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सीएसआईआर-भारतीय समवेत औषध संस्थान, जम्मू-180001 (भारत)

CSIR-INDIAN INSTITUTE OF INTEGRATIVE MEDICINE

(COUNCIL OF SCIENTIFIC AND INDUSTRIAL RESEARCH)

JAMMU-180001 (INDIA)

CONTENTS


IIIM

From the Director's Desk

I take this opportunity to present the Annual Report of CSIR- Indian Institute of Integrative Medicine, Jammu to its readers which highlights the scientific achievements and work done in the institute during the year 2016-2017.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. I am indeed happy to inform that the strides of progress have continued unabated towards excellence in research and development of innovative products for societal benefit. This period has been highly exiting for us as CSIR-IIIM; Jammu filed 17 patents applications both in India and in foreign countries and 03 patents were granted to IIIM. During this period, IIIM published a total of 188 scientific publications with an average impact factor of 3.049.

Several important events took place during this year. On the occasion of Platinum Jubilee celebration of CSIR through DD Live feed from New Delhi, Prime Minister released scented variety of rose developed by CSIR-IIIM, Jammu. Prof. Javed Musarat, Vice Chancellor, BGSB University delivered the CSIR foundation day lecture on the topic, "Small is not always beautiful". Dr. Harsh Vardhan, Union cabinet Minister for Science and Technology, Earth Sciences inaugurated cGMP a state of art, National facility for small and medium scale manufacturers accompanied by Dr. Jitendra Singh, Minister of State (MoS) (Independent Charge) for the Ministry of Development of North Eastern Region, Prime Minister Office, Personnel, Public Grievances and Pensions, Department of Atomic Energy and Department of Space along with Dr. Girish Sahni (Director General, CSIR and Secretary, DSIR). This facility will provide the products manufactured under GMP/GLP conditions besides its use for research in IIIM.

During this year laboratory hosted BIRAC workshop on Bio-entrepreneurship, Grant writing and IP. The objective of the workshop was to sensitize the target audience about BIRAC support for the entrepreneurs and the importance and relevance of intellectual property in the biotechnology regime. IIIM introduced Sea Buckthorn health drink, keeping all the medicinally important properties of the fruit, IIIM prepared health drink from its fruit packed in tetra-packs of 200 ml capacity.

This year 'Scientist of the year 2016' was awarded by the Essential Oil Association of India to Dr. Suresh Chandra, Chief Scientist and his team members. Dr. Sandip Bharate has been awarded for CSIR Young Scientist Award 2016 in Chemical Sciences and Dr. Nazia Abbas has been awarded with the prestigious INSA Medal for young scientist.

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, staff and the students of CSIR-IIIM who made possible this outstanding output for inclusion in this Annual Report.

(Ram Vishwakarma)

1.0 PLANT BIOTECHNOLOGY

1.1 In planta characterization of CYP710: A pivotal sterol 22-desaturase gene from *Withania somnifera*

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

Withania somnifera (L) Dunal produces a diverse array of steroidal lactones collectively called as withanolides. These are pharmacologically very important and belong to triterpenoids class of compounds which are synthesized via mevalonate and non-mevalonate pathways. To date, limited attempts have been made to identify the regulatory genes and decipher the biosynthetic pathway of withanolide biosynthesis. However, the downstream routes of their synthesis and different genes involved in the final formation are yet to be fully identified. Recent studies encompassing biosynthetic genes have covered broad areas like their regulation, spatial and temporal expression profiles about the metabolite accumulation, concerted dynamics brought about using various elicitations and physiological conditions. Most of the pathways for secondary metabolite biosynthesis deploy P450s at one or many steps to functionalize core structure of molecules which are still unexplored from *W. somnifera*. To get clear insight both at molecular and biochemical levels it requires extensive efforts to identify genes catalysing one or many reactions in biosynthetic pathway. Identification and characterization of P450s is essential for the elucidation of various biosynthetic pathways. In plants, a clear majority of sterols are present in membranes as a mixture of several major molecular species, including β-sitosterol, stigmasterol, campesterol, and cholesterol which modulate membrane permeability fluidity and microdomain formation. They also serve as precursors for the biosynthesis of plant steroid hormones involved in many different cellular processes. CYP710 is a sterol C-22 desaturase gene responsible for the biosynthesis of important plant sterols. Manipulation of its expression level leads to the direct modification of sterol composition in crop plants. Present study entails first comprehensive investigations related to identification and characterization of P450 monooxygenase CYP 710A from *W. somnifera*. We have successfully cloned and characterized CYP710A from *W. somnifera* including its in planta validation in *Nicotiana tobaccum*.

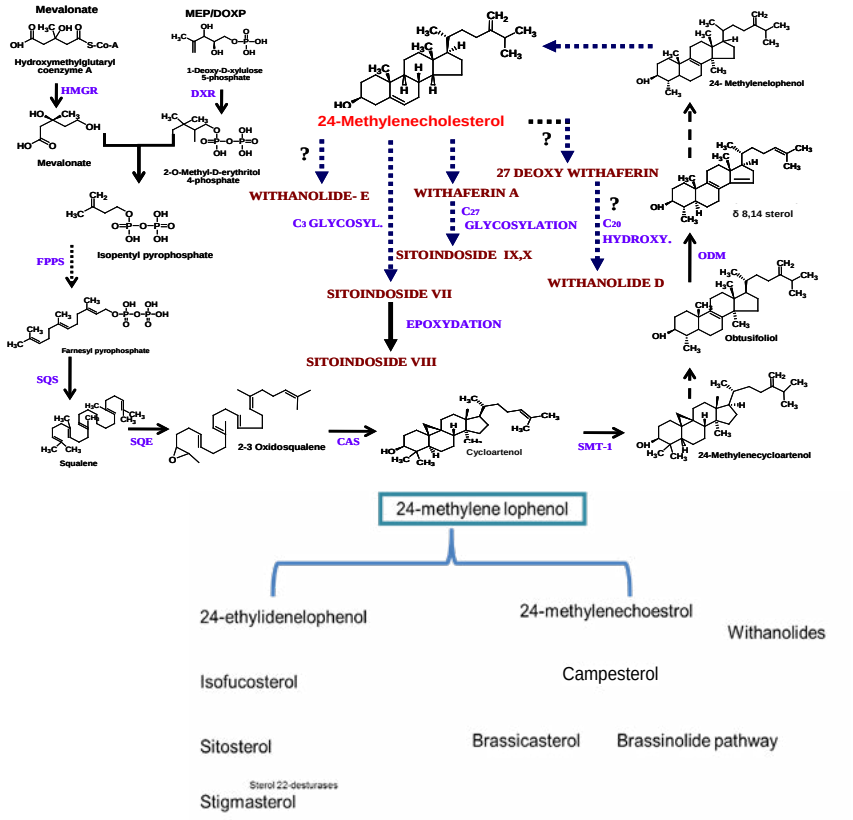


Fig 1.1.1. Biosynthetic pathway of triterpenoids in Withania somnifera. Mevalonate and Non-mevalonate pathway converge at IPP from where pathway proceeds in cytoplasm. 24 methylene cholesterol is diverging point of various triterpenoids viz withanolides, sterols and steroids

To know about the withanolide/ sterol biosynthetic pathway, we have successfully isolated and cloned the full-length ORF sterol 22 desaturases CYP710 gene from *Withania*, one of the putative gene involved in the sterol biosynthetic pathway. The open reading frame (ORF) for WsCYP710 was generated from aligning the core fragment, 5´and 3´ends and was comprised of 1530 nucleotide bases which confer to 503 amino acids with a predicted molecular mass of 53kDa Fig.1.1.2.

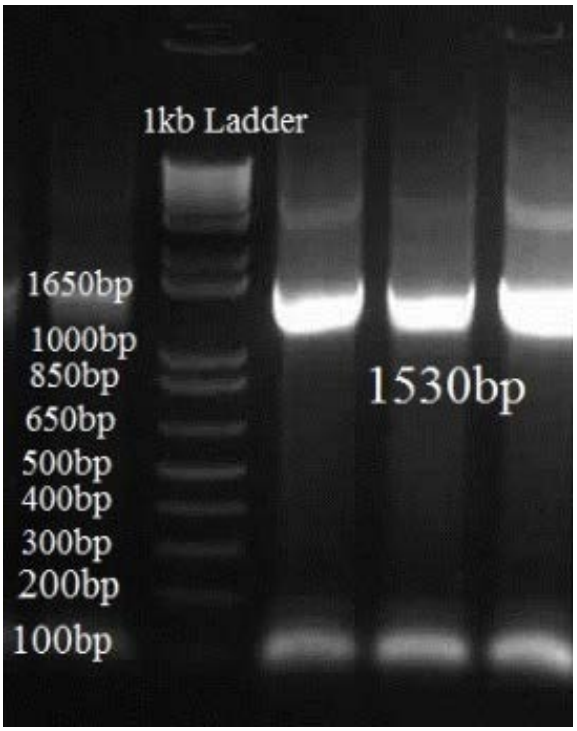


Fig. 1.1.2. Full length ORF of WsCYP710 cloned in pTZ

The WsCYP710 was also heterologously expressed in Schizosaccaromyces pombe. Extracts were prepared in 50% methanol and subjected to GC-MS analyses which confirmed its functionality on being compared to its respective standards and negative control (empty vector) which have been reported previously.

The nucleotide sequence so obtained was translated using translate tool. Translate tool and the properties of deduced amino-acid sequences (Fig1.1.3) were estimated using ProtParam. The open reading frame for CYP710 comprised of 1530 nucleotide bases. These nucleotide bases confer to 405 amino acids with predicted molecular mas of 54.43 kDa. The secondary structure was determined using SOPMA programme. The predicted structure of CYP85A1 showed the abundance of alpha helices (47.75) and random coils (32.15%) while as extended strands were in fewer amounts (14.42%) Fig.1.1.4.

The phylogenetic tree was constructed from different amino-acid sequences to ascertain the degree of evolutionary relatedness among different plant species. Protein sequences were retrieved from the GenBank through the BLASTp algorithm at the National Centre for Biotechnology Information (NCBI) using cloned full length sequences with the highest score from different were aligned using ClustalW2 tool using default parameters and Phylogenetic tree was constructed by neighbour-joining method using the MEGA5.2 software programme.

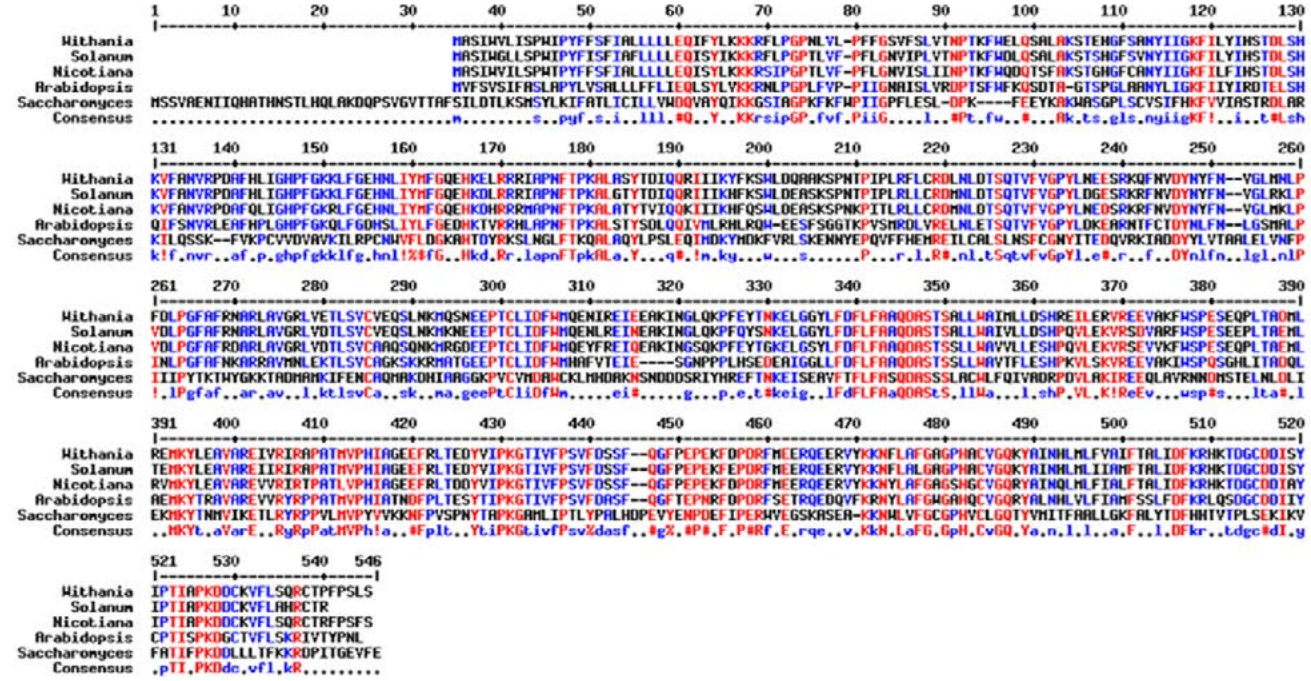


Fig. 1.1.3. Alignment of deduced amino-acid sequence of CYP710 gene from *Withania somnifera* with related species showing its conserved nature

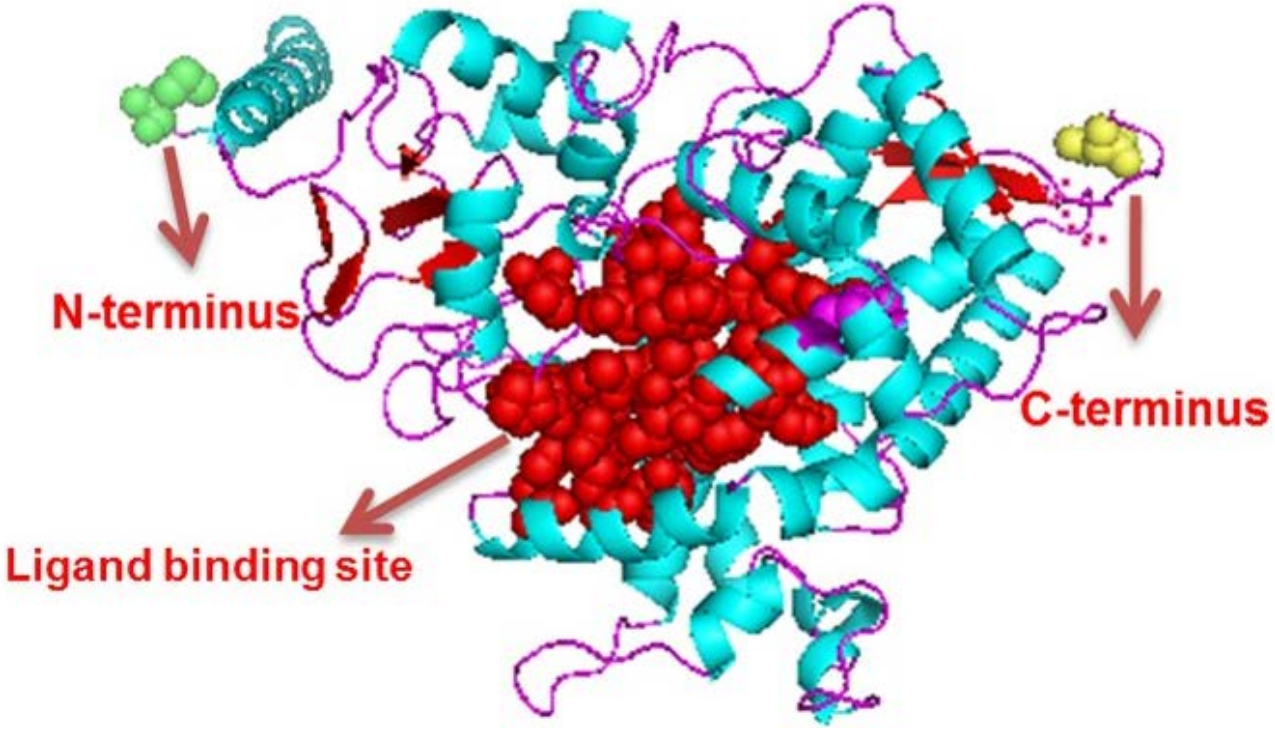


Fig. 1.1.4. 3D structure of the protein showing alpha helices (47%) and beta sheets (14%) with its ligand binding site shown in red colour, N-terminus in Green colour and C-terminus in yellow colour generated via Phyre server tool

