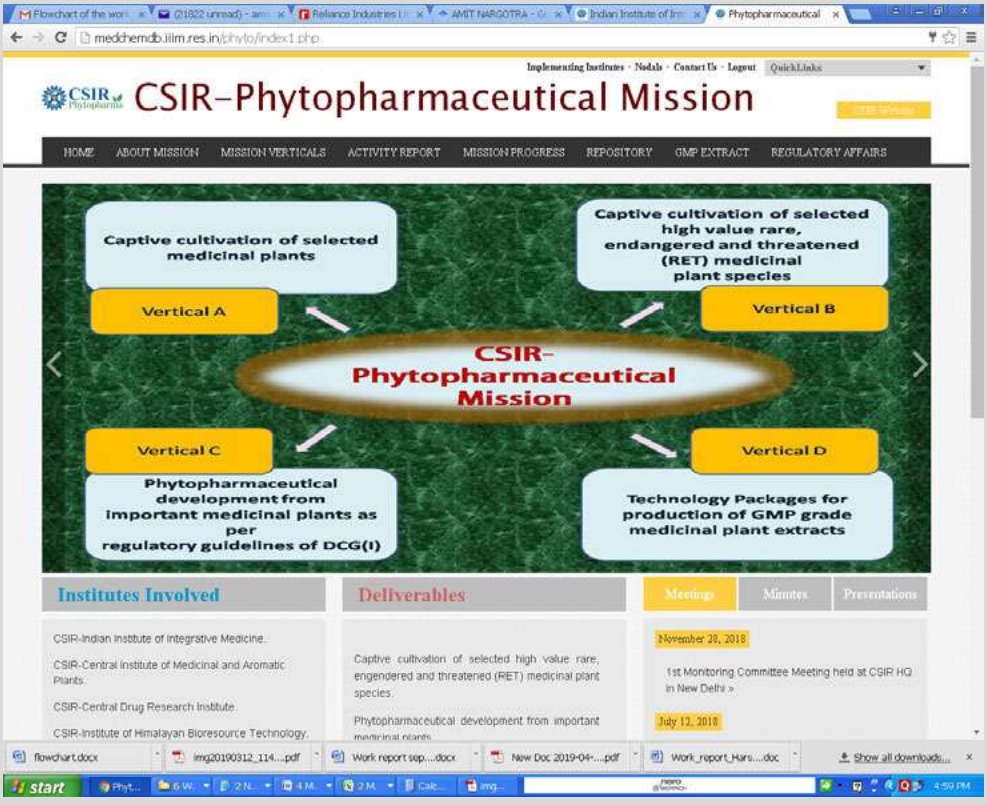


Figure 4.4.1. Home page of the CSIR-Phytopharmaceutical mission portal.

A separate compound repository is being made for the compounds submitted from the plants selected in the Phytopharmaceutical mission. Apart from the sub structural search database of this repository, the entire information about the compounds is also maintained in the Phytopharmaceutical mission portal also. Each compound submitted is tagged with a repository code, and the tab provides details about the code, structure, compound name, internal code, plant name, Institute, scientist name, CoA and purity data of each compound (as shown in figure 4.4.2). The same is accessible to all the participants with a password protection.

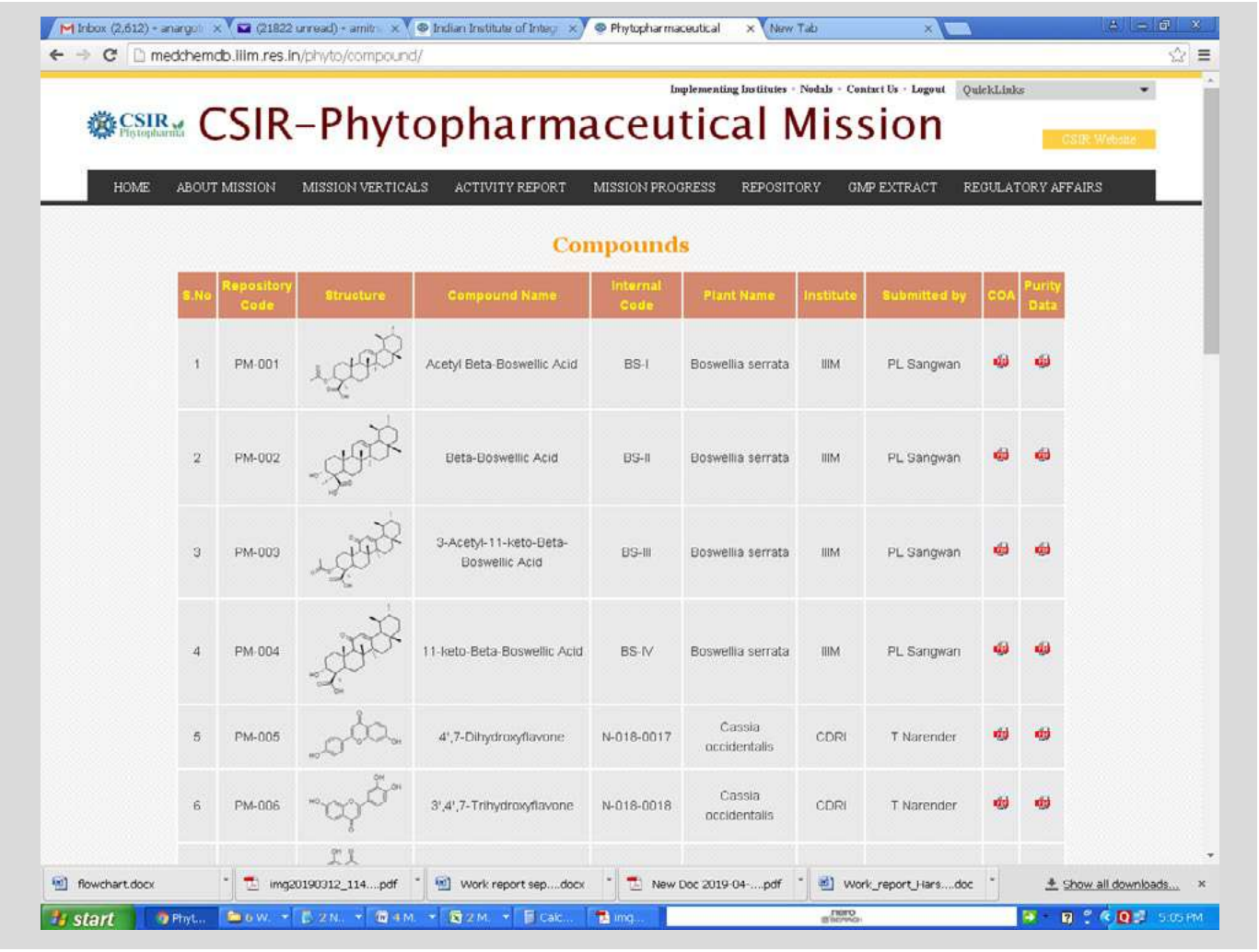


Figure 4.4.2. Snapshot of the repository page which provides information about the compounds submitted in the phytopharmaceutical mission repository.

4.5 Updation of Stem cell database (MedchemDB)

Rakhi Talwar, Monika Gupta, Amit Nargotra, Ram Vishwakarma.

Regular updation and enrichment of the stem cell portal was carried out. During the reported period crystal structure information of 9 structures were added and 4 new scaffolds were also added to the database. The portal is accessible over Internet at http://medchemdb.iiim.res.in/

4.6 Repository database updation and compound flow management

Monika Gupta, Amit Kumar, Amit Nargotra, Naresh Satti, Ram Vishwakarma

Updation of Institutional compound repository, which comprise of the Institutional pure natural compounds, new chemical entities as an outcome of all medchem projects and the externally procured library of drug like compounds. A total of 5 Natural Products and 23 new chemical entities from the med chem projects have been added in the reporting period to the repository along with the HPLC/HPTLC profile. All these compounds are also incorporated into the database for sub-structural search. This year a total of 785 compounds were issued for biological evaluation through this repository within and outside the Institute. The outcome of the compound repository from the discovery programs at IIIM is shown in figure 4.6.1.

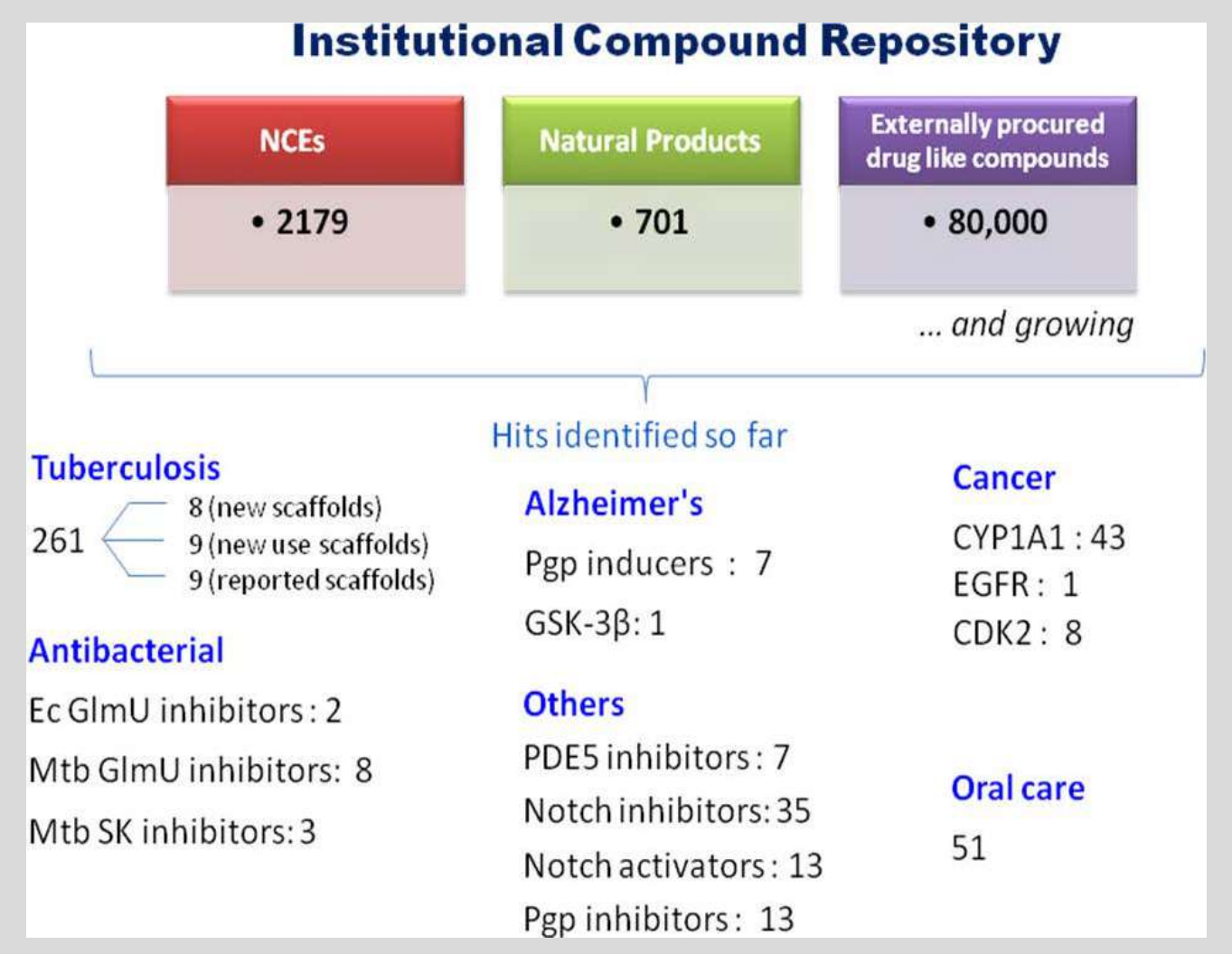


Figure 4.6.1. Discovery outcome of the Institutional compound repository

5.1 Chemical Investigation of Natural Products from *Psoralea corylifolia*

Nidhi Gupta, Arun Raina and P. L. Sangwan

Psoralea corylifolia (Leguminosae) is a well-known medicinal herb commonly known as Babchi or Bakuchi. It is a weed of winter season distributed all over the India in Himalayas, Uthrakhand, West-Bengal, Karnatka, Rajasthan, Punjab and U. P. It is also distributed in China and South-africa. The plant has been traditionally used in ayurvedic and chinese system of medicine as antihelmintic, antibacterial, antitumour, immunomodulatory, anti-inflammatory, antifungal and anti-oxidant. It is mainly used to treat various skin disorders such as leprosy, vitiligo, leukoderma and is also given the name 'Kushtanashini". *Psoralea corylifolia* seeds are used since ancient times because of their large medicinal value. *Psoralea corylifolia* (Leguminosae) is a medicinal plant which has been traditionally used in Ayurvedic and Chinese system of medicine and different extracts are reported for antihelmintic, antibacterial, antitumour, immunomodulatory, anti-inflammatory, antifungal and anti-oxidant activities. It is mainly used to treat various skin disorders such as leprosy, vitiligo, leukoderma and is also given the name "Kushtanashini". Meroterpenes (bakuchiol, 2,3-epoxybakuchiol), flavanoids (bavachin, bavachinin), coumarins (psoralen, isopsoralen), lipids (mono-, di- and tri-glycerides), resins and volatile oils (limonene, linalool) are some important bioactive constituents of the plant. In this section, isolation and characterization of 14 secondary metabolites (**1-14**) of different classes i.e. meroterpenes (**1**, **7** and **14**), coumarins (**2**, **3** and **9**) and flavanoids (**4-6**, **8** and **10-13**) (figure 5.1.1 is described. The structural elucidation of all the isolated compounds was performed by NMR, IR and HRESIMS. The isolated compounds were evaluated for *in-vitro* cytotoxic activity against four different human cancer cell lines: A549 (Lung), MCF-7 (Breast), HCT-116 (Colon) and PC-3 (Prostate). Different secondary metabolites exhibited potent anticancer activity. More significantly, compounds **5** and **9-14** displayed IC_{50} < 20μM against different cancer cell lines. Compound **13** (bavachin) was found as most potent natural product having IC_{50} < 5μM against all the examined cancer cell lines.

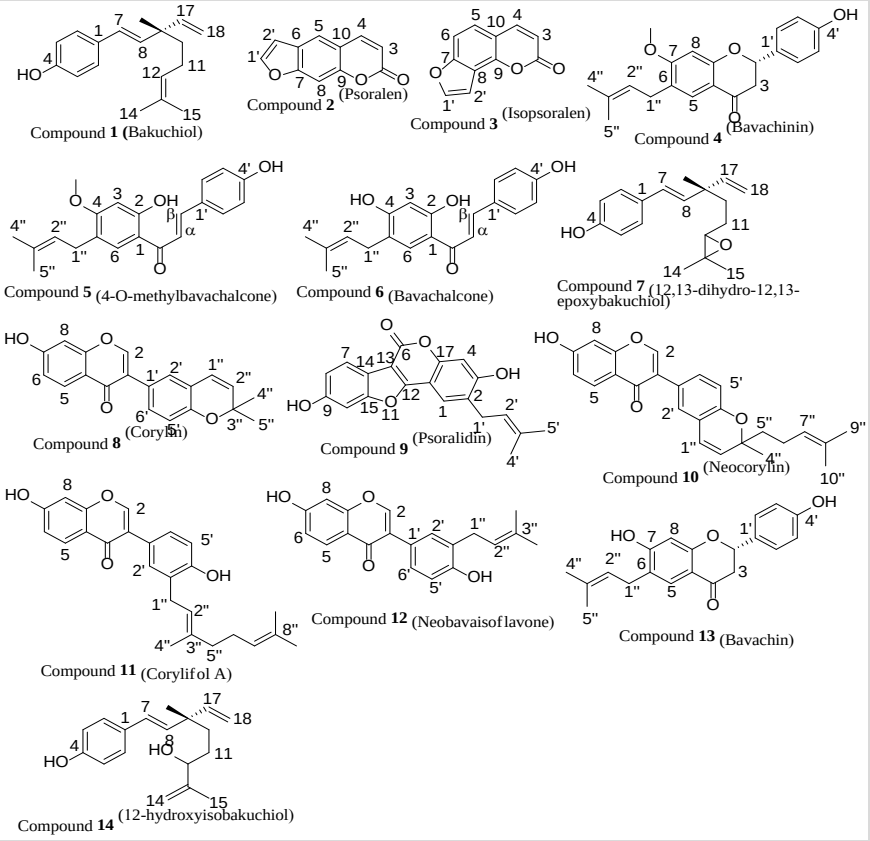


Figure 5.1.1. Natural products isolated from *Psoralea corylifolia*

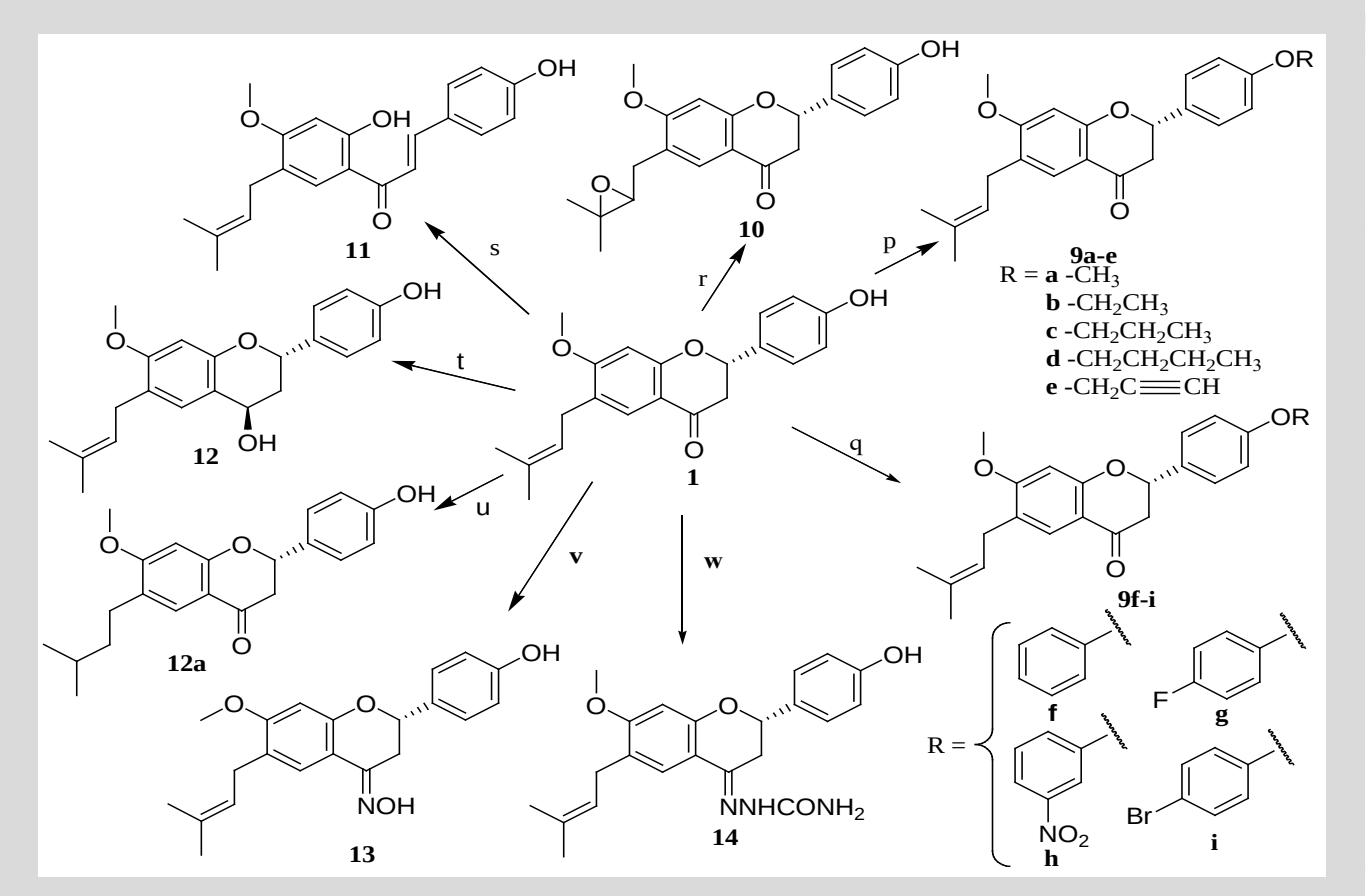
5.2 Synthesis and biological evaluation of novel bavachinin analogs as anticancer agents

Nidhi Gupta, Arem Qayum, Arun Raina, Ravi Shankar, Sumeet Gairola, Shashank Singh, and P. L. Sangwan

Flavanoids are one of largest classes of polyphenolic compounds that occur naturally in plants which possess broad spectrum of biological activities and are considered as suitable therapeutic agents against cancer. They generally possess a phenylbenzopyrone structure (C6-C3-C6) consisting of two aromatic rings, A and B connected by a central pyran ring C. The seeds of *Psoralea corylifolia* are major source of bavachinin and exhibit diverse pharmacological activities including anticancer, PPAR agonist, anti-inflammatory, anti-alzheimer and immune modulatory. Cytotoxic effects of bavachinin have also been studied on various cancer cell lines and possess 20S proteasome inhibitory activity that inhibits the signaling action of NFκB leading to cell death *via* apoptosis.

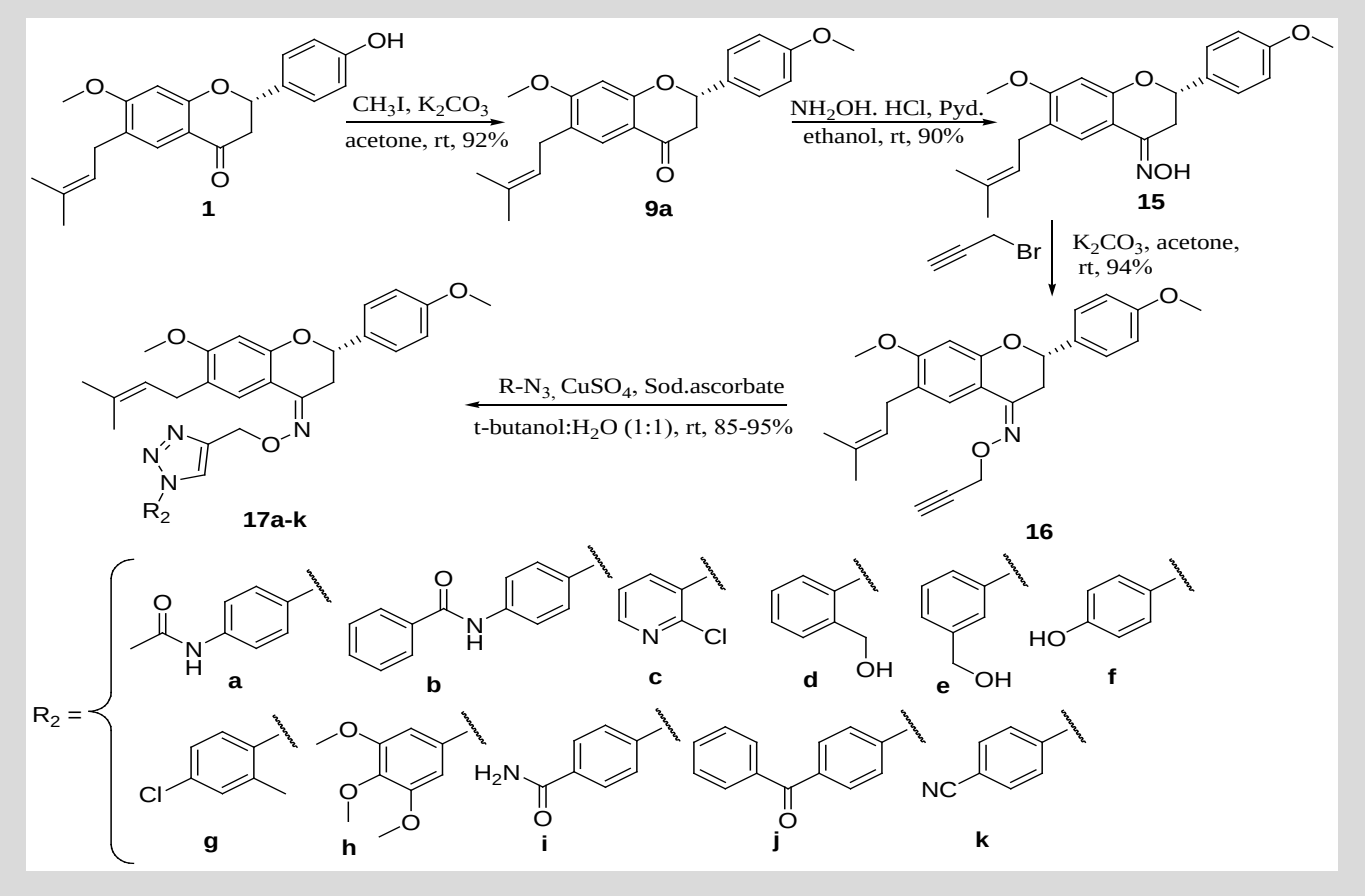
Bavachinin **1** was isolated in gram quantities from the seeds of *P. corylifolia* and was used for structural modification studies. The configuration at C-2 an asymmetric center in the molecule was observed (*S*) based on NOESY which was also confirmed by comparing the observed specific rotation value $[\alpha]_D$ = -20 (c = 1.0, $CHCl_3$) with literature. Different analogs of bavachinin **1** were synthesized with modifications at ring A, B, C and prenyl chain of the molecule as shown in scheme 5.2.1 and 5.2.2. Aliphatic ether analogs of bavachinin (**9a-e**) were synthesized by reacting **1** with appropriate alkyl halides in acetone in the presence of potassium carbonate as base. Analogs **9f-i**, aromatic ethers of bavachinin were synthesized through Chan-Lam coupling by reacting **1** with various aryl boronic acids in DCM in the presence of copper acetate and pyridine. Epoxide analog of bavachinin (**10**) was synthesized by reacting **1** with *m*-chloroperbenzoic acid (*m*-CPBA) in DCM as per earlier report. NOESY spectra are provided in supporting information. Compound **11**, chalcone analog of **1** was obtained by treating it with sodium hydride in ethanol. Compound **12**, carbonyl reduction analog was synthesized by reacting **1** with sodium borohydride ($NaBH_4$) in methanol as per our earlier report and its configuration was found 2*S*,4*R* at C-2 and C-4 position on the basis of 2D NMR (COSY, HSQC and HMBC) experiments including NOESY. Further the configuration was also confirmed through observed specific rotation $[\alpha]_D$ = +19 (c = 1.0, $CHCl_3$) which was found in comparison with literature. Compound **12a**, double bond reduced product was prepared by hydrogenation of bavachinin in presence of 10% Pd/C. Compounds **13** and **14**, oxime and semicarbazide analogs of bavachinin were synthesized by treating **1** with hydroxylamine hydrochloride and semicarbazide hydrochloride respectively in ethanol as solvent.

Bavachinin triazoles were synthesized at oxime moiety to prepare anticancer analogs in the light of literature. For this, methyl ether of bavachinin **9a** was reacted with hydroxylamine hydrochloride to prepare its oxime analog **15**. Compound **15** was reacted with propargyl bromide in acetone in presence of potassium carbonate to furnish compound **16** which was further subjected to Cu (I) catalyzed 1,3-dipolar cycloaddition reaction (click chemistry) using various substituted aromatic azides to provide 1,2,3-triazole derivatives **17a-k** in excellent yields (scheme 5.2.2). To confirm the configuration of C=N double bond in triazole analogs **17a-k**, NOESY experiment of one compound i.e. **17i** was recorded. On interpretation of data, the signal at δ 5.37 ($-OCH_2$) did not show any correlation with either of protons at C-3 ($-CH_2$) that rule out the *E* configuration while the same signal at δ 5.37 ($-OCH_2$) showing weak correlation with aromatic proton singlet at δ 7.63 (H-5) which indicate Z configuration of C=



Scheme 5.2.1. Reagents and conditions: p) R-X (-I, -Br), K_2CO_3, acetone, rt, 2h, 90-94% q) R-$B(OH)_2$, $Cu(OAc)_2$, Pyd., DCM, rt, 2-3h, 85-90% r) *m*-CPBA, DCM, 0°-rt, 2h, 78% s) NaH, ethanol, rt, 0.5h, 90% t) $NaBH_4$, MeOH, 0°- rt, 0.5h, 70% u) Pd/C, MeOH, rt, 2.0h, 80% v) NH_2OH. HCl, ethanol, rt, 1.5h, 85% w) $NH_2CONHNH_2$.HCl, ethanol, rt, 1.5h, 85%

Bio-evaluation studies exhibited better cytotoxic profile for many analogs compare to bavachinin. Best results were observed for a 1,2,3-triazole analog (**17i**) with IC_{50} values 7.72, 16.08, 7.13 and 11.67 µM against lung (A549), prostate (PC-3), colon (HCT-116) and breast (MCF-7) cancer cell lines respectively. This analog showed three and four fold improvement in cytotoxicity against HCT-116 and A549 cell lines than parent molecule (**1**). Structure activity relationship (SAR) study for all synthesized analogs was carried out. Further, mechanistic study of the lead molecule (**17i**) revealed that it inhibits colony formation and *in vitro* migration of human colon cancer cells (HCT-116). Also, it induced the morphological changes and mediated the apoptotic cell death of HCT-116 cells with perturbance in mitochondrial membrane potential (MMP) and PARP cleavage.



Scheme 5.2.2. Synthesis of bavachinin 1,2,3-triazole derivatives (**17a-k**)

5.3 Synthesis of α-santonin derivatives for diminutive effect on T and B-cell proliferation and their structure activity relationships

P. K. Chinthakindi, Jasvinder Singh, Shilpa Gupta, Amit Nargotra, Priya Mahajan, Anupurna Kaul, Zabeer Ahmed, Surrinder Koul, P. L. Sangwan

α-Santonin (**1**) was isolated from the aerial part of *Artemisia laciniata* and used as a starting material for chemical modification at three different reactive sites encompassing ring-A, B, and C of the molecule. The natural product (**1**) was subjected to Thiele reaction (rearrangement) with Ac_2O/H_2SO_4 to get acetyl α-desmotroposantonin (**2**) which on deacetylation afforded α-desmotroposantonin (**3**), the latter on nitration using nickel nitrate (II) hexahydrate in acetone/p-TSA resulted in the formation of 2-nitro α-desmotroposantonin (**4**) (Scheme 1). The presence of nitro group in **4** was confirmed by appearance of IR band at 1557 cm^{-1}, and disappearance of the aromatic proton signal (observed at δ 6.65 in **3**) in ^1H NMR. Observance of $[M^+]$ m/z at 291 in mass spectrum further confirms the structure of **4**. Hydrogenation of **4** with $NiCl_2/NaBH_4$ afforded 2-amino-α-desmotroposantonin (**5**) which showed disappearance of IR band at 1557 cm^{-1} and appearance of band at 3601 cm^{-1} (NH) in IR spectrum, and displayed $[M^+]$ m/z at 262 in the mass spectrum.

5.4 Synthesis of an unusual quinazoline alkaloid: theoretical and experimental investigations of its structural, electronic, molecular and biological properties

Shabir H. Lone, Salman Jameel, Muzzaffar A. Bhat, Rayees A. Lone, Ray J. Butcher and Khursheed A. Bhat

Alkaloids are a very important class of compounds as far as their role in metabolism and activity is concerned. They are among the oldest drugs used for the treatment of diseases and are still used as promising therapeutic agents. Deep sea environments are nowadays the focus of research for discovering newer alkaloids with potential therapeutic activities. New alkaloids are also being produced *via* chemical synthesis and natural product modifications with some of them being more active than the naturally obtained ones. In general alkaloids possess a range of biological activities which include analgesic, antiviral, antimalarial, antineoplastic, antimicrobial, anti-inflammatory, antioxidant antifungal, antibacterial, hemoglobinization agents of human leukemia cells, effects on the CNS, estrogenic effects *etc.* Based on these literature reports of alkaloids and our previous work on the isolation, and synthesis of bioactive compounds, we carried out the synthesis of an unusual self-condensation product of 2-aminobenzaldehyde by a method reported by Seidal and coworkers. In order to get deeper insights in to the molecular, structural and biological properties of the synthesized compound, we resorted to spectral, X-ray and DFT analysis. The experimentally obtained parameters were in close agreement to those obtained theoretically. Molecular electrostatic potential and frontier molecular orbital analysis was performed which permitted the calculation of HOMO–LUMO energy gap and related parameters. Based on PASS results, the molecule was evaluated against four different human cancer cell lines to explore its biological potential. Reduction of 2-nitrobenzaldehyde using iron powder in glacial acetic acid : ethanol : water system (2 : 2 : 1) under ultrasonic irradiation conditions for 1.5 h at 30 °C yielded the corresponding 2-aminobenzaldehyde. Refluxing 2-aminobenzaldehyde in ethanol with pyrrolidine yielded a reaction mixture containing an unusual self-condensation quinazoline alkaloid (**1**) (Fig. 5.4.1).

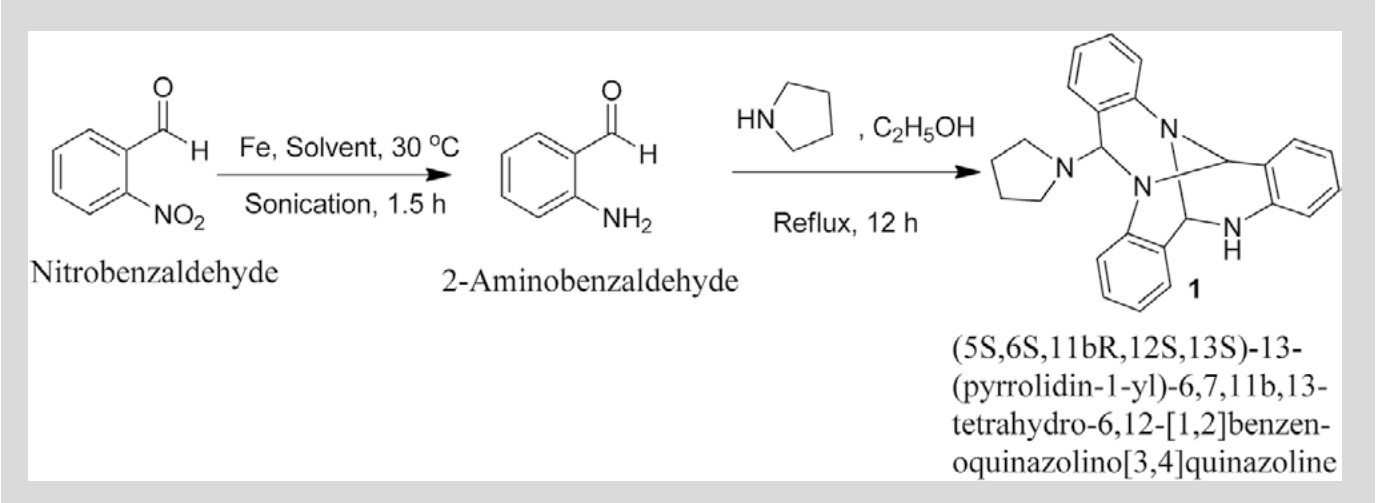


Figure. 5.4.1 Synthesis of an unusual quinazoline alkaloid (**1**).

Pure **1** was obtained when the reaction mixture was subjected to normal phase silica gel column chromatography. Its structure was elucidated while analyzing the spectral data in light of literature. The reaction proceeds *via* a series of nucleophilic additions of basic nitrogen of pyrrolidine ring on the highly electrophilic aldehyde group of 2-aminobenzaldehyde to give an intermediate which again condenses with two molecules of 2-aminobenzaldehyde to yield compound **1** (Fig. 5.4.2). The product was characterized using LC-MS, IR and NMR data analysis. LC-MS depicted m/z at 381 assignable to $[M + H]^+$ corresponding to its molecular formula $C_{25}H_{24}N_4$. H NMR depicted the presence of 12 aromatic protons assignable to three aromatic rings in the molecule whose presence was further supported by the appearance of 18 C signals in the aromatic region of the

molecule. Three downfield ^{1}H NMR singlets at δ 5.96, 5.29 and 4.52 ppm correspond to 3 CH groups present in the molecule which was supported by three carbon NMR resonances at δ 84, 71 and 64 ppm in its DEPT-NMR. Presence of upfield resonances at 51 and 23 ppm on the downside in DEPT NMR were assignable to four CH_2 groups of the pyrrolidine moiety which was supported by upfield resonances corresponding to 8 protons in H NMR.

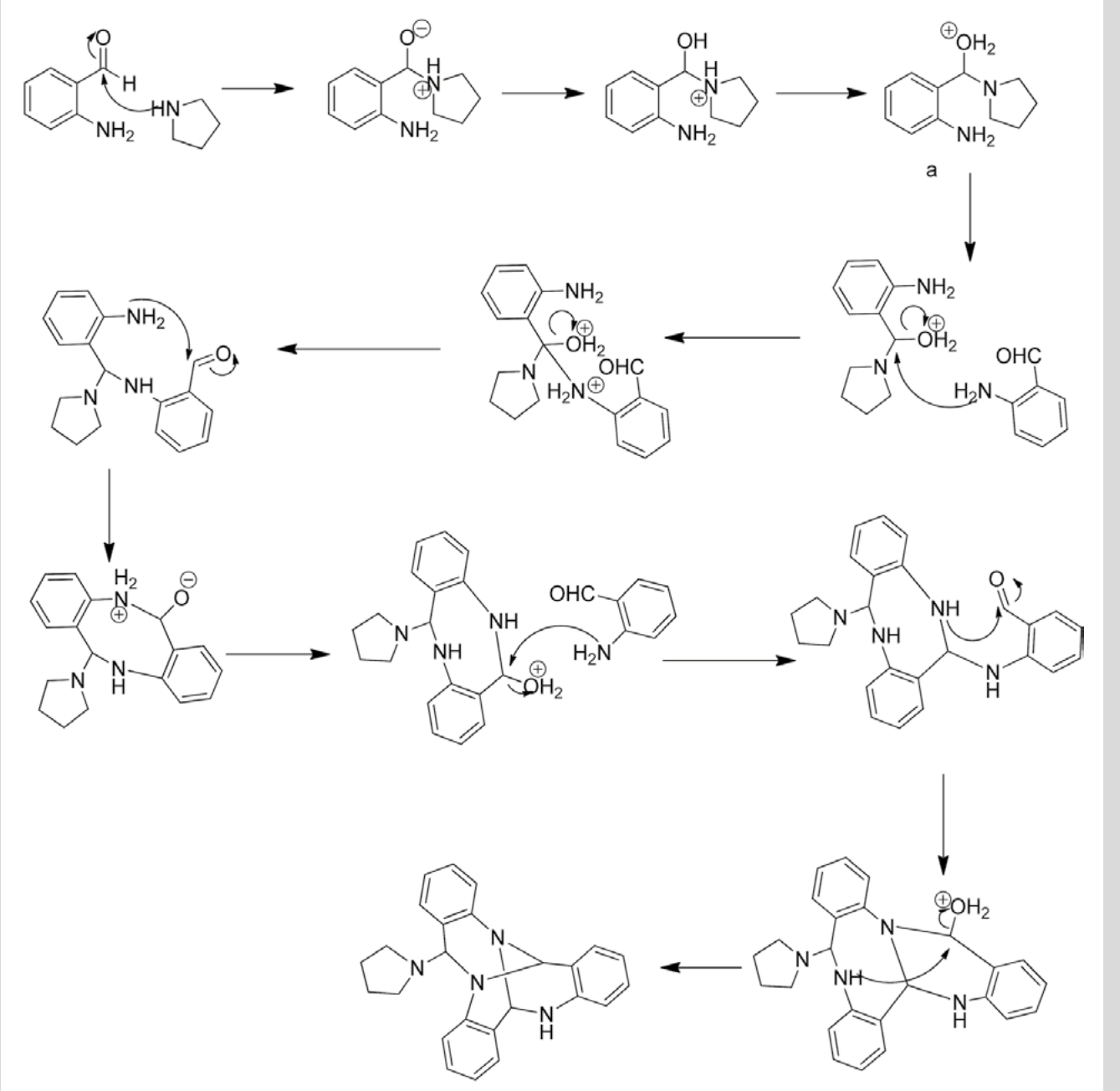


Figure 5.4. 2 Mechanism involved in the formation of quinazoline (**1**).