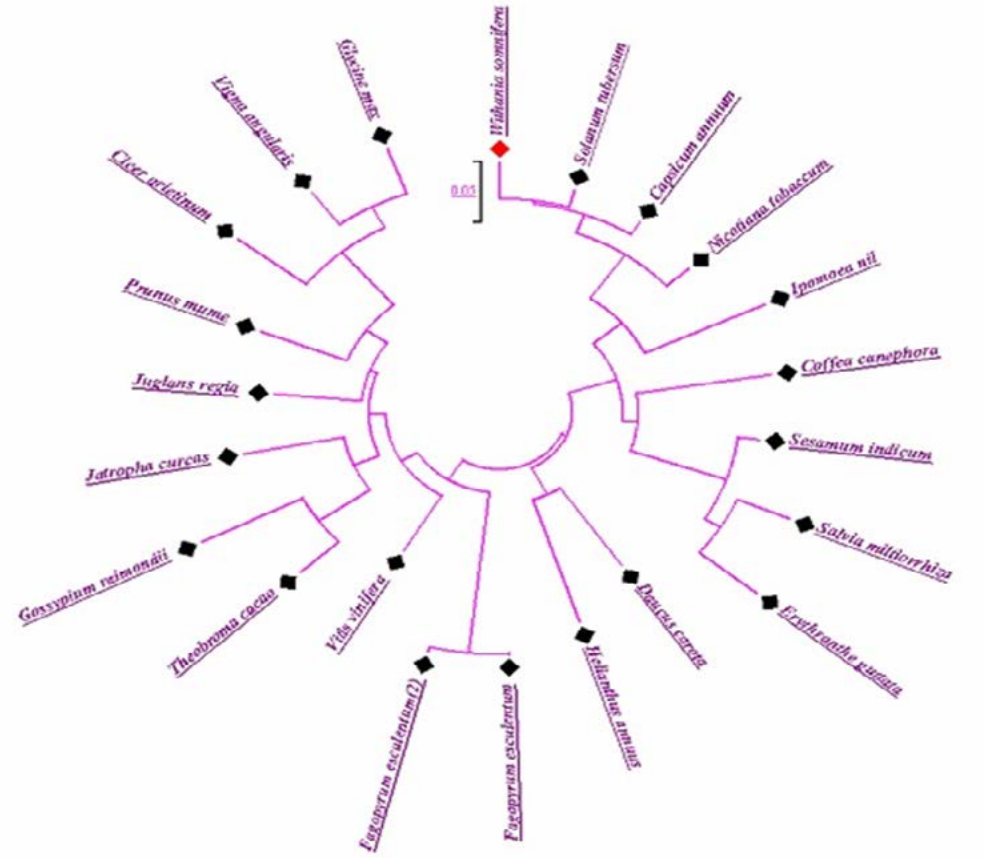


Fig. 1.1.5. Phylogenetic tree was constructed by using Mega6 software by aligning the amino-acid sequences from different species retrieved from NCBI

Previously, we have reported the expression profiles of WsCYP710 in different parts of plants viz leaves, stalk, roots, berries and inflorescence using quantitative Real time PCR. The analysis revealed highest transcript profile of CYP710 in leaves followed by stem whereas least expression was found in roots. In order to gain more insight to the role of CYP710 in *Withania*, HPLC analysis was performed by using dry extracts of different parts of plant to evaluate the concentration of withanolides/ phytosterols. Results revealed higher amounts of withaferin in leaves (60 µg mg-1 of the dry weight) whereas roots showed higher amount of withanolides (59 ng mg-1 of the dry weight) (Fig1.1.6).

In order to carry this work forward, construct of pCAMBIA1302-CYP710 was generated (Fig.1.1.7A) which was further used to transform *Agrobacterium rhizogenes* and *Agrobacterium tumefacien*. Leaves of *Withania* were infected with *A. rhizogenes* harbouring pCAMBIA-CYP710 and pCAMBIA (without) to induce transgenic hairy root lines (Fig.1.1.7B). The transgenic hairy roots so obtained were confirmed via PCR using rolB, GFP and GSPs (Fig.1.1.8A). Further, to analyze the copy number of CYP710 in transgenic roots, southern blot analysis was done which revealed the two allelic forms of CYP710 in roots (Fig.1.1.8B).

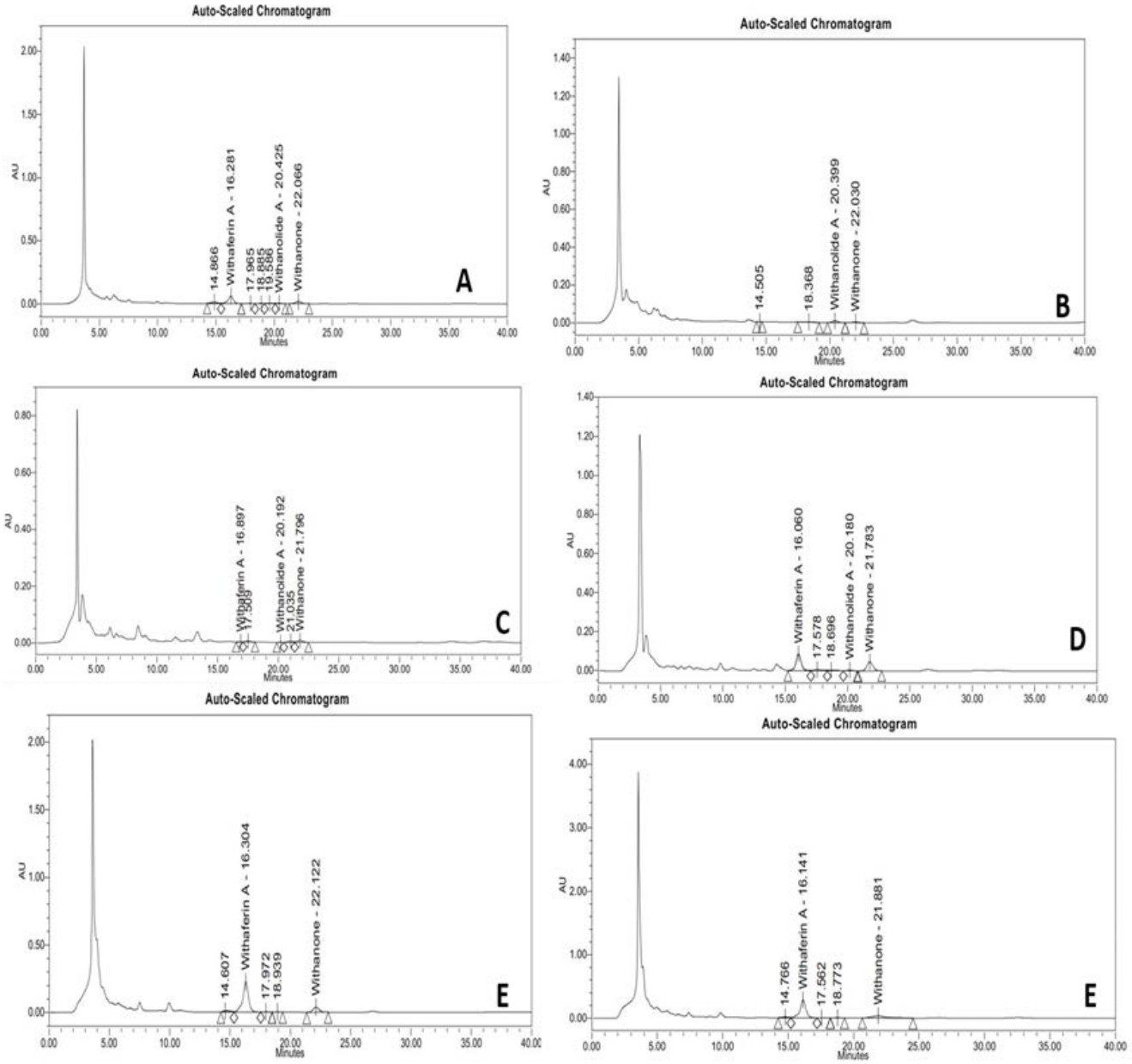


Fig. 1.1.6. HPLC chromatogram A) Stem B) Roots C) Berries D) Inflorescence E) Wild Leaves (60µg mg-1 of dry weight) F) Leaves transformed with *Agrobacterium tumefaciens* harbouring pCAMBIA-CYP710 showed enhanced production of withaferin A (80µg mg-1 of dry weight)

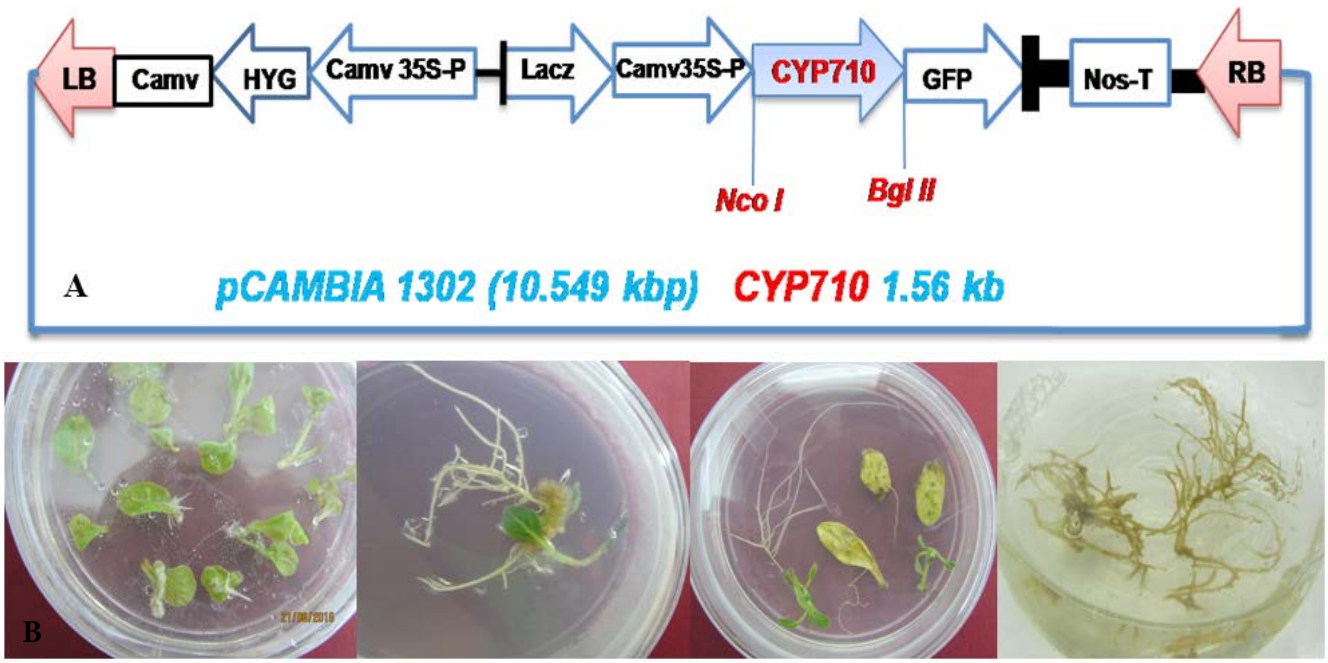


Fig. 1.1.7. A & 7.B) Construct of pCAMBIA-CYP710 in *A.rhizogenes* B) Hairy roots regeneration from leaves as explant using *A.rhizogenes* harbouring pCAMBIA-CYP710

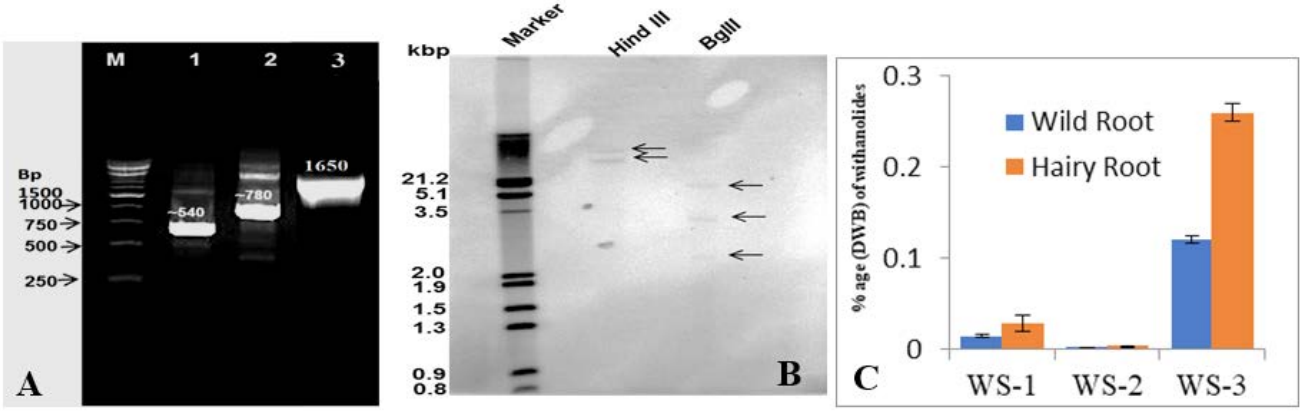


Fig. 1.1.8. A) Confirmation of transformed roots using rolB, GFP and GSP primers respectively. B- Southern blot analysis of roots of *Withania* depicting two bands in non-cutter lane and three bands in cutter lane thus revealing two forms of CYP710 in *withania* genome C- HPLC analysis of the wild and transformed hairy roots confirmed increase in the content of withanolides.

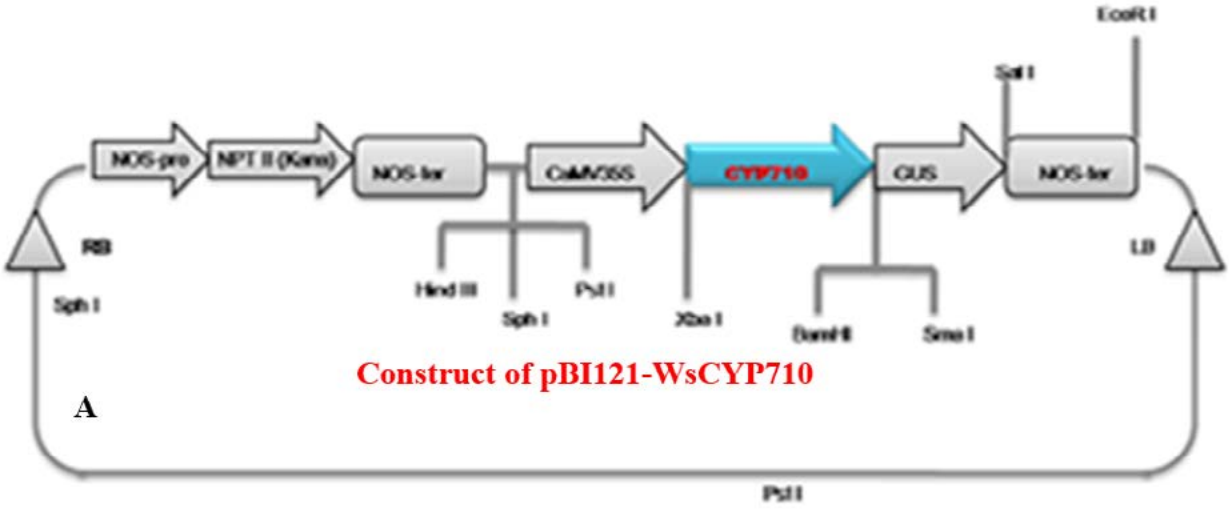


Fig.1.1.9. A) Construct of pBI121-CYP710 in *A.tumefaciens* Gv3101 B) Initiation of callus upon infection with Gv3101 cells C) Regeneration of plantlets from callus after 35 days D) Whole plant proliferation after 3 months

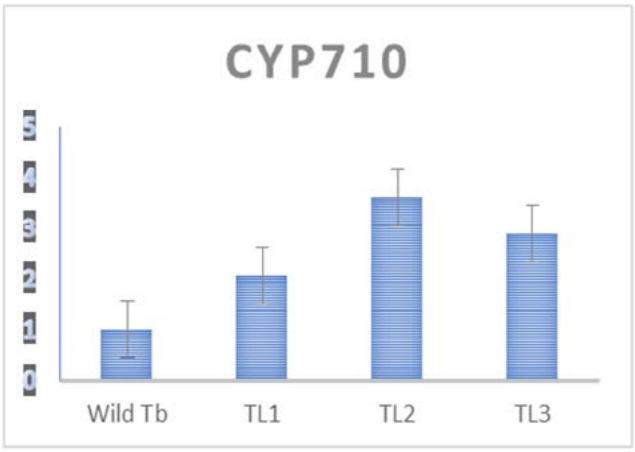


Fig.1.1.10. Real time analysis of control, transgenic line1, 2 and 3 showing increase in the content of sterols as compared to wild Tobacco plant

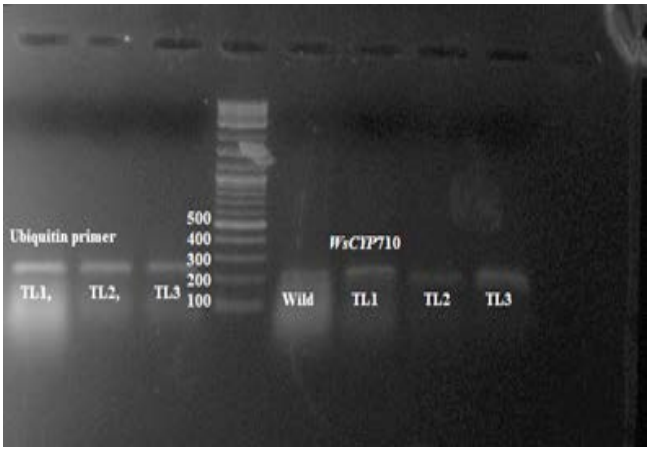


Fig.1.1.11. Semi-quantitative analysis of control, transgenic line1, 2 and 3 by using ubiquitin and gene specific primers

For in planta validation of CYP710A, transgenic tobacco lines were established. For this, construct of pBI121-CYP710A and vector (without gene) were transformed in *Agrobacterium tumefaciens* Gv3101 strain (Fig.1.1.9A-D). These constructs were then used to transform tobacco plants. The transgenic tobacco lines so developed were confirmed by using quantitative RT-PCR (Fig.1.1.10) which showed around 3x fold increase in the accumulation of sterol content in transgenic lines as compared to the wild Tobacco plants that confirmed the successful transformation of plants. Moreover, these lines were also analyzed using semi-quantitative technique using ubiquitin universal primers and WsCYP710 primers (Fig. 1.1.11) showing very light band of CYP710 in wild Tobacco as compared to the transgenic lines.

Efforts are underway to develop and evaluate phytosterols/ withanolides in F1 generation to understand the influence of CYP710 on metabolite production in Tobacco plant.

1.2 Rnai mediated down-regulation of CYP76B6, a cytochrome p450 from Nothapodytes nimmoniana (Graham) Mabb.

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

Monoterpene indole alkaloids (MIA) are plant-derived bioactive compounds with a wide spectrum of high-value pharmacological activities. Vinblastine,Vincristine, Camptothecin like MIAs used as anticancer drugs, are produced in extremely low levels, leading to high market prices and poor availability. Their low yields and lengthy production timeline have elicited intense efforts to engineer higher titers of these medicinally important MIAs.

Nothapodytes nimmoniana is a richest source of monoterpene indole alkaloid Camptothecin (CPT). CPT a potent anticancer drug produced via MIA pathway of which downstream pathway has not yet been fully elucidated. In the first step of MIA pathway, head to tail condensation of IPP and DMAPP leads to formation of geraniol diphosphate which is converted to geraniol. Geraniol-10-hydroxylase

(CYP76B6) is a membrane-bound cytochrome-P450 monooxygenase that catalyzes the hydroxylation of geraniol at the C-10 position to form 10-hydroxygeraniol which is suggested to be a potential site for regulation of monoterpenoid indole alkaloids. Previous studies indicate that increased CYP76B6 gene transcripts and enzyme activity may be implicated with the increased accumulation of MIAs.

In the present investigation full length NnCYP76B6 was isolated from leaf tissue by RACE and full length gene-specific primers designed from transcriptomic resource of *N. nimmoniana* (previously reported).

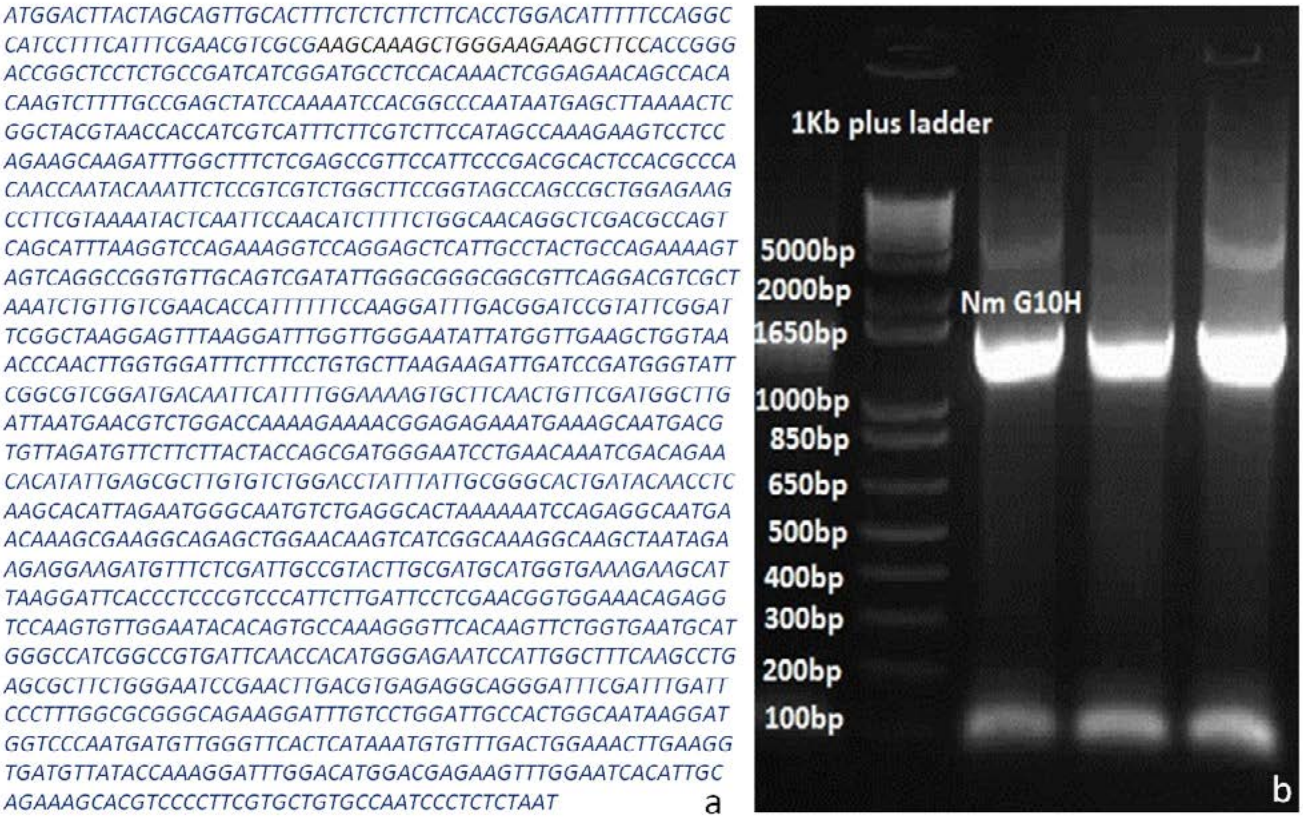


Fig. 1.2.1 Full length isolation and cloning of geraniol-10-hydroxylase: a- sequenced full length NnG10H(1497bp) using an automated DNA sequencer (ABI Prism 3130XL). b- Colony pcr of cloned NnG10H in *E.coli* DH5α strain with M13 primers.

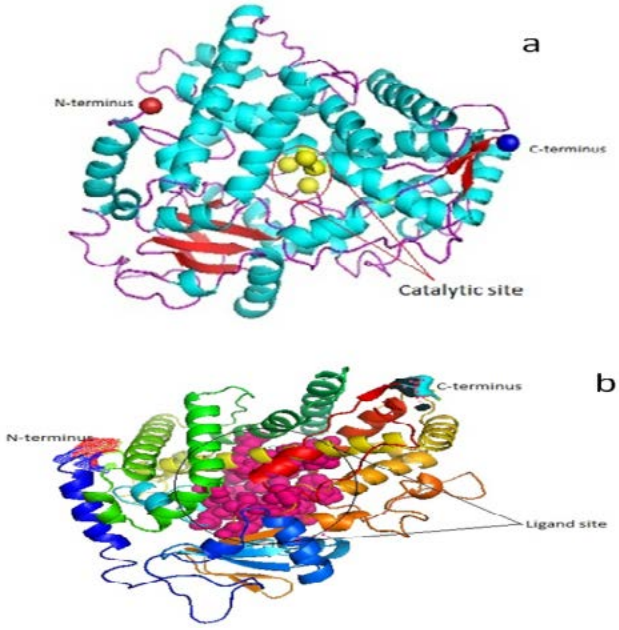


Fig. 1.2.2 Three dimensional models of G10H: a- 3D Cartoon display structure of G10H showing catalytic site in yellow predicted by PHYRE2 web server; b- Predicted ligand (shown in red) binding sites as predicted by 3DLigandSite Web Server

The full length NnCYP76B6 containing an open reading frame (ORF) of 1497bp encoding a polypeptide of 499 amino acids displaying 77% sequence identity with CYP76B6 of *Ophiorrhiza pumila* (Sequence ID: BAP90522.1) and *Rauvolfia serpentine* (Sequence ID: AGX93053.1) Fig.1.2.1. The theoretical isoelectric point (pI) and molecular weight of the deduced CYP76B61 protein was predicted to be 8.99 and 55.95 kDa, respectively. The nucleotide sequence of full length NnCYP76B6 cDNA identified from *N. nimmoniana* was submitted to NCBI GenBank under accession number KX129913.Three dimensional (3D) protein models were also determined using Phyre2 tool Fig.1.2.2. Six templates were selected to model CYP76B6 protein using crystal structure of human microsomal p450 1a2 in complex 2 with alpha- naphthoflavone. Homology modelling was performed with 100% confidence. Four amino acids aspartic acid (D), threonine (T), phenylalanine (F) and cysteine(C) were found to be involved in the formation of catalytic site having 305,306,434 and 441 positions respectively. Secondary structure analysis of CYP76B6 protein by SOPMA program revealed that 42.1% protein is in α-helix form and the remaining consists of extended strand (18.88%),beta turn (6.02%) and random coil (32.92%).Signal peptide region at N-terminal (1-19) was determined by PHOBIUS program. Cyotchrome p450 Heme iron ligand signature was found at amino acid position 434-443 using Prosite server. 3D ligand biding site web server results revealed that 27 amino acids were involved in ligand binding site rich in leucine.

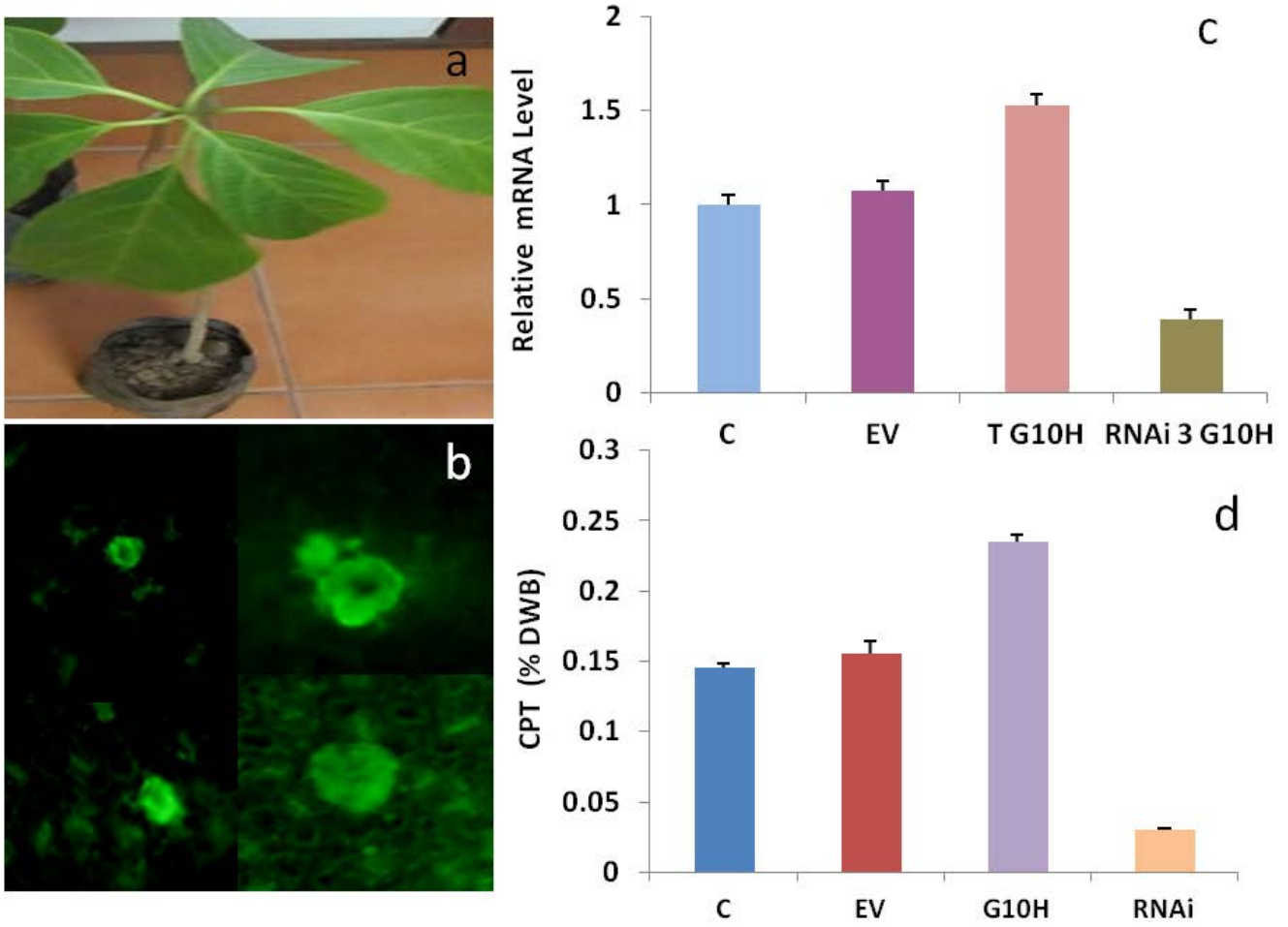


Fig. 1.2.3 Transient expression and RNAi mediated down-regulation of NnG10H. a- Agro-infiltered full-length coding region of NnG10H fused with GFP reporter gene in the vector pCAMBIA1302 in *N. nimmoniana*; b-Expression of contruct driven by the 35S promoter examined by fluorescent microscopy; c-qRT-PCR analysis of transcript abundance; d-HPLC determination of CPT accumulation

Geraniol 10 hydroxylase was further tested in planta. Construct of CYP76B6 in pCAMBIA 1302 at the 5′-terminal of the GFP gene under the control of CaMV 35S promoter and empty vector pCambia1302 was introduced into host plant via agroinfiltration. Expression of construct along with GFP was examined by fluorescent microscopy.