The actual structure was however arrived at using single crystal X-ray analysis (Fig. 5.4.3). Pure crystals of **1** were obtained by its crystallization from chloroform and ethanol at room temperature. The molecule crystallizes in a triclinic system with *P* $\bar{1}$ space group having 2-units in one unit cell. An X-ray ortep structure of compound **1** depicted four different conformations as shown in (Fig. 5.4.3).

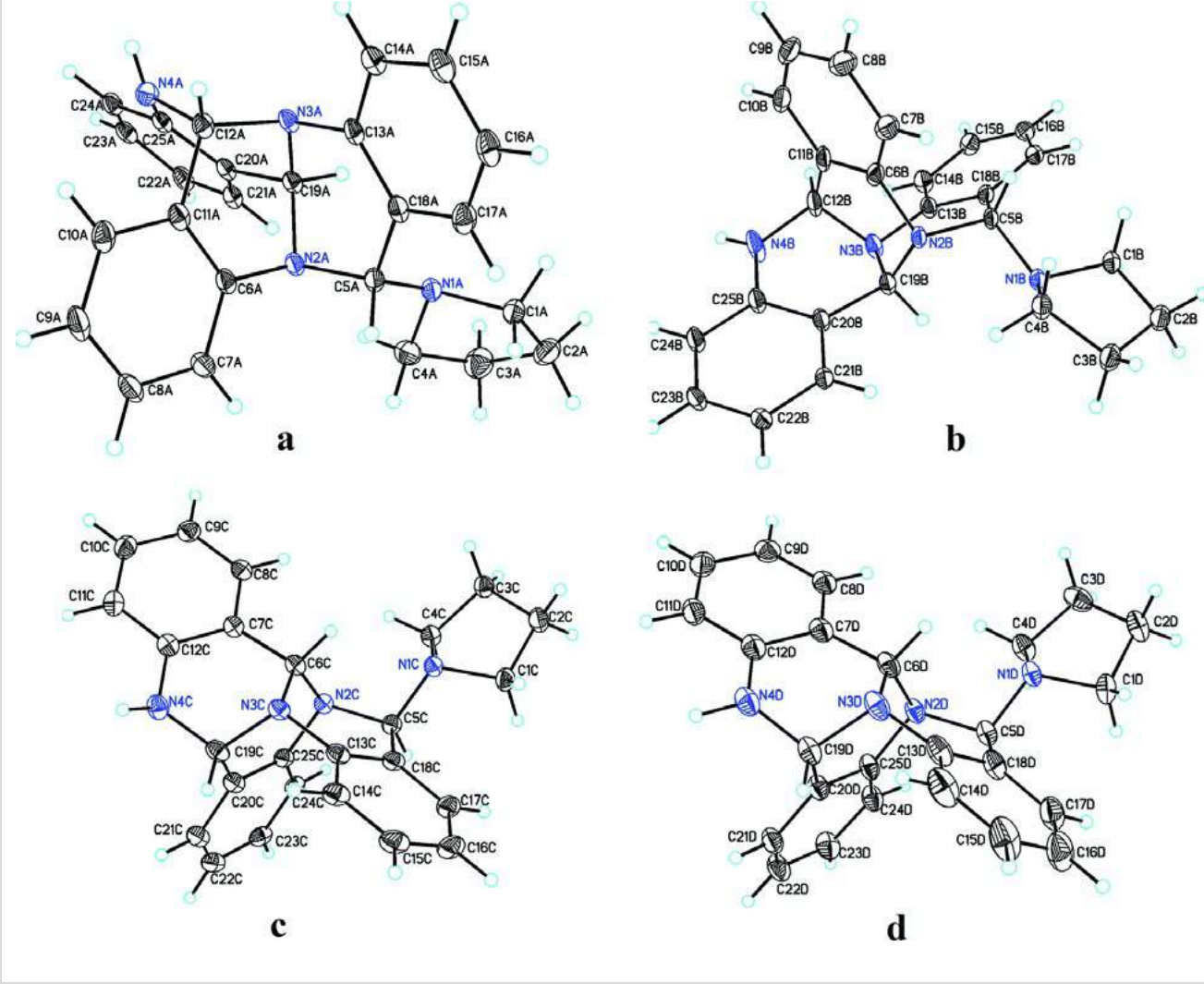


Figure 5.4.3 Four different conformations (**a–d**) of compound **1** as shown by single crystal X-ray analysis.

The crystal refinement of the molecule is shown in Table 5.4.1.

Table 5.4.1 Crystal data and structure refinement of compound **1**

Identification code	Shelx
Empirical formula $C_{101}H_{97}Cl_3N_{16}$	
Formula weight	1641.29
Temperature	153 (2) K
Wavelength	1.54184 Å
Crystal system	Triclinic
Space group	$P\bar{1}$
Unit cell dimensions	a = 12.8967 (4) Å b = 13.9278 (3) Å c = 23.2246 (7) Å
Volume	4093.1 (2) Å^3
Z	2
Density (calculated)	1.332 mg m^{-3}
Absorption coefficient	1.497 mm^{-1}
F(000)	1732
Crystal size	0.345 × 0.275 × 0.233 mm^3
Theta range for data collection	3.492 to 76.684°
Index ranges	$-16 \le h \le 16$, $-11 \le k \le 17$, $-29 \le l \le 28$
Reflections collected	29 828
Independent reflections	16 636 [R(int) = 0.0333]
Completeness to theta = 67.684°	99.8%
Absorption correction	Gaussian
Max. and min. transmission	1.000 and 0.322
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	16 636/12/1111
Goodness-of-fit on F^2	1.045

Table 5.4.2 Comparative analysis of experimentally obtained bond lengths of four conformers with that obtained theoretically (notable ones have been shown, for all refer to ESI file)

Bond	Exp. bond length (Å) of Conf. A	Exp. bond length (Å) of Conf. B	Exp. bond length (Å) of Conf. C	Exp. bond length (Å) of Conf. D	Theo. bond length (Å)
N(4)–H(4)	0.80	0.88	0.86	0.96	1.0138
C(2)–C(3)	1.496	1.531	1.527	1.566	1.5385
C(3)–C(4)	1.518	1.520	1.523	1.485	1.5335
C(6)–C(7)	1.399	1.383	1.511	1.512	1.420
C(11)–C(12)	1.525	1.514	1.399	1.399	1.487
C(21)–C(22)	1.388	1.385	1.377	1.386	1.398

The four conformers have slight variations among bond lengths and bond angles. Only a few significant differences with regard to bond lengths have been mentioned in Table 5.4.2. The characteristic feature of crystal packing view (Fig. 5.4.4) is the hydrogen bonding network in the form of N···H–N, Cl···H–C. The molecules are interconnected by means of these hydrogen bonds. Another interesting hydrogen bond is the one involving Cl···H–C (Table 5.4.3). Since crystallization of the molecule has been carried out in $CHCl_3$: EtOH solvent, it is likely that one of $CHCl_3$ molecule per unit cell has intruded inside during the process of crystallization providing additional stability to the unit cell.

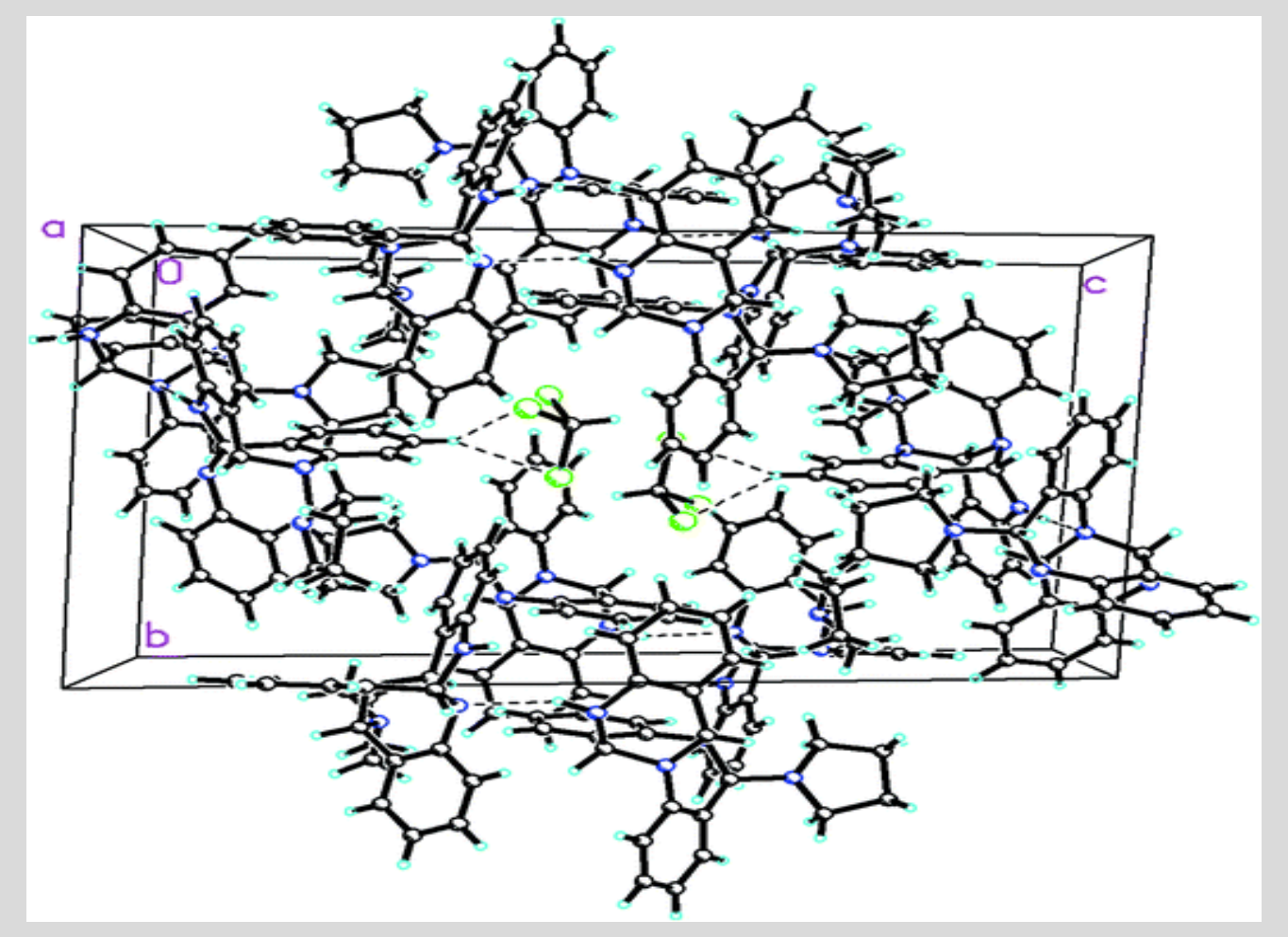


Figure 5.4.4 A perspective view of the crystal packing in the compound **1**.

Table 5.4.3 Hydrogen bonds for compound **1** [Å and °]

D–H···A	*d*(D–H)	*d*(H···A)	*d*(D···A)	∠(DHA)
N(4B)–H(4B)···N(3A)	0.88(5)	2.34(5)	3.143(4)	153(4)
N(4D)–H(4D)···N(3C)	0.96(6)	2.25(6)	3.125(4)	151(4)
C(5D)–H(5DA)···Cl(1T)	1.00	2.96	3.718(7)	133.1

5.5 Microwave-Assisted Synthesis of Andrographolide Analogues as Potent β-Glycosidase Inhibitors

Masood ur Rahman, Iram Ayoob, Shakeel u Rehman, Khursheed A. Bhat

Andrographolide, a bioactive compound isolated from *Andrographis paniculata* exhibits multiple pharmacological activities, in- cluding anti-HIV, antiplatelet aggregation, hepatic lipid peroxidation protective, hepatoprotective, choleretic, and anticancer effects. Herein, we report the synthesis of diverse analogues of andrographolide along with their β-glucosidase inhibitory activity against sweet almond β-glu- cosidase. The parent compound, **And-1**, displayed moderate inhibitory activity against the sweet almond β-glucosidase with IC50 of 142.5 μM. Among the synthesised analogues **And-10** showed the best activity, with IC50 of 92.4 μM, whereas the oxidised products (**And-4** and **And-5**) were moderately active against the tested enzyme. Additionally, com- pounds **And-6**, **And-7**, **And-8**, and **And-10** exhibited better β-glucosi- dase inhibitory activity than the positive control Castanospermine, with IC50 of 100.2, 102.4, 106.5, and 92.4 μM, respectively. These results highlight the importance of an electron-withdrawing NO2 group on the phenyl moiety in attaining the better β-glucosidase inhibition. It is noteworthy that the effect of a particular group plays a significant role in bioactivity. This study thus highlights an important aspect with re- gard to the most active compounds, which could extend the arsenal of compounds affecting the corresponding enzymes after further polish- ing and fine tuning.

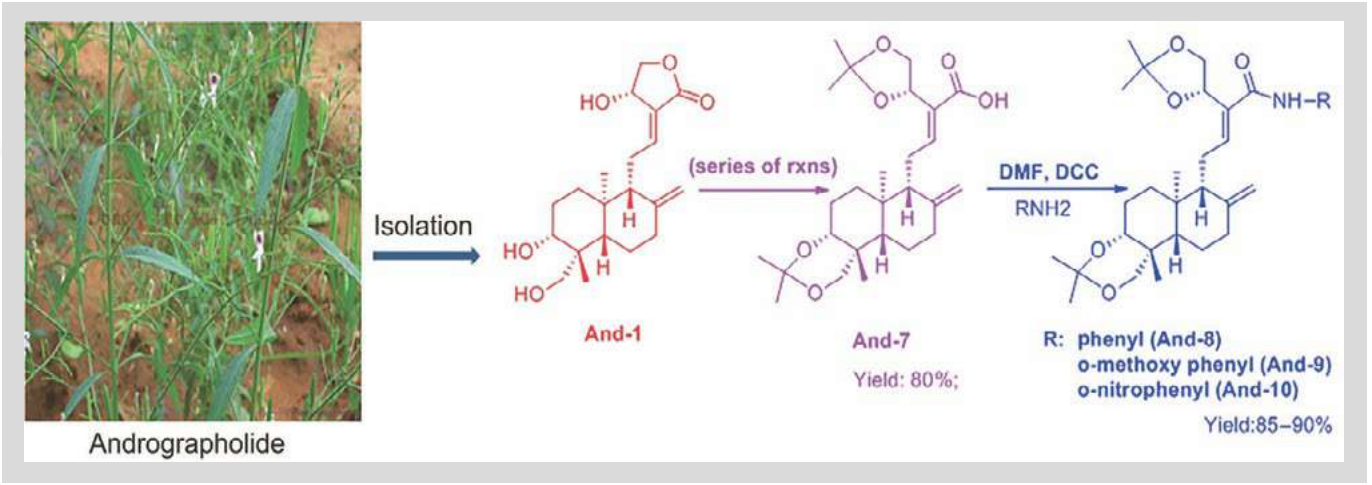
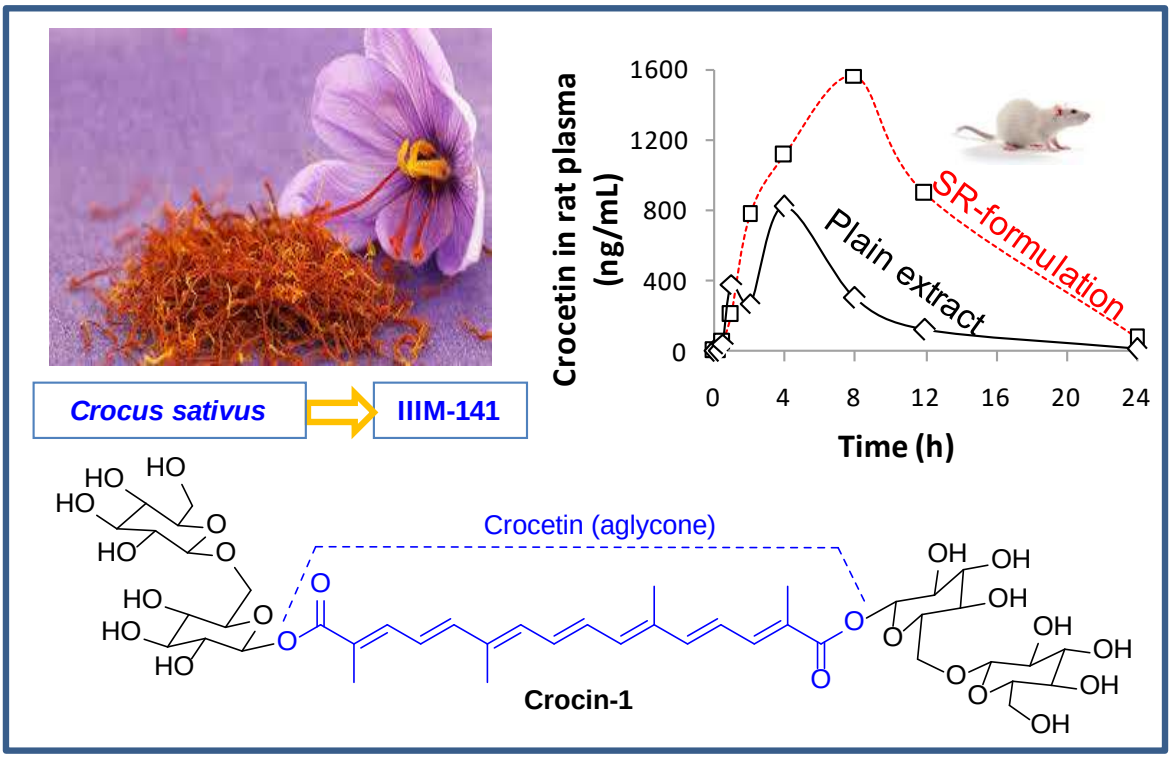


Figure 7.5.1. Expressions of AKT isoforms in clinical samples

6.0 MEDICINAL CHEMISTRY

6.1 Preclinical development of *Crocus sativus* based botanical lead IIIM-141 for Alzheimer's disease (ACS Omega, 2018, 3, 9572−9585)

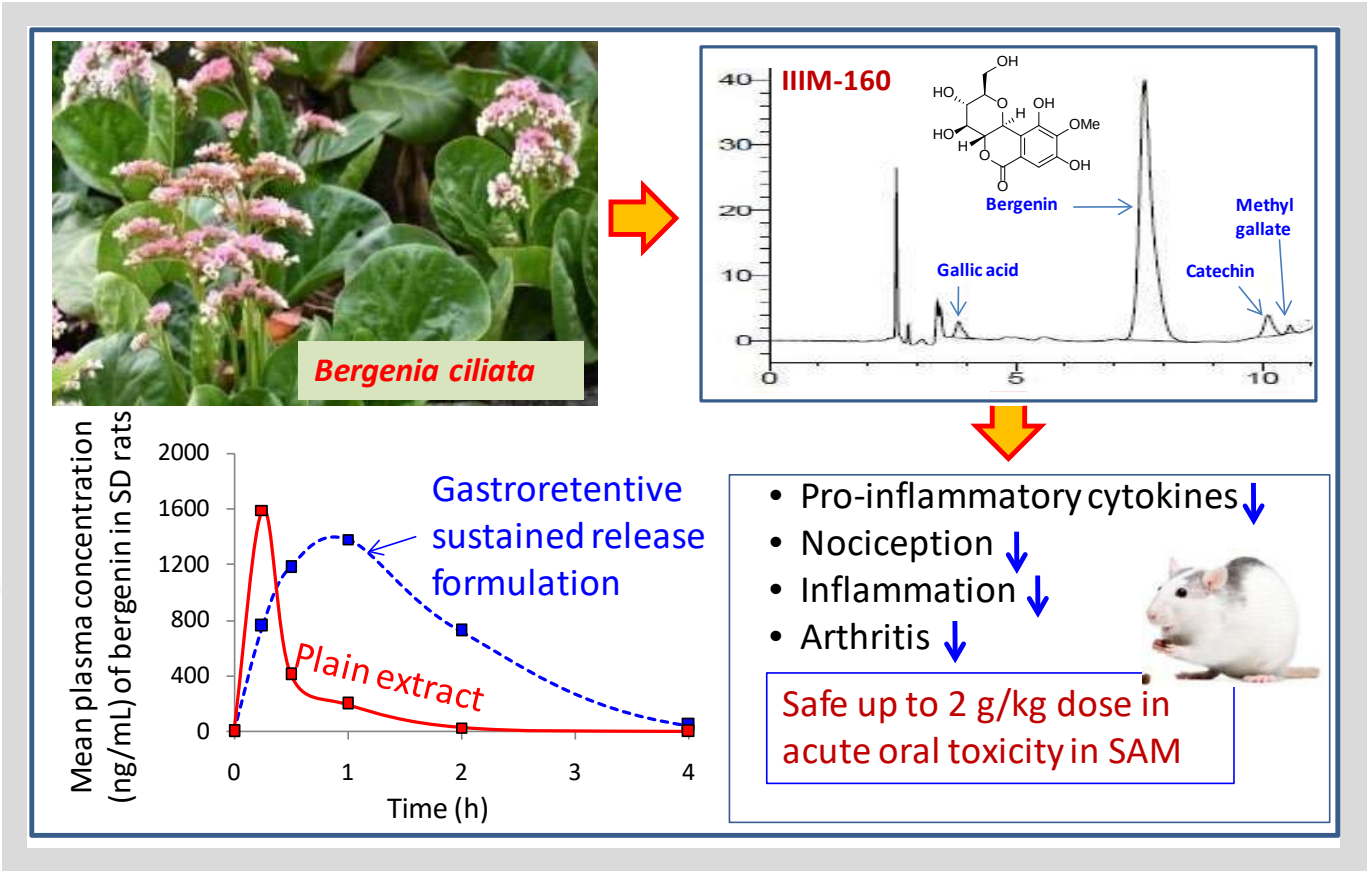
Sonali S. Bharate, Vikas Kumar, Gurdarshan Singh, Amarinder Singh, Mehak Gupta, Deepika Singh, Ajay Kumar, Ram A. Vishwakarma and Sandip B. Bharate



Crocus sativus L. (Family: Iridaceae) has been documented in traditional medicine with numerous medicinal properties. Recently, we have shown that *Crocus sativus* extract (IIIM-141) display promising efficacy in a genetic mice (5XFAD) model of Alzheimer's disease (AD) (*ACS Chem. Neurosci.* 2017, 8, 1756). To translate the available traditional knowledge and scientifically validated results into a modern medicine, herein we aimed to carry out its preclinical development. IIIM-141 is primarily a mixture of crocins containing *trans*-4-GG-crocin (36% w/w) as the principal component. The *in vitro* studies have shown that IIIM-141 has protective as well as therapeutic properties in assays related to AD. It induces the expression of P-gp, thereby enhancing the amyloid-β clearance from AD brain. It also inhibits NLRP3 inflammasome and protects SH-SY5Y cells against amyloid-β and glutamate-induced neurotoxicity. In behavioral models, it decreased the STZ-induced memory impairment in rats and recovered the scopolamine-induced memory-deficit in Swiss albino mice at 100 mg/kg dose. The acute oral toxicity study has shown that IIIM-141 is safe up to the dose of 2000 mg/kg, with no effect on the body weight, and biochemical/hematological parameters of the rats. The repeated oral administration of IIIM-141 for 28-days at 100 mg/kg dose, does not caused any pre-terminal deaths and abnormalities in Wistar rats. The pharmacokinetic analysis indicated that after oral administration of IIIM-141, the majority of crocin gets hydrolyzed to its aglycone crocetin. The sustained release capsule formulation was developed, which showed improved *in vitro* dissolution profile and significantly enhanced plasma exposure in the pharmacokinetic study. The sustained release formulation has resulted in 3.3-fold enhancement in the AUC of crocetin and doubling the crocetin: crocin ratio in plasma compared with the extract. The data presented herein will serve as the benchmark for the further research on this botanical candidate.

6.2 Discovery and preclinical development of IIIM-160, *Bergenia ciliata*-based anti-inflammatory and anti-arthritic botanical drug candidate (Journal of Integrative Medicine, 2019, 17, 192-204)

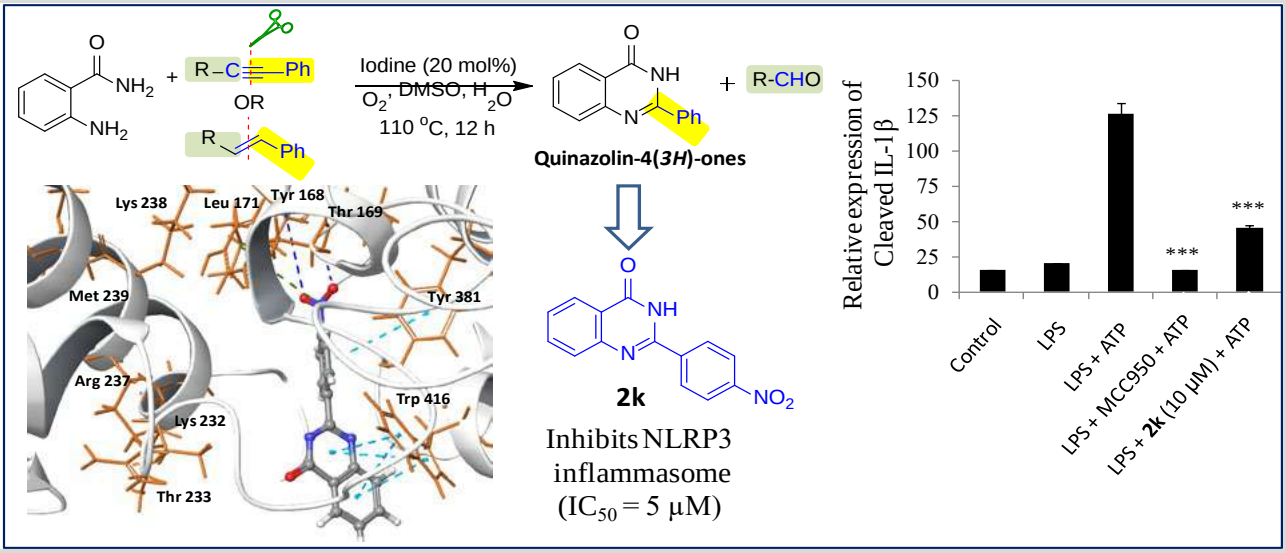
Sandip B. Bharate, Vikas Kumar, Sonali S. Bharate, Bikarma Singh, Gurdarshan Singh, Amarinder Singh, Mehak Gupta, Deepika Singh, Ajay Kumar, Surjeet Singh, Ram A. Vishwakarma



Bergenia ciliata (Haw.) Sternb. is used in the Indian traditional system of medicine to treat various ailments including rheumatism and to heal wounds. The objective of the present study was to perform a preclinical characterization of the *B. ciliata*-based botanical extract IIIM-160. IIIM-160 was chemically standardized and analyzed for heavy metal content, aflatoxins, and microbial load. The *in vitro* and *in vivo* efficacies were determined in suitable models of inflammation, arthritis and nociception. An acute oral toxicity study was performed in Swiss-albino mice. A suitable oral formulation was developed and characterized. Bergenin was found to be the major component (9.1% w/w) of IIIM-160. The botanical lead displayed inhibition of lipopolysaccharide-induced production of cytokines in THP-1 cells, with selectivity toward interleukin-6 (IL-6) and had an excellent safety-window. It showed anti-inflammatory, anti-arthritic and anti-nociceptive activity in animal models and was not toxic at oral doses up to 2 g/kg in Swiss-albino mice. The gastroretentive, sustained-release capsule formulation showed sustained-release of the bergenin over the period of 24 h, resulting in improved plasma-exposure of bergenin in Sprague Dawley rats. The dual-activity of IL-6 inhibition and anti-nociception mark the suitability of IIIM-160 for treating rheumatoid arthritis. This study will serve as the benchmark for further research on this botanical formulation.

6.3 Discovery of Quinazolin-4(3H)-ones as NLRP3 Inflammasome Inhibitors: Computational Design, Metal-free Synthesis and In-vitro Biological Evaluation (Journal of Organic Chemistry, 2019, 84, 5129-5140)

Mohd Abdullaha, Shabber Mohammed, Mehboob Ali, Ajay Kumar, Ram A. Vishwakarma, Sandip B. Bharate



NLRP3 inflammasome is an important therapeutic target for number of human diseases. Herein, a computationally-designed series of quinazolin-4(*3H*)-ones were synthesized using iodine-catalyzed coupling of arylalkynes (or styrenes) with *O*-aminobenzamides. Key event in this transformation involves oxidative-cleavage of C–C triple bond and the release of formaldehyde. Reaction relies on the C-N bond formation along with C-C bond cleavage under metal-free conditions. The nitro-substituted quinazolin-4(*3H*)-one **2k** inhibited NLRP3-inflammasome (IC_{50} 5 μM) *via* suppression of IL-1β release from ATP-stimulated J774A.1 cells.

6.4. Orally Effective Aminoalkyl 10H-Indolo-[3,2-b]quinoline-11-carboxamide Kills the Malaria Parasite by Inhibiting Host Hemoglobin Uptake (ChemMedChem, 2018, 13, 2581-2598)

Ramesh Mudududdla, Dinesh Mohanakrishnan, Sonali S. Bharate, Ram A. Vishwakarma, Dinkar Sahal, and Sandip B. Bharate

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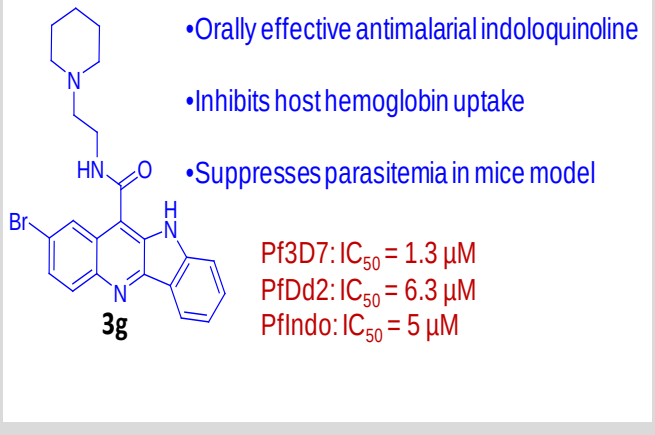


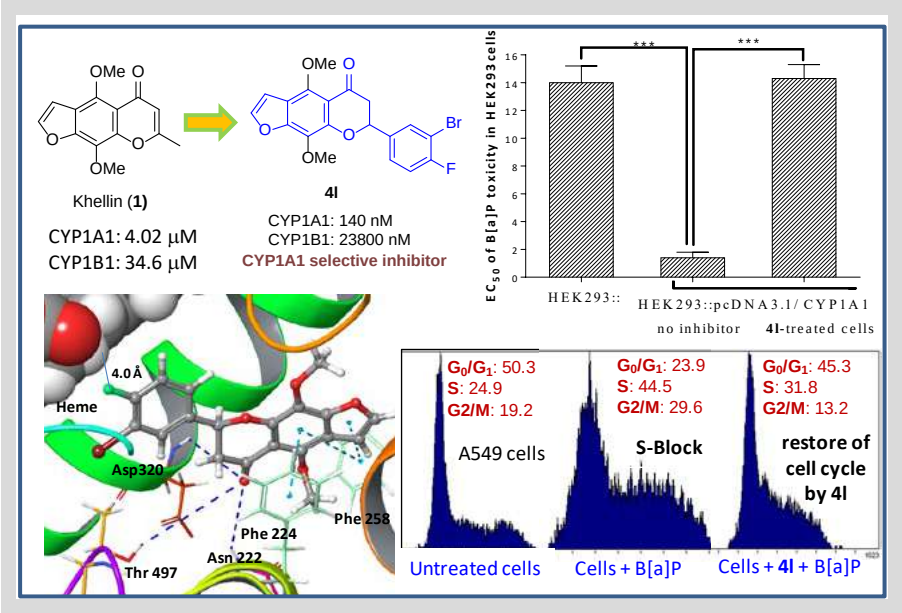
series of indolo[3,2-b]quinoline-C11-carboxamides were synthesized by incorporation of amino-alkyl side chains into the core of indolo[3,2-b]quinoline-C11-carboxylic acid. Their in vitro antiplasmodial evaluation against *Plasmodium falciparum* has led to the identification of 2-(piperidin-1-yl) ethanamine linked analog [2-bromo-*N*-(2-(piperidin-1-yl) ethyl)-10H-indolo[3,2-b]quinoline-11-carboxamide, **3g**] (IC_{50} 1.3 μM) as the most promising compound exhibiting good selectivity-indices against mammalian cell lines. The kill-kinetics on erythrocytic-stage parasites revealed that **3g** causes complete killing of only the trophozoite-stage parasites. Mechanistic studies have shown that **3g** targets the food vacuole of parasite, and inhibits the hemoglobin

uptake, β-haematin formation and basic endocytic processes of the parasite. Analog **3g** was found to be orally bioavailable and its curative antimalarial studies at 50 mg/kg, p.o. against *Plasmodium berghei* (ANKA)-infected mouse model showed that the **3g**-treated mice showed 27-35% suppression of parasitemia with increased life-span of treated as compared to untreated-control mice. Thus, the present work has demonstrated a proof-of-concept for oral efficacy of indolo[3,2-b] quinoline-C11-carboxamides.

6.5. Khellinoflavanone, a Semisynthetic Derivative of Khellin, Overcomes Benzo[a]pyrene Toxicity in Human Normal and Cancer Cells that Express CYP1A1 (ACS Omega, 2018, 3, 8553–8566)

Rajni Sharma, Ibidapo S. Williams, Linda Gatchie, Vinay R. Sonawane, Bhabatosh Chaudhuri, Sandip B. Bharate

Cytochrome P450 family 1 (CYP1) enzymes catalyze the metabolic activation of environmental procarcinogens such as benzo[a] pyrene, B[a]P, into carcinogens, which initiate the process of carcinogenesis. Thus, stopping the metabolic activation of procarcinogens can possibly prevent the onset of cancer. Several natural products have been reported to show unique ability in inhibiting CYP1 enzymes. We found that khellin, a naturally occurring furanochromone from *Ammi visnaga*, inhibits CYP1A1 enzyme with an IC_{50} value of 4.02 μM in CYP1A1-overexpressing human HEK293 suspension cells. To further explore this natural product for discovery of more potent and selective CYP1A1 inhibitors, two sets of semisynthetic derivatives were prepared. Treatment of khellin with alkali results in opening of a pyrone ring, yielding khellinone (**2**). Claisen-Schmidt condensation of khellinone (**2**) with various aldehydes in presence of potassium hydroxide, at room temperature, provide a series of furanochalcones **3a-v** (khellinochalcones). Treatment

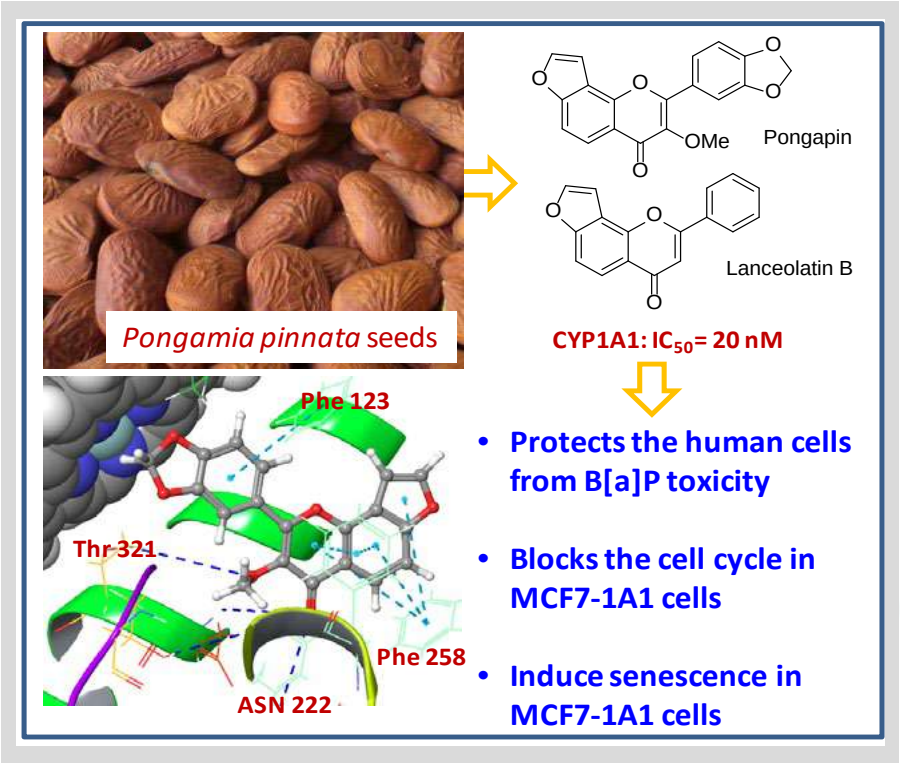


of khellinone (**2**) with aryl aldehydes in presence of piperidine, under reflux, affords the flavanone series of compounds **4a-p** (khellinoflavanones). The khellinoflavanone **4l** potently inhibited CYP1A1 with IC_{50} value of 140 nM in live cells, with 170-fold selectivity over CYP1B1 (IC_{50} for CYP1B1 = 23.8 μM). Compound **4l** at 3 x IC_{50} concentration for inhibition of CYP1A1, completely protected HEK293 cells from CYP1A1-mediated B[a]P toxicity. Lung cancer cells, A549 ($p53^{+}$) and Calu-1 (p53-null), blocked in growth at the S-phase by B[a]P were restored into the cell cycle by compound **4l**. The results presented herein strongly indicate the potential of these khellin derivatives for further development as cancer chemopreventive agents.