Furthermore, phytochemical analysis of transformed leaf showed higher levels of CPT accumulation (0.235 % DWB) in comparison to control (0.145 % DWB). Additionally, the expression analysis of CYP76B6 was carried out in transformed leaf that showed significant 0.53 fold increase in transcript level in comparison to control fig. 3c. Similarly RNAi mediated siliencing of CYP76B6 was investigated by qRT-PCR and CPT quantification. Suppression of CYP76B6 by antisense construct showed 0.59 fold reduction of CYP76B6 mRNA transcript level which led to marked reduction of CPT accumulation in comparison to control fig.3c & d. Plausibly these results are indicative that CYP76B6 can produce a synergistic effect on CPT accumulation and efficiently play a regulatory role for over-production.

1.3. Camptothecin biosynthesis and transcription analysis of key pathway genes in context to pathway diversion through in vitro homologous modulation via inhibitors in Nothapodytes nimmoniana

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

Nothapodytes nimmoniana (Graham) Mabb.; Syn. *Mappia foetida* Meirs or Nothapodytes foetida (Wight) Sleumer (Family-Icacinaceae) is a medium sized medicinal tree species found in Western Ghats of India which represents a biodiversity hotspot. The tree is the richest source of a potent anti-cancer monoterpene indole alkaloid camptothecin (CPT) and 9-methoxycamptothecin. CPT is a complex compound and a potent inhibitor of DNA topoisomerase I. Monoterpene indole alkaloids (MIAs) are high-value natural products composed of a secoiridoid moiety and an indole moiety. Owing to the complexity of these compounds, their chemical synthesis is prohibitive and complex. Irinotecan and topotecan, two water-soluble semi-synthetic analogs of CPT are approved drugs (FDA, US) for treating colorectal and ovarian cancers. It is also effective against several types of brain tumours in children. The global demand of CPT exceeds an annual market value of about US$ 4 billion.

Biosynthetic pathway of CPT is highly complicated and has been investigated for many years, and still its downstream pathway is not fully deciphered. Dimethylallyl pyrophosphate (DMAPP) and isopentenyl pyrophosphate (IPP) contributed via MEP or MVA pathway provides a strong flux for the production of monoterpene indole alkaloids. Yet, the crosstalk between the two pathways in plants is still unclear. Some exchanges of IPP between the cytoplasm and plastids do appear to occur, although with low efficiency. In order to validate and broaden the conceptual base, an in vitro strategy was deployed to have an insight into the flux of upstream pathway precursors to assess the turnover of CPT in response to known inhibitors of MVA and MEP pathways. To begin with, an efficient and reproducible in vitro system via indirect organogenesis and forced auxiliary bud induction was established. Additionally, *Agrobacterium rhizogenes* mediated transformed hairy roots were also induced to scale up their culture. This two pronged strategy is being envisaged for homologous modulation/enhanced production of CPT under manipulative conditions. For the initiation and establishment of axenic cultures, nodal segments were used as explants. These were cultured on Woody Medium (WM) supplemented with different phytohormone combinations and concentrations. The results are summarized in Table.1.3.1

Table 1.3.1 A comparative response of shoot regeneration percentage from explants on WM minimal medium supplemented with different combinations and concentrations of of Kn/IBA and BAP/IAA and TDZ/IBA, after 9 weeks of culture (Mean ± S.E). Values followed by same letter are not significantly different ($p \leq 0.05$) as per Duncan's multiple range test.

Woody Medium + growth regulator (mg/L)			**Regeneration %age ±SE**
Kinetin	IBA	TDZ	
1	1	-	23 ±0.93 f,g
2	1	-	28 ±0.48 e
3	1	-	34 ±0.56 c,d
4	1	-	19±0.09 f
-	1	1	40 ±0.54 b
-	1	2	52 ±1.06 a
-	1	3	37 ±0.34 c
BAP	IAA		
1	1	-	26 ±0.73 d,e
2	1	-	31 ±0.09 c
3	1	-	43.7 ±0.2 b
-	1	1	22 ±0.82 f,g
-	1	2	49 ±0.64 a
-	1	3	43 ±0.87 b

Maximum shoot regeneration was observed on WM medium fortified with TDZ (2 mg/L) and IBA (1mg/L) Figure 1.3.1

Fig.1.3.1 In vitro cultures, of *N. nimmoniana*; a &b - Callus induction, meristemoid differentiation and shoot regeneration; c- Multiple shoot induction (WM + kinetin+ IBA) ; d &e- Regenerated plants ; f- Static-liquid culture (TDZ+IBA); g- In vitro rooting (WM + IBA + Kinetin); h-; i- Tissue culture raised plant before hardening and after transplantation.

Agrobacterium rhizogenes mediated hairy root induction was carried out using in vitro/axenic leaf as explants. Emergence of vary small hairy roots were observed after 15th day of infection. These were confirmed by pcr amplification of rolb gene taking genomic DNA as template Fig.1.3.2. Three Agrobacterium rhizogenes strains, ATCC, LBA 9402 and A4 strain were tested at different concentrations of acetosyringone. Results are summarized in Table 1.3.2. A4 strain promoted maximum (66±0.52) hairy roots at 400-500 µM acetosyringone concentration. Hairy roots were further cultured in hormone free liquid 1/2MS medium for three weeks and harvested for chemoprofiling Fig.1.3.2c.

Agrobacterium rhizogenes				
Infection period (min.)	**Co-cultivation period (hr)**	**Acetosyringone concentration µM**	**Days required for induction**	**Transformation %age±SE**
LBA9402 strain				
45	36	100	20-25	35±0.66
45	36	200	20-25	26±0.33
45	36	400	15-20	48±0.45
45	36	600	15-20	57±0.23
ATCC15834 strain				
45	36	100	20-25	33±0.11
45	36	200	20-25	37±0.28
45	36	400	20-25	44±0.67
45	36	600	20-25	17±0.45
A4 strain				
45	36	100	15-20	35±0.78
45	36	200	15-20	46±0.37
45	36	400	15-20	66±0.52
45	36	600	15-20	52±0.78

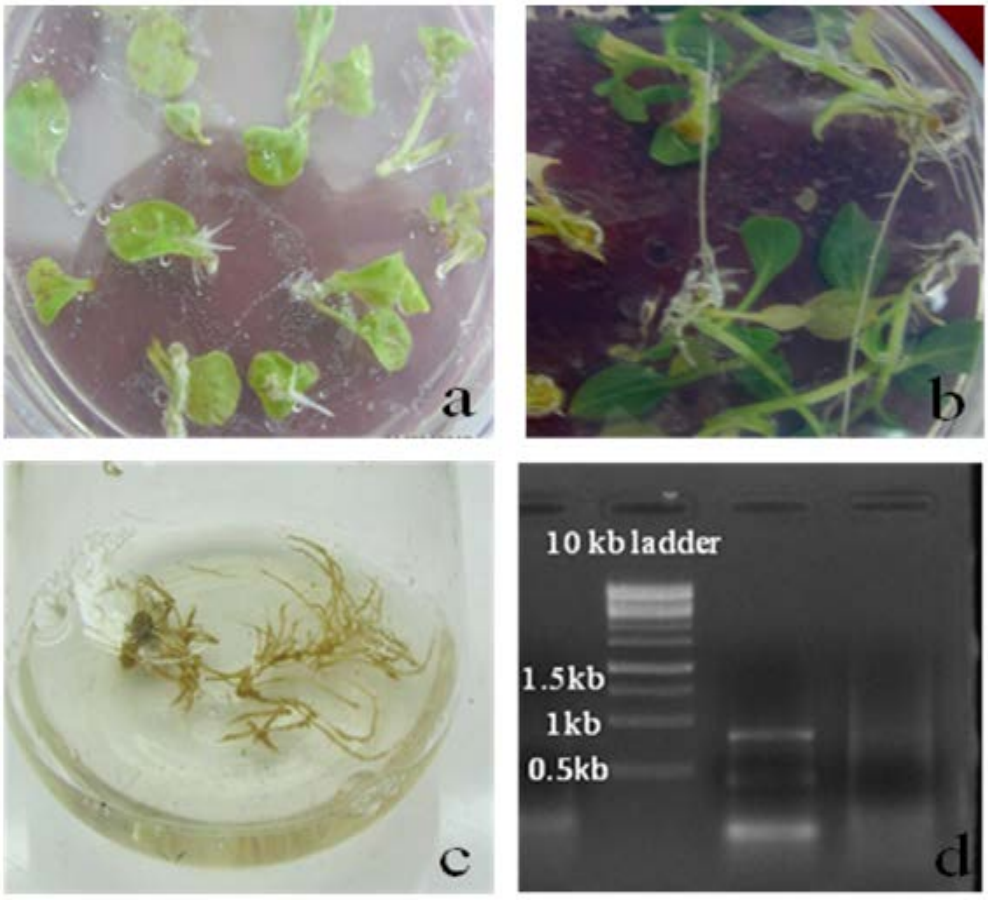


Fig. 1.3.2. Hairy root induction after two weeks (a,b); liquid suspension culture (c); pcr amplification of rol b (d)

Methanolic extracts were prepared for quantifying CPT content from in vitro shoot, in vivo leaf, in vitro root, in vivo root, hairy root and callus samples.

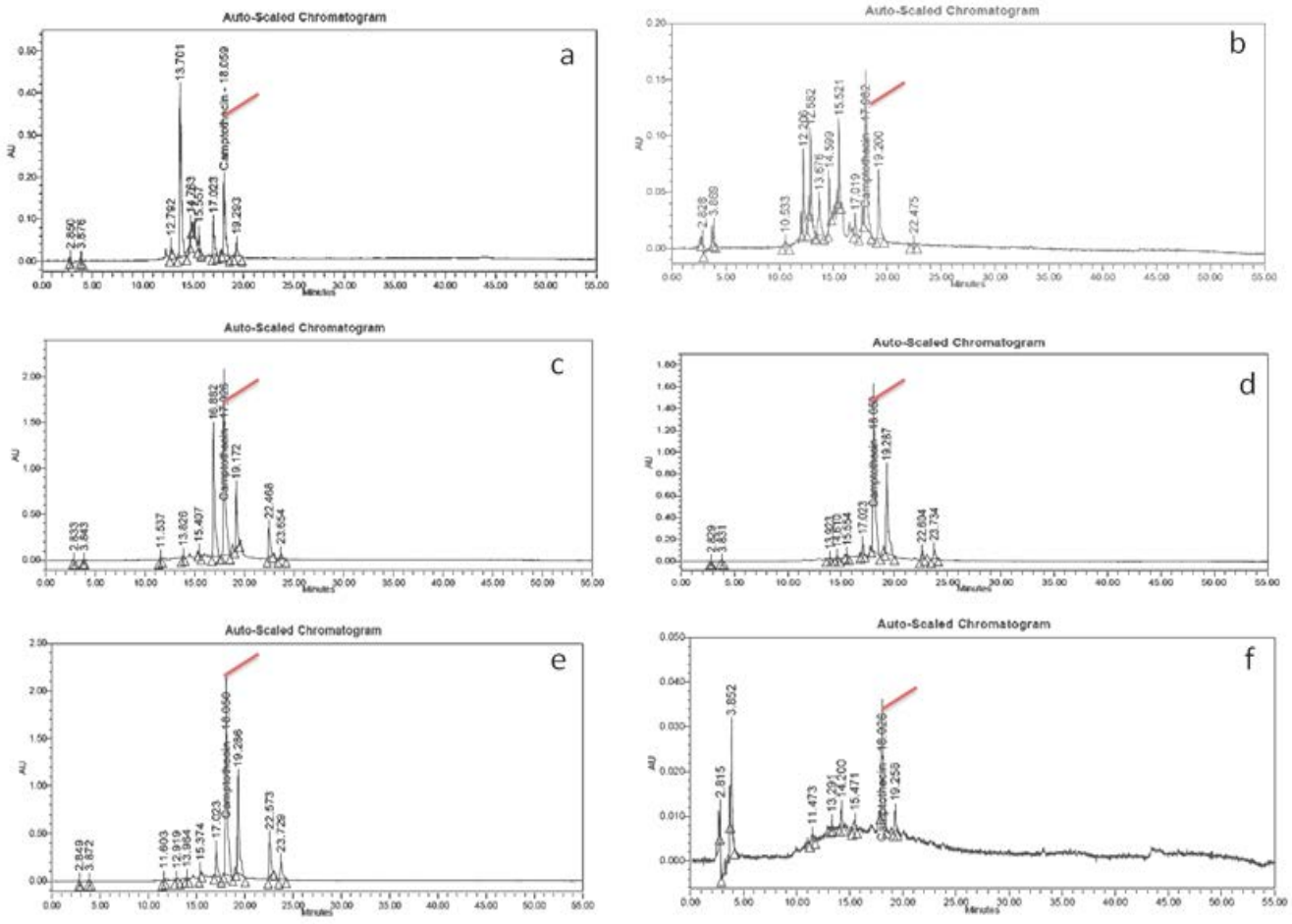


Fig 1.3.3. HPLC Chromatograms : a-Leaf in vivo; b-Leaf in vitro; c- Root in vivo; d- Root in vitro; e- Hairy root; f- Callus

The quantification of CPT by standard HPLC method revealed slightly higher concentration of CTP in in-vivo tissues (leaf, root) as compared to respective in vitro tissues (Fig. 3a-f). On the other hand CPT content of transformed hairy roots was recorded higher to those of their other in vitro cultures (Fig. 1.3.4).

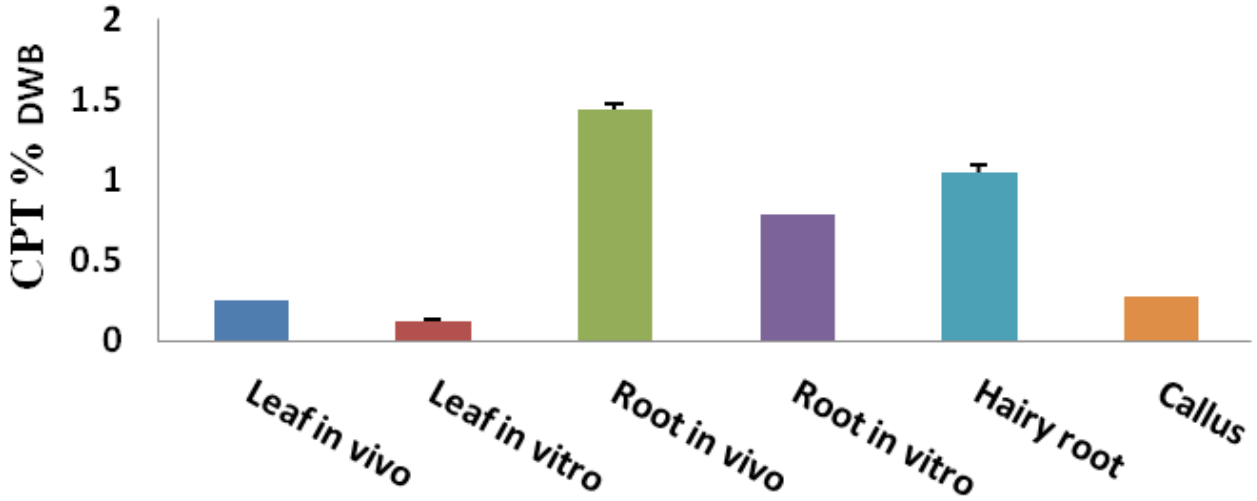


Fig.1.3.4. HPLC quantification of CPT content: in vivo leaf, in vitro leaf, in vivo root, in vitro root, hairy root and callus.

Monoterpene moiety exerts strong flux control for production of monoterpene indole alkaloids (MIA). To ascertain the contribution of monoterpene moiety two specific pathway inhibitors fosmidomycin and lovastatin were used to block DXPR and HMG enzymes of MEP and MVA pathway respectively as shown in Fig.1.3.5.

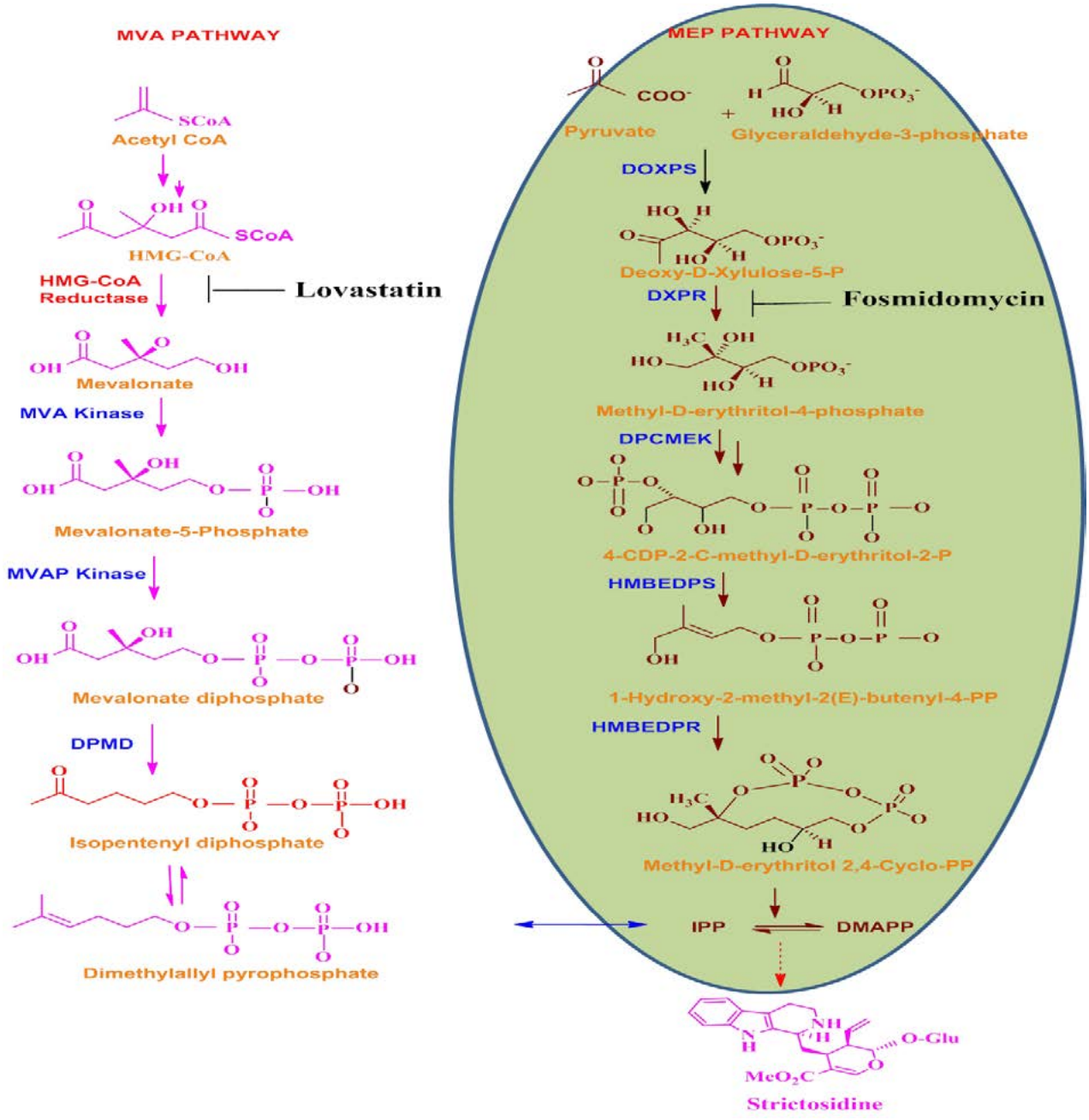


Fig.1.3.5. An overview of Mevalonate and Non mevalonate pathway in biosynthesis of MIA: DXPR- deoxy-xylulose-5-phosphate reductoisomerase; MEPCT-methyl erythritol-4-phosphate cytidyltransferase; DPCMEK-diphosphocytidyl-2-methyl-D-erythritol kinase;MECDPS-methyl-D-erythritol 2,4-cyclodiphosphate synthase; HMBEDPR-hydroxy-3-methyl but-2-enyl diphosphate reductase; HMG; Hydroxymethylglutaryl-CoA reductase; MK-mevalonate kinase;PMK-phosphomevalonate kinase; DPMD-diphosphomevalonate decarboxylase.

Fosmidomycin, and fosmidomycin / lovastatin treated cultures showed significant reduction of 91.11% and 92.3% respectively in CPT accumulation at 10th day. There was about 18.86% reduction in CPT content after lovastatin treatment. Further reduction of 93.4%, 95.6% and 9.2% was observed at 20th day of fosmidomycin, fosmidomycin/ lovastatin and lovastatin cultures respectively.

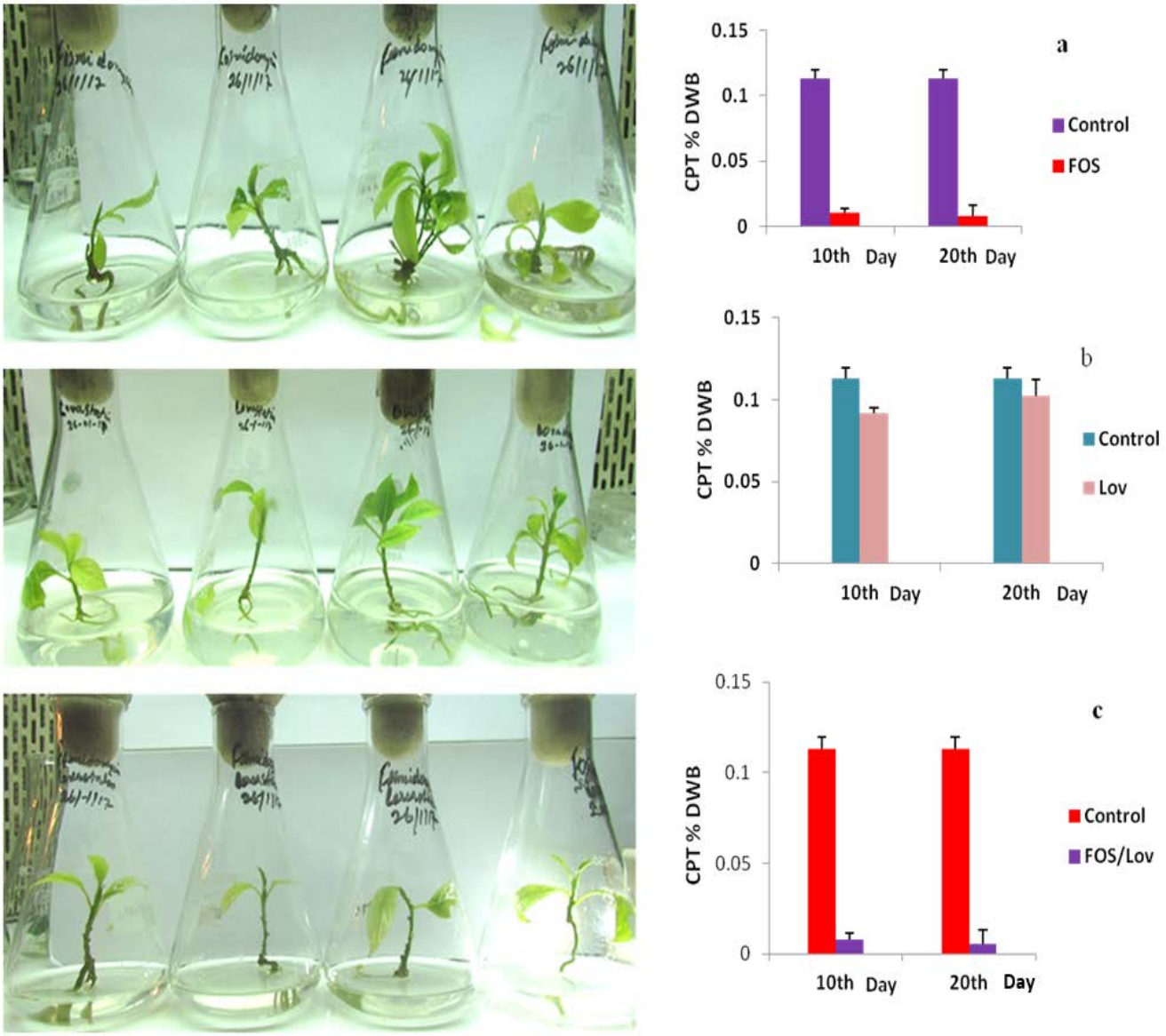


Fig.1.3.6. Effect of inhibitors on CPT accumulation: 1a & 2a- Fosmidomycin 150µM static Cultures and chemoprofiling of CPT content; 1b & 2b- Lovastatin 100µM static cultures and HPLC of CPT; 1c &2c Both Fosmidomycin/Lovastatin and HPLC of CPT content

These results tend to indicate that inhibition of mevalonate pathway channelizes the flux toward CPT production. Further, expression analysis of fosmidomycin treated target genes revealed that there is 0.81-0.44 fold reduction in transcript levels of DXPR, MEPC, DPCMEK, MECDPS and HMBEDPR in comparison to control at both 10th and 20th day respectively.

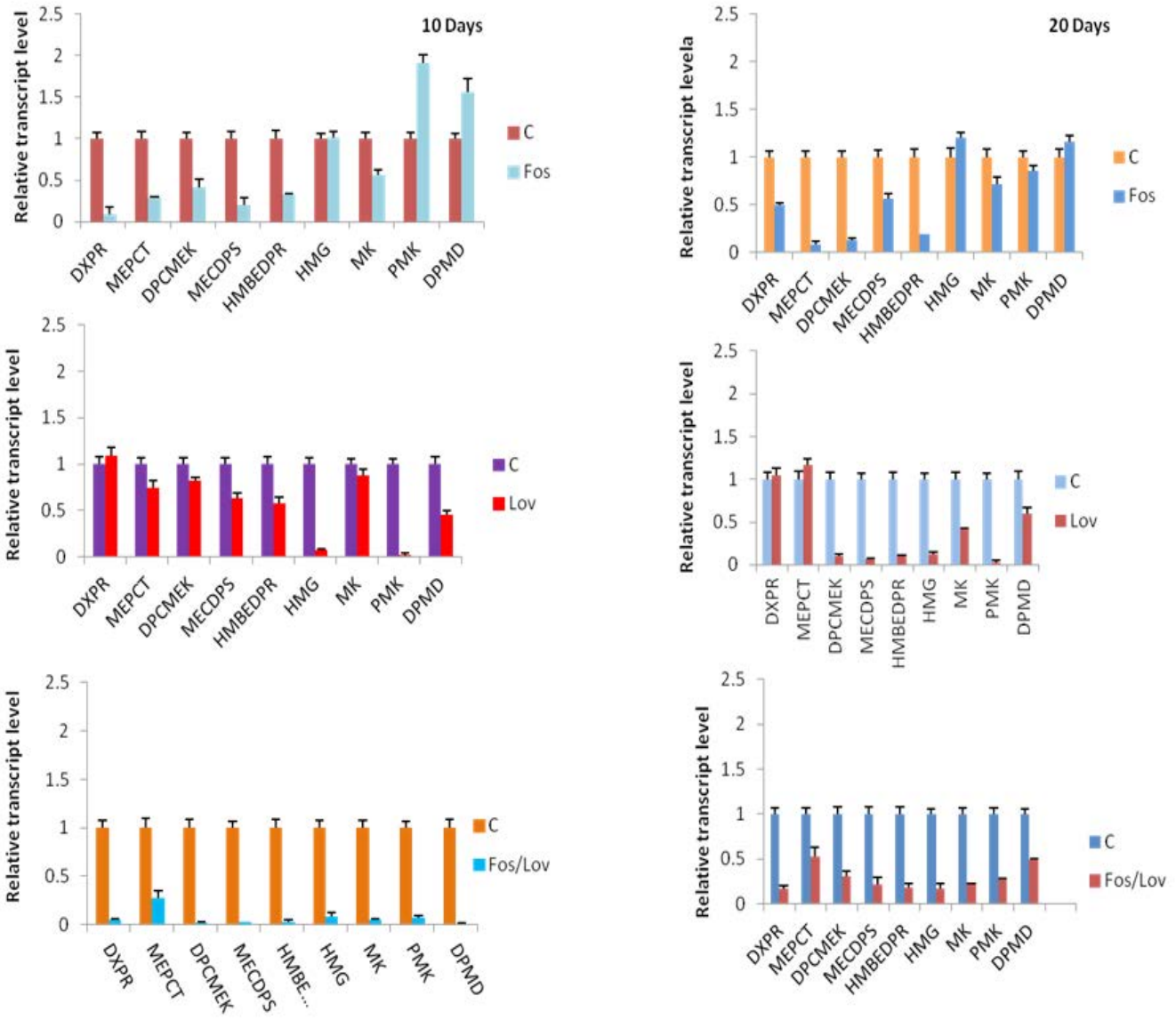


Fig.1.3.7. Effect of fosmidomycin and lovastatin on transcript level of target as well as downstream genes of CPT biosynthetic pathway: DXPR- deoxy-xylulose-5-phosphate reductoisomerase: MEPCT-methyl erythritol-4-phosphate cytidyltransferase; DPCMEK-diphosphocytidyl-2-methyl-D-erythritol kinase;MECDPS-methyl-D-erythritol 2,4-cyclodiphosphate synthase; HMBEDPR-hydroxy-3-methyl but-2-enyl diphosphate reductase; HMG; Hydroxymethylglutaryl-CoA reductase; MK-mevalonate kinase;PMK-phosphomevalonate kinase; DPMD-diphosphomevalonate decarboxylase.

Lovastatin showed somewhat higher reduction of target genes from 0.89- 0.5 folds. However fosmidomycin/ lovastatin also showed reduction in transcript levels of DXPR and HMG along with almost all downstream genes of MEP and MVA pathway. Hitherto, experimental evidence suggests that CPT biosynthetic flux proceeds predominantly via MVA pathway.

1.4. Some novel cytotypes: Cytological and phytochemical evaluation of major bioactive compounds from five species of genus Rumex L.

Syed Mudassir Jeelani and Surrinder K. Lattoo

The species of genus *Rumex L.* (Polygonaceae) are widely distributed at 1600 - 4000 m altitudes in the Kashmir Himalayas. The roots and aerial parts of Rumex have been and are still being used in ancient and current traditional herbal medicine all over the world for

various therapeutic purposes and pharmacological activities. The occurrence of polyploidy within the genus is of special interest to plant systematists and biologists. The present research aims to explore chemical diversity in various cytotypes of five species of *Rumex* supplemented with cytological studies to determine chromosome numbers from the Kashmir Himalayas. To reveal the comparative chemo-profiles of the different cytotypes/species of *Rumex*, standard LC-MS method was employed (Table 1.4.1). The study suggests positive correlation between metabolite accumulation in relation to plant parts, ploidy level and altitudinal gradients. All this is noteworthy to identify elite cytotypes/chemotypes for pharmaceutical and commercial purposes.