6.6. Furanoflavones Pongapin and Lanceolatin B Blocks the Cell Cycle and Induce Senescence in CYP1A1-overexpressing Breast Cancer Cells (Bioorganic & Medicinal Chemistry, 2018, 26, 6076-6086)

Rajni Sharma, Ibidapo S. Williams, Linda Gatchie, Vinay R. Sonawane, Bhabatosh Chaudhuri, Sandip B. Bharate

Expression of cytochrome P450-1A1 (CYP1A1) is suppressed under physiologic conditions but is induced (a) by polycyclic aromatic hydrocarbons (PAHs) which can be metabolized by CYP1A1 to carcinogens, and (b) in majority of breast cancers. Hence, phytochemicals or dietary flavonoids, if identified as CYP1A1 inhibitors, may help in preventing PAH-mediated carcinogenesis and breast cancer. Herein, we have investigated the cancer chemopreventive potential of a flavonoid-rich Indian medicinal plant, *Pongamia pinnata* (L.) Pierre. Methanolic extract of its seeds inhibits CYP1A1 in CYP1A1-overexpressing normal human HEK293 cells, with IC_{50} of 0.6 µg/mL. Its secondary metabolites, the furanoflavonoids pongapin/ lanceolatin B, inhibit CYP1A1 with IC_{50} of 20 nM. Although the furanochalcone pongamol inhibits CYP1A1 with IC_{50} of only 4.4 µM, a semisynthetic pyrazole-derivative **P5b**, has ~10-fold improved potency (IC_{50}, 0.49 µM). Pongapin/ lanceolatin B and the methanolic extract of *P. pinnata* seeds protect CYP1A1-overexpressing HEK293 cells from B[a]P-mediated toxicity. Remarkably, they also block the cell cycle of CYP1A1-overexpressing MCF-7 breast cancer cells, at the G_0-G_1 phase, repress cyclin D1 levels and induce cellular-senescence. Molecular modeling studies demonstrate the interaction pattern of pongapin/lanceolatin B with CYP1A1. The results strongly indicate the potential of methanolic seed-extract and pongapin/lanceolatin B for further development as cancer chemopreventive agents.



7.1 Analyzing role of cannabinoids as modulators of Wnt/β-catenin signaling pathway

Yedukondalu Nalli, Mohd Saleem Dar, Nasima Bano, Javeed Ur R. Najara, Aminur R. Sarkar, Junaid Banday, Aadil Qadir Bhat, AsifAli and Mohd Jamal Dar

Cannabinoids are comprised of naturally occurring active compounds of the *Cannabis sativa* and *Cannabis indica*, endogenous cannabinoids and synthetic cannabinoids. Cannabinoids are primarily used to alleviate pain, anxiety and depression. Neuro-protective properties of cannabinoids have been studied in several *in-vitro* and *in-vivo* neuro-degeneration models. The mechanisms involved in the neuro-protection provided by cannabinoids include cannabinoid receptor-independent as well as cannabinoid-receptor dependent effects. Recently synthetic cannabinoids have been approved as prescription medicine in some countries for their use in the treatment of many diseases including convulsion and epilepsy. Wnt/β-catenin signaling is a highly conserved pathway that is involved in regulating cell proliferation and differentiation during various stages of development, particularly, nervous system development. Wnt/β-catenin signalling has recently been shown to play a major role in the pathogenesis of neuropathic pain Since Wnt/β-catenin signalling pathway is involved in regulating neuropathic pain and cannabinoids are known to alleviate pain, we examined the impact of these cannabinoids on modulating Wnt/β-catenin signalling pathway.

Isolation and characterization of cannabinoids: We isolated six compounds (1- 6) from *Cannabis sativa,* and synthesized an epoxy derivative (**2a) from** compound **2**. These compounds were then characterized by 1D and 2D NMR spectral data (**Figure-7.1.1**). Thereafter, we assessed the anti-proliferative activity of these cannabinoids on a panel of cancer cell lines.

***In-vitro* cytotoxicity (IC50) of cannabinoids on a panel of selected cancer cells:** These cannabinoids were evaluated for their impact on cytotoxicity on a panel of cancer cell lines that include HCT-116, OVCAR, A549, MCF7, PC-3, HepG2 and SH-SY5Y cells spanning different tumour types (colon, ovary, lungs, breast, prostate, liver and neuroblastoma). The concentrations tested were from 1 μM to 100 μM for 72 hours. The results shown in **Table-7.1.1** indicate varying degrees of growth inhibition across different cell lines. Since HepG2 cells are considered a standard cell line for screening small molecule inhibitors of Wnt/β-catenin signalling, we calculated IC_{50} values for these compounds in HepG2 cells. Compounds **3**, **4**, **5** and **6** were seen to be relatively less effective than **1**, **2** and **2a**. We compared the effect of **1**, **2** and **2a** in HepG2 cells with that of salinomycin, a natural product-based inhibitor of Wnt/β-catenin signalling. Interestingly, compounds **1**, **2** and **2a** are seen to be less toxic than salinomycin in these cells when tested under similar conditions.

Cannabinoids are involved in regulating Wnt/β-catenin signaling pathway: We then examined the impact of these cannabinoids on regulating Wnt/β-catenin signaling pathway activity in in HepG2 by monitoring TCF-dependent β-catenin mediated transcription activity using Top-Flash reporter assay. Four hours post-transfection with approriate Top-Flash reporter plasmids, HepG2 cells are treated with cannabinoids in a concentration-dependent manner (well below their IC_{50} values), and luminescence was measured at 24h post-treatment. To perform these experiments, we used salinomycin as a positive control. Interestingly, compound **1**, **2** and **2a** were seen to significantly decrease the TopFlash activity in a dose-dependent manner when compared to solvent control (DMSO). Salinomycin treatment resulted in a decrease in Top-Flash activity in a dose-dependent manner under similar conditions (**Figure- 7.1.2).** Thus, we show that these compounds are relatively lesss toxic and could be developed as effective neuroprotective agents for the management of neuropathic pain because of their ability to modulate activity of Wnt/β-catenin signaling pathway.

Table 7.1.1. *In-vitro* cytotoxicity of cannabinoids on a panel of selected cancer cells post-72 hr treatment

Molecule / Cell line	Compound 1	Compound 2	Compound 2A	Compound 3	Compound 4	Compound 5	Compound 6
HCT-116	13±3.33	18±1.00	15.3±1.30	83±2.98	80±3.23	42±1.97	60±3.22
OVCAR	57±3.01	50±3.00	56.8±4.28	75±5.32	77±4.01	63±2.75	65±4.44
A549	39±2.10	40±2.40	45.2±4.22	90±3.20	91±3.98	45±4.44	60±1.88
MCF7	53±2.60	55±2.20	47.2±3.50	80±2.97	81±3.44	57±3.86	40±2.32
PC-3	44±1.88	12±0.90	17.6±3.06	79±3.09	78±4.11	65±5.07	40±1.79
HepG2	64±4	42.8±1.19	53±2.54	75±4.22	74±5.08	59±3.29	60±4.02
SH-SY5Y	55±5.32	48±5.12	51±2.49	95±4.27	97±5.05	50±2.99	77±5.82

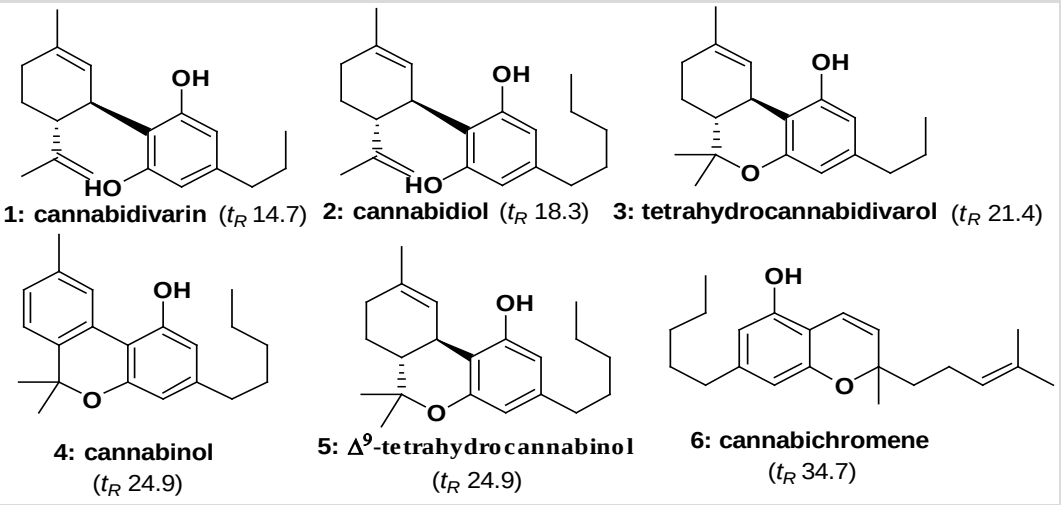


Figure-7.1.1.

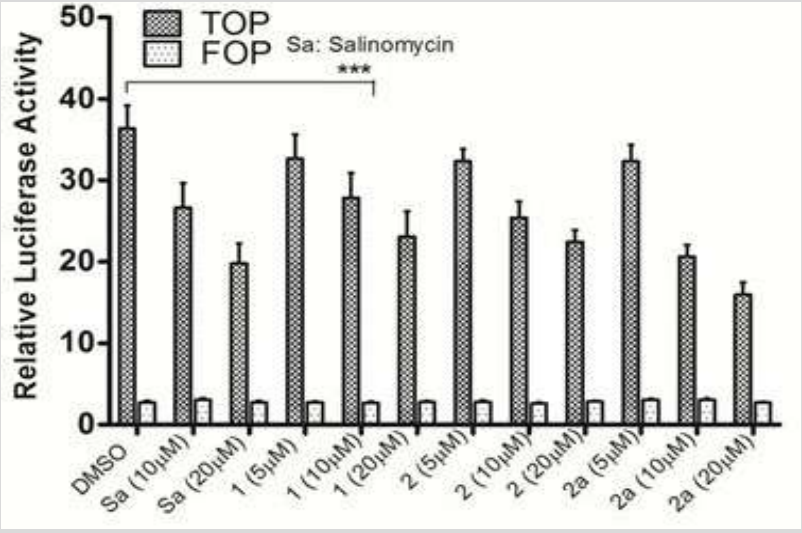
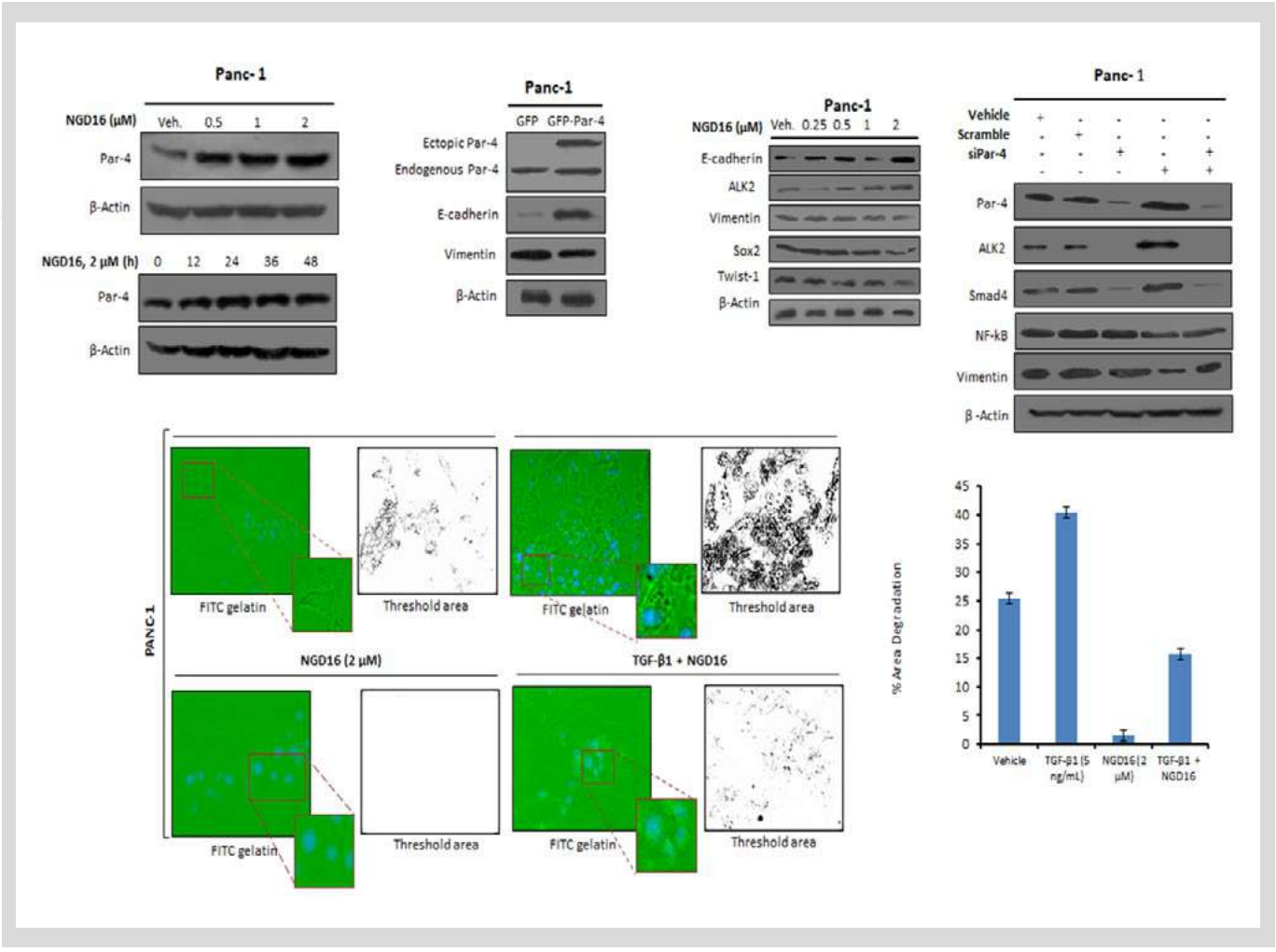


Figure 7.1.2. Top-Flash activity of cannabinoids in HepG2 cells: Reporter activity was determined upon co-transfection of TopFlash (TOP) or FopFlash (FOP) and Renilla plasmids into HepG2 cells under basal and serum-free conditions.

7.2 Dual role of Par4 in abrogation of EMT and switching on Mesenchymal to Epithelial Transition (MET) in metastatic pancreatic cancer cells

Archana Katoch, Sujit Suklabaidya, Souneek Chakraborty, Debasis Nayak, Reyaz U. Rasool, Deepak Sharma, Debaraj Mukherjee, Anmol Kumar, Parduman R. Sharma, Shanti bhusan Senapati, Lekha D. Kumar, Anindya Goswami.

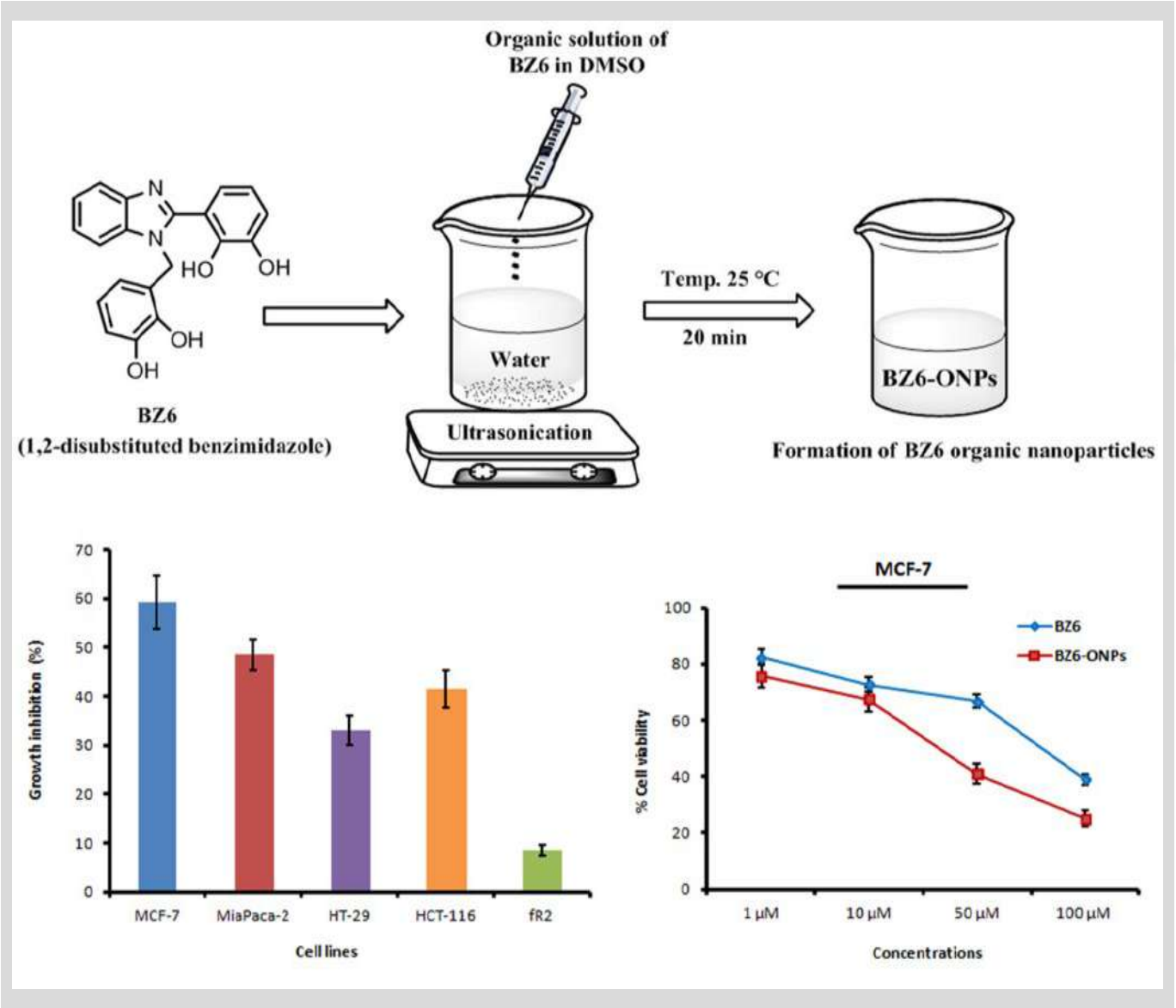
Here, we conceive a dual mechanism of Par-4-mediated inhibition of EMT and induction of MET in metastatic pancreatic cancer cells. First, we demonstrated that 1,1′-β-D-glucopyranosyl-3,3′-bis (5-bromoindolyl)-octyl methane (NGD16), an N-glycosylated derivative of medicinally important phytochemical 3,3′-diindolylmethane (DIM) abrogates EMT by inducing pro-apoptotic protein Par-4. Induction of Par-4 (by NGD16 or ectopic overexpression) strongly impedes invasion with inhibition of major mesenchymal markers viz. Vimentin and Twist-1 epithelial marker- E-cadherin. Further, NGD16 triggers MET phenotypes in pancreatic cancer cells by augmenting ALK2/ Smad4 signaling in a Par-4-dependent manner. Additionally, we demonstrate that intact Smad4 is essential for Par-4-mediated maintenance of E-cadherin level in MET induced cells.

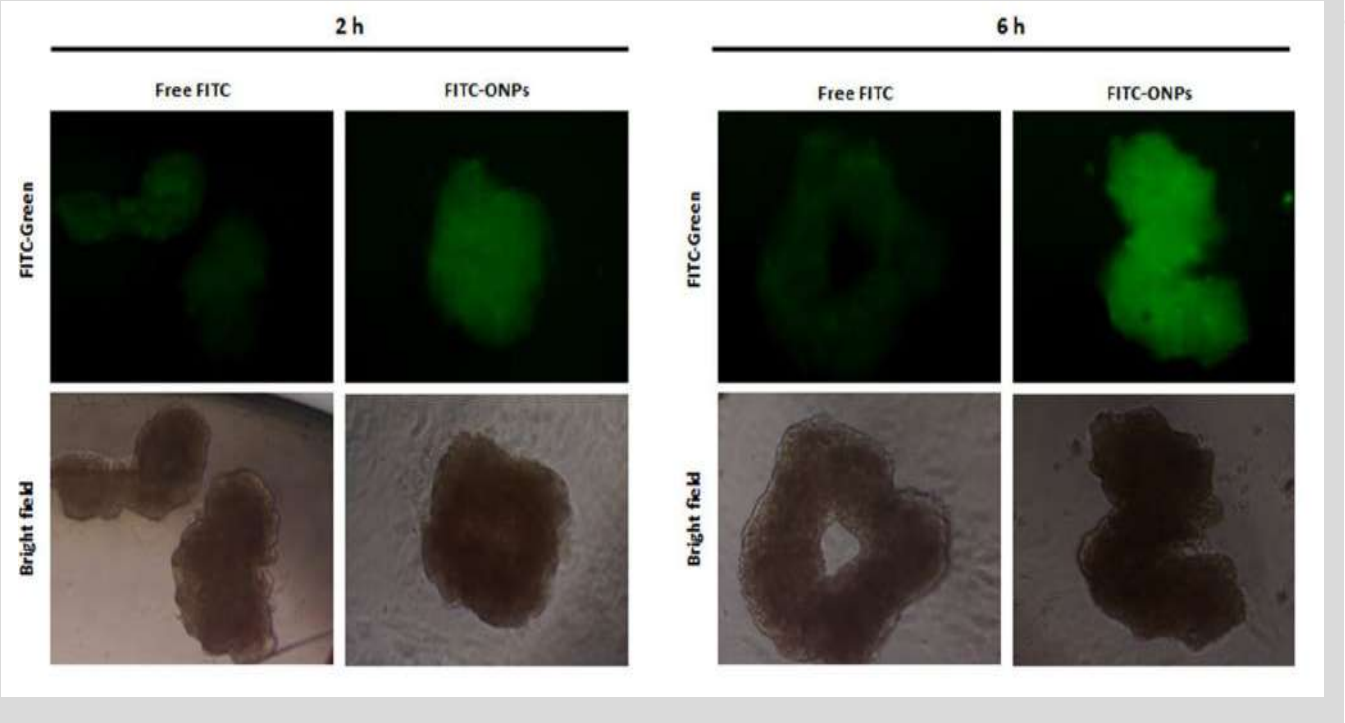


7.3 Self-assembled organic nanoparticles of benzimidazole analogue exhibit enhanced uptake in 3D tumor spheroids and oxidative stress induced cytotoxicity in breast cancer.

Dhanwal V, Katoch A, Singh A, Chakraborty S, Faheem MM, Kaur G, Nayak D, Singh N, Goswami A, Kaur N.

This study describes the preparation, characterization and biological evaluation of aqueous phase ONPs of potent 1,2-disubstituted benzimidazole derivative (BZ6) for anticancer activity. BZ6-ONPs were characterized through UV-absorption and fluorescence spectroscopic analysis for their photo-physical properties. DLS, TEM and SEM studies were carried out for morphological and structural analysis. Cytotoxicity determination on a panel of four different cancer cell lines (MCF-7, MiaPaca-2, HT-29 and HCT-116) revealed that the BZ6-ONPs show highest activity in human breast cancer MCF-7 cells. Additionally, the FITC-ONPs showed enhanced uptake in 3D tumor spheroids of MCF-7 cells compared to the free FITC.





7.4 Synthesis and Investigation of the Role of BenzopyranDihydropyrimidinone Hybrids in Cell Proliferation, Migration and Tumor Growth

Dash AK, Nayak D, Hussain N, Mintoo MJ, Bano S, Katoch A, Mondhe DM, Goswami A, Mukherjee Da

Two types of novel hybrids were synthesized efficiently from benzopyran aldehydes, ethylacetoacetate and urea under heteropolyacid catalysis. Compound 3 was found to be the most potent hybrid among the synthesized compounds with consistent cytotoxic activities against four human cancer cell lines (IC50 values: 0.139 - 2.32 μM). Compound 3 strongly inhibited proliferation abilities of A549 cells in colony formation assay. Compound 3 exerted oxidative stress-mediated mitochondrial dysfunction, in which mitochondrial reactive oxygen species (ROS) generation as a mechanism of its anti-proliferative effects was analyzed. Further, the molecule abrogated migration and cell scattering properties of aggressive PANC-1 cells. Mechanistic studies revealed that compound 3 modulated NF-kB expression and its downstream oncogenic proteins involved in cancer cell proliferation and invasion. Finally, compound 3 confirmed its in vivo anti-tumor efficacy; there observed 41.87% tumor growth inhibition at a dose of 30 mg/kg/body weight against a mouse model of Ehrlich solid tumor.

7.5 Differential manifestation of AKT isoforms in TN breast cancers and in cisplatin response.

Bhumika Wadhwa, Masroor Ahmad, Sameer Khan, Sameer Mir and Fayaz Malik

AKT, a serine threonine kinase, exists in three different isoforms and is known for regulating several biological processes including tumorigenesis. In this study, we investigate the expression and net effect of the individual isoforms in triple negative breast cancers and response to cisplatin treatment using cellular, mice models and clinical samples. Interestingly, analysis of the expressions of AKT isoforms in clinical samples showed relatively higher expression of AKT1 in primary tissues; whereas lung and liver metastatic samples showed elevated expression of AKT2. Similarly, Triple-negative breast cancer cell lines, BT-549 and MDA-MB-231, with high proliferative and invasive properties, displayed higher expression levels of AKT1/2. By

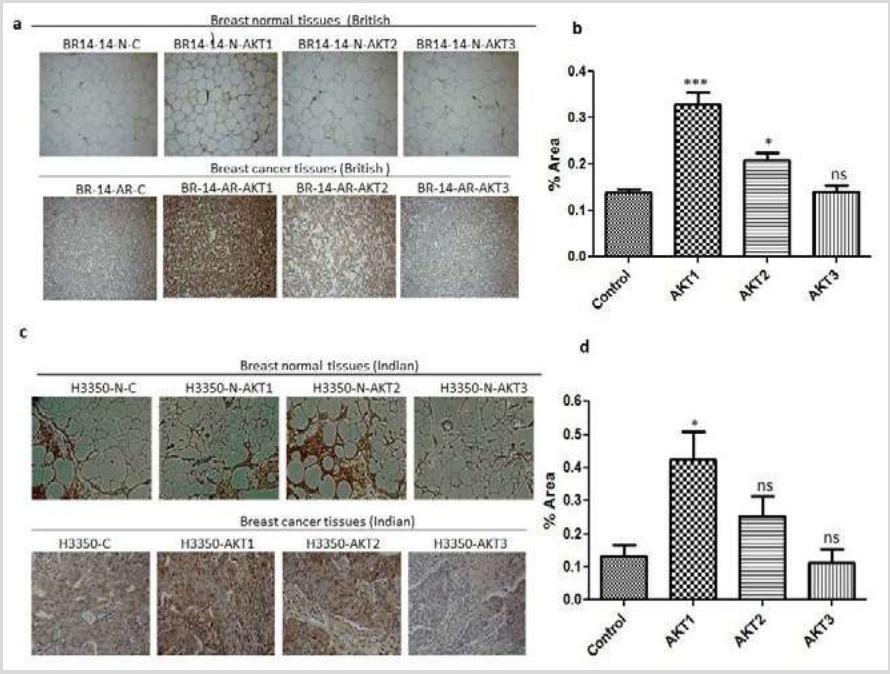


Figure 7.5.1. Expressions of AKT isoforms in clinical samples

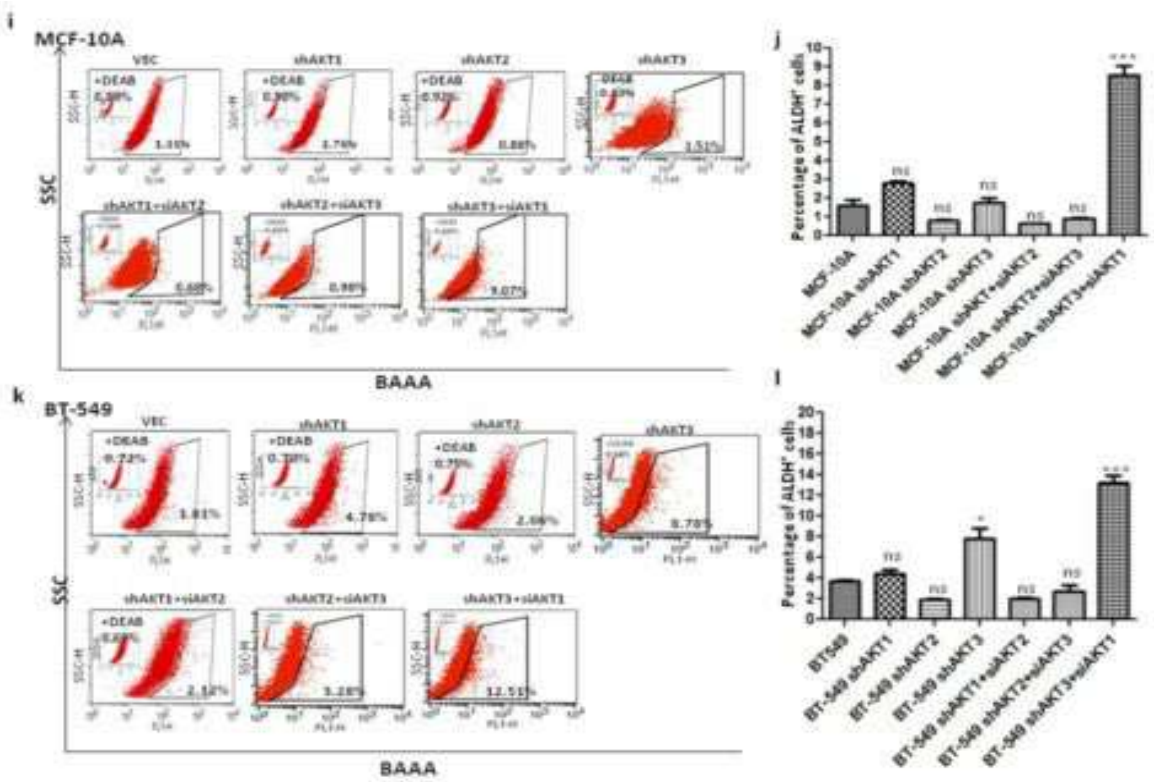


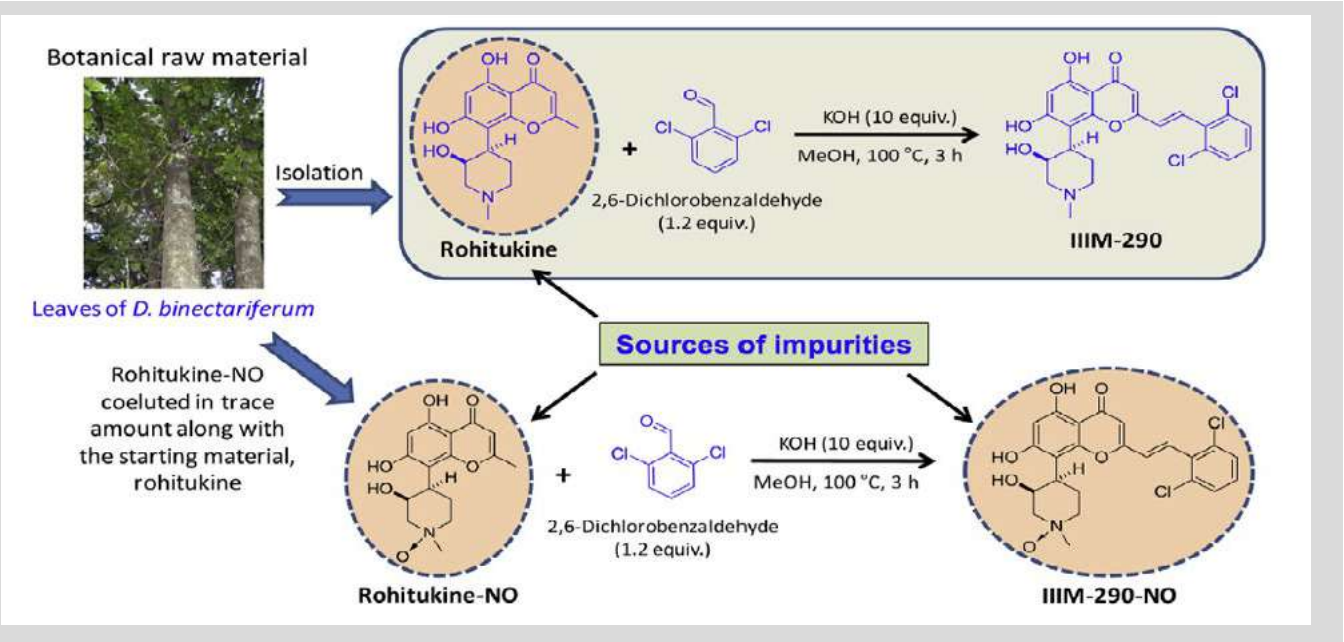
Figure 7.5.2. Effect of AKT isoforms knockdown on Cancer Stem Cell Populations

modulating AKT isoform expression in MCF-10A and BT-549 cell lines, we found that presence of AKT2 was associated with invasiveness, stemness and sensitivity to drug treatment. It was observed that the silencing of AKT2 suppressed the cancer stem cell populations, mammosphere formation, and invasive and migratory potential in MCF-10A and BT-549 cells. It was further demonstrated that AKT2 isoform is associated with reduced sensitivity towards cisplatin treatment in Triple-negative breast cancers cellular and syngeneic mice models. The decrease in cisplatin treatment response in AKT2 expressing cells was allied with the upregulation in the expression oftransporter protein ABCG2, whereas silencing of ABCG2 restored cisplatin sensitivity in these cells through AKT/SNAIL/ABCG2 axis. In conclusion, our study demonstrated thevaried expression of AKT isoforms in TN breast cancer and also confirmed differential role of isoforms in stemness, invasiveness and response towardsthe cisplatin treatment.

PK-PD and Toxicology

7.6 Impurity profiling of anticancer preclinical candidate, IIIM-290 (Journal of Pharmaceutial and Biomedical Analysis, 2019, 166, 1-5)

Vikas Kumar, Deendyal Bhurt, Ankita Sharma, Puneet Kumar, Sandip B. Bharate, Ram A. Vishwakarma, Sonali S. Bharate

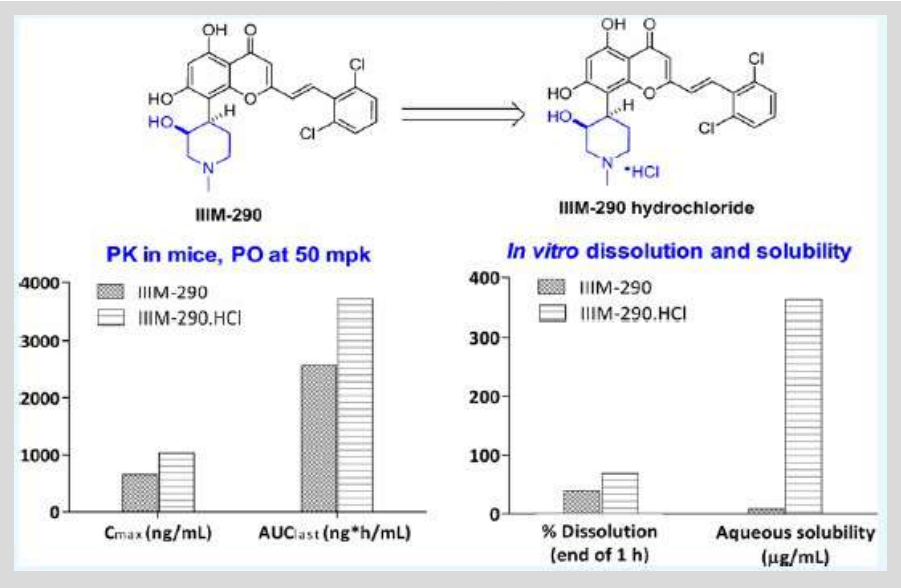


IIIM-290, an orally bioavailable preclinical candidate is effective in human xenograft models of leukemia, colon and pancreatic cancer. The promising preclinical data of this lead candidate has shown its potential for clinical development. As a part of its preclinical development, impurity profiling of pilot scale batches is one of the most important component of the CMC documentation. Herein, we report impurity profiling, its quantification in different scale-up batches and analytical method validation. Three impurities ranging from 0.09 to 1.25% in preclinical anticancer candidate, IIIM-290 were detected by validated HPLC method. The impurities (Imp-A, Imp-B and Imp-F) were isolated from the partially purified batch of IIIM-290 using semi-preparative HPLC. Isolated impurities were characterized by 1H, 13C NMR, FTIR and ESI–MS spectral data. Based on the characterization data, the sources of these impurities were identified as unreacted starting material (Imp-A), impurity from botanical raw material (Imp-B; impurity carried from starting material) and the chemically transformed product (Imp-F) of Imp-B, respectively.

7.7 Selection of a Water-Soluble Salt Form of a Preclinical Candidate, IIIM-290 (ACS Omega 2018, 3, 8365−8377)

Vikas Kumar, Sandip B. Bharate, Ram A. Vishwakarma, and Sonali S. Bharate

IIIM-290, a semisynthetic derivative of natural product rohitukine, is an orally bioavailable Cdk inhibitor, efficacious in the xenograft models of colon, pancreatic, and leukemia cancer. Its low aqueous solubility (8.6μg/mL) could be one of theA reasons for achieving optimal in vivo efficacy relatively at a higher dose. Being a nitrogenous compound, salt formation was envisaged as one of the ideal approaches to enhance its solubility and dissolution profile. Thus, herein, a solubility-guided miniaturized 96-well plate salt screening protocol was devised for identification of the suitable salt form of this preclinical candidate. The solubility-guided strategy has resulted in the identification of hydrochloride as the most favorable counterion, resulting in 45-fold improvement in aqueous solubility. The HCl salt was then scaled up at a gram size and characterized using 1H and 13C NMR, scanning electron microscopy, powder X-ray diffraction, Fourier transform infrared, and differential scanning calorimetry studies. The HCl salt displayed enhancement in the in vitro dissolution profile as well as improved plasma exposure in the pharmacokinetic study. The oral administration of the IIIM-290·HCl salt in BALB/c mice resulted in >1.5-fold improvement in areas under the curve, Cmax, and half-life. The prepared salt also did not alter its cyclin-dependent kinase (Cdk)-2 and Cdk-9 inhibition activity. This biopharmaceutically improved lead has a potential to investigate further in preclinical studies. The solubility-guided salt screening strategy implemented herein could be utilized for other preclinical leads.



8.0 cGMP and CHEMICAL ENGINEERING

Indian Institute of Integrative Medicine (IIIM) Jammu is a national institute under Council of Scientific & Industrial Research of India, with primary focus on new drug discovery from Natural products. The mandate of institute is discovery of novel pharmacologically active natural products from plants and translating them in to drug leads and candidates by medicinal chemistry, preclinical pharmacology and clinical development after bringing them under captive cultivation.

Product Development of Standardized Plant Extract in the form of capsule

❖ ***Hippophae rhamnoides*** (Sea Buckthorn):

CSIR-IIIM Jammu is mainly focus on Natural product chemistry, New Phyto-pharmaceutical (GSR 702 E), new drug discovery, Plant biotechnology etc., *Hippophae rhamnoides* (Sea Buckthorn) is a nutraceutical products. This institute is focused on safe & quality innovative product (Herbal) make available to the public through Govt. of India. The present invention comprising an effective amount of Pulp/ lyophilized powder along with one or more pharmaceutical acceptable additives/ carriers. This invention envisages the potential of an extract obtained from the fruit of the plant to act as an effective therapy against anti-oxidative suppressor property as well as Muti-vitamins source. Contains Vitamin A, B1, B2, B6, B9, B12, C, E, K and malic acid. The overall dose of the tablets is 750 mg with active ingredients of 300 mg. The dissolution time of formulated tablets are

(Sea Buckthorn) Nutraceuticals formulation

❖ ***Epimedium elatum:*** (Roots & Shoot) Herbal formulation

Part used for development of Extract of *Epimedium elatum* is dry roots and shoots of *Epimedium elatum* plant. Extract of supplied Epimedium plant material, has been developed as per SOP, the extract is developed in cGMP pilot plant and dried in lyophilizer. Capsules formulation developed at cGMP plant, the dosage of said capsule is around 400 mg (API). Overall weight of the capsules is around 545 mg. The total quantity of capsules manufactiured is around 1200 in size "0". The developed formulations prepared under "Development of nutraceuticals product from (RRLH-22330) and sample submitted for CMC study for both extract & Formulation.

Epimedium elatum : Nutraceuticals formulation (Capsule)

Non classical formulation (Capsules)

❖ **Thrombup:**

"Thrombup" is a non classical formulation manufactured for third party at cGMP pilot plant. The manufactured formulation is very well known for generation of Red Blood cells especially in fever of dengue. The non classical formulation is the mixture of three different botanical extract i.e. *Carica Papaya*, *Tinospora cordifolia* and *Andrographis paniculata*. The total quantity of capsules manufactured and packed in blister packing is around 50,000 size "0". The third party formulation prepared for M/s. Phyto Specialties Pvt. Ltd. Chennai.

❖ ***Hippophae rhamnoides*** (Sea Buckthorn):

Nutraceuticals formulation Natural Flavour | Flavoured with Vanilla

CSIR-IIIM Jammu is mainly focus on Natural product chemistry, *Hippophae rhamnoides* (Sea Buckthorn) is a nutraceutical products. This institute is focus on safe & quality innovative product (Herbal) make available to the public through Govt. of India. The present invention comprising an effective amount of Pulp/ lyophilized powder along with one important metal constituents i.e. Zinc Gluconate. This invention envisages the potential of an extract obtained from the fruit of the plant to act as an effective therapy against anti-oxidative suppressor property as well as Muti-vitamins source plus deficiency of metals especially in male nutritional children's as well as women's. Sea –Zing is the proposed brand name of the formulated tablets. The overall dose of the tablets is 750 mg. CMC studies on pulp and formulated products are going on with active ingredient 300 mg of Sea Buckthorn and 50 mg of Zinc Gluconate.

Sickle Cell Anaemia Mission Project

As on day, there is no any clinical studies were conducted on Indian population for the indication of Sickle cell anaemia. So, IIIM Jammu is seeking permission to conduct interventional bio-available and bio-equivalence (BA/BE) studies on the Indian population with a comparator of reference listed drug (RLD) i.e. Droxia, 400 mg, to make available to the Indian patients. In this connection, IIIM Jammu has been applied for the License for import of Droxia, 400 mg (RLD) to make Equivalent formulation and the same has been got, bearing license number: TL/NZ/18/000289, dated: 27/03/2018 in favour of IIIM Jammu from the Govt. of India, CDSCO, Ministry of Health and family welfare, New Delhi.

The cGMP department developed Standardized extract from Cannabis sativa (Alcoholic Cold Extraction) Leaves of Cannabis sativa processed at normal temperature and pressure with 1:8 solute solvent ratio (Plant material: Alcohol), extract filtered, and concentrated with the help of distillation. The concentrated extract dried in vacuum tray dryer and semi solid extract stored at low temperature.

Service to Industry:

Sl. No	Title of the project	Project Type/ Category	Amount received with your initiative	Govt./ Industry	Lab Reserve generation
1	Development of extract of *Pterocarpus santalinus* (Red Sanders)	Consultancy project	1.4 Lakh	M/s. Andhra Fogaku (P) Ltd. Hyderabad	1.4 Lakh
2	Development of capsule formulation of "**Thrombup**"	Third Party Manufacturing	0.25 Lakh	M/s. Phyto Specialties Pvt. Ltd. Chennai	0.25 Lakh
3	Skill development programme through (TBI)	Training	13.60 Lakhs	Private/University	13.60 Lakhs

Field Distillation Trail Runs:

Field distillation trail runs, under CSIR-AROMA Mission project was taken on 29th January 2019 to 02nd February at Jamnagar (Gujarat) and Jalna (Maharashtra) During the visit cum trail runs, interaction with the farmers and local individuals done and immobilized them for moving from traditional crops cultivation to medicinal/aromatic crops cultivation. After successful completion of trail runs of field distillation unit at Jamnagar and Jalna, the sample collected from both the location and submitted for the analysis in quality control and quality assurance department.

Interaction with farmers

Trail at Jalna (KVK)

Oil recovery

Trail at Jamnagar

Field Visit at Jamnagar

Oil recovery

TBI-Skill Development Program

cGMP Unit, CSIR-IIIM Jammu, provide opportunity to new entrepreneurs/SMEs engaged in manufacture of standardised extracts and botanical drug formulations, natural products etc., to evaluate their research leads and eventually graduate as entrepreneurs so that more number of industries can be setup and employment can be generated. This facility will also be used as the Technology Business Incubator (TBI), for which Department of Science and Technology has already approved a project. Biotech Industrial Training Programme under BCIL, have been selected for dissertation training programme in Technology Business Incubator of Indian Institute of Integrative Medicine (TBI-IIIM), Jammu, for the batch commencing in January/February, 2018.Training was imparted through lectures by the experts and through Practical in the area of extraction, formulation, QA/QC, and Utilities etc. The main objective of CSIR- IIIM is conducting One/three month certificate course to create a stream of highly trained manpower by enhancing practical and regulatory skills of science, pharmacy and medicine graduates in the area of extraction and formulation of phyto-pharmaceutical drugs.

Technology Business Incubator
CSIR-Indian Institute of Integrative Medicine
Gestate fledgling researches to full fledged technologies

STUDENTS SELECTED FOR DISSERTATION TRAINING PROGRAMME

This is to notify thatthe following applicantshave been selected for dissertation training programme in Technology Business Incubator of Indian Institute of Integrative Medicine (TBI-IIIM), Jammu, for the batch commencing in January/February, 2018.

List of students selected for the dissertation training programme starting from January/February, 2018: -

S.NO	STUDENT	UNIVERSITY	Duration	Particulars
1	Nisha Saini	Lovely Professional University	4 months	Jan- April'18
2	PriyaPandey	Lovely Professional University	4 months	Jan – April '18
3	Rajashri Paul	Lovely Professional University	4 months	Jan – April '18
4	Jubin J. Kurichiyil	Mar Athanasios College For Advanced Studies Tiruvalla	3 months	Feb – April '18
5	Nikhil A.N	Mar Athanasios College For Advanced Studies Tiruvalla	3 months	Feb – April '18
6	AbhishekSingodia	Amity University Rajasthan	6 months	Jan – June '18
7	AnkitShakyawal	Amity University Rajasthan	6 months	Jan – June '18
8	Prerna Sharma	Amity University Rajasthan	6 months	Jan – June '18
9	ShobitVaishnav	Amity University Rajasthan	6 months	Jan – June '18
10	Mohammad Mosa Mubarak	University of Kashmir	6 months	Jan – June '18
11	Vijay Kumar	Dr. R.M.L.A. University, Faizabad	6 months	Jan – June '18
12	Arya Pratap Rao	Dr. R.M.L.A. University, Faizabad	6 months	Jan – June '18
13	Ishita Bhattacharyya	Baba Farid Institute of Technology	4 months	Jan – April '18
14	SonaliSaini	Jaipur National University	6 months	Jan – June '18
15	Nisha	Jaipur National University	6 months	Jan – June '18
16	Avinash Kumar	Jaipur National University	6 months	Jan – June '18
17	Bikash Kumar Das	Siksha 'O' Anusandhan University	6 months	Jan – June '18
18	Sourav Garg	Mangalayatan University Beswan, Aligarh	5 months	Jan – May '18
19	Rahul Kumar	Mangalayatan University Beswan, Aligarh	5 months	Jan – May '18
20	Mohammad Imam Modassir	Samastipur college	3 months	Jan – March '18

Department involved in the following projects

Sl. No.	Title of Project	Project Category	Participating Agencies
1	CSIR-Phytopharmaceuticals Mission (HCP-0010) Project cost:Rs.988.00 Lakhs (Three years)	R&D	CSIR
2	Development of Phytopharmaceutical product for Boovine Mastitis (GAP-2141) Project cost:Rs.104.732 Lakhs (Three years)	R&D	DBT
3	"CSIR Aroma Mission" (HCP-0007) Project cost:Rs.2327.00 Lakhs (Three years)	R&D	CSIR
4	CSIR-Sickle Cell Anaemia (HCP-0008) Project cost:Rs.1367.00 Lakhs (Three years)	R&D	CSIR
5	Technology Business Incubation Programme (GAP-2160) Project cost:Rs.491.54 Lakhs (Five years)	R&D	DST
6	"Phytopharmaceutical Development of *Ficus semicordata* Buch.-Ham. ex Sm. as per regulatory guidelines of DCGI (under the Phytopharmaceutical Mission for North East Region)"	R&D	DBT
7	Development of Skin care products	R&D	CSIR
8	Chemical Engineering (STS-0004)	R&D	CSIR
9	Science and Technology Support Project (STS-1111)	R&D	CSIR

Other Activities:

- Conduct visit with the AYUSH department representatives for business development for cGMP plant.
- Developed standardized process for extraction of different medicinal/Botanical plants i.e. *Tinospora cordifolia, Boswellia serrata, Colebrookea oppositifolia, Woodfordia fruticosa, Glycrezza glabra* etc.
- Prepared Detailed Project Report for NITCO as per "Scheme of Fund for Regeneration of Traditional Industries (SFURTI)" guide lines for ECF generation where CSIR-IIIM Jammu has to act as Technical Agency.
- Facility provided to the various departmental laboratories for grinding of plant material, preparation of extract etc.
- Trained nos. of students from different prestigious collages under skill development program/TBI.
- Imparted training for entrepreneur development of programme for industrial personnel.
- Conduct visit of nos. of school students on various occasion of CSIR/IIIM Jammu foundation and as well as National Science Day, foundation day of CSIR and foundation day of CSIR-IIIM Jammu i.e. 28th February, 26 September & 02 Nov.
- Conduct visit of nos. administrative services probationers from New Delhi.
- Sr. Scientist Anil Kumar Katare enrolled for PhD program in Chemical engineering discipline under Rajeev Gandhi Technical University, Bhopal under the **Co-Supervision of Dr. Ram A. Vishwakarma**.

9.0 ANIMAL HOUSE

9.1 Evaluation of genetic diversity after 20th generation of full-sib mating of Balb/c mice by using microsatellite markers

Govind Yadav and Satheesh Kumar Panneer

BALB/c strain is the most commonly used animal research model in biology/ Bio-medical research. It is used for many inbred, outbred, and transgenic models establishment and being used in drug discovery and development for the betterment of humans as well as domestic animals. Still in India, we were deficient to developing new rodent models for human diseases due to lack of genetic quality of rodent stains. At CSIR-IIIM, Jammu animal house facility conducted study for genetic quality evaluation. Animals were maintained in environmentally controlled facility with routine health monitoring. Selection was conducted based on reproduction performance of the mother's. An unselected control line was maintained throughout the experiment. After, 20th generation of full sib mating results obtain three different lines. All the three lines of BALB/c strain shows standardized litter size of 8 pups at birth. All line mice were genotyped by using established 14 pair of microsatellite markers and genetic diversity analyzed. Here we are reporting that 1 allele varied for within line and 2 for between the lines. The Effective number of alleles was reported 1.021±0.016 in overall experimental population. Shannon's Index for within lines was 0 and among lines was 0.019±0.014. The Estimated Diversity (u) was 0 for within lines, 0.052 ±0.036 for control lines and 0.013±0.009 for among population. Polymorphic information content (PIC) observed in D11Mit260 and D1Mit71. Line1 was showing little higher Genetic distance with Line2 (0.154) followed by control line (0.114) and Line3 (0.074). Control line and Line2 were observed very close genetic distance (0.010). It is concluded that BALB/c strain at IIIM has no diversity within line and very little diversity between lines.

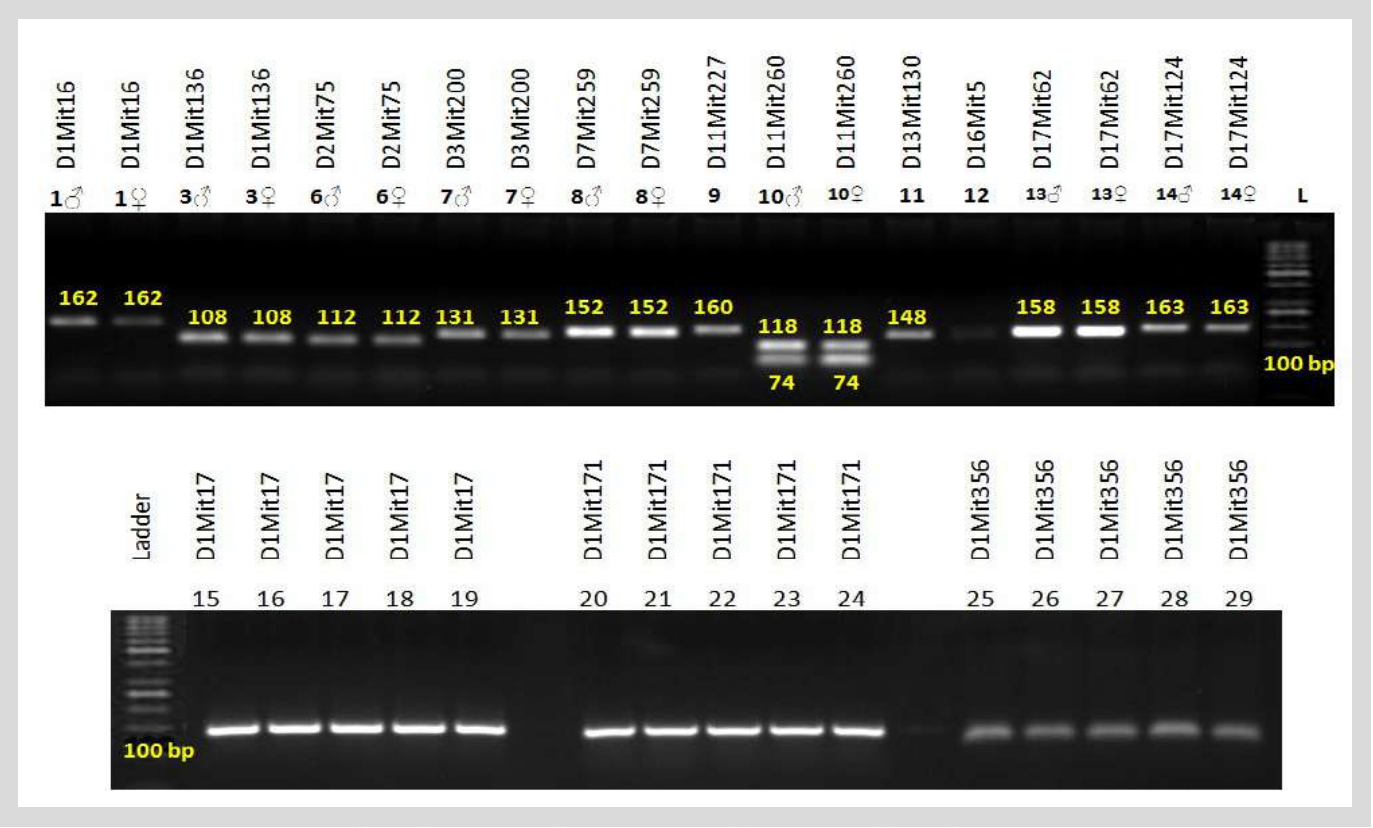
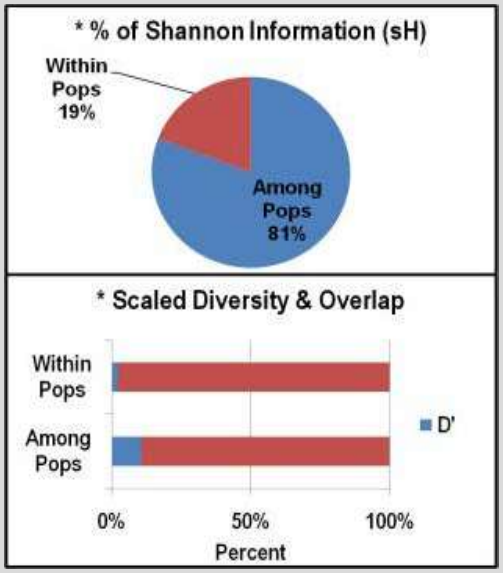


Figure 9.1.1. BALB/c male and female shows uniform allelic pattern in 2% agarose gel electrophoresis.



*** Genetic Distance (Nei) - Pairwise Population Matrix**

Line1	Line 2	Line 3	Control	
0.000				Line1
0.154	0.000			Line2
0.074	0.074	0.000		Line3
0.114	0.010	0.035	0.000	Control

Figure 9.1.2. Genetic analysis done by Population genetic software GenAlEx 6.5(2015)

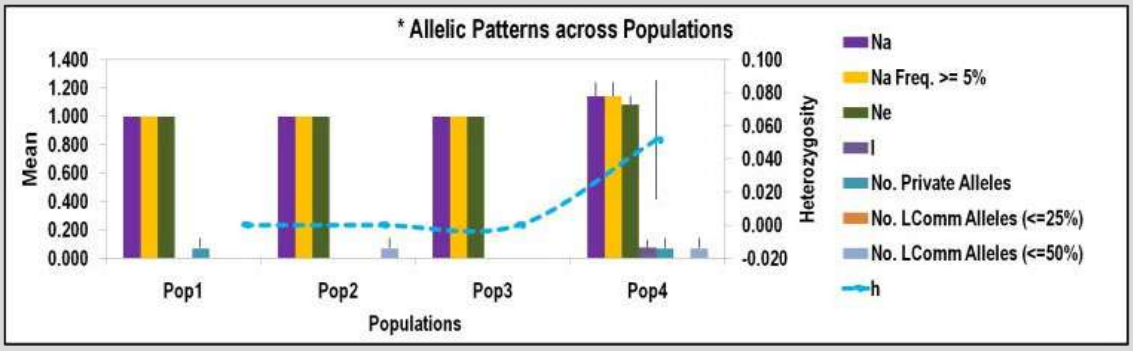
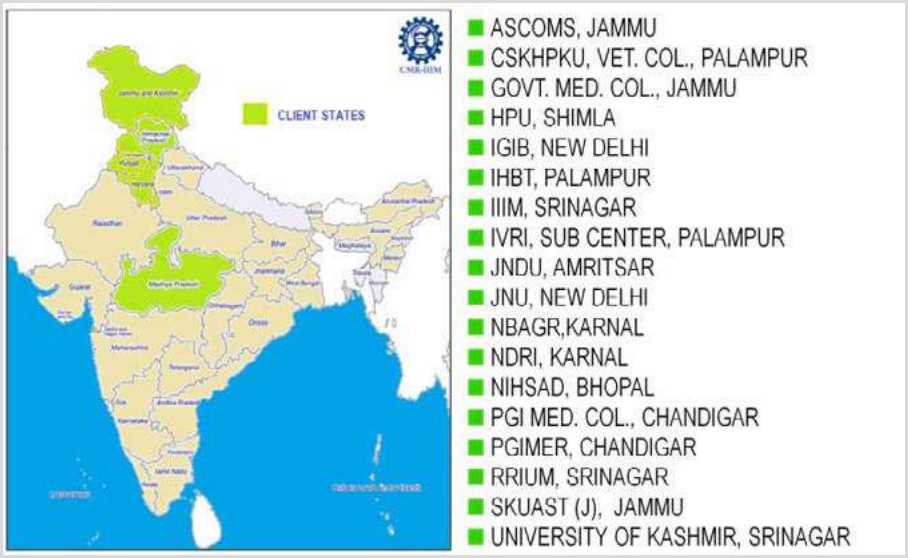


Figure 9.1.3. Heterozygosity analysis by using bioinformatics tools.

Outcome: *List of institutions using Balb/c/iiim Mice and benefited*



Poster Presentation Presented at SOCDAB Conference-2019, ICAR-NBAGR, Karnal

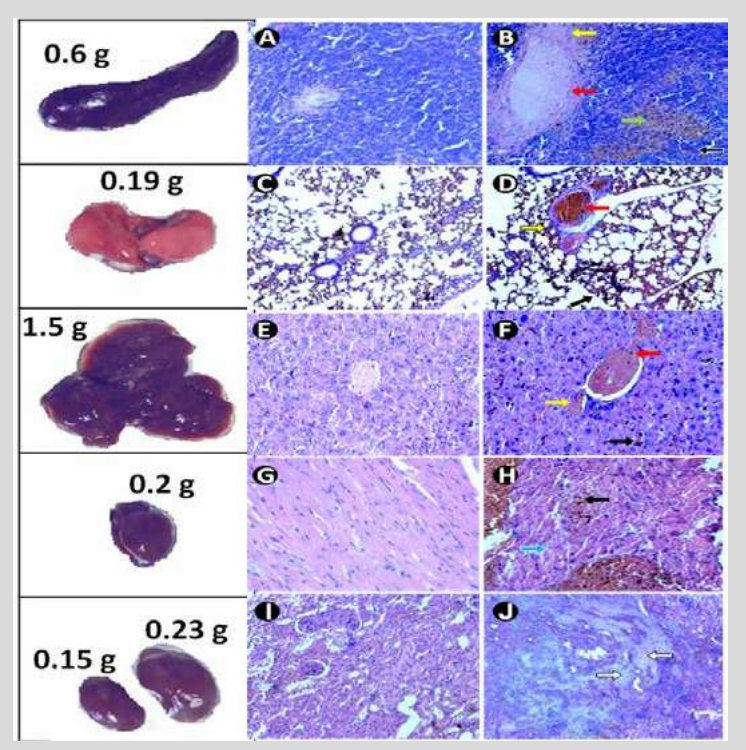
9.2 Establishment of genotyping based breeding program for transgenic Sickle Cell Anemic Mice and confirmation of its pathological conditions at CSIR-IIIM, Jammu

Govind Yadav, Narendra chauhan, Irfan Paswal, Amit Kumar and Satheesh Kumar Panneer

Many of murine models have been developed to mimic human sickle cell (SS) disease. Of these, the Jackson Lab – STOCK *Hba*^{tm1Paz} *Hbb*^{tm1Tow} Tg(HBA-HBBs)41Paz/J (003342) model has targeted deletions of murine α and β globins ($\alpha^{-/-}$, $\beta^{-/-}$) with a transgene containing human α, β^{s}, $^{A}\gamma$, $^{G}\gamma$, and β globins; thus, these mice express human sickle hemoglobin almost exclusively. At Animal House, CSIR-IIIM, Jammu we successfully determined the different globins genotypes in progenies of sickle mice by using standard PCR genotyping methods. Relatively complex attention has been given for genotyping of sickle mice for subsequent breeding program. So, we were tried to simplify the genotyping and breeding protocols for last six month. Allelic patterns (Figure 9.2.2.) of sickle and non-sickle mice were identified. These patterns are standards for selecting mice for breeding and help to identifying sickle mice in young age from there tail samples.Little attention has been given to comparison of the natural progression of chronic organ injury in sickle mice model with that in human sickle cell disease.

Figure 9.2.1: Sickle cell mice/iiim

Figure 9.2.2. Allelic Patterns of sickle and non-sickle Mice



We found that the Jackson mice have several hematologic as well as histopathologic (Figure 9.2.3) similarities with Published data. Which includes erythrocytic sickling, intravascular hemolysis, vascular ectasia, severe anemia, leukocytosis, elevations of inflammatory cytokines, renal infarcts, glomerulo-sclerosis, pulmonary congestion, hepatomegaly and splenomegaly with exuberant splenic hematopoiesis in Homozygous Sickle mice. For utilizing the full potential strengths of murine models of sickle cell disease which necessary to have a detailed understanding of the rate of development and severity of visceral pathology in sickle mice.

Figure 9.2.3. Sickle mice organs followed by microscopic findings of unaffected portions (A, C, E, G, I) with affected portions (B, D, F, H, J)

A, B – Spleen → *Sinusoidal congestion (yellow arrow), vascular ectasia (red arrow), increased hematopoietic cells (green arrow), siderosis (black arrow)*

C, D – Lung → *Sinusoidal congestion (yellow arrow), vascular ectasia (red arrow), siderosis (black arrow)*

E, F – Liver → *Sinusoidal congestion (yellow arrow), vascular ectasia (red arrow), siderosis (black arrow)*

G, H – Heart → *Appeared as loss of normal striations (Blue arrow), siderosis (black arrow)*

I, J – Kidney → *Renal infarcts (White arrow) in the sickle mice.*

9.3 Status of Pedigree of IIIM strains and its evaluation of different pharmacological studies

Govind Yadav and Satheesh Kumar Panneer

1. IIIM Animal House Facilitated R&D activities for proof of concept studies by providing Laboratory Animals of four different species viz., Mice, Rat, Guinea Pig, and Rabbit (Fig1). Currently available strains are being maintained by as per the ethical guidelines (Health Monitoring and Genetic Monitoring) and accredited with CPCSEA. Since last six years our animal house facility systematically programmed to establish pedigree from available stock of strains. Now pedigrees were maintained by standard selection procedures, systematic mating methods and strict record keeping. Our selection program gave the better results in production and reproduction performance of line and sub-lines. These pedigreed rodent lines being evaluated for their suitability in different pharmacological procedures in the area of drug discovery and development (Table.9.3.2). In our facility each line's upcoming filial generations were genetically improved by minimizing the traits variances within the line through scientific selections. Similarly, for outbred stocks were genetically improved by maximize the variance by avoiding inbreeding through maintains effective population size. New comers of Nude Mice and transgenic sickle mice were added during the year of April 2018 to March 2019.

Fig1:IIIM Strains (Apr 2018- Mar 2019)

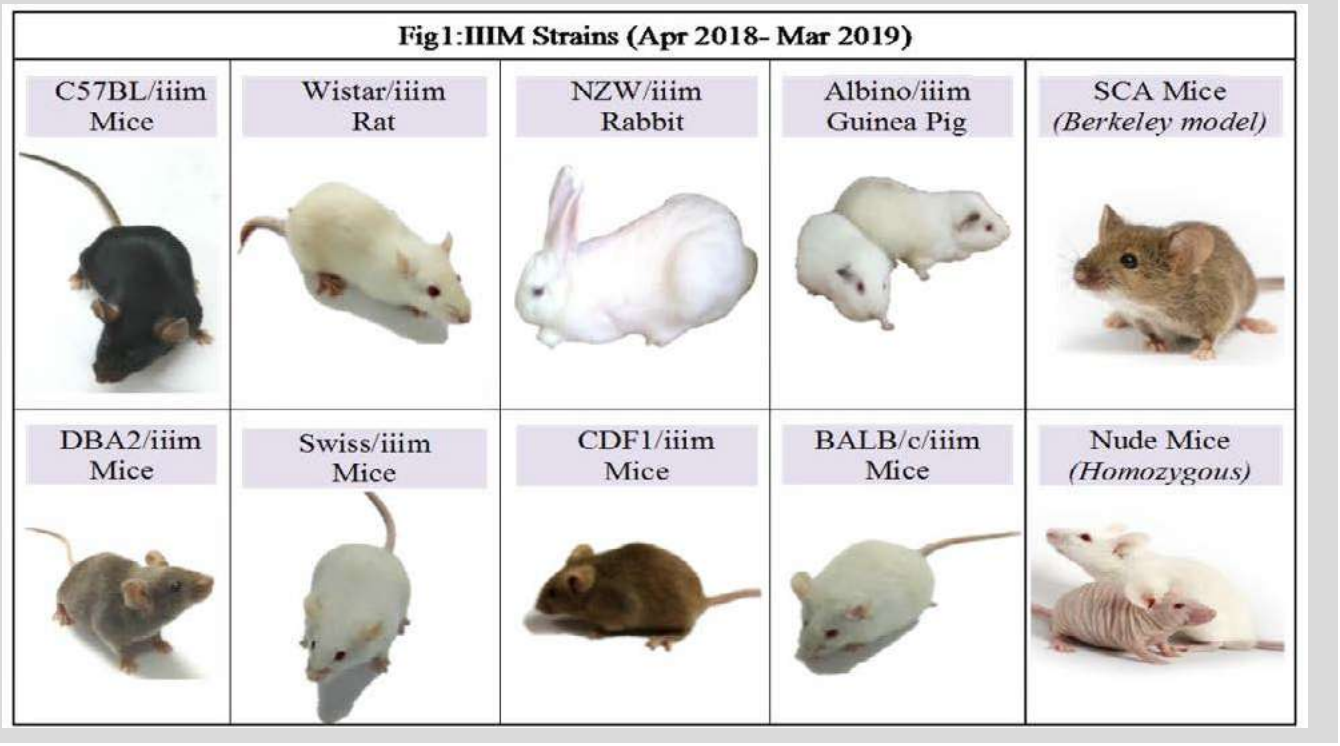


Table.9.3.1 Breeding performance from 1 April 2018 to 31, March 2019

S. No	Strain	No of sub-lines developed	1 April 2018		31 March 2019		Developed by
			Matting Group	Filial generation	Matting Group	Filial generation	
1	*C57BL/iiim Mice*	*3*	*MG-121*	*F-31*	*MG-128*	*F-33*	*Full Sub-Mating*
2	*DBA2/iiim Mice*	*3*	*MG-153*	*F-31*	*MG-166*	*F-33*	*Full Sub-Mating*
3	*BALBc/iiim Mice*	*3*	*MG-418*	*F-22*	*MG-454*	*F-23*	*Full Sub-Mating*
4	*SWISS/iiim Mice*	*2**	*MG-25*	*F-2*	*	*	*Selective Mating*
5	*Wister Rat*	*2**	*MG-172*	*F25*	*	*	*Selective Mating*

Table 9.3.2 List of studies and details of the strains used for IIIM R & D from 1 April 2018 to 31, March 2019

Projects:

- Development of phyto-pharmaceutical product for bovine mastitis: To provide the solution for treatment of mastitis (related to farmers keeping dairy animals for livelihood)
- *IND-Enabling studies (Mutagenecity):* No. of compound/extracts evaluated for mutagencity
- *Sickle Cell Anemia Mission:* CSIR-Sickle Cell Anemia Mission Project

Training programme

Six trainees were trained in handling, designing Animal studies and care of experimental animals, cell culture, microbial culture and PCR.

No of Clients:

14 clients added from Scientific Institutions

Jigysa programme:

Students and Teachers from various Kendriya Vidyalaya and other Schools introduced to Laboratory animals uses in biomedical research

Funds generated (from Apr 2018 – Mar 2019) is = Rs. 28,78,867

S.No.	Fund Generated	Revenue
1	Cost of animals provided in house R&D	(Table.2)Rs.12,58,000
2	Animals sold	Rs.4,02,867
3	Trainings	Rs.80,000
4	Ext. Project	Rs.11,38,000
	Total funds generated	Rs.**28,78,867**

New initiatives:

a. Evaluation of genetic diversity after 20th generation of full-sib mating of Balb/c mice by using microsatellite markers.

b. Successful establishment of genotyping based breeding program for transgenic Sickle Mice at CSIR-IIIM, Jammu and its microscopic pathological conditions for CSIR-Sickle Cell Anemia Mission Project

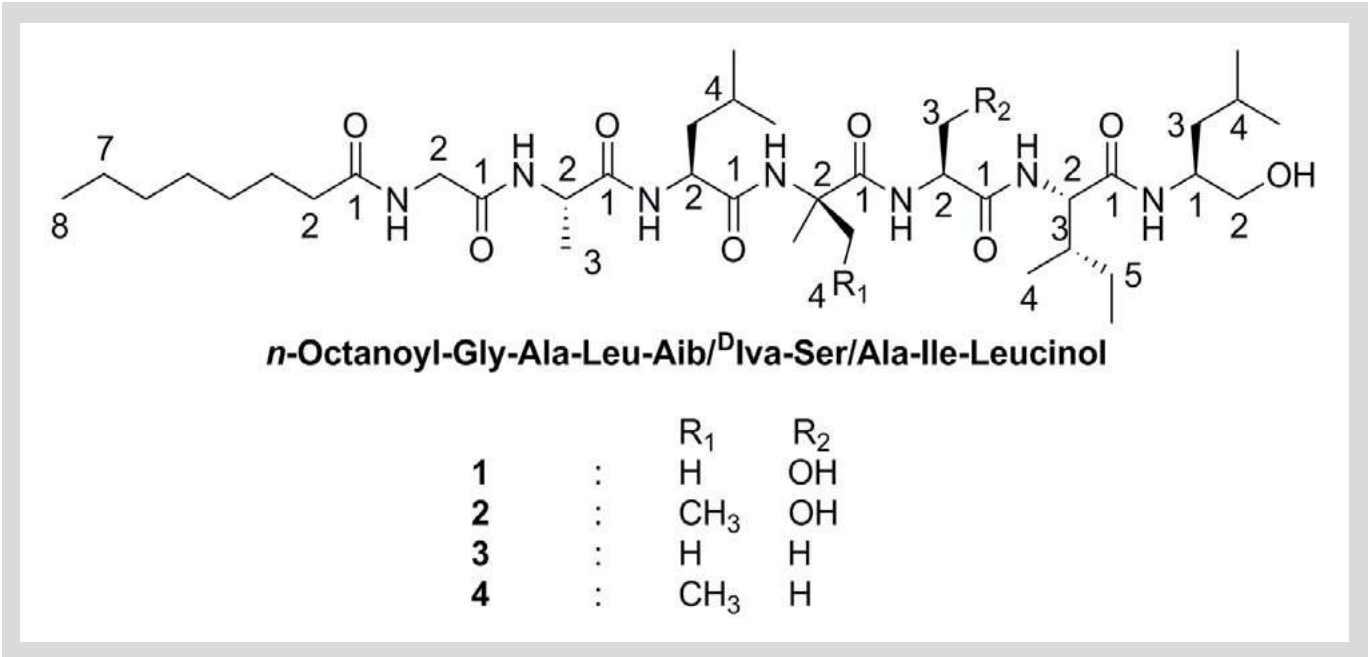
c. Addition of new strains(NUDE/J(002019), 129S1/SvImJ(002448), C57BL/J(000664) and SCA -Tg Mice Hba^{tm1Paz} Hbb^{tm1Tow} Tg(HBA - HBBs) 41Paz/J (003342) to IIIM Animal House Facility to support IIIM R & D Programs

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

10.1 Lipovelutibols A-D: Cytotoxic Lipopeptaibols from the Himalayan Cold Desert Fungus *Trichoderma velutinum* (J Nat Prod. 2018, 81 (2), 219-226)

Varun Pratap Singh, Nalli Yedukondalu, Vandana Sharma, Manoj Kushwaha, Asha Chaubey, Anil Kumar, Deepika Singh, Ram A. Vishwakarma

Enormous microbial diversity exists in the Himalayan cold desert region and is largely unexplored. Study was carried out for isolationof novel non-ribosomal peptides from soil-borne filamentous anamorphic fungus,*T. velutinum*, isolated from the cold Shiwalik regions of North-Western Himalayas. Four novel lipovelutibols A (**1**), B (**2**), C (**3**) and D (**4**) containing six amino acid residues with leucinol at the *C*-terminus and a fatty acyl moiety (*n*-octanoyl) at its *N*-terminus were isolated from the psychrotrophic fungus *Trichoderma velutinum*. Lipopeptaibols**2** and **4** were found to contain D-isovaline, a non-proteinogenic amino acid but lacked α-aminoisobutyric acid, characteristicof peptaibols. Cytotoxic activity of **2** and **4** was observed against HL-60, LS180, MDA-MB-231 and A549 cancer cell lines.