Table 1.4.1: SIM positive LC-MS optimized operating conditions for the quantification of Rutin, Piceatannol, Reversetrol, Naringenin, Kaempferol, Emodin and Physcion

Name of compound and [M+ H]+	Retention time (min)	Regression equation	R2	Linear range (µg/ml)	LOQ (ng/ml)	LOD (ng/ml)	Fragmentor voltage (V)
Rutin [611.5]	4.9	y=2345.535x+1018.662	0.997	0.39–100	300	100	160
Piceatannol [244.9]	7.1	y=1910.229x+5224.830	0.987	0.39–100	250	80	120
Resveratrol [228.9]	8.4	y=1379.803x+426.086	0.998	0.39–100	250	80	105
Naringenin [272.9]	12	y=3780.241x+11121.096	0.983	0.39–100	300	100	105
Kaempferol [287]	12.5	y=4783.164x+13674.126	0.981	0.39–100	240	80	140
Emodin [270.9]	24.2	y=1534.494x-1868.123	0.996	0.39–100	300	100	140
Physcion [284.8]	27	y=174.687x-82.422	0.982	0.39–100	300	100	140

Table 1.4.2: Information on chromosome count, ploidy level and locality recorded in different populations of five species of genus Rumex from Kashmir Himalayas

S. No.	Observed chromosome number ('n')	Ploidy level	Locality
R. crispus L.			
P1	30	Hexaploid (2n = 6x = 60)	Kanzalwan (34°36′N, 74°42′E; 2500 m)
P2	40	Octaploid (2n = 8x = 80)	Dawar (34°38′N, 74°47′E; 2600 m)
R. dentatus L.			
P3	20	Tetraploid (2n = 4x = 40)	Izmarg (31°20′ N, 78° 20′E; 2300 m)
P4	60	Dodecaploid (2n = 12x = 120)	Yosmarg (33º47'N, 74º39'E; 3 000 m)
R. hastatus D. Don			
P5	9	Diploid (2n = 2x = 18)	Kanzalwan (34°36′N, 74°42′E; 2300 m)
R. nepalensis Spreng			
P6	30	Hexaploid (2n = 6x = 60)	Dawar (34°38′N, 74°47′E; 2400 m)
P7	40	Octaploid (2n = 8x = 80)	Patalwan (34°35′N, 74◦52′E; 2700 m)
P8	50	Decaploid (2n = 10x = 100)	Aharbal (33°38′ N, 74°47′ E; 2800 m)
P9	60	Dodecaploid (2n = 12x = 120)	Mahadev (34°10′ N, 75°00′ E; 2900 m)
***R. orientalis Bernh.* ex Schult.f.**			
P10	30	Hexaploid (2n = 6x = 60)	Gurinullah (34°34′ N, 75°44′ E; 2500 m)

The wild plants of *R. crispus*, *R. dentatus*, *R. hastatus*, *R. nepalensis* and *R. orientalis* were collected from different localities of the Kashmir Himalayas (Table 1.4.2). Voucher specimens were deposited in the Janaki Ammal Herbarium, Indian Institute of Integrative Medicine (CSIR; Acronym, HRRL) Jammu, India.

The cytological studies were carried out on population basis. Detailed investigation of these populations/species revealed occurrence of different chromosomal races in *R. crispus* (n = 30, 40), *R. dentatus* (n = 20, 60) and *R. nepelensis* (n = 30, 40, 50, 60) (Fig. 1.4.1a-h). The chromosome number n = 40 in *R. crispus* and n = 60 in *R. dentatus* are new reports for these species. On the other hand, all the studied populations of *R. hastatus* and *R. orientalis* depicted chromosome number n = 9 and n = 30 respectively (Fig. 1.4.1). The existence of intraspecific polyploids in *R. crispus*, *R. hastatus* and *R. nepalensis* is indicative of the fact that the genome of such species is still in constant evolution, probably to increase the adaptive and survival rate under diverse ecological niches of Himalayas.

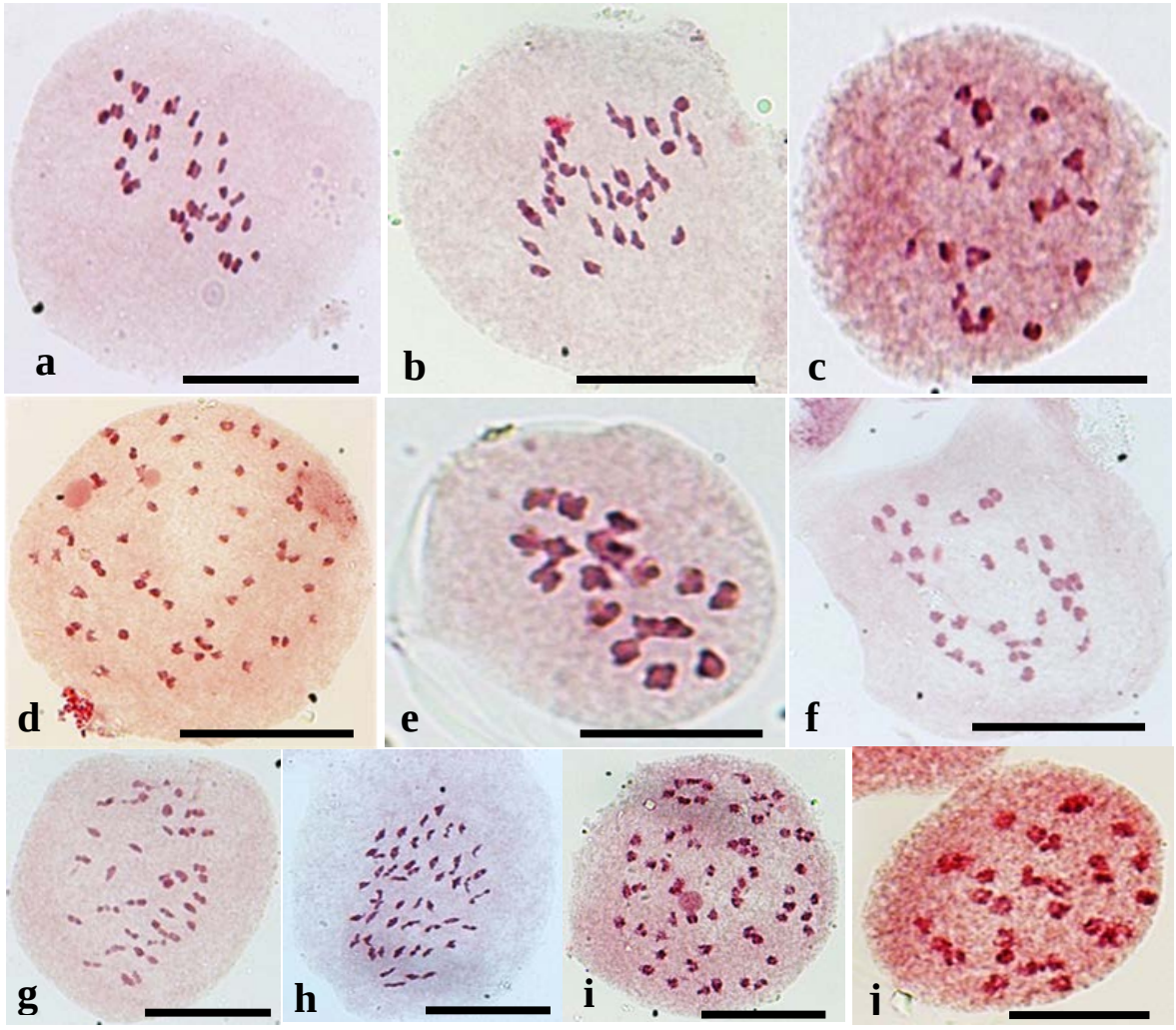
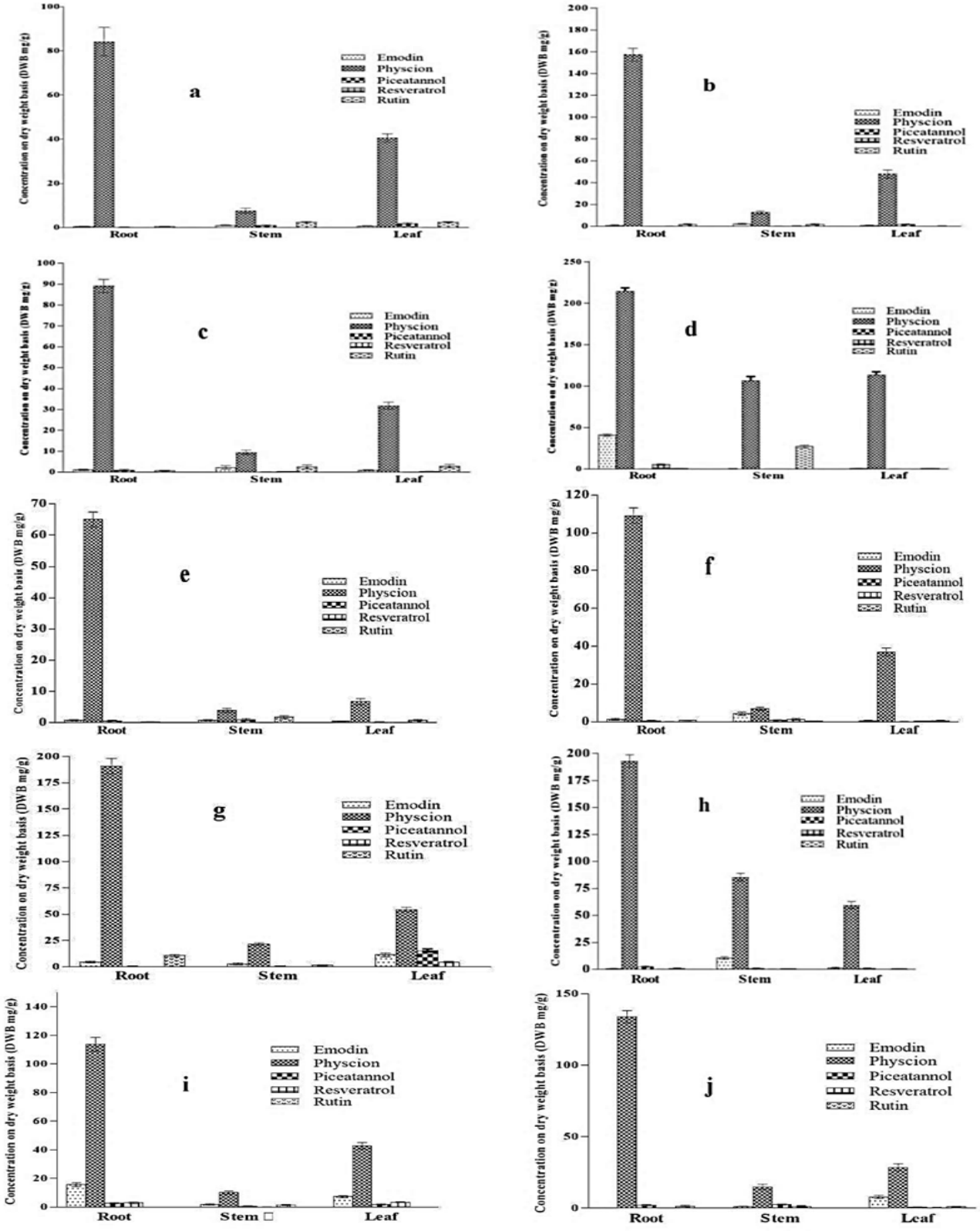


Fig. 1.4.1. Meiotic chromosome numbers in different populations of: a) *Rumex crispus*, PMC at metaphase- II showing thirty bivalents (hexaploid; Kanzalwan); b) *R. crispus* PMC showing forty bivalents (octaploid, Dawar); c) *R. dentatus*, PMC at metaphase- I showing forty bivalents (tetraploid, Izmarg); d) *R. dentatus*, PMC at diakinesis showing sixty bivalents (Dodecaploid ,Yosmarg); e) *R. hastatus*, PMC at metaphase-I showing nine bivalents (diploid, Kanzalwan); f) *R. nepalensis*, PMC at metaphase-I showing thirty bivalents (hexaploid, Dawar); g) *R. nepalensis*, PMC at metaphase-I showing forty bivalents (octaploid, Patalwan); h) *R. nepalensis*, PMC at metaphase-I showing fifty bivalents (decaploid, Aharbal); i) *R. nepalensis*, PMC at metaphase-I showing sixty bivalents (dodecaploid, Mahadev); j) *R. orientalis*, PMC at metaphase-I showing thirty bivalents (dodecaploid, Gurinullah). Scale bar = 10 µm.

The tissue-specific chemo-profiling revealed relative dominance of these bioactive compounds in roots followed by leaves and stems respectively in the studied species/cytotypes (Fig. 1.4.2, 1.4.3). The results also showed interesting differences in the content of phytoconstituents

(rutin, piceatannol, resveratrol, emodin, physcion) against a definite ploidy level. However, concentration of naringenin and kaempferol was below detection level. In general, a well-marked increasing trend in the concentration of these compounds was recorded from lower to higher ploidy levels along the altitudinal gradient (Fig. 1.4.2).



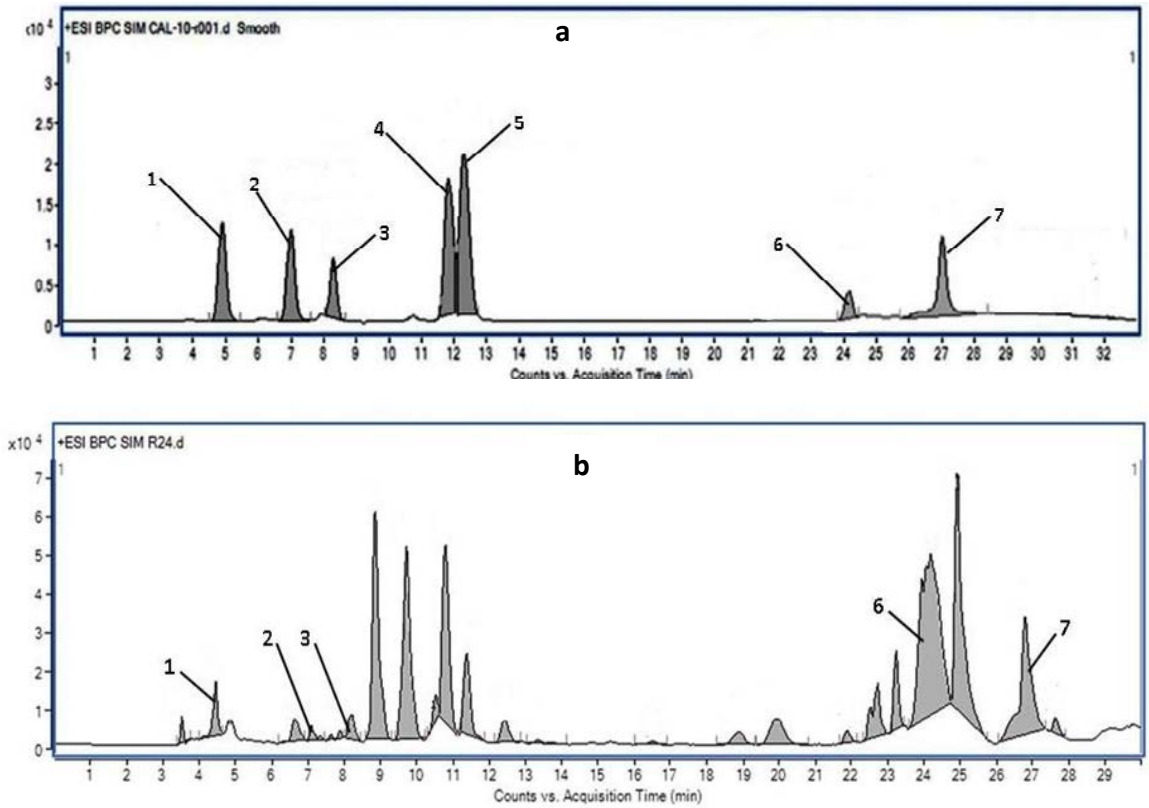


Fig. 1.4.2. Graphical representation of concentration of major bioactive compounds in: a) *R. crispius* hexaploid cytotype; b) *R. crispius* octaploid cytotype; c) *R. dentatus* tetraploid cytotype; d) *R. dentatus* dodecaploid cytotype; e) *R. hastatus* diploid cytotype; f) *R. nepalensis* hexaploid cytotype; g) *R. nepalensis* octaploid cytotype; h) *R. nepalensis* decaploid cytotype; i) *R. nepalensis* dodecaploid cytotype; j) *R. orientalis* Hexaploid cytotype.