Cytotoxicity activity of isolated lipovelutibols

S. No	IC50 (µM) ±SD			
	HL-60	**LS-180**	**MDA-MB-231**	**A549**
1	>30	>30	>30	30±1.2
2	2±0.1	>30	4±0.1	30±2.7
3	16±0.8	>30	16±0.7	17±1.0
4	4±0.1	7±0.2	5±0.1	4±0.2
Paclitaxel (nM)	2±0.1	2.8±0.1	3.0±0.1	6.8±0.1

Quality Control and Quality Assurance Division, is a NABL (National Accreditation Board for Testing and Calibration Laboratories) accredited laboratory for chemical testing. QCQA division has undergone desktop audit in Dec 2018 for renewal of certificate and successfully completed the audit. The accreditation continued in accordance with standard ISO/IEC 17025: 2005 having certificate no TC-6948, Issue date 01 Mar 2018, valid until 29 Feb 2020.

National Accreditation Board for Testing and Calibration Laboratories

(A Constituent Board of Quality Council of India)

CERTIFICATE OF ACCREDITATION

QUALITY CONTROL AND QUALITY ASSURANCE DIVISION,
CSIR-INDIAN INSTITUTE OF INTEGRATIVE MEDICINE

has been assessed and accredited in accordance with the standard

ISO/IEC 17025:2005

"General Requirements for the Competence of Testing & Calibration Laboratories"

for its facilities at

Canal Road, Jammu-Tawi, Jammu & Kashmir

in the field of

TESTING

Certificate Number TC-6948 *(in lieu of 1021)*

Issue Date 01/03/2018 Valid Until 29/02/2020

This certificate remains valid for the Scope of Accreditation as specified in the annexure subject to continued satisfactory compliance to the above standard & the relevant requirements of NABL.

(To see the scope of accreditation of this laboratory, you may also visit NABL website www.nabl-india.org)

Signed for and on behalf of NABL

N. Venkateswaran
Program Director

8907697010003000889

Anil Relia
Chief Executive Officer

QCQA Division, CSIR-IIIM Jammu stands approved by GOI, Ministry of Health and Family Welfare. QCQA division worked towards establishment of Food testing lab {(FSSAI) Food Safety Standard Authority of India} for food commodities as per the NABL scope. Notification S.O. 3648 (E) was published in Gazette of India, Extraordinary, Part-II, section 3, Sub-section (ii), dated 12 Dec 2018 under section 43 of FSS Act, 2006. Registration number allotted was 55/N/FSSAI/2018.

fssai
Referral lab for
Nuts, Honey & Nutraceuticals

The Scope of accreditation is on following commodities with competencies as given below.

To render analytical services of highest quality associated with degree of professional satisfaction & confidence to customer.

Scope of Accreditation

Food & Agricultural products
- Nuts
- Honey
- Alcoholic Drinks & Beverages
- Spices & Condiments

AYUSH Products
- Ayurvedic Drugs
- Unani drugs
- Herbal Formulations

Cosmetic & Essential Oils
- Qualitative analysis

Animal Food & feeds

Nutraceuticals

Competencies

Chromatographic Fingerprinting by HPTLC
Assay of active constituents by HPLC / LCMS/MS
Pesticides residue analysis
Heavy metals
Micronutrients
Adventitious Toxins; Aflatoxins
Physico chemical analysis
Antibiotic Drug Residues
Energy value
Microbial load
Quality analysis of Water
Vitamins

The Division is also dedicatedly involved in Chemistry Manufacturing & Control (CMC) of botanical raw material, extracts and formulations. Generation of CMC data on the following high value medicinal plants has been undertaken as given below using analytical instruments.

Boswellia serrata	Batch code for CMC study
Plant Material	BS/Pl Mat/B-02
Dried Extract Powder	BS/CMC/B-08 EEXTD 0023
Dried Extract Powder	BS/CMC/B-07 EEXTD 0022
Dried Extract Powder	BS/CMC/B-06 EEXTD 0014
Dried Extract Powder	BS/CMC/B-06 EEXTD 0015

Bergenia ciliata	Batch code for CMC study
Hydroalcoholic extract	B-01, B-02 and B-03
Hydroalcoholic extract	BC/CMC/B-14 EEXTD 0008,
Hydroalcoholic extract	BC/CMC/B 14 EEXTD 0008,
Hydroalcoholic extract	BC/CMC/B-12 DEXTD 0024

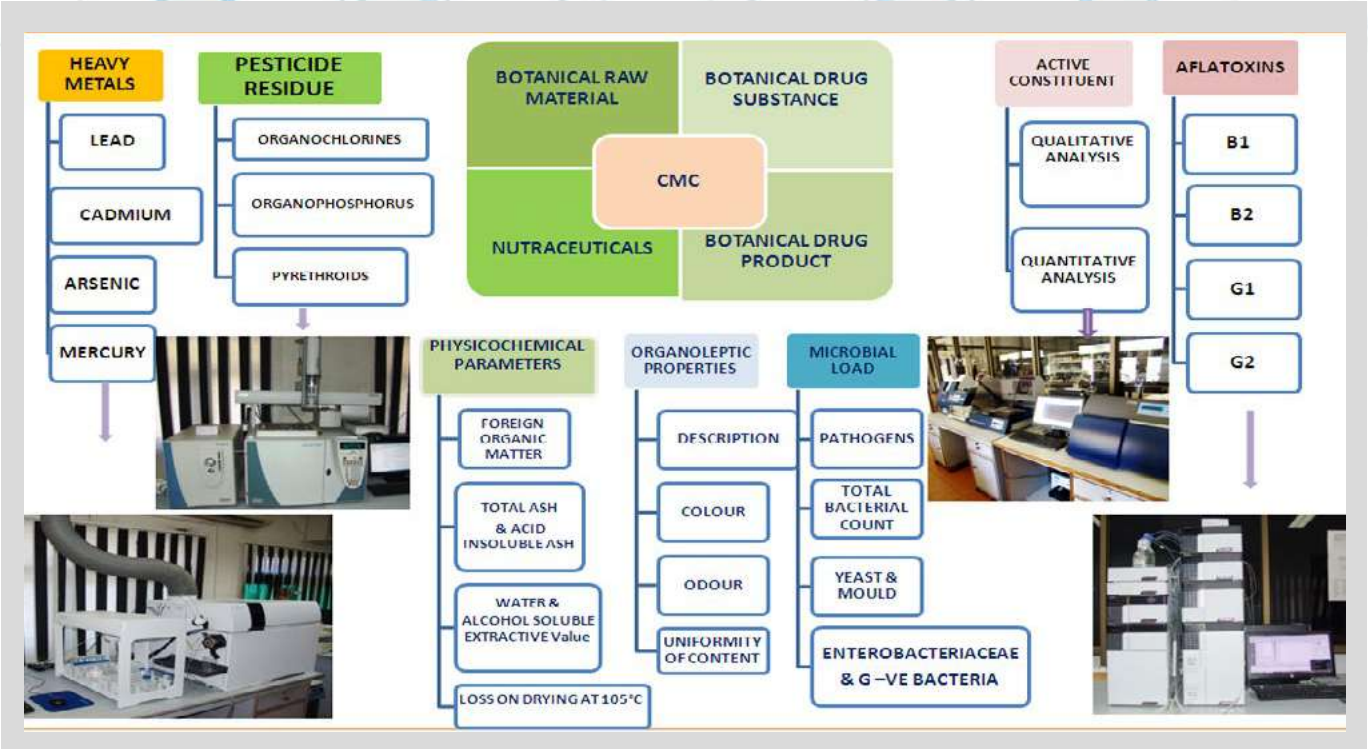
Trillum govandinum	Batch code for CMC study
Plant Material	Trillium/B-01/Pl. Mat.

Piper bitle	Batch code for CMC study
Extract	PB/CMC/01 EEXTD 0012

Withania somnifera	Batch code for CMC study
Dried Alcoholic extract	WS/CMC/B-06 EEXTD 0015
Plant Material	WS/CMC/B-05 EEXTD 0013
Plant Material	WS/CMC/B 03 DEXTD 0006

Colebrookea oppositifolia	Batch code for CMC study
Grinded Powder of leaves	CO-07/CMC
Dried EXTRACT Powder	CO-06/CMC/EEXTD 0002
Dry powder Extract	CO + Maltodextrin 10 ml + 1.25 g, 10ml + 2.5 g, 10ml + 3.75 g
Plant Material (Grinded)	CO-08 (only aflatoxins)

Glycyrriza glabra	Batch code for CMC study
Extract Powder	GG/CMC/B-05 EEXTD 0020
Extract powder	GG/CMC/B-04 EEXTD 0019
Extract powder	GG/CMC/B-02 EEXTD 0005



QCQA division has accrued many benefits to Society and industry as follows:

The QCQA division is proudly moving ahead for being designated as Drug Testing Laboratory (DTL Ayurveda). As the testing of AYUSH drugs is now covered under the provision of Drug and Cosmetic Act 1940, this requires application to be submitted to licensing authority as well as AYUSH department, New Delhi. Application is under process for approval on Form 48 as private AYUSH drug testing laboratory under Rule 160 A -J to the Drugs & Cosmetic Rules. 37 percent of drug samples submitted from the office of Indian Systems of medicine, J & K Jammu were found to be substandard. Commercial samples were carried out for food, spices and condiments, alcoholic drinks and beverages analysis of heavy metals, pesticides, aflatoxins, various physicochemical parameters like total ash, acid insoluble ash, crude fiber, peroxide value, free fatty acids were carried out. Physiochemical testing and microbial load in water from various public and private schools, universities, hospitals, small- and large-scale industries from J&K state and from other parts of India were also analyzed. As a part of Skill Development Program (SDP), manpower trainings were also conducted on analytical instruments for postgraduate students, giving them hands on experience on modern high-end analytical instruments.

Trichoderma velutinum as potential source of bioactive compounds and enzymes

The genus *Trichoderma*, a filamentous fungus is known to possess diverse metabolic capabilities to produce secondary metabolites with wide applications. It is also well known to produce nonribosomal peptides (NRPs) including peptaibols, lipopeptaibols, and lipoaminopeptides. About fourty species have been reported for peptaibiome production from this genus. Fermentation Technology Division has been actively involved in the isolation of microorganisms from the unexplored niches of North-Western Himalayas and has recently reported the psychtrophic microorganisms which are capable to produce small peptides/ peptaibols and has shown potential biocontrol activity.

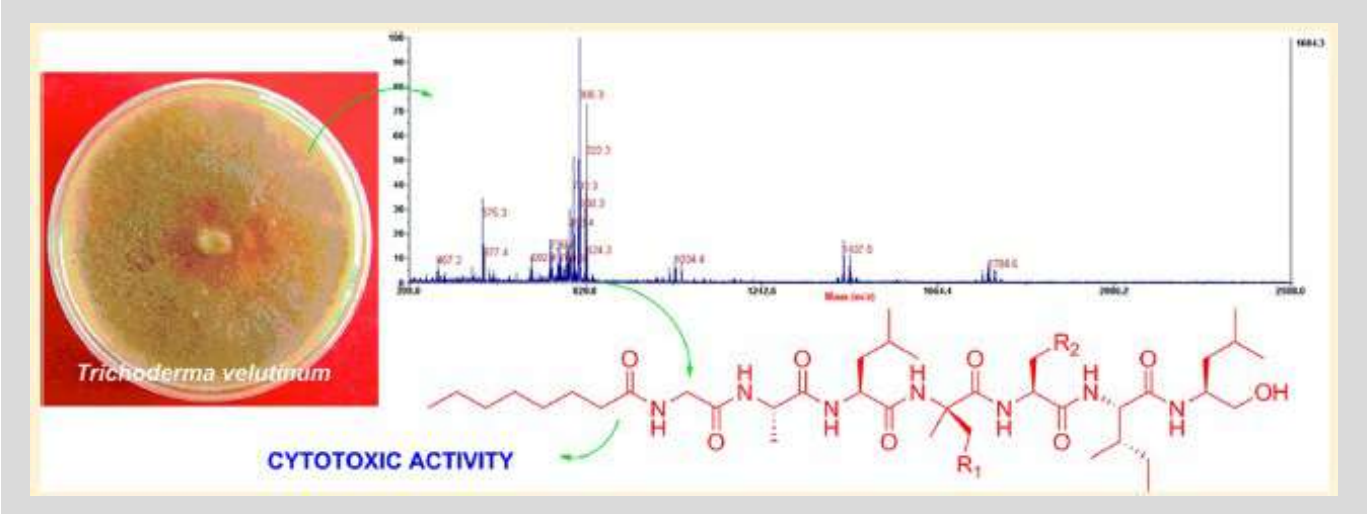


Figure 11.1: Maldi-MS profile of the bioactives produced by Trichoderma velutinum ACR-P1

The mycelia were grown on more than hundred petriplates under optimized conditions and were handed over to Medicinal Chemistry Division, where, the mycelia were harvested, and the biomass was extracted with ethyl acetate. The combined organic filtrate was evaporated to obtain a crude extract. The crude extract thus obtained was then subjected to purification through semipreparative RP-HPLC. Four pure compounds were isolated and characterized followed by cytotoxic activity evaluation at Cancer Pharmacology Division.

Potential for cell wall degrading enzyme production

Cellulase assay: Fungal strain ACR-P1 showed potential to metabolize CMC as sole source of carbon and energy and as a cellulase enzyme inducer. Strain grew radially with little sporulation or conidia formation towards the circumference of the petridish upon incubation up to 4 days. Results obtained from agar well diffusion assay were in agreement with CMC metabolization assay showing clear faded halos around the wells.

Chitinase assay: Strain ACR-P1 was observed to be the best metabolizer of colloidal chitin as sole carbon and energy source and as a chitinase inducer. The fungus grew with immense potential on chitin agar plates with abundant sporulation near the peripheries of the petridish. Also, dye indicator assay (BCP) showed potential of the fungus ACR-P1 for the chitinase enzyme by converting the dark yellow color of the medium (supplemented with BCP) to purple color due to pH shift taking place as a result of digested colloidal chitin upon growth. This assay provided the most reliable results illustrating chitinase producing potential of the strain ACR-P1. Also agar well diffusion assay further signified the chitinase activity of fungal strain with formation of purple colored zones around the wells with the fungal broth and CFE respectively.

Protease assay: Strain ACR-P1 was shown to be potential protease producer as it very vigorously metabolized the milk protein casein as sole source of carbon and energy. Also, agar well diffusion assay for protease well established the protease producing capabilities of the strain ACR-P1 resulting into clear zones around the wells with both fungal broth and CFE respectively.

Being a psychrotrophic fungus, and its biocontrol potential studied, efforts are now being made to develop a formulation that can be used as biocontrol agent during winters in the regios which suffer from extreme cold conditions.

Isolation and characterization of actinomycetes as potential bioactives

Actinomycetes are considered to be one of the most potential bacteria for pharmacological activity. With the advent of deleterious diseases, there is an urgent need for the isolation of new and beneficial compounds to combat these threats. The potential isolates may be further investigated for novel antibiotics development, biocontrol agents, plant growth harmones and agroactive compounds. The present work highlights the results of the studies on actinomycetes isolated from unexplored Shivalik region of Jammu (India) were screened for bioactivities against common human pathogens. The producers showing potential activity are being further investigated to isolate bioactive compounds. The pure isolates were inoculated in test tubes containing 10 ml or 500 ml Erlenmeyer flasks containing 100 ml ISP-2 medium and incubated for 7-10 days at 28˚C under shaking conditions. After incubation, supernatant were extracted with ethyl acetate and biomass was extracted using methanol. Isolated cultures were grown in ISP-2 medium at 28˚C under shaking conditions for 7-10 days. The fermented broth is used to check antimicrobial activity. All the test pathogens used in the present work were from Microbial Type Culture Collection and American Type Culture Collection. The antimicrobial activity was performed by agar well diffusion method. The isolates showing antimicrobial activity were further grown in one litre broth and solvent extracts were prepared.

Figure 11.2: Representative bioactive compounds producing actinomyces

Out of 46 pure isolates of actinomycetes 13 cultures showed antimicrobial activity. Only 2 cultures i.e GR 1 and PR-1, showed antimicrobial activity against both gram positive and gram negative bacteria, 11 cultures have antimicrobial activity only against gram negative bacteria and 3 cultures showed activity against fungal pathogens.

Service to Industry

- M/S Eco Force Pest Control India Pvt. Ltd. MoU signed for product (formulation) development for mosquito eradication
- M/S Bills Biotech Pvt. Ltd : Tripartite Non Disclosure Agreement was signed through NRDC for Microbial Fermentation Process of DHA

S&T Services

Participating in DBT sponsored project on "Characterization, Recombinant expression, Process Scale up and Validation of Selected Hydrolases from Native Actinobacteria for Commercial Exploitation" for scale-up studies of Chitinase enzyme.

12. KNOWLEDGE RESOURCE CENTER (LIBRARY)

Introduction

Library in this campus was in existence even during pre-independence days. During those times, it was known as 'Drug Research Laboratory (DRL) - Library' which was renamed as 'Regional Research Laboratory (RRL) - Library' in 1957 when CSIR took-over DRL and renamed the Institution as 'Regional Research Laboratory (RRL)'. Library shifted to its new building (present building) on 13th September, 1974. Subsequently, with the renaming of RRL as 'CSIR-Indian Institute of Integrative Medicine (IIIM)' and renaming of CSIR Libraries as 'S&T Knowledge Resource Centres', it is presently known as "IIIM S&T Knowledge Resource Centre (KRC)."

Objectives:

The objectives of IIIM-KRC are to further the interests of 'Users' by providing library services to enable them to keep a track of significant development in their fields of interest. It supports its Scientists, Students and other S&T users with current and even evolving knowledge in their respective spheres of R&D activities.

Membership:

IIIM KRC caters to the information requirements of not only internal users but also of external users, like - postgraduate students, faculty members of colleges & universities; and corporate members. However, the membership for external users is on nominal payment basis.

Collection:

(a) Print Collection:

Over the decades, IIIM has developed its rich Library resources. It has more than 100 year old rare research documents in its collection. It has grown into one of the most valuable research library in the country. It has a rich collection of books, periodicals, databases and other intellectual material. Broadly speaking, its collection covers subject areas of - Biotechnology, Botany, Medicinal Chemistry, Natural Products Chemistry (NPC), Pharmacology, Quality Control and Agrotechnology & Cultivation of Medicinal and Aromatic plants.

During financial year 2018-19, IIIM KRC added 81 books and reference resource, including books in Hindi language, in its collection.

The holding status as on 31.03.2019 is as under:

No. of purchased documents: 27836

No. of Periodicals Bound Volumes: 17187

(b) E-Resources:

IIIM is an important member of 'National Knowledge Resource Consortium (NKRC)'. Through this consortium, KRC provides access to thousands of journals published by various publication groups - like American Chemical Society, Emerald, IEEE, JCCC, Nature Publishing Group, Oxford University Press, Royal Society of Chemistry, Taylor and Francis, Wiley, etc. It also subscribes other e-resources which are not available through NKRC consortium.

The total budget allocation during the financial year 2018-19 was Rs.93.00 lakh.

It has computerized all its in-house activities using 'KOHA' open source software. These services are being maintained and updated on a regular basis.

Services:

Presently, following services are being provided to the users:

> Online access to e-Journals and Databases.
> Electronic Document Delivery Service (EDDS).
> Information search and retrieval facility.
> Plagiarism Detection Service.
> Reprographic & Print facilities.

Other initiatives:

KRC has developed its website with the help of IIIM-IT Cell. It can be accessed on URL: http://onlinelibrary.iiim.res.in/. Besides other useful information, links to all the subscribe e-resources; NKRC resources, etc. are available on this website.

13 AcSIR Activities at CSIR- IIIM, Jammu

CSIR-IIIM, Jammu is an important unit of AcSIR System. The Institute offers PhD programme to eligible candidates in the following research areas:

a) Biological Sciences;

b) Chemical Sciences.

The admission takes place twice in a year i.e., for the January & July/August sessions. In July/August, 2018 session a total of thirty three (33) PhD Students were registered at IIIM, Jammu. Similarly, in January, 2019 session twelve (12) students were selected for admission to PhD programme.

The Academic Cell at IIIM is taking necessary initiatives to ensure smooth functioning of all AcSIR Academic activities, viz. student's Admission Processes, Course Work, DAC formation and arranging of meetings, Pre and post thesis submission formalities, etc. It acts as a liaison between AcSIR Headquarter Office, AcSIR Lab Coordinator, Ph.D Supervisors, Students, DAC Members & other External Experts.

As course curriculum, a student has the choice to select his/her Course Work topic and has to undergo various mandatory examinations from time to time. This includes – four DACs (Doctoral Advisory Committee Meetings); Comprehensive Examination; Course-work examination; Open Collegiums, and Viva-Voce (OEBs). The Comprehensive Examination and Viva Voce (OEB) of the student involve at least one 'External Expert Member'.

During this period, a total of eighteen (18) DAC-I; fourteen (14) DAC-II/Comprehensive Examinations; eighteen (18) – DAC-III; and twenty three (23) DAC-IV Meetings were conducted. Also, twenty two (22) AcSIR students submitted their final thesis and successfully defended their viva voice (OEB) examination. This includes:

Biological Sciences – 17 candidates

Chemical Sciences – 05 candidates

It is taking utmost care in proper record-keeping; to ensure that rules & guidelines are followed in a timely manner at local level; handling of Students Fee issues; providing hospitality services to the invited External Experts; timely processing of their TA/DA payments and other related matters.

LIST OF PUBLICATIONS

CALENDER YEAR 2018

S. No.	Title	Author	Impact Factor
1	4-aryl/heteroaryl-4H-fused Pyrans as Anti-proliferative Agents: Design, Synthesis and Biological Evaluation. *Anti-cancer agents in medicinal chemistry* **(2018),** 18(1), 57-73	Kumar Dinesh; Sharma Pooja; Bedi P M S; Jain Subheet K; Kumar Dinesh; Sharma Pooja; Singh Gurpreet; Qayum Arem; Mahajan Girish; Mintoo M J; et al	2.556
2	4-Formyl-Pyrazole-3-Carboxylate: A Useful Aldo-X Bifunctional Precursor for the Syntheses of Pyrazole-fused/ Substituted Frameworks. JOURNAL OF HETEROCYCLIC CHEMISTRY **(2018),** 55(2), 373-390.	Devi, N; Shankar, R; Singh, V	1.241
3	A Mechanistic Study to Determine the Structural Similarities Between Artificial Membrane Strat-M® and Biological Membranes and Its Application to Carry Out Skin Permeation Study of Amphotericin B Nanoformulations. *AAPS PharmSciTech* **(2018)**, 19(4), 1606-1624,	Kaur Lakhvir; Jain Subheet Kumar; Singh Kanwaldeep; Paul Surinder; Singh Sukhprit; Singh Shashank	2.666
4	A new clerodane furano diterpene glycoside from Tinospora cordifolia triggers autophagy and apoptosis in HCT-116 colon cancer cells. *Journal of Ethnopharmacology* **(2018)**, 211, 295-310. DOI:10.1016/j.jep.2017.09.034	Sharma, Neha; Kumar, Ashok; Sharma, P. R.; Qayum, Arem; Singh, Shashank K.; Dutt, Prabhu; Paul, Satya; Gupta, Vivek; Verma, M. K.; Satti, N. K.; et al	3.115
5	A Novel Approach to Access Aryl Iodides and Disulfides via Dehydrazination of Arylhydrazines and Arylsulfonylhydrazides. *ChemistrySelect* **(2018)**, 3(10), 2800-2804. DOI:10.1002/slct.201800188	Balgotra, Shilpi; Kumar Verma, Praveen; Kour, Jaspreet; Gupta, Sorav; Vishwakarma, Ram A.; Sawant, Sanghapal D.	1.505
6	A Simple and Efficient Approach for the Synthesis of 1,3-Oxazolidines from beta-Amino Alcohols Using Grinding Technique. *CHEMISTRYSELECT* **(2018),** 3 (48), 13675-13681	Singh, N; Dar, AA; Kumar, A	1.505
7	A strain of Streptomyces sp. isolated from rhizospheric soil of Crataegus oxycantha producing nalidixic acid, a synthetic antibiotic. *Journal of Applied Microbiology* **(2018)**, 124(6), 1393-1400. DOI:10.1111/jam.13736	Arora, N.; Kumar, S.; Satti, N. K.; Ali, A.; Gupta, P.; Katoch, M.	2.16
8	Acyl Radicals from Terminal Alkynes: Photoredox-Catalyzed Acylation of Heteroarenes. *Chemistry - A* European Journal **(2018),** 24(42), 10617-10620. DOI:10.1002/chem.201801628	Sultan, Shaista; Rizvi, Masood Ahmad; Kumar, Jaswant; Ali Shah, Bhahwal	5.16
9	Aglaonema nebulosum (araceae), range extension and first record from India. *J. Bot. Res. Inst. Texas* **(2018),** • 12, pp. 239-243.	Singh B, Adhikari D, Barik SK	NOT KNOWN
10	AKT Inhibition Modulates H3K4 Demethylase Levels in PTEN-Null Prostate Cancer. *Molecular cancer therapeutics* **(2018)**, 18(2):356-363. doi: 10.1158/1535-7163	Khan MI, Hamid A, Rath S, Ateeq B, Khan Q, Siddiqui IA, Adhami VM, Choudhry H, Zamzami MA, Mukhtar H	5.365
11	Allosteric Site Inhibitor Disrupting Auto-Processing of Malarial Cysteine Proteases. *Scientific reports* **(2018)**, 8(1), 16193.	Pant A; Verma S; Dixit R; Pandey K C; Pant A; Verma S; Pande V; Kumar R; Wani N A; Rai R; et al	4.122
12	Amide hydrolyzing potential of amidase from halotolerant bacterium Brevibacterium sp. IIIMB2706. *Biocatalysis and Biotransformation* **(2018)**, Ahead of Print. DOI:10.1080/10242422.2018.1494733	Sharma, Hitesh; Singh, Rahul Vikram; Raina, Chand; Babu, Vikash	1.06

S. No.	Title	Author	Impact Factor
13	Antiproliferative efficacy of curcumin mimics through microtubule destabilization. *European journal of medicinal chemistry* **(2018),** 15151-61	Khwaja S, Fatima K, Hasanain M, Behera C, Kour A, Singh A, Luqman S, Sarkar J, Chanda D, Shanker K, Gupta AK, Mondhe DM, Negi AS	4.816
14	Antitumour, acute toxicity and molecular modeling studies of 4-(pyridin-4-yl)-6-(thiophen-2-yl) pyrimidin-2(1H)-one against Ehrlich ascites carcinoma and sarcoma-180. *Heliyon* **(2018),** 4(6), e00661	Kumar Dinesh; Sharma Pooja; Nepali Kunal; Singh Gurpreet; Jain Subheet K; Kumar Dinesh; Sharma Pooja; Mahajan Girish; Mintoo Mubashir J; Singh Amarinder; et al	SCImago Journal Rank (SJR): 0.355
15	Assessing ethnic traditional knowledge, biology and chemistry of Lepidium didymum L., lesser-known wild plants of Western Himalaya. *Proc. Natl. Acad. Sci. India Sect. B.* Biol. Sci. **(2018),** pp. 1-8. DOI: 110.1007/s40011-018-1027-4	Singh B, Singh S, Singh B, Kitchlu S, Babu B	0.396
16	Assessment of chemical and genetic variability in Tanacetum gracile accessions collected from cold desert of Western Himalaya. *3 Biotech* **(2018),** *8, pp. 284. DOI:10.1007/s13205-018-1299-7*	Mahajan V, Chouhan R, Kitchlu S, Bindu K, Koul S, Singh B, Bedi YS, Gandhi SG	1.497
17	Attenuation of Glutamate-Induced Excitotoxicity by Withanolide-A in Neuron-Like Cells: Role for PI3K/Akt/MAPK Signaling Pathway. *Molecular Neurobiology* **(2018)**, 55(4), 2725-2739. DOI:10.1007/s12035-017-0515-5	Dar, Nawab John; Satti, Naresh Kumar; Dutt, Prabhu; Hamid, Abid; Ahmad, Muzamil	5.076
18	Azoalkyl ether imidazo[2,1-b]benzothiazoles as potentially antimicrobial agents with novel structural skeleton. BIOORGANIC & MEDICINAL CHEMISTRY LETTERS **(2018),** 28(14), 2426-2431.	Maddili, SK; Li, ZZ; Kannekanti, VK; Bheemanaboina, RRY; Tuniki, B; Tangadanchu, VKR; Zhou, CH	2.448
19	Bacillus amyloliquefaciens induces production of a novel blennolide K in coculture of Setophoma terrestris. *Journal of Applied Microbiology* **(2018)**, 124(3), 730-739. DOI:10.1111/jam.13683	Arora, D.; Chashoo, G.; Singamaneni, V.; Sharma, N.; Gupta, P.; Jaglan, S.	2.16
20	Bioactive compounds and pharmacological and food applications of Syzygium cumini - a review. *FOOD & FUNCTION* **(2018),** 9(12), 6097-6116	Chhikara, N; Kaur, R; Jaglan, S; Sharma, P; Gat, Y; Panghal, A	3.241
21	Biotransformation, Using Recombinant CYP450-Expressing Baker's Yeast Cells, Identifies a Novel CYP2D6.10(A122V) Variant Which Is a Superior Metabolizer of Codeine to Morphine Than the Wild-Type Enzyme. ACS OMEGA **(2018),** 3(8), 8903-8912.	Williams, IS; Gatchie, L; Bharate, SB; Chaudhuri, B	2.584
22	Bovine mastitis: An appraisal of its alternative herbal cure. *Microbial pathogenesis* **(2018),** 114357-361	Mushtaq Saleem; Shah Aabid Manzoor; Shah Aiyatullah; Lone Sajad Ahmad; Hussain Aehtesham; Hassan Qazi Parvaiz; Ali Md Niamat	2.332
23	Broad-Spectrum Antibacterial Activity of Proteolytically Stable Self-Assembled αγ-Hybrid Peptide Gels. *Biomacromolecules* (2018), 19(3), 782-792	Malhotra Kamal; Singh Yashveer; Shankar Sudha; Rai Rajkishor; Shankar Sudha; Rai Rajkishor	5.738
24	Camphor sulphonic acid mediated quantitative 1,3-diol protection of major Labdane diterpenes isolated from Andrographis paniculata. *Natural product research* **(2018)**, 32(15), 1751-1759,	Sharma Venu; Dhar Manoj K; Kaul Sanjana; Kapoor Kamal K; Mukherjee Debaraj; Gupta Vivek K	1.928
25	Carbon-carbon and Carbon-heteroatom Bond Formation Reactions using Unsaturated Carbon Compounds. *Chemical Record* **(2018),** Ahead of Print. DOI:10.1002/tcr.201800095	Sultan, Shaista; Shah, Bhahwal Ali	4.891

S. No.	Title	Author	Impact Factor
26	Catalyst Free Selective Monobenzoylation of Diols with Benzoyl Cyanide: A Robust and Regioselective Strategy. *ChemistrySelect* **(2018)**, 3(2), 828-831. DOI:10.1002/slct.201702893	Abdul Waseem, Malik; Lone, Ali Mohd.; Teli, Bisma; Bhat, Bilal A.	1.505
27	CD44 targeted PLGA nanomedicines for cancer chemotherapy. *European journal of pharmaceutical sciences* : official journal of the European Federation for Pharmaceutical Sciences **(2018),** 12147-58,	Saneja Ankit; Arora Divya; Dubey Ravindra Dhar; Kumar Robin; Panda Amulya K; Gupta Prem N	3.466
28	Characterization of the gene encoding 4-coumarate:CoA ligase in Coleus forskohlii. *Journal of Plant Biochemistry and Biotechnology* **(2018)**, Ahead of Print. DOI:10.1007/s13562-018-0468-4	Awasthi, Praveen; Mahajan, Vidushi; Jamwal, Vijay Lakshmi; Chouhan, Rekha; Kapoor, Nitika; Bedi, Yashbir S.; Gandhi, Sumit G.	0.774
29	Chemical investigation of Cannabis sativa leading to the discovery of a prenylspirodinone with antimicrobial potential. *Tetrahedron Letters* **(2018),** 59(25), 2470-2472. DOI:10.1016/j.tetlet.2018.05.051	Nalli, Yedukondalu; Arora, Palak; Riyaz-Ul-Hassan, Syed; Ali, Asif	2.125
30	Chitosan Engineered PAMAM Dendrimers as Nanoconstructs for the Enhanced Anti-Cancer Potential and Improved In vivo Brain Pharmacokinetics of Temozolomide. *Pharmaceutical research* (2018), 35(1), 9.	Sharma Ashok Kumar; Gupta Lokesh; Sahu Hitesh; Gupta Umesh; Qayum Arem; Singh Shashank K; Nakhate Kartik T; Ajazuddin	3.335
31	Citrus medica: nutritional, phytochemical composition and health benefits - a review. FOOD & FUNCTION **(2018),** 9(4), 1978-1992.	Chhikara, N; Kour, R; Jaglan, S; Gupta, P; Gat, Y; Panghal, A	3.241
32	Contribution to Biodiversity Hotspot: Assessment of forest types, floristic composition and economic wealth of Nokrek biosphere reserve in Northeast India. I*ndian For.***(2018),** 144(8), 734-741.	Singh B, Singh B, Borthakur SK, Phukan SJ	NOT KNOWN
33	Corrigendum to "Short hybrid peptides incorporating β- and γ-amino acids as antimicrobial agents" [Peptides 97 (2017) 46-53]. *Peptides* (New York, NY, United States) **(2018),** 104, 85. DOI:10.1016/j.peptides.2018.04.007	Wani, Naiem Ahmad; Singh, Gurpreet; Shankar, Sudha; Sharma, Arushi; Katoch, Meenu; Rai, Rajkishor	2.851
34	Cross dehydrogenative coupling of sugar enol ethers with terminal alkenes in the synthesis of pseudo-disaccharides, chiral oxadecalins and a conjugated triene. ORGANIC & BIOMOLECULAR CHEMISTRY **(2018),** 16(15), 2666-2677.	Hussain, N; Tatina, MB; Mukherjee, D	3.49
35	Cyclodipeptide c(Orn-Pro) Conjugate with 4-Ethylpiperic Acid Abrogates Cancer Cell Metastasis through Modulating MDM2. *Bioconjugate Chemistry* **(2018),** 29(1), 164-175. DOI:10.1021/acs.bioconjchem.7b00670	Shankar, Sudha; Faheem, Mir Mohd; Nayak, Debasis; Wani, Naiem Ahmad; Farooq, Saleem; Koul, Surrinder; Goswami, Anindya; Rai, Rajkishor	4.485
36	Cytophilic Antibodies Against Key Plasmodium falciparum Blood Stage Antigens Contribute to Protection Against Clinical Malaria in a High Transmission Region of Eastern India. *The Journal of infectious diseases* **(2018)**, 218(6), 956-965.	Kana IH, Garcia-Senosiain A, Singh SK, Tiendrebeogo RW, Chourasia BK, Malhotra P, Sharma SK, Das MK, Singh S, Adu B, Theisen M	5.186
37	De novo transcriptome analyses reveals putative pathway genes involved in biosynthesis and regulation of camptothecin in Nothapodytes nimmoniana (Graham) Mabb. *Plant Molecular Biology* **(2018),** 96(1-2), 197-215. DOI:10.1007/s11103-017-0690-9	Rather, Gulzar A.; Sharma, Arti; Pandith, Shahzad A.; Kaul, Veenu; Nandi, Utpal; Misra, Prashant; Lattoo, Surrinder K.	3.543

S. No.	Title	Author	Impact Factor
38	Design and synthesis of 1,4-substituted 1H-1,2,3-triazolo-quinazolin-4(3H)-ones by Huisgen 1,3-dipolar cycloaddition with PI3Kγ isoform selective activity. *Bioorganic & Medicinal Chemistry Letters* **(2018),** 28(6), 1005-1010. DOI:10.1016/j.bmcl.2018.02.032	Srinivas, M.; Singh Pathania, Anup; Mahajan, Priya; Verma, Praveen K.; Chobe, Santosh S.; Malik, Fayaz A.; Nargotra, Amit; Vishwakarma, Ram A.; Sawant, Sanghapal D.	2.442
39	Design, Synthesis and In vitro Evaluation of Piperazine Incorporated Novel Anticancer Agents. *Letters in Drug Design & Discovery* **(2018),** 15(8), 866-874., DOI:10.2174/1570180815666171211161501	Singh, Mahaveer; Jadhav, Hemant R.; Kumar, Amit	0.924
40	Detailed account on activation mechanisms of ruthenium coordination complexes and their role as antineoplastic agents. *European journal of medicinal chemistry* **(2018),** 150419-445	Pal Mousumi; Nandi Utpal; Mukherjee Debaraj	4.816
41	Determination of ZSTK474, a novel Pan PI3K inhibitor in mouse plasma by LC-MS/MS and its application to Pharmacokinetics. *Journal of pharmaceutical and biomedical analysis* **(2018),** 149387-393	Singh Amarinder; Singh Gurdarshan; Thatikonda Thanusha; Singh Parvinder Pal; Vishwakarma Ram; Kumar Amit; Wazir Priya; Nandi Utpal; Tikoo Manoj K; V Vijayabhaskar; et al	3.107
42	Development of ultra performance liquid chromatography tandem mass spectrometry method for simultaneous identification and quantitation of potential osteogenic phytochemicals in Butea monosperma. *J. Chromatogr. Sci.* **(2018),** 56(8), pp. 738-745. DOI: 10.1093/chromsci/bmy050	Bajpai V, Singh A, Singh P, Sharma K, Singh B, Singh BP, Sahai M, Maurya R, Kumar B	1.169
43	Direct N-heterocyclization of hydrazines to access styrylated pyrazoles: synthesis of 1,3,5-trisubstituted pyrazoles and dihydropyrazoles. *RSC Advances* **(2018)**, 8(47), 26523-26527. DOI:10.1039/C8RA04550J	Vunnam Venkateswarlu, Jaspreet Kour, K. A. Aravinda Kumar, Praveen Kumar Verma, G. Lakshma Reddy, Yaseen Hussain,ab Aliya Tabassum, Shilpi Balgotra, Sorav Gupta, Abhinandan D. Hudwekar, Ram A. Vishwakarmaa and Sanghapal D. Sawant	2.936
44	Discovery and Preclinical Development of IIIM-290, an Orally Active Potent Cyclin-Dependent Kinase Inhibitor. *Journal of Medicinal Chemistry* **(2018),** 61(4), 1664-1687. DOI:10.1021/acs.jmedchem.7b01765	Bharate, Sandip B.; Kumar, Vikas; Jain, Shreyans K.; Mintoo, Mubashir J.; Guru, Santosh K.; Nuthakki, Vijay K.; Sharma, Mohit; Bharate, Sonali S.; Gandhi, Sumit G.; Mondhe, Dilip M.; et al	6.253
45	Discovery of 2-aminothiazolyl berberine derivatives as effectively antibacterial agents toward clinically drug-resistant Gram-negative Acinetobacter baumanii. EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY **(2018),** 146, 15-37.	Gao, WW; Gopala, L; Bheemanaboina, RRY; Zhang, GB; Li, S; Zhou, CH	4.833
46	Domestication and nutrient management of Monarda citriodora Cer.ex Lag. in Sub Tropical region of Jammu (India). *International Journal of Chemical Studies* **(2018)**, 6(2Pt.R), 1-5.	Koli, Brijendra; Gochar, Rajendra; Meena, Sr; Chandra, Suresh; Bindu, Kushal	0.565
47	Drug targets exploited in Mycobacterium tuberculosis: Pitfalls and promises on the horizon. *Biomedicine & Pharmacotherapy* **(2018)**, 103, 1733-1747. DOI:10.1016/j.biopha.2018.04.176	Bhat, Zubair Shanib; Rather, Muzafar Ahmad; Maqbool, Mubashir; Ahmad, Zahoor	3.457
48	Dual role of Par-4 in abrogation of EMT and switching on Mesenchymal to Epithelial Transition (MET) in metastatic pancreatic cancer cells. *Molecular carcinogenesis* **(2018)**, 57(9), 1102-1115.	Katoch Archana; Chakraborty Souneek; Nayak Debasis; Rasool Reyaz U; Sharma Parduman R; Goswami Anindya; Katoch Archana; Chakraborty Souneek; Nayak Debasis; Rasool Reyaz U; et al	3.851