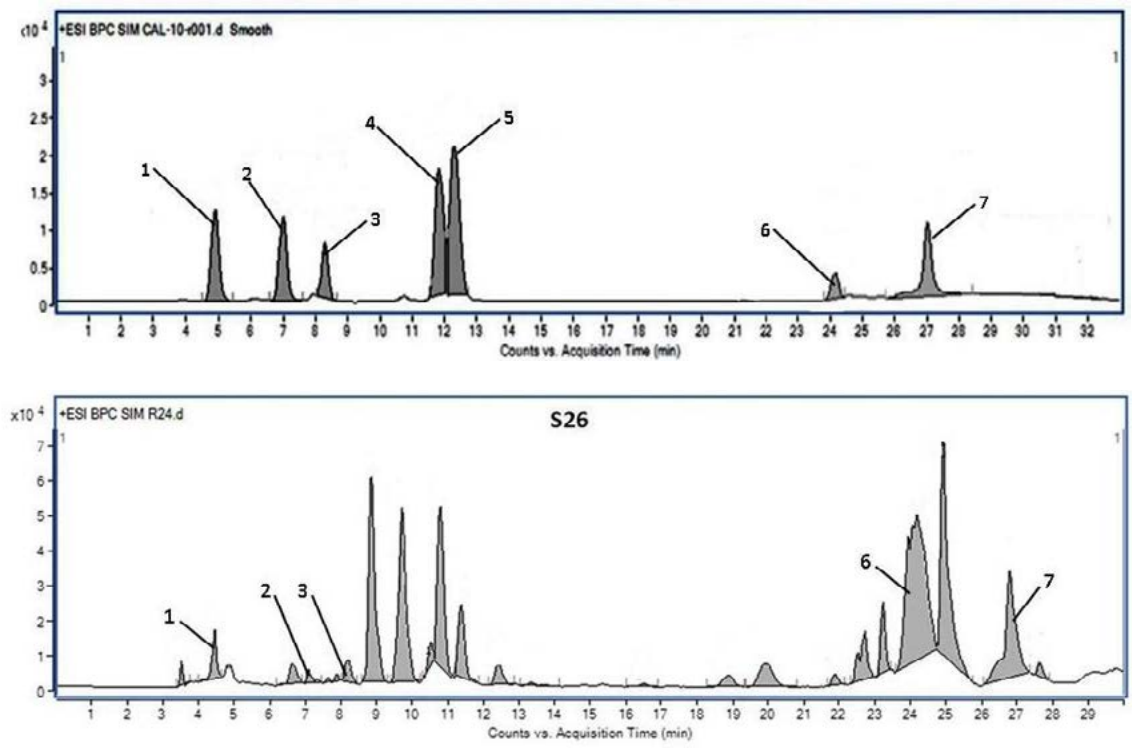


Fig. 1.4.3a LCMS chromatogram of investigated compounds, rutin (1), piceatannol (2), resveratrol (3), naringenin (4), kaempferol (5), emodin (6) and physcion (7). b) LC-MS chromatogram of dodecaploid cytotype.

In the present investigation, occurrence of different cytotypes has been reordered in *R. crispus*, *R. dentatus* and *R. nepalensis* with ploidy levels ranging from tetraploidy to dodecaploidy except diploidy in *R. hastatus* and hexaploidy in *R. orientalis*. The polyploid races n = 40 in *R. crispus* and n = 60 in *R. dentatus* are hitherto unreported. Chemo-profiling through LCMS based on seven major bioactive compounds of different species/ cytotypes in root, stem and leaf from various altitudinal gradients presented an appreciable variability in emodin, physcion, piceatannol, resveratrol and rutin contents. The increasing trend of metabolite accumulation by and large seems to be in conformity with the increasing altitude and ploidy status. Due to cytological variation the species also presents robust adaptability and ecological plasticity. Further, the study has a prospect to explore desirable species/cytotype of Rumex with maximum concentration of phytoconstituents for commercial and pharmacological uses.

1.5 Understanding the chemical heterogeneity of cell suspension culture of *Glycyrrhiza glabra*

Saima Khan, Pooja Goyal, Malik Muzafar Manzoor, Pankaj Pandotra, Ajai P Gupta, Ram Vishwakarma, Ashok Ahuja, Suphla Gupta

The effect of various basal media and plant hormones were also investigated to study growth and glycyrrhizin production in root callus. Three different basal media (Gamborg's, White & MS) were tested (PCTOC, 2016). Root explants showed callusing in White and MS basal media only. Glycyrrhizin content was found better in MS medium (three folds higher) than White medium. Further medium engineering was employed to increase the glycyrrhizin contents in the callus regenerating form MS medium. Different phytohormones in various concentrations and combinations were tried in MS medium. Results showed good callus growth, producing higher glycyrrhizin in KG4 and F6 mediums. LC-MS based phytochemical analysis of the 4 weeks old callus revealed KG4 medium produced higher glycyrrhizin(6.3 µg/g) , isoliquisitin (2.1 µg/g)and quericitin (0.6 µg/g), while F6 medium showed glycyrrhizin(9.3 µg/g) , isoliquisitin (0.8 µg/g), quericitin (0.1 µg/g), and higher contents of hispaglabsidin A (0.5 µg/g) and formomentin (8.9 µg/g). White's medium although showed lower contents of glycyrrhizin but root callus grown in this medium had very high contents of glabridin (2.5 µg/g)), hispaglabsidin B(3.0 µg/g) butin (2.1 µg/g) and formomentin (1.1 µg/g) . Since, our objective was to persue higher glycyrrhizin production we choose F6 medium for all our future experiments.

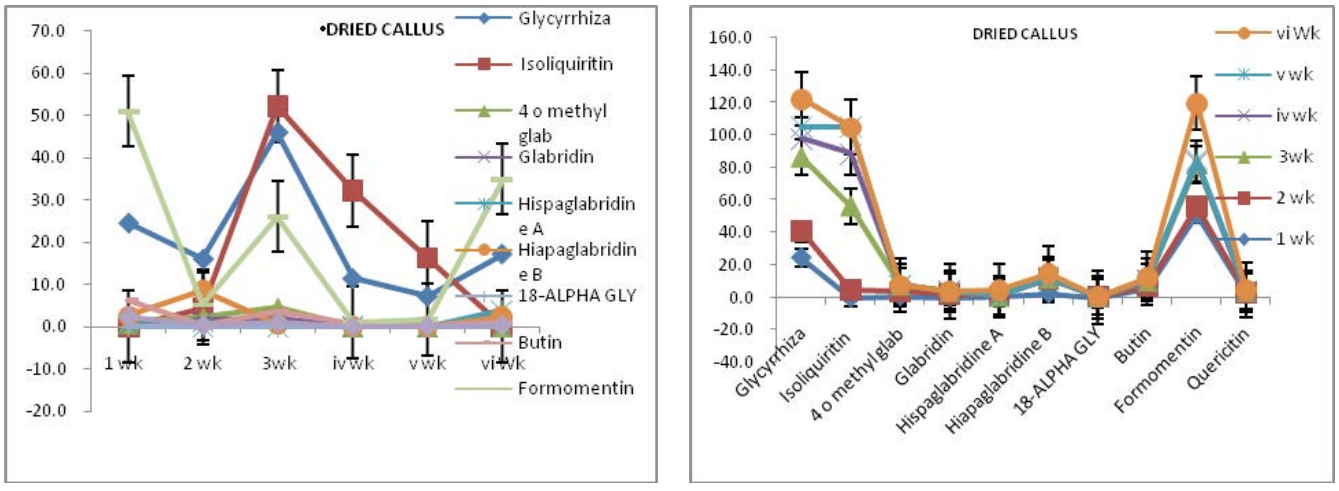


Fig. 1.5.4: A) Time Course Chemical profile of dried callus of G. Glabra. **B)** Quantification of compounds in dried callus

The root explants in F6 medium manifested two types of callus (1) brown color (2) green color. These callus were separated and sub-cultured in F6 medium for 1 month. Varied chemical composition was also observed in different callus morphology. Green callus mass gave higher glycyrrhizin (39.7 µg/g) as compared to brown callus (17.1). The differential chemical profile obtained in different basal media, both by phytohormones composition and availability of macro- and micro-nutrients, indicated modulation of the terpenoids and flavonoids contents in the invitro culture in *Glycyrrrhiza glabra*.

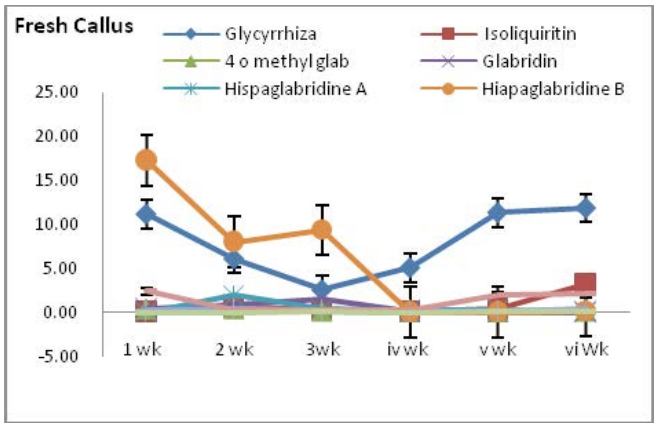


Fig. 1.5.3a) Time Course Chemical Profile of fresh callus of *G. Glabra*

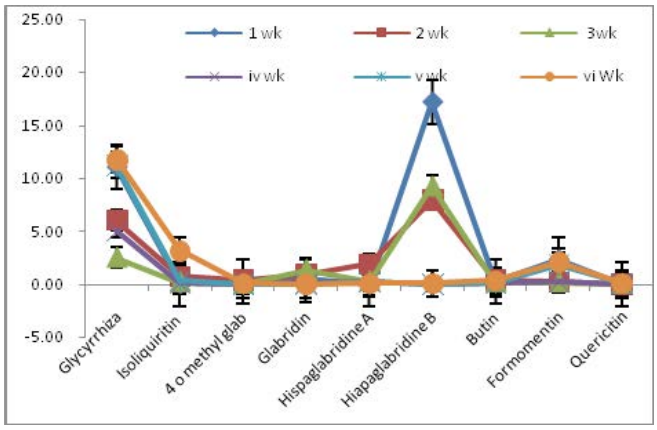


Fig. 1.5.3b) Quantification of 10 chemical compounds in fresh callus of *G. glabra*

The F6 medium was used to produce fine callus suspension, as maximum glycyrrhizin could be detected in these calluses, in minimum time. Both green and brown colored callus were similarly suspended in liquid F6 medium, kept under same conditions in shaker having a rotary motion of 80 rpm for 5 weeks. Time bound chemical profile assessment was conducted to understand heterogeneity of the suspension culture with time. The callus was harvested every week from both green and brown color containing flasks. One week old suspension culture, did not produce good amount of glycyrrhizin, however brown aggregates produced appreciable amounts of hispaglabsidine B(3.3 µg/g). A sharp increase in 2 week old green callus (63.1 µg/g) and glycyrrhizin content was observed in brown callus (3.8 µg/g). In the second week the suspension callus consisted of fine mass as well as cell aggregates. Fine mass was carefully sieved into a fresh F6 medium and aggregates were transferred to separate fresh F6 medium.

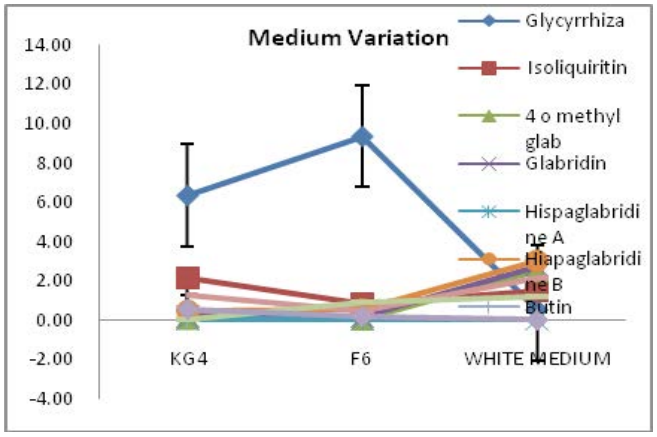


Fig. 1.5.1: Chemical profiling of *G. Glabra* cells suspension culture investigated under different basal medium

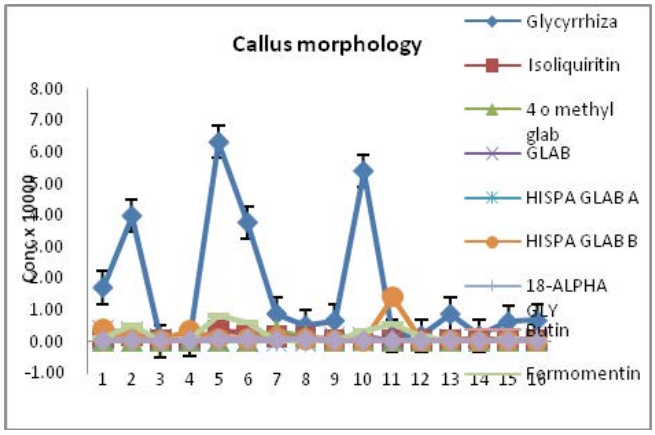


Fig. 1.5.2: Chemical sprectra and callus myoshology (green brown color) in *G. glabra*

Further, it was observed that 4-o-methyl glabridine was detected only in 3 weeks old culture, glabridine and hispaglabridine A were however, observed in all the stages studied in the present study. Most of the flavonoids were detected in appreciable quantity in third week of culturing. Glycyrrhizin, 4-o-methyl glabridine were found maximum in 2 week old green callus, isoliquistin and hispaglabsidine A &B were found maximum in four week old culture. Glabridine, formomentin and quericitine followed no definite pattern of accumulation with time; however formomentin was seen to accumulate only in green root cell suspension cultures only. The coarse suspension was carefully sieved to get fine mass of green and brown callus. Three week old fine mass (from green and brown) and cell aggregates (green and brown) were analyzed. Green aggregates showed higher glycyrrhizin (8.6 µg/g) than the brown aggregates cell mass (5.0 µg/g). The green aggregates had higher 4-O-methyl-glabsidin (3.2 µg/g vs1.5 µg/g), glabridine (1.6 µg/g vs 0.6 µg/g) and hispaglabsidine B(1.3 µg/g vs 0.5 µg/g) than the brown aggregate of the same age kept under similar conditions. Two weeks old green

callus in F6 suspension medium had higher isoliquisitin (3.3 µg/g vs 2.6 µg/g) and formomentin (8.0 µg/g vs 5.6 µg/g). Further, it was observed that fine suspension cell mass in F6 medium after 3 weeks showed higher concentration (5.4 µg/g) as compared to brown cell mass (6.4 µg/g), thereafter the glycyrrhizin concentrations in particular declared in subsequent weeks. Following conclusions can be drawn relating callus ,morphology with the time course chemical profile of the cell suspension green callus and fine suspensions are the better source of glycyrrhizin, isoliquistin, glabsidine and formomentin. Two weeks old green suspension showed maximum concentrations of glycyrrhizin (6.3 µg/g), isoliquistin and hispaglabsidine were present in all the stages in all the weeks studied however, isoliquistin concentration was found to decrease after 3 weeks. White's medium and MS media composition differs largely in terms of source of nitrogen and phosphate micro elements. White's medium has biotin while MS medium contains Thiamine for carbohydrate metabolism. These elements might be one of the reasons behind differential chemical response of the regenerated callus.