S. No.	Title	Author	Impact Factor
49	Enantioselective resolution of 2-arylpropionic acid derivatives employing immobilization of lipase from Bacillus subtilis strain Kakrayal_1 (BSK-L). *Bioresource technology* **(2018),** 269581-585	Bhushan Indu; Saraswat Rashmi; Gupta Pankaj; Shah Bhahwal A	5.807
50	Enasidenib: First Mutant IDH2 Inhibitor for the Treatment of Refractory and Relapsed Acute Myeloid Leukemia. *Anti-cancer agents in medicinal chemistry* **(2018),** Oct 24. doi: 10.2174/1871520618666181025091128	Dogra Raghav; Bhatia Rohit; Shankar Ravi; Bansal Parveen; Rawal Ravindra K	2.556
51	Establishment of LCMS Based Platform for Discovery of Quorum Sensing Inhibitors: Signal Detection in Pseudomonas aeruginosa PAO1. *ACS Chemical Biology* **(2018),** 13(3), 657-665. DOI:10.1021/acschembio.7b00875	Kushwaha, Manoj; Jain, Shreyans K.; Sharma, Nisha; Abrol, Vidushi; Jaglan, Sundeep; Vishwakarma, Ram A.	4.592
52	Ethylene and Polyamines in Counteracting Heavy Metal Phytotoxicity: A Crosstalk Perspective. JOURNAL OF PLANT GROWTH REGULATION **(2018),** 37(4), 1050-1065	Asgher, M; Khan, MIR; Anjum, NA; Verma, S; Vyas, D; Per, TS; Masood, A; Khan, NA	2.179
53	Exploring a broad spectrum nitrilase from moderately halophilic bacterium Halomonas sp. IIIMB2797 isolated from saline lake. *Journal of Basic Microbiology* **(2018),** 58(10), 867-874. DOI:10.1002/jobm.201800168	Singh, Rahul Vikram; Sharma, Hitesh; Koul, Anshela; Babu, Vikash	1.58
54	Four new carbazole alkaloids from Murraya koenigii that display anti-inflammatory and anti-microbial activities. *Organic & Biomolecular Chemistry* **(2018),** 16(11), 1994. Language: English, Database: CAPLUS, DOI:10.1039/C8OB90030B	Nalli, Yedukondalu; Khajuria, Vidushi; Gupta, Shilpa; Arora, Palak; Riyaz-Ul-Hassan, Syed; Ahmed, Zabeer; Ali, Asif	3.423
55	Furanoflavones pongapin and lanceolatin B blocks the cell cycle and induce senescence in CYP1A1-overexpressing breast cancer cells. *Bioorganic & Medicinal Chemistry* **(2018),** 26(23-24), 6076-6086. DOI:10.1016/j.bmc.2018.11.013	Sharma, Rajni; Williams, Ibidapo S.; Gatchie, Linda; Sonawane, Vinay R.; Chaudhuri, Bhabatosh; Bharate, Sandip B.	2.881
56	Hemisynthesis, computational and molecular docking studies of novel nitrogen containing steroidal aromatase inhibitors: testolactam and testololactam. NEW JOURNAL OF CHEMISTRY **(2018),** 42(6), 4579-4589.	Lone, SH; Bhat, MA; Lone, RA; Jameel, S; Lone, JA; Bhat, KA	3.069
57	Identification of a unique loss-of-function mutation in IGF1R and a crosstalk between IGF1R and Wnt/β-catenin signaling pathways. *Biochimica et biophysica acta. Molecular cell research* **(2018)**, 1865(6), 920-931,	amwal Gayatri; Singh Gurjinder; Dar Mohd Saleem; Singh Paramjeet; Bano Nasima; Syed Sajad Hussain; Sandhu Padmani; Akhter Yusuf; Monga Satdarshan P; Dar Mohd Jamal	4.651
58	Identification of Degradant Products of Saroglitazar by UPLC Tandem Mass Spectroscopy and Attenuated Total Reflection FTIR Techniques. INDIAN JOURNAL OF PHARMACEUTICAL EDUCATION AND RESEARCH **(2018),** 52(4), 635-643.	Kumar, TNVG; Vidyadhara, S; Narkhede, NA; Silpa, NYS; Lakshmi, MR	0.425
59	Identification of karanjin isolated from the Indian beech tree as a potent CYP1 enzyme inhibitor with cellular efficacy via screening of a natural product repository. *MedChemComm* **(2018)**, 9(2), 371-382. DOI:10.1039/C7MD00388A	Joshi, Prashant; Sonawane, Vinay R.; Williams, Ibidapo S.; McCann, Glen J. P.; Gatchie, Linda; Sharma, Rajni; Satti, Naresh; Chaudhuri, Bhabatosh; Bharate, Sandip B.	2.342
60	Identification, isolation, and synthesis of seven novel impurities of anti-diabetic drug Repaglinide. *Drug testing and analysis* **(2018)**, 10(1), 212-221	Kancherla Prasad; Alegete Pallavi; Khagga Mukkanti; Kancherla Prasad; Keesari Srinivas; Alegete Pallavi; Das Parthasarathi	2.993

S. No.	Title	Author	Impact Factor
61	Identification, phylogenetic analysis and expression profiling of ABC transporter family of Crocus sativus L: A step towards understanding apocarotenoid transport. *Plant Gene* **(2018)**, 14, 1-6. DOI:10.1016/j.plgene.2018.02.001	Mohiuddin, Tabasum; Baba, Shoib Ahmad; Ashraf, Nasheeman	SCImago Journal Rank (SJR): 0.650
62	Impact of Concomitantly Administered Curcumin on Pharmacokinetics of Daclatasvir in Mice Under the Frame of Herb-Drug Interaction. INDIAN JOURNAL OF PHARMACEUTICAL EDUCATION AND RESEARCH **(2018)**, 52(4), s11--S15	Magotra, A; Kotwal, P; Bhatt, S; Dogra, A; Singh, G; Nandi, U	0.425
63	Impurity profiling of anticancer preclinical candidate, IIIM-290. *Journal of pharmaceutical and biomedical analysis* **(2018)**, 1661-5	Kumar Vikas; Bhurta Deendyal; Sharma Ankita; Kumar Puneet; Bharate Sandip B; Vishwakarma Ram A; Bharate Sonali S	2.831
64	In perspective: Potential medicinal plant resources of Kashmir Himalayas, their domestication and cultivation for commercial exploitation. JOURNAL OF APPLIED RESEARCH ON MEDICINAL AND AROMATIC PLANTS **(2018),** 8, 10-25.	Jeelani, SM; Rather, GA; Sharma, A; Lattoo, SK	1.966
65	*In silico* evaluation of the resistance of the T790M variant of epidermal growth factor receptor kinase to cancer drug Erlotinib. *Journal of biomolecular structure & dynamics* **(2018),** 36(16), 4209-4219	Singh Inderpal; Verma Vijeshwar; Chandra Ratna; Singh Inderpal; Verma Vijeshwar; Singh Shashank; Uversky Vladimir N; Uversky Vladimir N	3.107
66	*In vitro* acaricidal activity of Piper nigrum and Piper longum fruit extracts and their active components against Rhipicephalus (Boophilus) microplus ticks. *Experimental & applied acarology* **(2018)**, 75(3), 333-343.	Godara R; Katoch R; Yadav A; Verma M K; Dutt P; Satti N K; Katoch M	1.929
67	*In vitro* antimycobacterial activity of 2-(((2-hydroxyphenyl) amino)methylene)-5,5-dimethylcyclohexane-1,3-dione:anew chemical entity against Mycobacterium tuberculosis. *International Journal of Antimicrobial Agents* **(2018)**, 52(2), 265-268. DOI:10.1016/j.ijantimicag.2018.02.022	Rather, Muzafar Ahmad; Bhat, Zubair Shanib; Lone, Ali Mohd; Maqbool, Mubashir; Amin, Shajrul; Bhat, Bilal A.; Ahmad, Zahoor	4.253
68	Indolyl-isoxazolidines attenuate LPS-stimulated pro-inflammatory cytokines and increase survival in a mouse model of sepsis: Identification of potent lead. *European journal of medicinal chemistry* **(2018)**, 15356-64	Singh Gagandeep; Singh Gurjit; Bhatti Rajbir; Gupta Mehak; Kumar Ajay; Sharma Ankita; Singh Ishar Mohan Paul	4.816
69	Intervention of curcumin on oral pharmacokinetics of daclatasvir in rat: A possible risk for long-term use. *Phytotherapy Research* **(2018),** 32(10), 1967-1974. DOI:10.1002/ptr.6123	Dogra, Ashish; Bhatt, Shipra; Magotra, Asmita; Sharma, Anjna; Kotwal, Pankul; Gour, Abhishek; Wazir, Priya; Singh, Gurdarshan; Nandi, Utpal	3.349
70	*In-vitro* and in-vivo pharmacokinetics of IS01957, p-coumaric acid derivative using a validated LC-ESI-MS/MS method in mice plasma. *Journal of Pharmaceutical Investigation* **(2018),** 48(5), 565-574. DOI:10.1007/s40005-017-0350-8	Sharma, Anjna; Magotra, Asmita; Rath, Santosh Kumar; Wazir, Priya; Nandi, Utpal; Koul, Surrinder; Sangwan, Payare Lal; Gupta, Ajai Prakash; Singh, Gurdarshan	NOT KNOWN
71	In-vitro assessment of cytotoxicity, antioxidant and anti-inflammatory activities of Ficus palmata. JOURNAL OF HERBAL MEDICINE **(2018),** 13, 71-75.	Khajuria, V; Gupta, S; Bhagat, A; Ahmed, Z	1.554
72	Iodine-NH4OAc mediated regioselective synthesis of 2-aroyl-3-arylimidazo[1,2-a]pyridines from 1,3-diaryl-prop-2-en-1-ones. ORGANIC & BIOMOLECULAR CHEMISTRY **(2018),** 16(8), 1330-1336.	Kour, D; Gupta, A; Kapoor, KK; Gupta, VK; Rajnikant; Singh, D; Das, P	3.49

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73	Juniperus chinensis L. (Cupressaceae): A New Taxa Record for Himalaya and Extension of Geographic Distribution in South Asia. NATIONAL ACADEMY SCIENCE LETTERS-INDIA **(2018),** 41(1), 69-73.	Singh, B; Sultan, P; Bedi, YS	NOT KNOWN
74	Kaempferol-3-o-β-D-glucuronate exhibit potential anti-inflammatory effect in LPS stimulated RAW 264.7 cells and mice model. *International Immunopharmacology* **(2018)**, 57, 62-71. DOI:10.1016/j.intimp.2018.01.041	Khajuria, Vidushi; Gupta, Shilpa; Sharma, Neha; Tiwari, Harshita; Bhardwaj, Subhash; Dutt, Prabhu; Satti, Naresh; Nargotra, Amit; Bhagat, Asha; Ahmed, Zabeer	3.118
75	Khellinoflavanone, a Semisynthetic Derivative of Khellin, Overcomes Benzo[a]pyrene Toxicity in Human Normal and Cancer Cells That Express CYP1A1. *ACS Omega* **(2018)**, 3(8), 8553-8566. DOI:10.1021/acsomega.8b01088	Sharma, Rajni; Williams, Ibidapo S.; Gatchie, Linda; Sonawane, Vinay R.; Chaudhuri, Bhabatosh; Bharate, Sandip B.	2.584
76	Lactococcus lactis provides an efficient platform for production of disulfide-rich recombinant proteins from Plasmodium falciparum. *Microbial cell factories* **(2018),** 17(1), 55	Singh SK, Tiendrebeogo RW, Chourasia BK, Kana IH, Singh S, Theisen M	3.831
77	Lipovelutibols A-D: Cytotoxic Lipopeptaibols from the Himalayan Cold Habitat Fungus Trichoderma velutinum. *Journal of Natural Products* **(2018)**, 81(2), 219-226. DOI:10.1021/acs.jnatprod.6b00873	Singh, Varun Pratap; Yedukondalu, Nalli; Sharma, Vandana; Kushwaha, Manoj; Sharma, Richa; Chaubey, Asha; Kumar, Anil; Singh, Deepika; Vishwakarma, Ram A.	3.885
78	Mechanochemical feedback control of dynamin independent endocytosis modulates membrane tension in adherent cells. *Nature communications* **(2018)**, 9(1), 4217	Joseph Jose Thottacherry, Anita Joanna Kosmalska, Amit Kumar, Amit Singh Vishen, Alberto Elosegui-Artola, Susav Pradhan, Sumit Sharma, Parvinder P. Singh, Marta C. Guadamillas, Natasha Chaudhary, Ram Vishwakarma, Xavier Trepat, Miguel A. del Pozo, Robert G. Parton, Madan Rao, Pramod Pullarkat, Pere Roca-Cusachs & Satyajit Mayor	12.353
79	Meet Our Editorial Board Member. *Recent Patents on Drug Delivery & Formulation* **(2018)**, 12(1), 1. DOI:10.2174/1872211312010180529124916	Gupta, Prem N.	NIL
80	Modulation of dietary folate with age confers selective hepatocellular epigenetic imprints through DNA methylation. *Journal of Nutritional Biochemistry* **(2018),** 53, 121-132. DOI:10.1016/j.jnutbio.2017.10.007	Najar, Rauf Ahmad; Wani, Nissar Ahmad; Bhat, Javeed Ahmad; Dar, Nawab John; Rahat, Beenish; Gupta, Ajai Prakash; Kaur, Jaspreet; Kaur, Jyotdeep; Hamid, Abid	4.414
81	Multifunctional neuroprotective effect of Withanone, a compound from Withania somnifera roots in alleviating cognitive dysfunction. *Cytokine+* **(2018)**, 102, 211-221. DOI:10.1016/j.cyto.2017.10.019	Pandey, Anjali; Bani, Sarang; Dutt, Prabhu; Kumar Satti, Naresh; Avtar Suri, Krishan; Nabi Qazi, Ghulam	3.514
82	Murrayanine Attenuates Lipopolysaccharide-induced Inflammation and Protects Mice from Sepsis-associated Organ Failure. *Basic & clinical pharmacology & toxicology* **(2018),** May 2. doi: 10.1111/bcpt.13032. [Epub ahead of print]	Gupta Shilpa; Khajuria Vidushi; Wani Abubakar; Gupta Shilpa; Khajuria Vidushi; Bhagat Asha; Ahmed Zabeer; Wani Abubakar; Nalli Yedukondalu; Ali Asif	2.659
83	New cytochalasin from Rosellinia sanctae-cruciana, an endophytic fungus of Albizia lebbeck. *Journal of Applied Microbiology* **(2018),** 125(1), 111-120. DOI:10.1111/jam.13764	Sharma, N.; Kushwaha, M.; Arora, D.; Jain, S.; Singamaneni, V.; Sharma, S.; Shankar, R.; Bhushan, S.; Gupta, P.; Jaglan, S.	2.16
84	New distribution records of the leopard plants *Ligularia amplexicaulis* DC. and *Ligularia sibirica* (L.) Cass. (Asteraceae) in the Indian Himalaya. *J. Threat. Taxa.***(2018),** 10(13), pp. 12854-12858. DOI: 10.11609/jott.4005.10.13.12854-12858	Singh B, Singh S, Singh B	NOT KNOWN

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85	Nonantioxidant Tetramethoxystilbene Abrogates alpha-Synuclein-Induced Yeast Cell Death but Not That Triggered by the Bax or beta A4 Peptide. ACS OMEGA **(2018),** 3(8), 9513-9532	Derf, A; Mudududdla, R; Akintade, D; Williams, IS; Abdullaha, M; Chaudhuri, B; Bharate, SB	2.584
86	Novel carbazole-triazole conjugates as DNA-targeting membrane active potentiators against clinical isolated fungi. EUROPEAN JOURNAL OF MEDICINAL CHEMISTRY **(2018),** 155, 579-589.	Zhang, Y; Tangadanchu, VKR; Bheemanboina, RRY; Cheng, Y; Zhou, CH	4.833
87	Novel organophosphorus aminopyrimidines as unique structural DNA-targeting membrane active inhibitors towards drug-resistant methicillin-resistant Staphylococcus aureus. MEDCHEMCOMM **(2018),** 9(9), 1529- 1537.	Li, D; Bheemanaboina, RRY; Battini, N; Tangadanchu, VKR; Fang, XF; Zhou, CH	2.394
88	One-Pot Regioselective and Stereoselective Synthesis of C-Glycosyl Amides from Glycals Using Vinyl Azides as Glycosyl Acceptors. *Organic Letters* **(2018),** 20(13), 4036-4039. DOI:10.1021/acs.orglett.8b01602	Rasool, Faheem; Ahmed, Ajaz; Hussain, Nazar; Yousuf, Syed Khalid; Mukherjee, Debaraj	6.492
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91	Orally Effective Aminoalkyl 10H-Indolo[3,2-b]quinoline-11-carboxamide Kills the Malaria Parasite by Inhibiting Host Hemoglobin Uptake. *ChemMedChem* **(2018)**, 13(23), 2581-2598. DOI:10.1002/cmdc.201800579	Mudududdla, Ramesh; Mohanakrishnan, Dinesh; Bharate, Sonali S.; Vishwakarma, Ram A.; Sahal, Dinkar; Bharate, Sandip B.	3.009
92	Oscimum sanctum extract inhibits growth of Gram positive and Gram negative bacterial strains. *Microbial pathogenesis* **(2018)**, 118, 211-213	Khaliq Tahirah; Waseem Malik Abdul; Lone Ali Mohd; Hassan Qazi Parvaiz	2.332
93	p110α and p110β isoforms of PI3K are involved in protection against H2O2 induced oxidative stress in cancer cells. *Breast cancer* (Tokyo, Japan) **(2018),** ,	Singh Paramjeet; Bano Nasima; Hossain Md Mehedi; Basit Rafia; Dar Mohd Jamal; Singh Paramjeet; Bano Nasima; Hossain Md Mehedi; Basit Rafia; Dar Mohd Jamal	1.772
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95	Photoredox Generated Vinyl Radicals: Synthesis of Bisindoles and β-Carbolines. *Journal of Organic Chemistry* **(2018)**, 83(23), 14443-14456. DOI:10.1021/acs.joc.8b02193	Chalotra, Neha; Ahmed, Ajaz; Rizvi, Masood Ahmad; Hussain, Zakir; Ahmed, Qazi Naveed; Shah, Bhahwal Ali	4.805
96	Physicochemical, pharmacokinetic, efficacy and toxicity profiling of a potential nitrofuranyl methyl piperazine derivative IIIM-MCD-211 for oral tuberculosis therapy via in-silico-in-vitro-in-vivo approach. *Pulmonary Pharmacology & Therapeutics* **(2018)**, 48, 151-160. DOI:10.1016/j.pupt.2017.11.006	Magotra, Asmita; Sharma, Anjna; Singh, Samsher; Ojha, Probir Kumar; Kumar, Sunil; Bokolia, Naveen; Wazir, Priya; Sharma, Shweta; Khan, Inshad Ali; Singh, Parvinder Pal; et al	2.406

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98	Potential herb-drug interaction of a flavone glycoside from Cuminum cyminum: Possible pathway for bioenhancement of rifampicin. INDIAN JOURNAL OF TRADITIONAL KNOWLEDGE **(2018),** 17(4), 776-782.	Sharma, A; Magotra, A; Bhatt, S; Dogra, A; Wazir, P; Satti, NK; Singh, G; Bhusari, SS; Nandi, U	0.92
99	Preclinical Development of Crocus sativus-Based Botanical Lead IIIM-141 for Alzheimer's Disease: Chemical Standardization, Efficacy, Formulation Development, Pharmacokinetics, and Safety Pharmacology. *ACS Omega* **(2018)**, 3(8), 9572-9585. DOI:10.1021/acsomega.8b00841	Bharate, Sonali S.; Kumar, Vikas; Singh, Gurdarshan; Singh, Amarinder; Gupta, Mehak; Singh, Deepika; Kumar, Ajay; Vishwakarma, Ram A.; Bharate, Sandip B.	2.584
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102	Radicicol rescues yeast cell death triggered by expression of human α-synuclein and its A53T mutant, but not by human βA4 peptide and proapoptotic protein bax. *Bioorganic chemistry* **(2018)**, 85152-158.	Derf Asma; Verekar Shilpa A; Deshmukh Sunil K; Jain Shreyans K; Bharate Sandip B; Chaudhuri Bhabatosh	3.929
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104	Recent advances in near-infrared light-responsive nanocarriers for cancer therapy. *Drug discovery today* **(2018)**, 23(5), 1115-1125	Saneja Ankit; Kumar Robin; Panda Amulya K; Arora Divya; Jaglan Sundeep; Kumar Sandeep	6.848
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109	Room Temperature Metal-Catalyzed Oxidative Acylation of Electron-Deficient Heteroarenes with Alkynes, Its Mechanism, and Application Studies. *Journal of Organic Chemistry* **(2018)**, 83(20), 12420-12431. DOI:10.1021/acs.joc.8b01475	Sharma, Shweta; Kumar, Mukesh; Vishwakarma, Ram A.; Verma, Mahendra K.; Singh, Parvinder Pal	4.805

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110	Screening of antitubercular compound library identifies novel ATP synthase inhibitors of Mycobacterium tuberculosis. *Tuberculosis* (Oxford, United Kingdom) **(2018)**, 108, 56-63. DOI:10.1016/j.tube.2017.10.008	Kumar, Sunil; Mehra, Rukmankesh; Sharma, Sumit; Bokolia, Naveen Prakash; Raina, Diksha; Nargotra, Amit; Singh, Parvinder Pal; Khan, Inshad Ali	2.727
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113	Soluble Aβ1-42 suppresses TNF-α and activates NLRP3 inflammasome in THP-1 macrophages. *Cytokine+* **(2018)**, 111, 84-87. DOI:10.1016/j.cyto.2018.07.026	Gupta, Mehak; Wani, Abubakar; Ul Ahsan, Aitizaz; Chopra, Mani; Vishwakarma, Ram A.; Singh, Gurdarshan; Kumar, Ajay	3.514
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115	Streptomyces puniceus strain AS13., Production, characterization and evaluation of bioactive metabolites: A new face of dinactin as an antitumor antibiotic. *Microbiological Research* (2018), Volume 207, March 2018, Pages 196-202. doi.org/10.1016/j.micres.2017.12.004	Hussain Aehtesham; Ahmad Rather Muzafar; Ahmad Zahoor; Saleem Dar Mohd; Qayum Arem; Jamal Dar Mohd; Dangroo N A; Aga Mushtaq A; Manzoor Shah Aabid; Parvaiz Hassan Qazi	2.777
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117	Synthesis and biological evaluation of novel bavachinin analogs as anticancer agents. *European Journal of Medicinal Chemistry* **(2018),** 145, 511-523. DOI:10.1016/j.ejmech.2018.01.006	Gupta, Nidhi; Qayum, Arem; Raina, Arun; Shankar, Ravi; Gairola, Sumeet; Singh, Shashank; Sangwan, Payare L.	4.816
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119	Synthesis and in vitro evaluation of substituted 3-cinnamoyl-4-hydroxy-pyran-2-one (CHP) in pursuit of new potential antituberculosis agents. *MedChemComm* **(2018)**, 9(1), 165-172. DOI:10.1039/C7MD00366H	Bhat, Zubair Shanib; Ul Lah, Hafiz; Rather, Muzafar Ahmad; Maqbool, Mubashir; Ara, Tabassum; Ahmad, Zahoor; Yousuf, Syed Khalid	2.342
120	Synthesis and Investigation of the Role of Benzopyran Dihydropyrimidinone Hybrids in Cell Proliferation, Migration and Tumor Growth. *Anti-cancer agents in medicinal chemistry* **(2018),** Sep 2. doi: 10.2174/1871520618666180903101422. [Epub ahead of print]	Dash Ashutosh K; Hussain Nazar; Mukherjee Debaraj; Nayak Debasis; Mintoo Mubashir Javed; Bano Sumera; Katoch Archana; Mondhe Dilip Manikaro; Goswami Anindya	2.556
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122	Synthesis of pyrazole acrylic acid based oxadiazole and amide derivatives as antimalarial and anticancer agents. *Bioorganic chemistry* **(2018),** 77106-124.	Verma Garima; Khan Mohemmed Faraz; Akhtar Wasim; Akhtar Mymoona; Alam Mohammad Mumtaz; Chashoo Gousia; Ali Asif; Ali Israr; Shaquiquzzaman Mohammad	3.929
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124	Tacrolimus: An updated review on delivering strategies for multifarious diseases. *European Journal of Pharmaceutical Sciences* **(2018),** 114, 217-227. DOI:10.1016/j.ejps.2017.12.017	Dheer, Divya; Jyoti; Gupta, Prem N.; Shankar, Ravi	3.466
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126	The shikimate pathway enzyme that generates chorismate is not required for the development of Plasmodium berghei in the mammalian host nor the mosquito vector. *International journal for parasitology* **(2018),** 48(3-4), 203-209	Choudhary Hadi Hasan; Srivastava Pratik Narain; Singh Subhash; Kumar Kota Arun; Mishra Satish	3.078
127	Therapeutic applications of betulinic acid nanoformulations. *Annals of the New York Academy of Sciences* **(2018),** 1421(1), 5-18.	Saneja Ankit; Kumar Robin; Panda Amulya K; Saneja Ankit; Arora Divya; Dubey Ravindra Dhar; Gupta Prem N; Saneja Ankit; Arora Divya; Gupta Prem N	4.277
128	Therapeutic applications of resveratrol nanoformulations. *Environmental Chemistry Letters* **(2018),** 16(1), 35-41. DOI:10.1007/s10311-017-0660-0	Arora, Divya; Jaglan, Sundeep	3.125
129	Transformation of Substituted Glycals to Chiral Fused Aromatic Cores via Annulative π-Extension Reactions with Arynes. *Organic Letters* **(2018),** 20(6), 1572-1575. DOI:10.1021/acs.orglett.8b00319	Hussain, Nazar; Jana, Kalyanashis; Ganguly, Bishwajit; Mukherjee, Debaraj	6.492
130	Trigonelline prevents high cholesterol and high fat diet induced hepatic lipid accumulation and lipo-toxicity in C57BL/6J mice, via restoration of hepatic autophagy. *Food and Chemical Toxicology* **(2018)**, 121, 283-296. DOI:10.1016/j.fct.2018.09.011	Sharma, Love; Lone, Nazir A.; Knott, Rachel M.; Hassan, Adil; Abdullah, Tasduq	3.977
131	Valproic acid induces three novel cytotoxic secondary metabolites in Diaporthe sp., an endophytic fungus from Datura inoxia Mill. *Bioorganic & Medicinal Chemistry Letters* **(2018)**, 28(12), 2217-2221. DOI:10.1016/j.bmcl.2018.04.018	Sharma, Vishal; Singamaneni, Venugopal; Sharma, Nisha; Kumar, Amit; Arora, Divya; Kushwaha, Manoj; Bhushan, Shashi; Jaglan, Sundeep; Gupta, Prasoon	2.442
132	Why Are the Majority of Active Compounds in the CNS Domain Natural Products? A Critical Analysis. *Journal of Medicinal Chemistry* **(2018)**, 61(23), 10345-10374. DOI:10.1021/acs.jmedchem.7b01922	Bharate, Sonali S.; Mignani, Serge; Vishwakarma, Ram A.	6.253
133	Y X-Ray Study of 7a-(2-Chlorophenyl)-7a,8a,9,10,11,12a-hexadronaptho [1 ‘,2 ‘:4,5]furo[3,2-d]pyrrolo[2,1-b]oxazole and 2-(4-fluorophenyl)-2-hydroxynaptho[2,1-b]furan-1(2H)-one. CRYSTALLOGRAPHY REPORTS **(2018),** 63(3), 382-387.	Kumar, B; Battini, N; Ahmed, QN; Ali, A; Gupta, VK	0.751

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1	0179NF2017/IN	Sustained Release Formulations Of Dysoxylum Binectariferum	Bharate Sonali Sandip, Kumar Vikas, Gupta Mehak, Gandhi Sumit, Kumar Ajay, Bharate Sandip Bibishan, Vishwakarma Ram	---	19/Apr/2018	201811014818
2	0191NF2017/IN	A Novel Process For -C-Aryl-Mannosylation And Its Application In The Synthesis Of Dapagliflozin	Debaraj Mukerjee, Nazar Hussain, Sushil Raina, Ram Vishwakarma	08/May/2018	---	201811017232
3	0039NF2018/IN	Solid Dispersion Comprising An Anticancer Compound With Improved Solubility And Efficacy	Bharate Sonali Sandip, Kumar Vikas, Mintoo Mubashir Javed, Mondhe Dilip Manikrao, Bharate Sandip Bibishan, Vishwakarma Ram	---	13/Jul/2018	201811026240

Filed in Foreign

S No	NFNO	Country	Title	Inventors	Comp. Filing Date	Application No.
1	0222NF2015/CA	CA	Fused Pyrimidines As Isoform Selective Phosphoinositide-3-Kinase-Alpha Inhibitors And Process For Preparation Thereof	Bharate Sandip Bibishan, Bhushan Shashi, Mohammed Shabber, Guru Santosh Kumar, Bharate Sonali Sandip, Kumar Vikas, Mahajan Girish, Mintoo Mubashir Javed, Mondhe Dilip Manikrao, Vishwakarma Ram	07/May/2018	3004534
2	0222NF2015/US	US	Fused Pyrimidines As Isoform Selective Phosphoinositide-3-Kinase-Alpha Inhibitors And Process For Preparation Thereof	Bharate Sandip Bibishan, Bhushan Shashi, Mohammed Shabber, Guru Santosh Kumar, Bharate Sonali Sandip, Kumar Vikas, Mahajan Girish, Mintoo Mubashir Javed, Mondhe Dilip Manikrao, Vishwakarma Ram	08/May/2018	15/774520
3	0222NF2015/EP	EP	Fused Pyrimidines As Isoform Selective Phosphoinositide-3-Kinase-Alpha Inhibitors And Process For Preparation Thereof	Bharate Sandip Bibishan, Bhushan Shashi, Mohammed Shabber, Guru Santosh Kumar, Bharate Sonali Sandip, Kumar Vikas, Mahajan Girish, Mintoo Mubashir Javed, Mondhe Dilip Manikrao, Vishwakarma Ram	14/May/2018	16834199.8
4	0211NF2015/EP	EP	3-Pyrimidinyl Pyrrolo [2,3-B] Pyridine As New Anticancer Agents And The Process For The Preparation Thereof	Umed Singh, Gousia Chashoo, Girish Mahajan, Thanusha Thatikonda, Priya Mahajan, Hari Prasad Aruri, Satish Sonbarao Gudup, Amit Nargotra, Dilip Manikrao Mondhe, Ram Asrey Vishwakarma, Parvinder Pal Singh	21/Jun/2018	16834200.4

S No	NFNO	Country	Title	Inventors	Comp. Filing Date	Application No.
5	0169NF2015/ CN	CN	Substituted Aurone Alkaloids As Anti-Mycobacterial Agents	Satish Sonbarao Gudup, Sanjay Kumar, Hari Prasad Aruri, Umed Singh, Gurunadham Munagala, Kushalava Reddy Yempalla, Samsher Singh, Inshad Ali Khan, Vishwakarma Ram Asrey, Parvinder Pal Singh	03/ Sep/2018	201780014936.1
6	0169NF2015 /EP	EP	Substituted Aurone Alkaloids As Anti-Mycobacterial Agents	Satish Sonbarao Gudup, Sanjay Kumar, Hari Prasad Aruri, Umed Singh, Gurunadham Munagala, Kushalava Reddy Yempalla, Samsher Singh, Inshad Ali Khan, Vishwakarma Ram Asrey, Parvinder Pal Singh	04/ Sep/2018	17725779.7
7	0120NF2017/ WO	WO	Gastroretentive Sustained Release Formulations Of Bergenia Ciliata	Bharate Sonali Sandip, Singh Rohit, Gupta Mehak, Singh Bikarma, Katare Anil Kumar, Kumar Ajay, Bharate Sandip Bibishan, Vishwakarma Ram	11/ Sep/2018	PCT/ IN2018/050588
8	0092NF2017/ WO	WO	Sustained Release Formulations Of Crocus Sativus	Bharate Sonali Sandip, Kumar Vikas, Singh Rohit, Rani Sarita, Gupta Mehak, Kumar Ajay, Bharate Sandip Bibishan, Vishwakarma Ram	04/ Oct/2018	PCT/ IN2018/050629
9	0210NF2017/ WO	WO	A Process For Thr Preparation Of Natural Crystallized Thymol From Monarda Citriodora (Jammu Monarda) Oil	Shankar Ravi, Chandra Suresh, Meena Siya Ram, Verma Mahendra Kumar, Bindu Kushal, Vij Bhavna, Dheer Divya, Jyoti, Vishwakarma Ram Asrey	03/Jan/2019	PCT/ IN2019/050003
10	0294NF2015/ US	US	Furanochalcones As Inhibitors Of Cyp1a1, Cyp1a2 And Cyp1b1 For Cancer Chemoprevention	Bharate Sandip Bibishan, Sharma Rajni, Joshi Prashant, Vishwakarma Ram, Chaudhuri Bhabatosh	12/ Feb/2019	16/325002
11	0294NF2015/ CA	CA	Furanochalcones As Inhibitors Of Cyp1a1, Cyp1a2 And Cyp1b1 For Cancer Chemoprevention	Bharate Sandip Bibishan, Sharma Rajni, Joshi Prashant, Vishwakarma Ram, Chaudhuri Bhabatosh	12/ Feb/2019	3033569
12	0294NF2015/ EP	EP	Furanochalcones As Inhibitors Of Cyp1a1, Cyp1a2 And Cyp1b1 For Cancer Chemoprevention	Bharate Sandip Bibishan, Sharma Rajni, Joshi Prashant, Vishwakarma Ram, Chaudhuri Bhabatosh	11/ Mar/2019	17801507.9

Granted in India

S No	NFNO	Title	Inventors	Prov. Filing Date	Application No.	Grant Date	Patent No.
1	0236NF2006/IN	An Aromatic Inhibitor Of Venom Phospholipase A2	Nargotra Amit, Koul Surrinder, Singh Jaswant, Ahmed Zabeer, Bhagat Asha, Taneja Subhash Chandra, Raina Ravinder Kumar, Qazi Ghulam Nabi	05/Mar/2008	0532DEL 2008	02/Jul/2018	298398
2	0472NF2004 /IN	Aromatic Amides As Potentiators Of Bioefficacy Of Anti-Infective Drugs	Surrinder Koul, Jawahir Lal Koul, Subhash Chandra Taneja, Pankaj Gupta, Inshad Ali Khan, Zahid Mehmood Mirza, Ashwani Kumar, Rakesh Kamal Johri, Monika Pandita, Anita Khosa, Ashok Kumar Tikoo, Subhash Chander Sharma, Vijeshwar Verma, Ghulam Nabi Qazi	31/Mar/2005	0718DEL 2005	25/Jul/2018	299207

Granted in Foreign

S No	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Grant Date	Patent No.
1	0219NF2012/US	Rohitukine Analogs As Cyclin-Dependent Kinase Inhibitors And A Process For The Preparation Thereof	Vishwakarma Ram Asrey, Bharate Sandip Bibishan, Bhushan Shashi, Mondhe Dilip Manikrao, Jain Shreyans Kumar, Meena Samdarshi, Guru Santosh Kumar, Pathania Anup Singh, Kumar Suresh, Behl Akanksha, Mintoo Mubashir Javed, Bharate Sonali Sandip, Joshi Prashant	14/Oct/2015	14/784489	03/Apr/2018	9932327
2	0127NF2014/US	Novel 1,3,5 -Triazine Based Pi3k Inhibitors As Anticancer Agents And A Process For The Preparation Thereof	Thatikonda Thanusha, Kumar Suresh, Singh Umed, Mahajan Priya, Mahajan Girish, Nargotra Amit, Malik Fayaz, Mondhe Dilip Manikrao, Vishwakarma Ram Asrey, Singh Parvinder Pal	19/May/2017	15/528435	24/Apr/2018	9951040

S No	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Grant Date	Patent No.
3	0195NF2011/ GB	Design, Synthesis And Biological Evaluation Of Isoform Selective Analogs Of Liphagane Scaffold As Anticancer Agents: P13k-Alpha/ Beta Inhibitors	Ram A Vishwakarma, Sanghapal Damodhar Sawant, Parvinder Pal Singh, Abid Hamid Dar, Parduman Raj Sharma, Ajit Kumar Saxena, Amit Nargotra, Kolluru Anjaneya Aravind Kumar, Mudududdla Ramesh, Asif Khurshid Qazi, Aashiq Hussain, Nayan Chanauria	10/Sep/2014	13723567.7	16/ May/2018	2828269
4	0195NF2011/ EP	Design, Synthesis And Biological Evaluation Of Isoform Selective Analogs Of Liphagane Scaffold As Anticancer Agents: P13k-Alpha/ Beta Inhibitors	Ram A Vishwakarma, Sanghapal Damodhar Sawant, Parvinder Pal Singh, Abid Hamid Dar, Parduman Raj Sharma, Ajit Kumar Saxena, Amit Nargotra, Kolluru Anjaneya Aravind Kumar, Mudududdla Ramesh, Asif Khurshid Qazi, Aashiq Hussain, Nayan Chanauria	10/Sep/2014	13723567.7	16/ May/2018	2828269
5	0106NF2013/ US	Novel Pyrazolopyrimidinones As Pde-5 Inhibitors	Sawant Sanghapal Damodhar, Ginnereddy Lakshma Reddy, Mahesuni Srinivas, Syed Sajad Hussain, Dar Mohd Ishaq, Nargotra Amit, Mahajan Priya, Vishwakarma Ram Asrey	29/Jul/2016	15/115573	10/Jul/2018	10017511
6	0036NF2014/ US	A Pharmaceutical Composition For The Treatment Of Multi-Drug Resistant Infections	Vishwakarma Ram, Kumar Ajay, Khan Inshad Ali, Bharate Sandip Bibishan, Joshi Prashant, Singh Samsher, Satti Naresh	06/ Mar/2017	15/509183	04/Sep/2018	10064840
7	0302NF2013/ US	N-Substituted Beta-Carbolinium Compounds As Potent P-Glycoprotein Inducers	Bharate Sandip, Kumar Ajay, Manda Sudhakar, Joshi Prashant, Bharate Sonali, Vishwakarma Ram	21/Apr/2017	15/521170	11/Sep/2018	10072009

S No	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Grant Date	Patent No.
8	0225NF2012/GB	6-Notro-2,3-Dihydroimidazo[2,1-B] Oxazoles And A Process For The Preparation Thereof	Parvinder Pal Singh, GURUNADHAM MUNAGALA, KUSHALAVA REDDY YEMPALLA, INSHAD ALI KHAN, NITIN PAL KALIA, VIKRANT SINGH RAJPUT, AMIT NARGOTRA, SANGHAPAL DAMODHAR SAWANT, RAM ASREY VISHWAKARMA	02/May/2016	14725544.2	24/Oct/2018	3052503
9	0225NF2012/ES	6-Notro-2,3-Dihydroimidazo[2,1-B] Oxazoles And A Process For The Preparation Thereof	Parvinder Pal Singh, GURUNADHAM MUNAGALA, KUSHALAVA REDDY YEMPALLA, INSHAD ALI KHAN, NITIN PAL KALIA, VIKRANT SINGH RAJPUT, AMIT NARGOTRA, SANGHAPAL DAMODHAR SAWANT, RAM ASREY VISHWAKARMA	02/May/2016	14725544.2	24/Oct/2018	3052503
10	0225NF2012/FR	6-Notro-2,3-Dihydroimidazo[2,1-B] Oxazoles And A Process For The Preparation Thereof	Parvinder Pal Singh, GURUNADHAM MUNAGALA, KUSHALAVA REDDY YEMPALLA, INSHAD ALI KHAN, NITIN PAL KALIA, VIKRANT SINGH RAJPUT, AMIT NARGOTRA, SANGHAPAL DAMODHAR SAWANT, RAM ASREY VISHWAKARMA	02/May/2016	14725544.2	24/Oct/2018	3052503

S No	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Grant Date	Patent No.
11	0225NF2012/ EP	6-Notro-2,3-Dihydroimidazo[2,1-B] Oxazoles And A Process For The Preparation Thereof	Parvinder Pal Singh, GURUNADHAM MUNAGALA, KUSHALAVA REDDY YEMPALLA, INSHAD ALI KHAN, NITIN PAL KALIA, VIKRANT SINGH RAJPUT, AMIT NARGOTRA, SANGHAPAL DAMODHAR SAWANT, RAM ASREY VISHWAKARMA	02/ May/2016	14725544.2	24/ Oct/2018	3052503
12	0176NF2014/ EP	SUBSTITUTED 1, 2, 3- TRIAZOL-1-YL-METHYL-2, 3-DIHYDRO-2-METHYL-6-NITROIMIDAZO [2, 1-B]OXAZOLES AS ANTI-MYCOBACTERIAL AGENTS AND A PROCESS FOR THE PREPARATION THEREOF	YEMPALLA KUSHALAVA REDDY, MUNAGALA GURUNADHAM, SINGH SAMSHER, SHARMA SUMIT, KHAN INSHAD ALI, VISHWAKARMA RAM ASREY, SINGH PARVINDER PAL	24/Apr/2017	15787313.4	07/ Nov/2018	3209669
13	0176NF2014/ GB	SUBSTITUTED 1, 2, 3-TRIAZOL-1-YL-METHYL-2, 3-DIHYDRO-2-METHYL-6-NITROIMIDAZO [2, 1-B] OXAZOLES AS ANTI-MYCOBACTERIAL AGENTS AND A PROCESS FOR THE PREPARATION THEREOF	YEMPALLA KUSHALAVA REDDY, MUNAGALA GURUNADHAM, SINGH SAMSHER, SHARMA SUMIT, KHAN INSHAD ALI, VISHWAKARMA RAM ASREY, SINGH PARVINDER PAL	24/Apr/2017	15787313.4	07/ Nov/2018	3209669
14	0036NF2014/ GB	A Pharmaceutical Composition For The Treatment Of Multi-Drug Resistant Infections	Vishwakarma Ram, Kumar Ajay, Khan Inshad Ali, Bharate Sandip Bibishan, Joshi Prashant, Singh Samsher, Satti Naresh	03/ Mar/2017	15807704.0	18/ Nov/2018	3212235

S No	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Grant Date	Patent No.
15	0036NF2014/ EP	A Pharmaceutical Composition For The Treatment Of Multi-Drug Resistant Infections	Vishwakarma Ram, Kumar Ajay, Khan Inshad Ali, Bharate Sandip Bibishan, Joshi Prashant, Singh Samsher, Satti Naresh	07/ Mar/2017	15807704.0	18/ Nov/2018	3212235
16	0059NF2014/ EP	10-Substituted Colchicinoids As Potent Anticancer Agents	Vishwakarma Ram, Bharate Sandip Bibishan, Kumar Ajay, Singh Baljinder, Kumar Ashok, Bhushan Shashi, Hamid Abid, Joshi Prashant, Guru Santosh Kumar, Kumar Suresh, Hussain Aashiq, Qazi Asif Khurshid, Bharate Sonali Sandip, Sharma Parduman, Saxena Ajit Kumar, Mondhe Dilip Manikrao, Mahajan Girish, Wani Zahoor	13/Apr/2017	15805323.1	12/ Dec/2018	3207026
17	0059NF2014/ GB	10-Substituted Colchicinoids As Potent Anticancer Agents	Vishwakarma Ram, Bharate Sandip Bibishan, Kumar Ajay, Singh Baljinder, Kumar Ashok, Bhushan Shashi, Hamid Abid, Joshi Prashant, Guru Santosh Kumar, Kumar Suresh, Hussain Aashiq, Qazi Asif Khurshid, Bharate Sonali Sandip, Sharma Parduman, Saxena Ajit Kumar, Mondhe Dilip Manikrao, Mahajan Girish, Wani Zahoor	13/Apr/2017	15805323.1	12/ Dec/2018	3207026
18	0117NF2013/ GB	6-Aryl-4-Phenylamino-Quinazoline Analogs As Phosphoinositide-3-Kinase Inhibitors	Vishwakarma Ram Asrey, Bharate Sandip Bibishan, Bhushan Shashi, Yadav Rammohan Rao, Guru Santosh Kumar, Joshi Prashant	27/Sep/2016	15720483.5	30/Jan/2019	3110801

S No	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Grant Date	Patent No.
19	0117NF2013/ EP	6-Aryl-4-Phenylamino-Quinazoline Analogs As Phosphoinositide-3-Kinase Inhibitors	Vishwakarma Ram Asrey, Bharate Sandip Bibishan, Bhushan Shashi, Yadav Rammohan Rao, Guru Santosh Kumar, Joshi Prashant	27/Sep/2016	15720483.5	30/Jan/2019	3110801
20	0060NF2014/ US	Polyalkylated Acyl And Benzoyl-Phloroglucinols As Potent P-Glycoprotein Inducers	Bharate Sandip, Kumar Ajay, Bharate Jaideep, Joshi Prashant, Wani Abubakar, Mudududdla Ramesh, Sharma Rohit, Vishwakarma Ram	18/Apr/2017	15/520063	12/Feb/2019	10202326
21	0117NF2013/ US	6-Aryl-4-Phenylamino-Quinazoline Analogs As Phosphoinositide-3-Kinase Inhibitors	Vishwakarma Ram Asrey, Bharate Sandip Bibishan, Bhushan Shashi, Yadav Rammohan Rao, Guru Santosh Kumar, Joshi Prashant	24/ Aug/2016	15/121328	12/Feb/2019	10202374
22	0058NF2014/ EP	Alkylidene Phosphonate Esters As P-Glycoprotein Inducers	Bharate Sandip, Kumar Ajay, Manda Sudhakar, Joshi Prashant, Bharate Sonali, Wani Abubakar, Sharma Sadhana, Vishwakarma Ram	20/ Mar/2017	15787031.2	27/ Mar/2019	320967

BOOKS & BOOK CHAPTERS

Books

- ***Singh Bikarma,*** *Vishawakarma RA, Barik SK, Khan IA, Sharma YP, Kumar B, Singh Bishander*, **et. al.** "Plants of Commercial Values" ISBN: 978-93-87973-50-3, © 2019, Editor, ***Bikarma Singh***, New India Publishing Agency, New Delhi, India.

Book Chapters

- ***Katare, Anil Kumar****, Inshad Ali Khan, Durga Prasad Mindala, Naresh Kumar Satti, Bal Kirshan Chandan, Gurdarshan Singh,Mowkashi Khullar, Neelam Sharma and Bikarma Singh* "*Colebrookea Oppositifolia* Sm., An Important Hepato-protective Phytopharma Plant in Drug Discovery" Published in "*Plants for Human Survival and Medicine*", pp 55-82 © 2019, Editor, Bikarma Singh, New India Publishing Agency, New Delhi, India

- ***Katare Anil Kumar, Khan,*** *IA, Mindala DP, Gupta PK, Singh S, Singh B.* "*Woodfordia Fruticosa* (L.) Kurz., a Potent Indian Medicinal Plant in Curing Peptic Ulcer" Published in "*Plants of Commercial Values*" ISBN: 978-93-87973-50-3, pp 17-36 © 2019, Editor, Bikarma Singh, New India Publishing Agency, New Delhi, India. [ISBN: 978-93-87973-503].

- *Rajendra Gochar, Bikarma singh, Manta Gochar, Rajendra Bhanwaria and* ***Anil Kumar Katare.*** *"Grewia asiatica L., an Important Plant of Shivalik Hills: Agro-technology and Product Development"* Published in "*Plants for Human Survival and Medicine*", pp 139-152 © 2019, Editor, Bikarma Singh, New India Publishing Agency, New Delhi, India.

- ***Singh Bikarma****, Sharma YP, Kumar B, Singh B, Lakhanpal TN. "Morchella esculenta* Dill. ex Pers., an important medicinal mushroom of Himalaya: traditional usages, phytochemistry, pharmacology and need for scientific intervention" Published in *Plants of Commercial Values*, pp 1-16 © 2019, Editor, Bikarma Singh, New India Publishing Agency, New Delhi, India. [ISBN: 978-93-87973-503].

- *Jeet S, Rahul VP, Bhanwaria R, Singh CP, Gochar R, Kumar A, Kumar K, Pal J,* ***Singh Bikarma*** "Exploring commercial cultivation of tissue cultured raised banana in Himalayan Shivalik range". Published in *Plants of Commercial Values*, pp. 133-145 © 2019, Editor, Bikarma Singh, New India Publishing Agency, New Delhi, India. [ISBN: 978-93-87973-503].

- *Singh S,* ***Singh Bikarma. "***Indian Rhododendrons and their value addition: revision and review" Published in *Plants of Commercial Values*; pp.293-316. © 2019, Editor, Bikarma Singh, New India Publishing Agency, New Delhi, India. [ISBN: 978-93-87973-503].

- ***Singh Bikarma,*** *Sneha, Anand R.* "Aromatic Wealth of Himalaya: value addition and product development from essential oil bearing plants" Published in *Plants of Commercial Values*; pp. 361-378 © 2019, Editor, Bikarma Singh, New India Publishing Agency, New Delhi, India. [ISBN: 978-93-87973-503].

- ***Gupta Suphla.*** "Epimedium elatum (Morr & Decne): An Emerging Therapeutic Medicinal Plant from Northwestern Himalayas in India" Published in *Plant and Human Health*; Vol. 1, pp. 619-656, Editor, M. Ozturk, K. R. Hakeem, Springer International Publishing AG, part of Springer Nature. [doi.org/10.1007/978-3-319-93997-1_17].

INVITED TALKS / SEMINARS / CONFERENCES / WORKSHOPS/ SYMPOSIUM / POSTER PRESENTATIONS

Invited Talks or Guest Lecturer in Seminars / Workshops:

- ***Dr Bikarma Singh, Plant Sciences*** Invited as Expert Member of BGCI programme on Global Seed Conservation Challenges-Conserving India's Threatened Flora, organized by Jammu University on 28th May to 1st June 2018**.**
- ***Dr Bikarma Singh, Plant Sciences*** Invited as Keynote Speaker in a workshop entitled "Field Taxonomy" and presented a talk entitled "Field taxonomy with reference to Vascular Plant Diversity of J&K State" on 28th July 2018, jointly organized by University of Jammu and J&K State Forest Department in Jammu.
- ***Dr Bikarma Singh, Plant Sciences*** Invited as Keynote Speaker in a workshop on "Scientist-Farmers Interaction Meet 2018" and presented a talk entitled "Farmers Income through Intervention of Science from Laboratory & Forest Resources" on 4th August 2018 organized by J&K State Forest Department in Jammu.
- ***Dr Bikarma Singh, Plant Sciences*** Invited as Keynote Speaker in National Seminar on Plant and Fungal Diversity: Status and Challenges & Symposium on Plant Ecology and presented a talk entitled "Orchid contribution to J&K state: diversity, distribution and future perspectives" held at Department of Botany, University of Jammu, J&K State, jointly organized by University of Jammu, J&K State & DST, New Delhi**.**
- ***Dr. Suphla Gupta,*** Delivered a Planetary Lecture on women in science: the meristem at 6th J&K Women Science Congress, February 26-28, 2019 Organised by Jammu University.
- ***Dr. Zahoor Ahmad Parry,*** Delivered an invited **Young Investigator talk** on 33rd Foundation Day of Department of Biotechnology on 26th February, 2019 at National Institute of Immunology (NII), New Delhi.
- ***Dr. Suphla Gupta,*** Delivered a Lecture/Presentation on *"Career in Science & Research" to* 500 students and faculties on an Educational Visit on 19th December 2018 to CSIR-IIIM, Jammu.
- ***Dr. Asha Chaubey,*** Delivered Invited talk on Microbial Natural products: Present scenario and future prospects in Women Science Congress (5-6 January 2019) during 106th Indian Science congress held at Lovely Professional University.
- ***Dr. Asha Chaubey,*** Delivered Invited talk on "Value addition in Medicinal and Aromatic plant products for human Welfare" during National conference on Women Empowerment through Agro-Entrepreneurships for livelihood security (WE-2019) held during 7-8 February 2019 held at Sher-e-Kashmir University of Agricultural Sciences and Technology, Chatha, Jammu (J&K).
- ***Dr. Asha Chaubey,*** Organized one day training program on "Utilization of Fermentation Technology for production of value added products using fruits and vegetables as raw materials" for J&K state Govt. employees on 29 October 2019.
- ***Dr. Asha Chaubey,*** Organized Two days Jigyasa workshop on "Science for Industry" for Kendriya Vidyala teachers and students on 25-26 March 2019.
- ***Dr. Sandip Bharate,*** Delivered Invited talk on " Exploring Indian Medicinal Plant and their secondary metabolities in the search of drugs and nutraceuticals" held on 17th. November 2018 in the 6th Binnenial Conference on New Developments in Drug Discovery from natural products and traditional medicines at NIPER, Mohali.

Radio Talks

- डॉ। सुफला गुप्ता, साल 2018 की **उपलब्धियां** : विज्ञान की नज़र से on Science Magazine Programme AIR Jammu, Jan 1, 2019

Conference Proceedings

- ***Er. Anil Kumar Katare*** participated/representation in Indian Science Congress held in LPU Jalandhar from 16-20 March 2018.
- ***Er. Anil Katare*** participated in "10th Agro vision exhibition at Nagpur from 23rd to 27th November 2018.
- *Bajpai V, Singh P,* ***Singh B****, Kumar B.* "LC-MS Method for simultaneous identification and quantitation of selected Cannabinoids in male and female samples of Cannabis sativa leaves." National Workshop and Seminar on HPLC Basics and Method Development. CSIR-CDRI, Lucknow, 18-23, June 2018.
- *Bhellum B,* ***Singh B.*** "Patterns of plant diversity and species composition of Jasrota subtropical forests in Shivalik Himalayas of India." XLI All India Botanical Conference of the Indian Botanical Society and National Symposium on Ecological Restoration, Carbon Sequestration and Biotechnological Approaches for Biodiversity Conservation. Gwalior, India: Jiwaji University, 25-27 October 2018. 87-88.
- *Bajpai V,* ***Singh B****, Kumar B.* "Identification and quantitation of phytochemicals in Cannabis sativa leaves using UPLC-ESI-QTRAP-MS/MS techniques." International Conference on New Age Opportunities and Challenges for Quality, Safety and GNPs in Herbal Drug Development. CSIR-NBRI, Lucknow, 22-23 February 2019.
- ***Singh B,*** *Bhanwaria R.* "RRL(J)ML-4 variety of mint as a rich source of Carvone and Limonene for value addition and product development." National Conference on Mints: Prospects, Challenges and Threats. CSIR-CIMAP Lucknow, 24-26 February 2019. 24-25.
- *Dutt A, YP Sharma,* ***Singh B***. "Ethnomedicinal plant knowledge and ethnoveterinary claims from Gujjar and Bakerwal tribes of district Poonch, J&K State, India." Plant and Fungal Diversity: Status and Challenges & Symposium on Plant Ecology. epartment of Botany, University of Jammu, J&K State, 18-19 March 2019. 59.
- ***B, Singh.*** "Orchid contribution to J&K state: diversity, distribution and future perspectives." Plant and Fungal Diversity: Status and Challenges & Symposium on Plant Ecology. Department of Botany, University of Jammu, J&K State, 18-19 March 2019. 17-18.
- *Nazir M,* ***Singh B.*** "Investigation on floristic composition and medicinal wealth of district Kupwara in Kashmir Himalaya, India." Plant and Fungal Diversity: Status and Challenges & Symposium on Plant Ecology. Department of Botany, University of Jammu, J&K State, 18-19 March 2019. 39.
- *Surmal O,* ***Singh B.*** "A cartographic representation on preliminary investigation of Woody pure strand forest vegetation around a District Doda (J&K State) of Western Himalaya." Plant and Fungal Diversity: Status and Challenges & Symposium on Plant Ecology. Department of Botany, University of Jammu, J&K State, 18-19 March 2019. 40-41.
- *Singh S,* ***Singh B.*** "Preliminary studies on diversity, composition and structure of vegetation in forests of Sarthal Mountains in J&K Himalayas." Plant and Fungal Diversity: Status and Challenges & Symposium on Plant Ecology. Department of Botany, University of Jammu, J&K State, 18-19 March 2019. 53.
- ***Gupta Suphla,*** *Manzoor, Malik Muzafar,* et al. "Understanding the role of UDP-dependent glycosyltransferases (UGTs) in Glycyrrhiza glabra under different growth conditions." National Conference on Recent Development in Plant Stress Biology (RDPSB): Translating Laboratory Research to Human Welfare. Department of Botany, Central University of Jammu, 11-12 December, 2018.
- ***Gupta Suphla,*** Manzoor, Malik Muzafar, et al. "Functional characterization and hetrologous expression of Squalene epoxidase Gene and Promoter from Glycyrrhiza glabra." Recent Advances on Interdisciplinary Sciences (International Conference). Jammu University, 11-12 Jan, 2019.
- ***Gupta Suphla****, Lone, Sajad Ahmad,* et al. "Dwindling status of epimedium elatum (morren & decne) and its geographical distribution in kashmir." Recent Advances on Interdisciplinary Sciences (International Conference). Jammu University, 11-12 Jan 2019.

- *Arti Sharma, Satiander Rana, Gulzar A. Rather,* ***Surrinder K. Lattoo*** (2018). *In planta* characterization of sterol 22-desaturase (CYP710A1) from *Withania somnifera* in heterologous host (*Nicotiana tabacum*) presented in 24th International conference on Frontiers in chemical and biology interface-2018 at Manipal University, Jaipur (January 11-13) Pp. P-128.

- *Arti Sharma, Gulzar A. Rather, Manoj K. Dhar and* ***Surrinder K. Lattoo*** (2018). Transient over-expression and aMIR-mediated silencing of *Ws*WRKY2 transcription factor revealed its regulatory role in the biosynthesis of triterpenoids in *Withania somnifera* presented *in* XLII All India Cell Biology Conference and International symposium on Functional Genomics organized by Bits Pillani, Goa (21-24 Dec., 2018) Pp. 211.

- *Arti Sharma, Gulzar A. Rather, Manoj K. Dhar and* ***Surrinder K. Lattoo*** (2018). Augmentation in withanolides content mediated through modulation in relative transcript levels of key rate-limiting genes in response to abiotic stress in *Withania somnifera* (L.) Dunal presented in National conference on recent developments in plant stress biology: translating laboratory research for human welfare organized by Central University, Jammu (8-9 Dec. 2018) Pp.165.

- *Arti Sharma, Gulzar A. Rather, Manoj K. Dhar and* ***Surrinder K. Lattoo*** (2018). From genes to transcription factors: Metabolic engineering of triterpenoids biosynthetic pathway in *Withania somnifera (L.)* Dunal presented in International conference on recent advances in interdisciplinary sciences by University of Jammu (11-12 Jan. 2019) Pp.250.

- *Gulzar A. Rather, Arti Sharma, Veenu Kaul,* ***Surrinder K. Lattoo*** (2018). Deciphering the role of key seco-iridoid pathway genes through transcriptomic and genomic approaches in relation to camptothecin biosynthesis presented in National Conference on Recent Developments in Plant Stress Biology: Translating Laboratory Research to Food Production (RDPSB-2018) at Central University Jammu (07th–08th December, 2018).

- *Gulzar A. Rather, Arti Sharma, Veenu Kaul,* ***Surrinder K. Lattoo*** (2019). Dynamics of camptothecin biosynthesis and molecular regulation of secologanin synthase, a key metabolic gene in *Nothapodytes nimmoniana* (Graham) Mabb presented in International Conference on Recent Advances in Interdisciplinary Sciences at University of Jammu (January 11-12, 2019).

- *Sweeta Manhas, Vikas Sahrma and* ***Asha Chaubey*** (2018). L-Asparaginase: A potential Therapeutic agent, poster presented in RASSA-2018, National Seminar on Smart Technologies to Boost Farm profitability and Socio-economic status of Rural India at Sher-e-Kashmir University of Agricultural Sciences and Technology, Chatha, Jammu (J&K) (19-20 November, 2018).

- *Ankita Magotra, Ravi S. Manhas and* ***Asha Chaubey*** (2018). Optimization of fermentation conditions for Terrein from *Aspergillus terrus,* poster presented in 59th Annual Conference of Association of Microbiologist of India conference at Hyderabad Central University, Hyderabad (9-12 December 2018).

- *Ravi S. Manhas and* ***Asha Chaubey*** (2019). Isolation and screening of actinomycetes for bioactives production, poster presented in Indian Science Congress at Lovely Professional University (3-7 January 2019).

- Diksha Koul, Ravi.S. Manhas, Devtulya Chander and ***Asha Chaubey*** (2019). Isolation and screening of serratiopeptidase producing bacteria, poster presented at Indian Science Congress in Lovely Professional University (3-7 January 2019).

Participations in Societal / Science & Technology

- ***Dr. Asha Cahubey*** Participated in 10th Agrovision—India's Premier Agri Summit"d at Nagpur during 23-26 November 2019.

- ***Dr. Asha Cahubey*** Participating in DBT sponsored project on "Characterization, Recombinant expression, Process Scale up and Validation of Selected Hydrolases from Native Actinobacteria for Commercial Exploitation" for scale-up studies of Chitinase enzyme

Research Grants Received

1. **Deciphering role of astrocytes in pathogenesis of central nervous system tuberculosis (CNS-TB) and exploiting its related pathways as potential therapeutic targets for CNS-TB.** Funding Agency: Indian Council of Medical Research (Govt. of India) Budget: Rs-8500000:00)-2019. Role: Principal Investigator.

2. **Investigating Multidrug Resistant Tuberculosis in Kashmir.** Funding Agency: Department of Science and Technology (Govt. of India) under **Teachers Associateship For Research Excellence** scheme (November 2018) (Budget: Rs-2000000:00) Role: Principal Investigator.

3. **Bio-prospection of Actinomycetes from high altitude Salt lakes of Leh – Ladakh for drug discovery against Tuberculosis**. Funding Agency: Department of Biotechnology (Govt. of India), (Just approved October 2018) (Budget: Rs-5600000:00) Role: Principal Investigator.

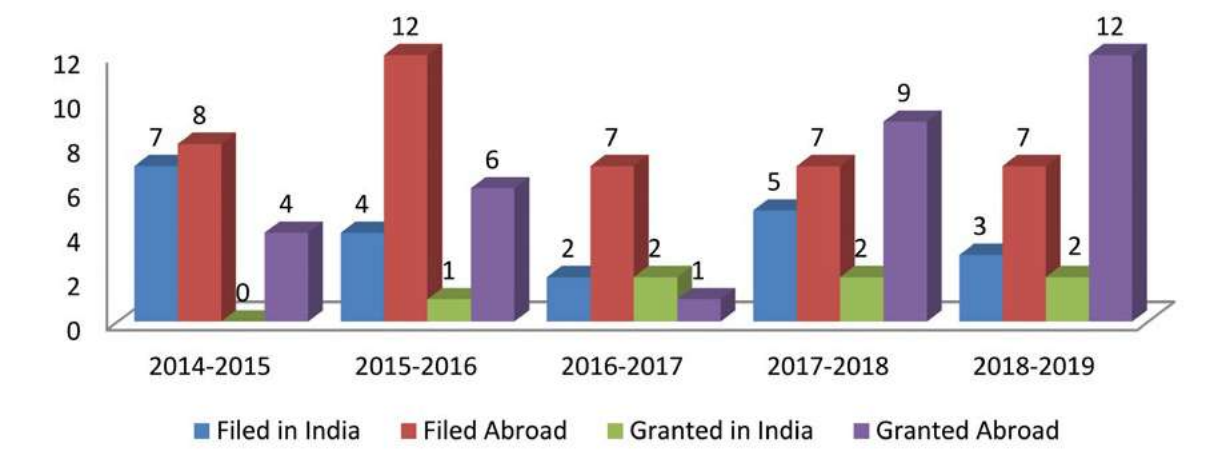
Awards / Recognition

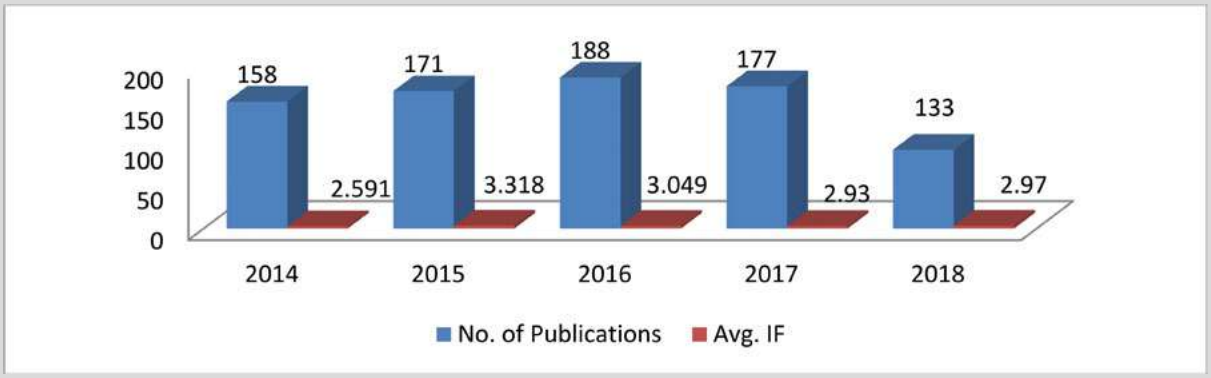
1. ***Dr. Zahoor Ahmad Parry***, Member of the **Expert Screening Committee of Innovative Young Biotechnologist Award** (IYBA) 2018.

2. ***Mr. Sajad A Lone*** was awarded AcSiR PhD Degree Award on his thesis work entitled, Molecular, Phytochemical & Cytological Characterization of *Epimedium elatum* (Morr & Decne) - A rare high altitude medicinal plant of Northwestern Himalayas in India.

3. ***CSIR-IIIM Aroma Mission team*** received the "Ultra International Team Award" at the International Congress & Expo-2018 organized by the Essential Oil Association of India, at Hotel Grand Sheraton, Bengaluru. A citation and cash award of Rs. 100000/- was given to the team for its contribution in implementing the the Mission and the Aroma Industry.

Patents



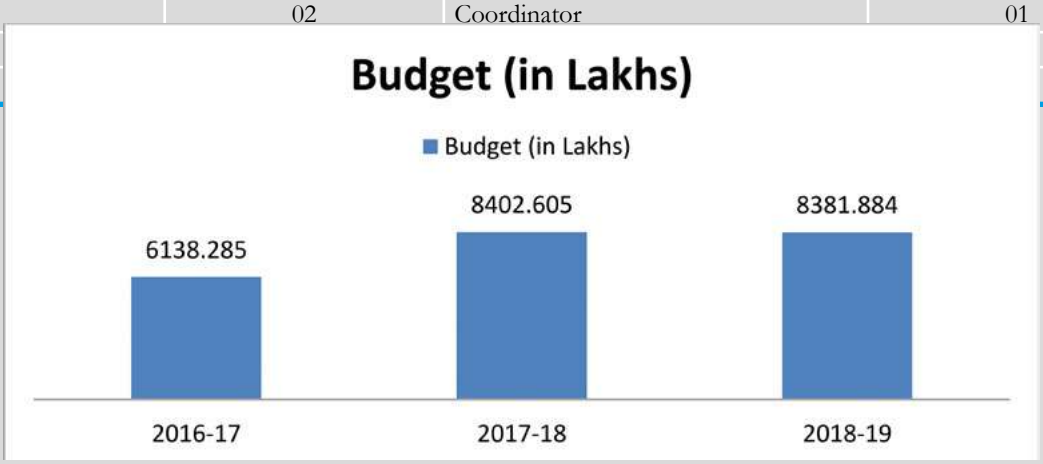


Publications

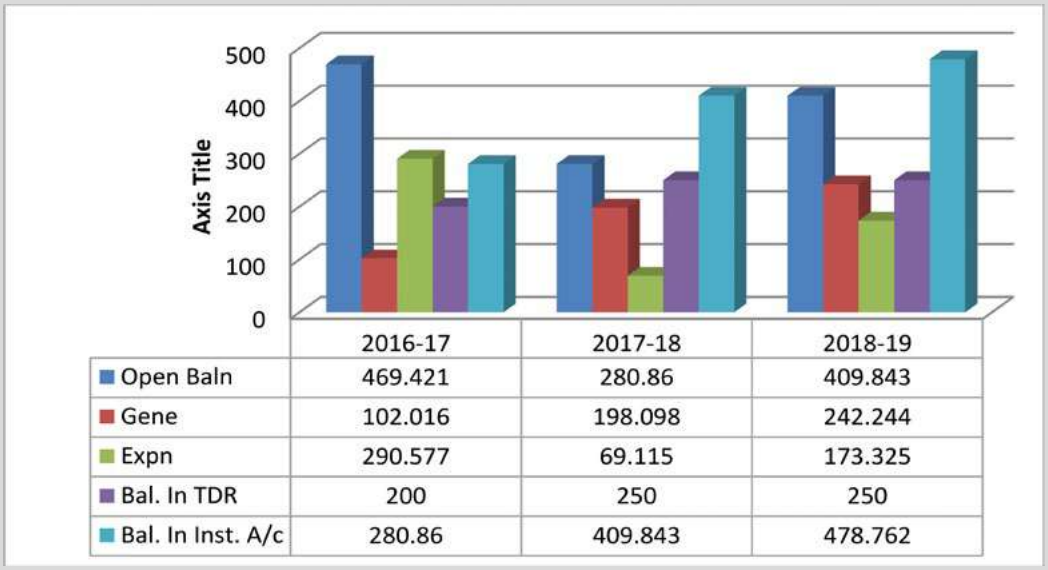
Fellows

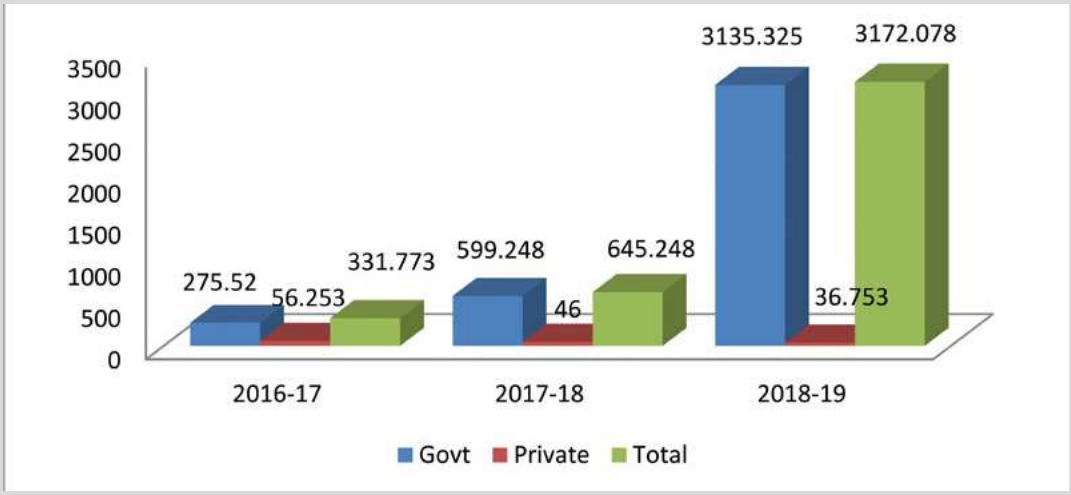
Fellowship	No. of Students	Fellowship	No. of Students
SRF (CSIR) GATE	01	JRF (DST)	01
SRF(CSIR)GPAT	02	Women Scientist	04
JRF(CSIR)	29	Young Scientist	03
SRF(CSIR)	28	Inspire Faculty	01
SRA (CSIR)	01	Post Doctoral Fellowship	10
RA(CSIR)	-	N.P.D.F.	01
JRF(UGC)	40	CSIR TWAS Fellowship	01
SRF (UGC)	16	Project Fellows	142
JRF(ICMR)	01	Senior Project Fellow	01
SRF(ICMR)	05	Research Associate	02
RA(ICMR)	01	Teacher Associate	02
JRF(DST)INSPIRE	09	Work Contract	02

SRF(DST)INSPIRE	05	Office Assistant	01
JRF(DBT)	02	Coordinator	01
SRF(DBT)			
RA (DBT)			



Budgets (Rs. In Lakhs)





Institute's Reserve (Rs. In Lakhs)

Institute's Reserve (Rs. In Lakhs)

I. ICB014-A002: Anti-Ulcer activity:

CSIR-IIIM, Jammu has been developed a standardized drug product i.e., ICB014-A002 Capsule, the manufacturing procedure has been scaled up in cGMP facility and all the manufacturing process has been optimized. Analytical method for drug substance and drug product has been developed and validated at QC/QA section. Drug product

CLINICAL TRIALS REGISTRY - INDIA
NATIONAL INSTITUTE OF MEDICAL STATISTICS
(INDIAN COUNCIL OF MEDICAL RESEARCH)

REF/2017/11/016022
CTRI Website URL - http://ctri.nic.in

Clinical Trial Details (PDF Generation Date :- Sat, 03 Feb 2018 10:31:58 GMT)

CTRI Number	CTRI/2018/01/011259 [Registered on: 10/01/2018] - **Trial Registered Prospectively**
Last Modified On	30/12/2017
Post Graduate Thesis	No
Type of Trial	Interventional
Type of Study	Ayurveda
Study Design	Non-randomized, Placebo Controlled Trial
Public Title of Study	Clinical trial to evaluate safety, tolerability and pharmacokinetic of herbal (ICB-014-A002) capsule in healthy adult volunteers.
Scientific Title of Study	A Phase-I, Dose Escalation Study to evaluate safety, tolerability and pharmacokinetic of ICB-014-A002 capsule in healthy adult volunteers.

Secondary IDs if Any

Secondary ID	Identifier
CRSC16005, version 01, date 09/08/2017	Protocol Number

Details of Principal Investigator or overall Trial Coordinator (multi-center study)

Details of Principal Investigator	
Name	Dr Dushyant Balat
Designation	MBBS, MD
Affiliation	Apollo Hospitals International Limited
Address	Apollo Hospitals International Limited, Health Check Department plot no. 1A, Bhat, GIDC Estate, Gandhinagar Gandhinagar GUJARAT 382428 India
Phone	9825015055
Fax	
Email	drdushyant.balat@gmail.com

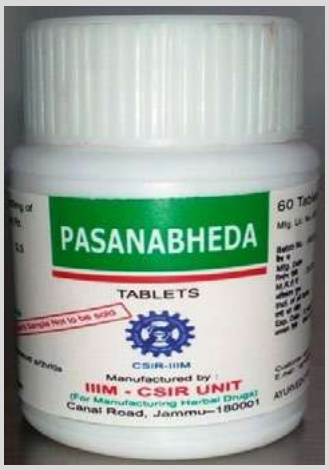
Details Contact Person (Scientific Query)

Details Contact Person (Scientific Query)	
Name	Dr Sanjay Patel
Designation	Manager-CRO
Affiliation	Cadila Pharmaceuticals Limited
Address	Cadila Pharmaceuticals Limited, 1389, Trasad Road, Dholka, Ahmedabad. Ahmadabad GUJARAT 387810 India
Phone	9825603307
Fax	
Email	sanjay.p@cadilapharma.co.in

Details Contact Person (Public Query)

Details Contact Person (Public Query)	
Name	Dr Sanjay Patel
Designation	Manager-CRO
Affiliation	Cadila Pharmaceuticals Limited
Address	Cadila Pharmaceuticals Limited, 1389, Trasad Road. Dholka, Ahmedabad. Ahmadabad GUJARAT 387810 India

was found to be stable when stored at 30°C±2°C & 65%±5%RH for 01 year in PVC bottle pack. The present invention comprising an effective amount of an extract or lyophilized extract at least one bioactive fraction obtained from ICB014 A002 (*Woodfordia fruticosa*) along with one or more pharmaceutically acceptable additives/carriers. This invention envisages the potential of an extract obtained from the flower of ICB014 A002 (*Woodfordia fruticosa*) to act an effective therapy against peptic ulcer disease.With this background data, CSIR-IIIM, Jammu compile a dossier (IND) to the AYUSH department to conduct the Phase-I Clinical trial on Healthy volunteer on 18/12/2017 through CRO with following study related documents viz.,



1. Clinical study protocol
2. Investigators Brochure
3. Case Record form, Single Dose study
4. Case Record form, Multiple Dose study
5. Patient information sheet & Informed consent form

As got approval from the AYUSH department/ Institutional ethics committee (Apollo Hospitals, Gujarat), Clinical study was registered in the Clinical trial Registry India (CTRI) with bearing registration number: **CTRI/2018/01/011259**, dated: **10/01/2018**

Woodfordia fructicosa (flowers) Ulcrine capsules

Phase-I Clinical trial of *ICB 014-A002* Capsules, Drug product from botanical source for the Prevention and management of Anti-ulcer activity.

Figure: Sea-zinc- a nutraceutic supplement of natural vitamin C and zinc gluconate

Phase-I Clinical trial conducted at Apollo Hospitals, Ahmadabad, Gujarat. WHO-CoPP certification also filed for the Ulcrine formulation.

II. II. IIIM 160-A002- Anti-Inflammatory & Rheumatoid arthritis:

CSIR-IIIM, Jammu has been developed a standardized drug substance (Extract) i.e., IIIM 160 A002, the manufacturing procedure has been scaled up in cGMP facility and all the manufacturing process has been optimized. Analytical method for drug substance and drug product has been developed and validated at QC/QA section. Drug product was found to be stable when stored at 30°C±2°C & 65%±5%RH for 02 year in LDPE bags. IIIM Jammu developed a prototype Novel drug delivery formulation (Gastro Retentive sustained release) on the standardised extract and has been granted a patent, bearing CSIR Granted No. 0120NF2017/IN. CSIR-IIIM Jammu also filled international patent for the same drug delivery formulation. The present invention comprising an effective amount of an extract or lyophilized extract at least one bioactive fraction obtained from IIIM 160 A002 (*Bergenia ciliata*) along with one or more pharmaceutically acceptable additives/carriers.

This invention envisages the potential of an extract obtained from the whole plant of IIIM 160 A002 (*Bergenia ciliata*) to act an effective therapy against Anti-inflammatory & rheumatoid arthritis. With this background data, CSIR-IIIM, Jammu has to be compiling a dossier (IND) to the AYUSH department to conduct the Phase-I Clinical trial on Healthy volunteer through CRO.

III. Proprietary Health Supplement (Formulation of natural vitamin C and Zinc gluconate)

CSIR-IIIM Jammu has developed a technology to convert glucose to gluconate salts using a fungal strain i.e. *Aspergillus niger* under certain specifically defined physico-chemical conditions. The gluconatte salts have several established pharmaceutical, agricultural and other industrial applications. Calcium, copper, ferrous and zinc salts find use in oral metal supplements for humans, animals and agricultural applications. During our recent efforts to develop new product

External and internal view of the walk in plant growth chamber

lines in nutraceutical sector, we attempted to blend highly nutraceutical fruit (Leh berry) of Laddakh region with Zinc gluconate to develop nutraceutical supplement.

I. Fractional Distillation Unit (cGMP)

IIIM Jammu as an emerging entrepreneur in the field of AROMA Industries. This institution set up a National cGMP facility for extraction, formulation and packing

Traditional ISM herbal medicine formulation dosage forms (Tablets, capsule, liquid oral dosage forms and churna). The order for the **Fractional Distillation Unit** was placed to M/s. M.P. Scientific & Instruments Luchnow (U.P.) for Installation of Fractional Distillation Unit (FDU).The facility is now installed and commissioned under the supervision of Dr. M.K. Verma with required successful trail runs. The capacity of **Fractional Distillation Unit** is around 100 litres per batch**;** the major portion of this unit is made of glass. The objectives of the installation of such facility are to develop fractions from essential oils and these fractions are having their own market with high economy. The partitioning Fractional Distillation Unit (FDU) at Chemical Engineering Division is completed by Civil Engineering.

II. Fractional Distillation Unit (Capacity: 100 L)

The facility is to cater to the needs of CSIR-IIIM in terms of preparation of Value added products such as face wash, mouth wash, toothpaste etc., under CSIR AROMA Mission project (HCP-0007) and also other NCEs that are being evaluated for IND potential. It may also prove a boon for small scale aroma industry (Commercialization) to take advantages of this facility which may not be accessible to them due to high cost and maintenance requirements.

III. Walk in Plant growth chamber

A walk in plant growth chamber was installed at plant sciences decision of the institute. The growth chamber has approximate external dimensions of 108"W x 132"D x 108"H with illuminated shelves for growing plants. The total growing area within the chamber is approximately 150 ft^2. The facility is useful for growing plants, particularly *Arabidopsis* and *Nicotiana* sp. under controlled conditions of light, temperature, photoperiod and humidity.

IMPORTANT EVENTS

HON'BLE VICE-PRESIDENT SH. M. VENKAIAH NAIDU VISITS CSIR-IIIM JAMMU

Vice President of India M. Venkaiah Naidu on 28th May 2018 visited CSIR- Indian Institute of Integrative Medicine,

Jammu. The Governor of Jammu and Kashmir, Shri N.N. Vohra, the Minister of State for Development of North Eastern Region (I/C), Prime Minister's Office, Personnel, Public Grievances & Pensions, Atomic Energy and Space, Dr. Jitendra Singh, the Deputy Chief Minister of Jammu and Kashmir, Shri Kavinder Gupta and other dignitaries also accompanied the visiting Vice President at CSIR-IIIM campus. On his arrival at CSIR-Indian Institute of Integrative Medicine, the Vice President addressed the scientists, scholars and other technical staff. The Vice President said that both science and religion are the tools in the hands of the people in their quest for prosperity and internal peace. Scientific advancements illuminate our understanding of the universe, where as the religion provides answers to the unexplored universe. Further in his speech said that that the process of questioning

and seeking solutions lies at the heart of research, the Vice President said that human progress is not possible without the quest for deeper understanding of the world around. Research and innovation make us grow and they transform the world we inhabit. The Vice President said that posing relevant questions and seeking answers must be a way of life. He said that children and young adults must be encouraged to ask questions and search for answers. Quality of research is an important indicator of the quality of an educational system and said that it also determines the pace of a country's development. Later, the Vice President took round of the institute, inspected the testing labs and evinced keen interest in the exhibition of medicinal and aromatic preparations by the scientists of the institute and being used by various companies for commercial production. Director CSIR-IIIM, Dr. Ram Vishwakarma welcomed the dignitaries and gave a resume

of the major research domains of the institute.

EXHIBITION ON "WOMEN EMPOWERMENT

2018"

A three-day mega exhibition on women empowerment was organised from 22nd June – 24th June 2018 at Ramada Hotel in Jammu.

On the occasion, Member Parliament Rajya Sabha, Shamsher Singh Manhas was the Chief Guest, who inaugurated the exhibition. Speaking on the occasion, Manhas appreciated the efforts for organizing this exhibition for the people of State. He asked the people of the State in general and youth in particular to take benefits of the schemes launched the central government for the welfare and take nation to the new heights. Anand Pal, member Paryas Exhibition, in his address, said that the three-day exhibition was organised with a view to empower and encourage women to step in the corporate world and set landmark. The government

Visit of Kendriya Vidyalaya (K.V.) School students and faculty members

departments which participated in the exhibition include Indian Space Research Organization (ISRO), Indian Council of Medical Research, Defence Research and Development Organization, National Skill Development Corporation, National Thermal Power Corporation (NTPC), National Committee on Plasticulture Applications in Horticulture (NCPAH), National Agricultural Cooperative Marketing Federation of India (NAFED), National Health Mission, Natural Resources Defense Council (NRDC), Central Pollution Control Board (CPCB), Technology Development Board, Department of Science and Technology and others.

During the exhibition, CSIR-IIIM displayed various posters on Research & Development done in the institute such as Agrotechnology, Leather Technology, Fermentation Technology, Technology Business Incubators (TBI), Quality Control and Quality Assurance (QCQA), cGMP, HRD etc to encourage and motivate the gatherings. Various IIIM Scientists explained the visitors on the R&Ds done in IIIM. Apart from this, we also displayed herbal products from cGMP, Fermentation and sold essential oil kits of 3ml and 6 ml to the visitors. Based on the objectives of the project, scientist explained about the Technology Business Incubator (TBI) at CSIR-IIIM Jammu to the chief guest,

who proves a boon for students, young entrepreneurs, and industry personals. The motto of IIIM was to attract as many as ***"Women to Science".***

CSIR-IIIM-VIBHA ORGANISES PRE-CURSOR EVENT OF IISF-2018

CSIR-IIIM organized Public Outreach Programme on 25th September 2018 as a part of pre-cursor event of the India International Science Festival (IISF-2018), which was organised jointly by Ministries of Science and Technology and Earth Sciences and Vijnana Bharati (VIBHA) at Lucknow from October 3 to 5, 2018. Er. Rajneesh Anand, Chief Scientist welcomed the guests, students and teachers. Dr Dhiraj Vyas, Nodal Scientist IISF-2018 elaborated the proceedings of the event and informed that more than 25 schools with about 1,000 students and teachers across Jammu participated in this event. Mr. Samir Vohra, VIBHA representative narrated the achievements of VIBHA since its inception. A video presentation of VIBHA was also screened to inspire young students. On the occasion, the institute observed open day for students and various competitions like quiz, extempore and science models were organized for the students. A visit to various divisions of the institute was organized where the scientists and technical staff demonstrated the research activities. An impressive exhibition was held in which achievements of CSIR-IIIM were put on display. Prof Kamal K Kapoor, Department of Chemistry, University of Jammu delivered popular science talk to the students. He encouraged the students to make science and research as their passion which would help them to discover the fundamental laws of nature and build their knowledge and creativity. Dr Ram Vishwakarma, Director said that young minds should think critically and challenge conventional set of thinking. He also pressed for the need to develop scientific temper among students for transformation of the youth and country. Dr Vishwakarma wished the budding scholars for successful scientific endeavour.

JIGYASA TRAINING PROGRAM

cGMP Unit, CSIR-IIIM Jammu, provide opportunity to K.V. School students and faculty members in manufacturing of standardised extracts and botanical drug formulations, natural products etc., to evaluate encourage the students at early

stage for research and eventually graduate as entrepreneurs/ researchers so that more number of young students can be setup and employment can be generated. This facility will also be used as the Technology Business Incubator (TBI), for which Department of Science and Technology has already approved a project. K.V. School students and faculty have been selected for dissertation training programme in cGMP Unit, CSIR-IIIM Jammu of Indian Institute of Integrative Medicine (TBI-IIIM), Jammu, and conducted training program in March, 2019.

CSIR - INDIAN INSTITUTE OF INTEGRATIVE MEDICINE CELEBRATES 76TH FOUNDATION DAY OF CSIR

CSIR-IIIM celebrates 76th foundation day of CSIR on 26th September, 2018. The celebrations, in this connection, were held at IIIM auditorium and were largely attended by eminent scientists, faculty members of research & educational institutions, entrepreneurs, invited dignitaries, guests, members of Press and staff members of CSIR-

IIIM.

Dr Rajesh S Gokhale, former Director, CSIR-Institute of Genomics and Integrative Biology (CSIR-IGIB) and Staff Scientist, National Institute of Immunology, New Delhi was the Chief Guest on the occasion. To celebrate the CSIR Foundation day, IIIM organized 2-day event at the main campus. On the first day of the programme, IIIM and VIBHA jointly organized a pre-cursor event, in which the institute observed 'Open-Day' for students wherein Quiz, Extempore and Science Models Competitions for the students of 9th to 12th class were organized. An impressive exhibition was also held in which aromatic and medicinal products developed by CSIR-IIIM were put on display.

CSIR - INDIAN INSTITUTE OF INTEGRATIVE MEDICINE CELEBRATES ITS 77TH FOUNDATION DAY

Indian Institute of Integrative Medicine, Jammu celebrated its 77th Foundation day on December, 2018. Ram Bahadur Rai, Veteran Journalist and President of Indra Gandhi National Centre for the Arts (IGNCA), Delhi, were the chief guest and Dr. C.K. Katiyar, C.E.O., Health Care, Emami Ltd.; Kolkatta was the Guest of Honour on the occasion. Dr. C.K. Katiyar, the guest of honour while speaking on the occasion said that India has very rich knowledge of Ayurvedic system of healing and health care but unfortunately we seldom bother to understand the insight of this novel and glorious system. Ram Bahadur Rai, the chief Guest of the function had delivered the foundation day lecture "Gandhi 150 Varsha: Mahatma Gandhi ke Sapanon Ki Rajya Vyavastha". During his lecture he dealt with the Gandhian principles of life and relevance of Gandhi in modern time. For the overall development of nation like India, Rai said that the governance should start from villages rather than from State or union capital. As part of Foundation day, the institute celebrates 30th November as OPEN DAY in which about 700 students drawn from different colleges and schools of Jammu city were also taken on a guided visit to the various research divisions and medicinal farms of the institute. The scientists and technical staff have demonstrated their indoor and field research activities to the visiting students and other dignitaries. Dr. Deepika Singh conducted the proceedings while Er. Abdul Rahim, Head PME and IT Divisions presented vote of thanks.

IIIM LICENSED TECHNOLOGY ON SAFFRON BASED NUTRACEUTICAL PRODUCT

CSIR-IIIM, Jammu has licensed a technology on a Saffron based nutraceutical product for brain health to Pharmanza Herbal Pvt. Ltd., Gujarat on 3rd July, 2018 for launching this product both in domestic and US market.

NATIONAL CONFERENCE-CUM-INDUSTRY-ACADEMIA MEET

September 13-14, 2018

National Conference-cum-Industry-Academia meet on "Opportunities and Challenges in Fermentation Based Industrial Processes" (IAMF-2018) organized by CSIR Integrative Medicine, Jammu (IIIM) concluded successfully on 14th. September 2018 after two days of intense deliberations on present state of knowledge and future of fermentation bas J&K state and India. The event was primarily sponsored by DBT, SERB, DRDO, IIIM-TBI and Ministry of AYUSH. Large numbers of well-known dignitaries from Government, Industry and Academia event. Many well known personalities from the fields of Fermentation, Ayurveda and Medicine presented their work. High quality research work of scholars was presented and various products & processes were displayed in the exhibition. Most of the participants and dignitaries agreed that this event was very much required to be conducted in J&K for development of the industry in the state. They also congratulated Dr. Ram Vishwakarma, Director IIIM and Dr Vikash Babu, Convener of the conference for huge success of the event. Event concluded with vote of thanks by Er Abdul Rahim.

SC/ST/OBC REPORT-I

ANNUAL STATEMENT SHOWING THE REPRESENTATION OF SCs, STs AND OBCs AS ON FIRST JANUARY OF THE YEAR AND NUMBER OF APPOINTMENTS MADE DURING THE PRECEDING CALENDER YEAR 2018

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH (DSIR) O/o INDIAN INSTITUTE OF INTEGRATIVE MEDICINE, JAMMU

	Representation of SCs/STs/OBCs (As on 01.01.2019)				Number of appointments made during the calendar year 2018									
					By Direct Recruitment				By Promotion			By Deputation		
Groups	Total number of Employees	SCs	STs	OBCs	Total	SCs	STs	OBCs	Total	SCs	STs	Total	SCs	STS
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Group A	79	11	03	08	NIL	--	--	--	--	--	--	--	--	--
Group B	83	18	02	11	NIL	--	--	--	--	--	--	--	--	--
Group C	81	26	01	05	NIL	--	--	--	--	--	--	--	--	--
Group D (Excluding Sweepers)	--	--												
Group D (Sweepers)														
TOTAL	243	55	06	24	NIL	--	--	--	--	--	--	--	--	--

SO (Estb)

O/o Indian Institute of Integrative Medicine, Jammu- 180001

SC/ST/OBC REPORT-II

ANNUAL STATEMENT SHOWING THE REPRESENTATION OF SCs, STs AND OBCs IN VARIOUS GROUP'A' SERVICES AS ON FIRST JANUARY AND NUMBER OF APPOINTMENTS MADE IN THE SERVICE IN VARIOUS GRADES IN THE CALENDER YEAR 2018

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH (DSIR) O/o INDIAN INSTITUTE OF INTEGRATIVE MEDICINE, JAMMU

	Representation of SCs/STs/OBCs (As on 01.01.2019)				Number of appointments made during the calendar year 2018									
					By Direct Recruitment				By Promotion			By Deputation		
Pay Band and Grade Pay	Total number of Employees	SCs	STs	OBCs	Total	SCs	STs	OBCs	Total	SCs	STs	Total	SCs	STS
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
PB-3 Rs.5400	10	02	01	01	--	--	--	--	--	--	--	--	--	--
PB-3 Rs.6600	17	04	--	04	--	--	--	--	--	--	--	--	--	--
PB-3 Rs.7600	36	04	--	04	--	--	--	--	--	--	--	--	--	--
PB-4 Rs.8700	16	01	--	--	--	--	--	--	--	--	--	--	--	--
PB-4 Rs.8900	05	01	02	--	--	--	--	--	--	--	--	--	--	--
PB-4 Rs.10,000	01	--	--	--	--	--	--	--	--	--	--	--	--	--
HAG+Above	01	--	--	--	--	--	--	--	--	--	--	--	--	--
TOTAL	86	12	03	09	--	--	--	--	--	--	--	--	--	--

SO (Estb)

O/o Indian Institute of Integrative Medicine, Jammu- 180001

ANNUAL STATEMENT SHOWING THE REPRESENTATION OF THE PERSONS WITH DISABILITIES IN SERVICES (AS ON 1ST JANUARY 2019)

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH (DSIR) O/o INDIAN INSTITUTE OF INTEGRATIVE MEDICINE, JAMMU

Group	Number of Employees				
	Total	In Identifiedposts	VH	HH	OH
1	2	3	4	5	6
Group A	79	03 (OH-2; HH-1)	--	**	02
Group B	83	02 (VH; HH)	*	**	02
Group C	81	02 (OH; HH)	--	**	01
Group D					
TOTAL	243				

Note:

(I) VH stands for Visually Handicapped (persons suffering from blinders or low vision).

(II) HH stands for Hearing Handicapped (persons suffering from hearing impairment).

(III) OH stands for Orthopaedically Handicapped (persons suffering from locomotor disability or cerebral palsy).

* One post under VH category is lying vacant.

**One post under HH category is lying vacant.

SO (Estb)

O/o Indian Institute of Integrative Medicine, Jammu - 180001

सीएसआईआर–भारतीय समवेत औषध संस्थान, जम्मू में राजभाषा की प्रगति में हिन्दी के कार्यक्रम

वित्तीय वर्ष 2018-19 में हिन्दी अनुभाग द्वारा संस्थान में निम्नलिखित कार्यक्रम व बैठकें आयोजित की गई:-

(क) नगर राजभाषा कार्यान्वयन समिति, जम्मू की अर्द्धवार्षिक बैठक दिनांक 21 जून, 2018 को सीएसआईआर-भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में सम्पन्न हुई।

भारत सरकार, गृह मंत्रालय, राजभाषा विभाग के निर्देशानुसार नगर राजभाषा कार्यान्वयन समिति, जम्मू की अर्द्धवार्षिक बैठक दिनांक 21 जून, 2018 (बृहस्पतिवार) को अपराह्न 3.00 बजे सीएसआईआर-भारतीय समवेत औषध संस्थान, जम्मू के कॉन्फ्रेंस हॉल में आयोजित हुई। बैठक की अध्यक्षता संस्थान के मुख्य वैज्ञानिक एवं नराकास, अध्यक्ष श्री रजनीश आनन्द ने की। इस अवसर पर ब्रिगेडियर रघु सढोत्रा जी, उपमहानिदेशक, राट्रीय कैडेट कोर निदेशालय, नहर मार्ग, जम्मू, डॉ. कृणा कुमारी, प्रभारी, क्षेत्रीय आयुर्वेदीय मूत्रविकार अनुसंधान संस्थान, बनतालाब, जम्मू, डॉ. शरद चन्द्र शर्मा, प्राचार्य, राट्रीय संस्कृत संस्थानम्, जम्मू, श्री वी.के.बक्शी, उपनिदेशक, कार्यालय महालेखाकार (लेखा परीक्षा), जम्मू एवं नराकास के केन्द्रीय कार्यालयों के सभी कार्यालयाध्यक्ष/राजभाषा अधिकारी/ हिन्दी अधिकारी/हिन्दी अनुवादक/प्रिन्ट व इलैक्ट्रॉनिक मीडिया के सभी संवाददाता तथा अन्य गणमान्य व्यक्ति उपस्थित थे।

सर्वप्रथम बैठक में उपस्थित कार्यालय प्रमुखों एवं उपस्थित अधिकारियों का स्वागत डॉ. रमा शर्मा, हिन्दी अधिकारी एवं सचिव, नराकास, जम्मू ने किया। उन्होंने अपने स्वागत संबोधन में सभी मंचस्थ एवं अन्य उपस्थित गणमान्य व्यक्तियों का स्वागत करते हुए मंचस्थ अध्यक्ष महोदय को आमंत्रित किया कि वे कार्यक्रम व बैठक का दीप प्रज्ज्वलित कर विधिवत् शुभारंभ करें तथा मंच पर बैठे सभी अधिकारियों से भी निवेदन है कि वे भी अध्यक्ष महोदय का साथ दें। दीप प्रज्ज्वलन हेतु कु. ज्योति ने सहायता की। अध्यक्ष महोदय की अनुमति से बैठक की कार्रवाई आरम्भ की गई। तदुपरान्त बैठक में प्रथम अक्टूबर, 2017 से 31 मार्च, 2018 के दौरान सभी सदस्य कार्यालयों के हिन्दी कार्यान्वयन संबंधी प्रगति रिपोर्ट की समीक्षा प्रस्तुत की। बैठक का मुख्य उद्देश्य केन्द्रीय कार्यालयों में हिन्दी का उत्तरोत्तर विकास करना तथा जम्मू 'ग' क्षेत्र को राजभाषा की प्रगति की ओर अग्रसर करने की दिशा में रहा ।

अपने अध्यक्षीय संबोधन में संस्थान के मुख्य वैज्ञानिक एवं नराकास अध्यक्ष श्री रजनीश आनन्द जी ने कहा कि नगर के सभी केन्द्रीय कार्यालयों के उपस्थित कार्यालय प्रमुख एवं अन्य गणमान्य व्यक्तियों का संस्थान एवं नराकास मंच की ओर से सबका हार्दिक स्वागत करता हूँ। जिसमें समिति के सभी सदस्य कार्यालयों के हिन्दी से संबंधित कार्यालयाध्यक्षों, नोडल अधिकारियों एवं राजभाषा अधिकारियों से अनुरोध है कि कृपया बैठक में खर्च होने वाले पैसे को समय-समय से भिजवाएं ताकि पत्रिका का समय से प्रकाशन किया जा सके। जम्मू नगर में राजभाषा की प्रगति में आप सभी महती भूमिका है, मैं आशा करता हूँ कि आप सभी के सहयोग से इस क्षेत्र में राजभाषा हिन्दी का कार्य दिन प्रतिदिन बढ़ता जा रहा है।

अन्त में संस्थान के श्री के.सी.पालीवाल, वित्त एवं लेखा अधिकारी ने धन्यवाद किया।

(ख) नगर राजभाषा कार्यान्वयन समिति, जम्मू की अर्द्धवार्षिक बैठक दिनांक 22 नवम्बर, 2018 को सीएसआईआर-भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में सम्पन्न हुई।

भारत सरकार, गृह मंत्रालय, राजभाषा विभाग के निर्देशानुसार नगर राजभाषा कार्यान्वयन समिति, जम्मू की अर्द्धवार्षिक बैठक दिनांक 22 नवम्बर, 2018 (बृहस्पतिवार) को पूर्वाह्न 11.00 बजे सीएसआईआर-भारतीय समवेत औषध संस्थान,

जम्मू के कॉन्फ्रेंस हॉल में आयोजित हुई। बैठक की अध्यक्षता संस्थान के मुख्य वैज्ञानिक एवं नराकास, अध्यक्ष श्री रजनीश आनन्द ने की। इस अवसर पर श्री एरदन एक्का, कमांडेंट, ग्रुप केन्द्र, केन्द्रीय रिजर्ब पुलिस, बनतालाब, जम्मू; डॉ. गोपेश कुमार शर्मा, अनु. अधिकारी, क्षेत्रीय आयुर्वेदीय मूत्रविकार अनुसंधान संस्थान, बनतालाब, जम्मू; प्रो. शरद चन्द्र, सहाचार्य, राट्रीय संस्कृत संस्थानम्, जम्मू; श्री पंकज बहादुर, नियंत्रक प्रशासन, भारतीय समवेत औषध संस्थान, जम्मू एवं नराकास के केन्द्रीय कार्यालयों के सभी कार्यालयाध्यक्ष/राजभाषा अधिकारी/ हिन्दी अधिकारी/हिन्दी अनुवादक तथा प्रिन्ट व इलैक्ट्रॉनिक मीडिया के सभी संवाददाता तथा अन्य गणमान्य व्यक्ति उपस्थित थे।

सर्वप्रथम बैठक में उपस्थित कार्यालय प्रमुखों एवं उपस्थित अधिकारियों का स्वागत श्री सँजय शर्मा, कार्यवाहक हिन्दी अधिकारी एवं सचिव, नराकास, जम्मू ने किया। उन्होंने अपने स्वागत संबोधन में सभी मंचस्थ एवं अन्य उपस्थित गणमान्य व्यक्तियों का स्वागत करते हुए मंचस्थ अध्यक्ष महोदय को आमंत्रित किया कि वे कार्यक्रम व बैठक का दीप प्रज्ज्वलित कर विधिवत् शुभारंभ करें तथा मंच पर बैठे सभी अधिकारियों से भी निवेदन किया कि वे भी अध्यक्ष महोदय का साथ दें। दीप प्रज्ज्वलन हेतु श्रीमती सुनीता कुमारी ने सहायता की। अध्यक्ष महोदय की अनुमति से बैठक की कार्रवाई आरम्भ की गई। तदुपरान्त बैठक में प्रथम अप्रैल, 2018 से 30 सितम्बर, 2018 के दौरान सभी सदस्य कार्यालयों के हिन्दी कार्यान्वयन संबंधी प्रगति रिपोर्ट की समीक्षा प्रस्तुत की गई। बैठक का मुख्य उद्देश्य केन्द्रीय कार्यालयों में हिन्दी का उत्तरोत्तर विकास करना तथा राजभाषा हिन्दी की प्रगति की ओर अग्रसर करने की दिशा में रहा ।

संस्थान के मुख्य वैज्ञानिक एवं नराकास अध्यक्ष श्री रजनीश आनन्द जी ने अपने अध्यक्षीय संबोधन में जम्मू नगर के सभी केन्द्रीय कार्यालयों के उपस्थित कार्यालय प्रमुख एवं अन्य गणमान्य व्यक्तियों का संस्थान एवं नराकास की ओर से सबका हार्दिक अभिनन्दन किया। समिति के सभी सदस्य कार्यालयों के कार्यालयाध्यक्षों/ हिन्दी अधिकारियों/हिन्दी अनुवादकों/नोडल अधिकारियों एवं राजभाषा अधिकारियों से अनुरोध किया कि हिन्दी तिमाही प्रगति रिपोर्ट समय से भिजवाएं ताकि हिन्दी के क्रिया-कलापों को बढ़ावा दिया जा सके। उन्होंने यह भी निवेदन किया कि सभी अपने कार्यालयों से अंशदान राशि भिजवाएं ताकि पत्रिका 'ज्ञानवार्ता' का समय से प्रकाशन किया जा सके। बैठक के अन्त में 23 सदस्य कार्यालयों को हिन्दी के कार्यान्वयन में विशिष्ट योगदान के लिए प्रशस्ति-पत्र प्रदान किए गए।

अन्त में श्री पंकज बहादुर, नियंत्रक प्रशासन,

भारतीय समवेत औषध संस्थान, जम्मू ने प्रशासन से संबंधित आदेश/अनुदेश के बारे में विस्तार से बताया और ध न्यवाद ज्ञापित कियज़ं

2. सीएसआईआर-भारतीय समवेत औषध संस्थान, जम्मू में हिन्दी दिवस/पखवाड़ा, 2018 का आयोजन

राजभाषा हिन्दी के उत्तरोत्तर विकास और अधिकारियों/कर्मचारियों में हिन्दी के प्रति जागरूकता उत्पन्न करने और रूचि जगाने के उद्देश्य से प्रत्येक वर्ष सितम्बर माह में हिन्दी दिवस/हिन्दी पखवाड़ा का आयोजन किया जाता है। वर्ष 2018 का आयोजन दिनांक 14 सितम्बर, 2018 से 28 सितम्बर, 2018 तक तत्संबंधी प्रतियोगिताएं हिन्दी निबन्ध लेखन, भाषण प्रतियोगिता (अन्तरविभागीय), हिन्दी में मूलकार्य, हिन्दी पखवाड़ा समापन समारोह आदि कार्यक्रम आयोजित किए गए और सभी स्टॉफ सदस्यों, शोध छात्रों एवं नराकास सदस्यों ने भी भाग लिया और 16 विजयी प्रतियोगियों को नकद राशि एवं प्रामण-पत्र प्रदान किए गए।

HUMAN RESOURCE

Director

Dr. Ram A. Vishwakarma

Chief Scientist

Er. Rajneesh Anand

Sr. Pr. Scientist

Dr. D.M. Mondhe

Er. Abdul Rahim

Pr. Scientist

Dr. Anindya Goswami

Dr. Inshad Ali Khan

Dr. Muzamil Ahmad

Dr. Gurdarshan Singh

Dr. Zabeer Ahmed

Dr. (Ms.) Asha Chubey

Sr. Scientist

Dr. Rajkishore Rai

Dr. Subash Singh

Dr. P. N Gupta

Dr.Zahoor Ahmad Parry

Sh. Shashank Kr. Singh

Dr. (Mrs.) Meenu Katoch

Dr. Abid Hamid Dar

Dr. Jamal Dar

Dr. Sandeep B. Bharate

Dr. Asif Ali

Dr. Qazi Naveed Ahmad

Dr. Prasoon Kumar Gupta

Dr. Sheikh Tasduq Abdullah

Dr. Fayaz Ahmed Malik

Dr. Dhiraj Kr. Vyas

Dr. Sumit Gandhi

Dr. Qazi Parvaiz Hassan

Dr. Syed Riyaz- Ul Hassan

Dr. Khursheed Ahma Bhat

Dr. S.D. Sawant

Dr. (Mrs.) Suphla Bajpai Gupta

Dr. Debaraj Mukherjee

Dr. Syed Sajad Hussain

Dr. Saurabh Saran

Mrs. Deepika Singh

Dr. Amit Nargotra

Dr. Pyare Lal Sangwan

Scientist

Dr. Govind Yadav

Sh. Anil Kumar Katare

Dr.Bilal Ahmad Bhat

Dr. Parvinder Pal Singh

Dr. Bhahwal Ali Shah

Dr. Sundeep Jaglan

Dr. (Mrs.) Nasheeman Ashraf

Dr. Sumit Gairola

Dr. Prashant Misra

Er. Shaghaf Mobin Ansari

Dr. Vikash Babu

Dr. Bikarma Singh

Dr. Ravi Shankar

Dr. Utpal Nandi

Dr. Sreedhar Madishetti

Dr. Rajendra Bhanwaria

Dr. Vishav Prakash Rahul

Dr. Sabha Jeet

Dr. Nazia Abbas

Principal Technical Officer

Dr. S.K. Lattoo

Sh. R.K. Khajuria

Dr. (Mrs.) Kanti Rekha

Mrs. Urmila Jamwal

Sr. Technical Officer (3)

Dr. A. P. Gupta

Mrs. Pinki Koul
Dr. Ajay Kumar
Mrs. Asha Devi
Sh. Rajinder Kumar

Sr. Technical Officer (2)

Dr. Phalisteen Sultlan
Sh. Buddh Singh

Sr. Technical Officer (1)

Dr. Siya Ram Meena
Dr. Satheesh Kumar P

Technical Officer

Sh. Ajit Prabhakaran
Dr. M.K. Verma
Sh. Vikrant Awasthi
Sh. Mukesh Jhangra
Mr. Gourav Sharma
Mrs. Bhavana Vij

Technical Assistant

Sh. Manish Kumar
Sh. Kamlesh Singh
Sh. Sumit Kumar
Sh. Arvind Kr. Yadav
Sh. Yogesh Kumar
Sh. Amit Kumar
Sh. Rajinder Gocher
Sh. Niteen Ashok Narkhede
Sh. Uma Shankar
Miss. Monika Gupta
Sh. Chandera Pal Singh
Sh. Durga Prasad Mindala
Sh. Ashok Kumar Bhargava
Mrs. Priya Wazir
Sh. Narinder Kumar
Sh. Sumit Roy
Sh. Habibullah
Sh.Yadunandan Sen

Medical Officer

Dr. Amit Sharma
Dr. (Mrs.) Anju Gupta

Supdt. Executive Engineer (Elect.)

Sh. Ashwani Chopra

Supdt. Executive Engineer (Civil)

Sh. G.P. Singh

Library Officer

Sh. Sanjay Sharma

Assistant Engineer (Civil)

Sh. S.N. Bharati

Jr. Engineer (Electrical)

Sh. Bikram Singh

Sr. Technician

Sh. Ajeet Singh
Mrs. Raj Kumari
Sh. Kuldip Raj
Sh. Vikram Abrol
Sh. Om Singh
Sh. Madan Lal
Sh. Jasbir Singh
Mrs. Manju Sambyal
Mrs. Neelam Sharma
Sh. Parshotam Kumar
Sh. Kuldeep Singh
Sh. Rajinder Kumar Gupta
Mrs. Sunita Devi
Mrs. Parveen Sharma
Mrs. Shabnam Khan
Sh. P.R. Mehta
Dr. Anil Prabhakar
Sh. Ashwani Sharma
Sh. Partap Chand
Sh. Samar Singh
Mrs. Kiran Koul
Sh. Satya Bhushan

Sh. Rajinder Kumar
Sh. Naresh Pal
Sh. Vijay Kumar
Sh. Ashok kumar
Sh. Kasturi Lal
Ms. Anjum Vashist
Sh. Rajesh KumarSahdev
Sh. Asad Ullah
Sh. Shabir Husen

Technician

Sh. Rahul Kalgotra
Sh. Karan Pal
Sh. Kirshan Kumar

Lab Assist.

Sh. Girdhari Lal Sharma
Sh. Bishan Kumar
Sh. Jasbir Singh
Sh. Sham Lal Bhagat
Sh. Abdul Hamid Dar
Sh. Neel Kamal
Sh. Rishi Kumar
Sh. Balwinder Singh
Sh. Manoj Kumar
Sh. Ajit Ram
Sh. Om Parkash
Sh. Girdhari Lal
Sh. Abdul Ahed Sheikh
Sh. Fayaz Ahmad Dar
Mrs. Darshana
Sh. Kuldeep kumar
Sh. Tarachand
Sh. Nagar Lal
Sh. Ashok Kumar

Controller ofAdministration

Sh. Pankaj Bhadur

Finance & Accounts Officer

Sh. Satish Kumar

Store & Purchase Officer

Sh. Praphul Kumar

Section Officer (G)

Sh. Rajesh Kumar Gupta

Section Officer (F&A)

Sh. Anil Gupta

Section Officer (S&P)

Sh. Ram Singh

Private Secretary

Sh. Ramesh Kumar

Security Officer

Sh. Yashpal Singh

Security Asst.

Sh. Bhupinder Singh
Sh. Balkrishan
Sh. Subash Chander

Assistant General Gr (1)

Sh. Romesh Kumar Mottan
Sh. U.S. Thappa
Mrs. Kusum Bali
Mrs. Neelam Razdan
Sh. Ranjeet Kr. Gupta
Sh. Manoj Kumar
Ms. Nisha Vij
Sh. Rajinder Singh

Asst.(F&A) Gr(1)

Sh. Umesh Malhotra
Sh. Harish K Gupta

Asst.(S&P) Gr(1)

Sh. Satish Sambyal
Mrs. Rajni Kumari

Senior Stenographer

Sh. V.K. Sharma

Receptionist

Mrs. Jyoti Prabha

Asstt. (G) Gr(II)

Mrs. Rekha Gupta

Sh. Mohd. Ayub Bhat

Asstt (F&A) Gr(II)

Sh. Vinod Kumar Meena

Mrs. Lovely Ganjoo.

Sh. Sanchit Kumar Sharma

Asstt (S&P) Gr(II)

Sh. Bua Ditta

Sh. Angrez Singh

Asstt (F&A) Gr(III)

Sh. Roshan Lal

Asstt (G) Gr(III)

Mrs. Sunita Kumari

Halwai

Sh. Janak Raj

Jr. Section Asstt.

Sh. Tarsem Kumar

Work Assist.

Sh. Milkhi Ram

Sh. Jagdish Singh

Sh. Romesh Kumar

Sh. Chaman Lal

Sh. Parshotam Lal

Sh. Mohd. Farooq Bhat

Sh. Ram Lal

Sh. Ashok Kumar

Sh. Tarseem Kumar (Appointed as LDC)

Sh. Pawan Kumar

Sh. Rajesh K. Tandon

Sh. Moses Tegi

Sh. Girdhari Lal.

Sh. Rashpal

Sh. Prithvi Raj

Sh. Mangal Dass

Sh. Sham Lal

Sh. Subash Chander

Sh. Girdhari lal

Sh. Suram Chand

Sh. Tara Chand

Sh. Rattan Lal

Sh. Sukhdev Raj

Sh. Kala Ram

Sh. Ashok Kumar

Sh. Munna

Sh. Dev Raj

Sh. Surinder Kumar

Sh. Ashok Kumar

Sh. Karnail Chand

Sh. Bachan Lal

Sh. Kali Das

Sh. Daleep Raj

Sh. Shyam Lal

Sh. Sodagar Lal