Among the eight flavonoids and two triterpenoids investigated in the dried callus mass grown for six weeks, a lot of chemical heterogeneity was observed in the dried callus. The dried weight of callus ranged between 0.2g (1 week) to 0.25 in 3 weeks old culture. Glycyrrhizin concentration ranged between a maximum of 46µg/g in 3 weeks to 7.2µg/g in 5 week. Glycyrrhizinic acid was detected in very small quantity in the three week old culture (0.3µg/g). Among the flavonoids investigated , isoliquistin was found maximum in three weeks old culture (52µg/g) and minimum was observed in two weeks old culture (4.3µg/g). Formomentin was found maximum 51.0µg/g in 1 week old culture and minimum 1.0µg/g was seen in 4 weeks old culture. Butin and quericitin were the third most abundant flavonoids in dried root callus mass of *G. glabra*. Butin and formomentin were present maximum in one week old cultures 6.2µg/g and 2.4µg/g, respectively. Their minimum concentration was observed in 2 weeks (0.3µg/g) and 4 weeks (.03µg/g) old cultures respectively. Hispaglabsidin B was detected maximum in 2 week old culture (8.6µg/g) and minimum in 5 weeks old culture (0.05µg/g), while Hispaglabsidin A concentration was much reduced in dried callus ranging between not detected in 5 weeks old culture to 0.4µg/g in one week old culture. Glabridine was present maximum in 3 weeks old culture (1.8µg/g) and not detected in 5 week old dried callus culture. In the fresh callus, the average weight of the callus after one week was 2.2 g which increased to 3.9 g in 4 weeks and thereafter reduced to 2.0 g in 6 weeks.

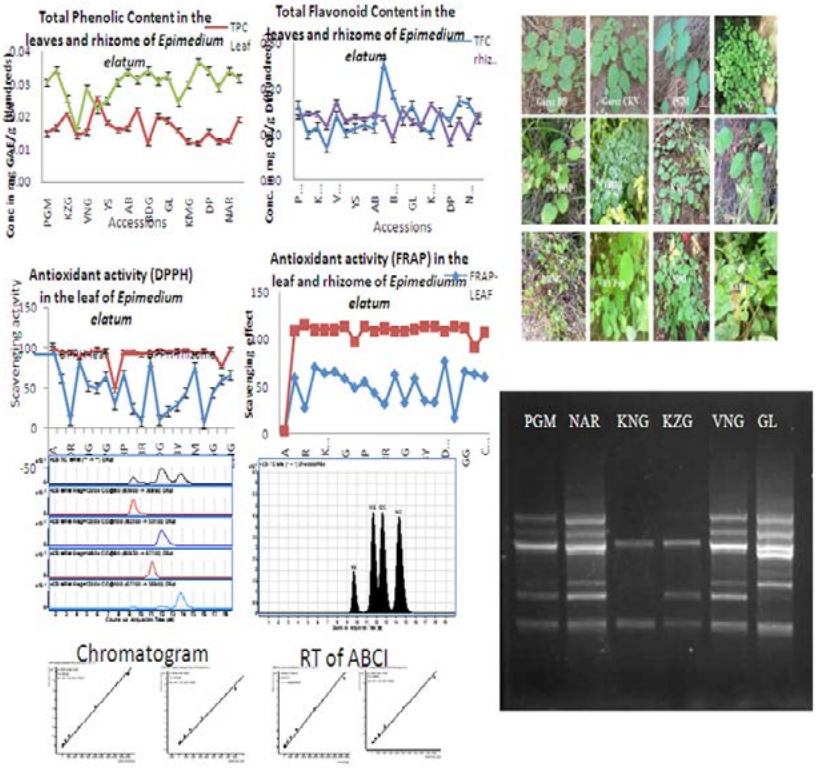
Chemically, the concentration of glycyrrhizin did not show increase in its content with time. It was maximum in 1 week (11µg/g), thereafter it decreased to 2.5µ/g in 3 weeks and 11 µg/g again in 5 &6 weeks. Isoliquiritin concentration was maximum 3.2µg/g in 6 weeks and minimum was seen in 1 week (.9µg/g) and 0.08µg/g in 4 weeks. Formomentin was observed maximum (2.4µg/g) after 1 week and 6 weeks (2.1µg/g). Butin & quericitin were seen to vary between 0.09µg/g (5 weeks) to 0.4µg/g (2 weeks) and (0.6µg/g) in 2 weeks to 0.12µg/g in 5 weeks,respectively. HispaglabridinB seems to vary maximum in six weeks. It ranged between 17.3µg/g (1 week) to 0.01µg/g in (4 weeks). HispaglabridinA was minimum in 1 week (0.04µg/g) and maximum in 2 weeks 109µg/g. Glabridine was not detected in 5 &6 weeks and was maximum in 3 week (1.4µg/g) while 4-o-methyl glabridine was detected only in first two weeks (0.3µg/g). in comparing the chemical profiles, following conclusion can be made. Dried callus showed higher contents glycyrrhizin, isoliquiritin and formomentin; (2) flavonoid concentration reduced drastically in forth week in the fresh callus, except formomentin and quericitn; and (3) hispaglabridine A&B were found in higher quantities in fresh callus.

1.6 Comprehensive assessment of antiosteoporosis prenylated flavonoids and genetic diversity in *Epimedium elatum*: an unexplored species from north western Himalayas

Sajjad Ahmad Lone, Manoj Kushwaha, Abubakar Wani, Ajay Kumar, Ajai P Gupta, Suresh Chandra, Suphla Gupta

Epimedium, a member of Podophyllum family, consists of more than 56 species, distributed mainly in northern hemisphere with 47 of them alone in China (Ma et al., 2011; Zhang et al., 2014). Five species *(E.sagittatum, E.koreanum, E.pubescens, E.wushanense, E.brevicornum)* of this perennial genera form an important ingredient of Herba epimedii. They have been used in folk medicine as a tonic, aphrodisiac and antirheumatic preparations in China, Japan and Korea for more than 2000 years (Ma et al., 2011). More than 260 phytochemical compounds have been isolated from different species of Herba Epimedii (Ma et al., 2011). Among them, four flavonoid glycosides 'ABCI' (Epimedin-A,

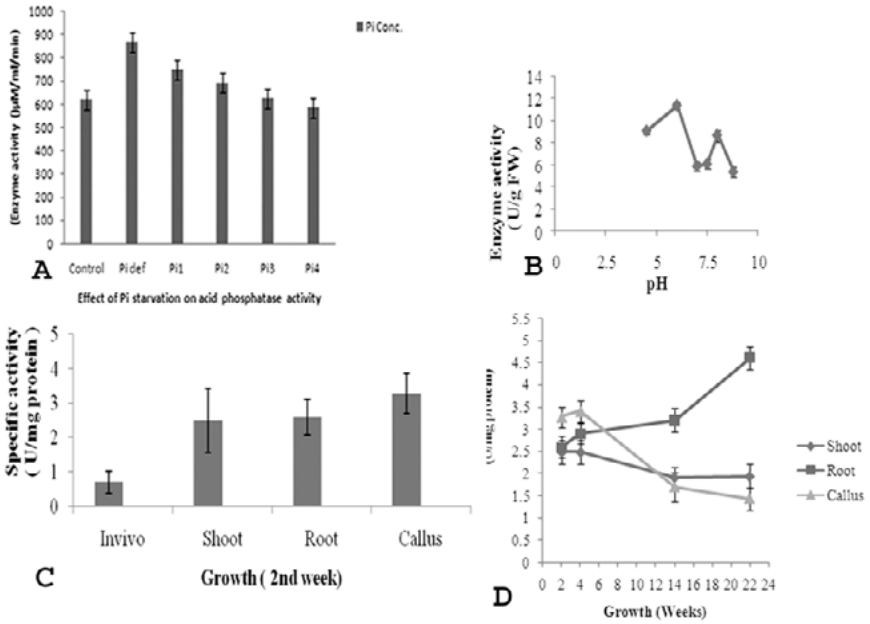
Epimedin-B, Epimedin-C and Icariin) constitute more than 50% of the plant secondary metabolites (Wu et al., 2003; Pei et al., 2007; Wang et al., 2007, 2010).These multi-flavonoid glycosides (ABCI) are recommended as quality markers (reference compounds) for *Herba Epimedii*. Species included in *Herba epimedii* have been extensively studied in China. Literature survey revealed different species of *Herba Epimedii* produce a significant variation in major flavonoids and even the same species from different locations exhibited chemotypic variation (Guo et al., 1996; Xu et al., 2013; Chen et al., 2015). Although, a comparatively less explored species of the genus Epimedium elatum C Morren & Decne, a perennial medicinal plant endemic to high altitudes shady forests of north western Himalayas (Nasir and Ali., 2005; Perveen et al., 2010), does not group under *Herba epimedii* recent reports have indicated its potential in bone related diseases (Arief et al., 2015) and potent PPAR-γ ligand-binding activity (Tantry et al.,, 2012). In addition, few reports on isolation and simultaneous quantification of its active constituents (Tantry et al., 2012; Sofi et al., 2014; Naseer et al., 2015; Arief et al., 2015) have also been reported. But modern science is still exploring the medicinal aspects of this species. Research on distributional and altitudinal aspects of rare and neglected *E elatum* species is poorly documented. No reports on the genetic diversity existing in the wild population of this species are available, till date. The present study examines the unexplored *Epimedium elatum* species in its natural habitat to assess its diversity and potential use as nutraceutical. We have collected wild populations from 20 unexplored high altitudes of Kashmir Himalayas, India in order to assess its; (1) distribution under natural habitat, (2) genetic diversity and chemotype variation of ABCI flavonoids, (3) total polyphenol (TPC) and flavonoid contents (TFC) and (4) antioxidant activities employing DPPH and FRAP model systems. Simultaneous determination of four prenylflavonoids (ABCI multiglycosides) in E.elatum led to the identification of four groups based on the relative composition of ABCI in the unexplored *E.elatum* collected from Northwestern Himalayan range of India. Genetic assessment of twenty accessions revealed a moderate to high genetic diversity. The accessions showed good antioxidant activity corresponding with a high content of total flavonoids. The aerial parts of the unexplored species can be a good source of ABCI multiglycosides while the underground parts can be exploited for potential anti-oxidant activity. These findings will serve to give a deeper understanding of the chemical spectrum of the *E.elatum* on four important phytochemicals. Systematic phytochemical characterization along with proper conservation strategy is essential to convert this understudied species into potential source of medicinal flavonoids. The study will have conservation and cultivation implications for *E.elatum*. Efforts are needed to domesticate the elite chemotypes of *E.elatum* at low altitude conditions in shade gardens for cultivation trials. This will help in germplasm conservation and exploiting the species as future nutraceutical with antiosteoporotic potential. The present study lays the foundation of assessing the gene pool and more studies are needed to elucidate the genetic basis and metabolic processes of *E.elatum*. Keeping in view the pharmacological potential of the Epimedium species, there is wide-ranging scope for *E. elatum* to become a future source of ABCI multiglycosides. Wild populations of this species could become threatened, if timely and effective protective measures are taken.



1.7 Assessment of Acid Phosphatase Production exploiting In vitro cultures of *Atropa acuminata*

Khan Saima, Katoch Meenu, Gupta Suphla, Mallubhotla Sharada, Sambayal Manju1, Ahuja Ashok

The potential of *Atropa acuminata* cultures of different morphogenetic nature were investigated for resourcing acid phosphohydrolase. The crude enzyme extract obtained from the various morphogenetic cultures were found to be a mixture of four enzyme forms, distinguishable by polyacrylamide gel electrophoresis (PAGE). The apparent molecular weight of the four native PAGE separated isoforms ranged between 215 kDa to 39 kDa. Proliferative shoots and roots of in-vitro plants and callus of *Atropa acuminata* showed higher specific activity (2.49, 2.60 and 3.28 U/mg protein, respectively) as compared to in-vivo grown plants (0.71 U/mg protein). Activity of acid phosphohydrolase in root tissue increased progressively (2.6 and 4.6 U/mg) during the entire growth period (2-22 weeks), whereas in case of shoot cultures the specific activity reached its maximum (2.49 U/mg protein) at 4 weeks and declined subsequently (1.92 U/mg protein). Similarly callus culture initially showed higher phosphohydrolytic activity (3.28-3.41 U/mg protein) till 4 weeks which decreased with the growth of cultures thereafter. The pH optima of the phoshohydrolytic enzyme was estimated at different pH, ranging between 4.5 to 8.8, at constant temperature of 25°C was found to be 5.4 (11.3 U/g FW). Enzyme activity tends to decline (5.3 U/g FW at pH 8.0) with the increase in pH. For resourcing phoshohydrolytic enzyme, various in-vitro culture lines and in- vivo plants of *Atropa acuminata* were analyzed for its comparison with field grown plant of the same age. Results demonstrated higher specific activity of the enzyme in 2 weeks old callus (3.28 U/mg protein), roots (2.60 U/mg protein) and proliferative shoots (2.49 U/mg protein) of in-vitro plants culture as compared to in-vivo grown plants (0.71 U/mg protein). Further, the dynamics of phoshohydrolytic enzyme activity with respect to growth of proliferative shoots, roots and callus of in-vitro plants of *Atropa acuminata* showed maximum specific activity in the callus (3.41 U/mg protein) and decrease in activity with the growth of these cultures (Fig 2). Values showed decline in specific activity by almost half as the callus cultures entered 14weeks (1.70 U/mg protein) to 22 weeks (1.44 U/mg protein). The higher enzyme activity in non-differentiated callus cultures observed in the present case in the early stages of callus growth suggested its involvement in the process of dedifferentiation during callus initiation. Increased ACP activity induced by phosphate (Pi) starvation has been demonstrated in a number of plants, including *Nicotiana tabacum, Solanum tuberosum, Solanum lycopersicum and Arabidopsis thaliana* (Bozzo et al., 2002; Kaida et al., 2003; Zimmermann et al.,2004; del Pozo et al., 1999). Consistent with these findings we found that ACP activity ascended while transition from Pi sufficiency to deficiency thereby revealing that these hydrolases might be involved in phosphate acquisition and mobilization processes. In terms of biomass, fivefold more biomass of callus can be produced in 22 weeks which would provide better enzyme units in comparison to root tissues. As such the present results indicated that callus cultures established from selected line could be obvious choice for the production of phosphohydrolase as enzyme activity peaks in the initial growth phase of the callus. Large scale production of phosphohydrolases in fermenters utilizing *Nicotiana tabacum* cell suspension cultures has been optimized (Ilieva et al., 2000). The process which has been commercially exploited for large scale production of phosphohydrolases provide basis and extend opportunity to exploit tissue culture system of *Atropa acuminata* for production of this commercially important enzyme.



1.8 Plant Collection, Authentication and Certification in Janaki Ammal Herbarium

Bikarma Singh, Sumeet Gairola, Vinay Kumar Gupta, Kiran Koul, Sudhir Nanda

Plant authentication and certification is a quality assurance process that ensures the correct identity of species and plant parts are used as raw material for herbal industries. 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. We authenticated hundreds of plant species and essential oil yielding plants growing in Himalaya belts. Janaki Ammal Herbarium is recognized as a National Referral Centre for plant identification and authentication.

During 2016-2017, many field tours for collection of plant materials were undertaken and more than 500 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. The identities of these plants were confirmed by following SOP followed in Janaki Ammal Herbarium.

Fig. 1.8.1 Plant collection, authentication and certification at Janaki Ammal Herbarium

1.9. Floristic Inventory, Population Mapping and Bioprospection of unexplored Kathua District

Sumit Singh, Bikarma Singh

Biodiversity inventories often known as the 'bio-blitz approach' include exhaustive "all-taxa" surveys that seek to identify the full complement of existing organisms within an area of interest. A more typical and pragmatic approach to biodiversity inventory is to target a particular species, ecological community, or taxonomic group. There are virtually no places where on-the ground inventories of biodiversity are considered complete. Increasingly, land managers are becoming proactive about biodiversity inventories, recognizing that it is cost-effective to document hot spots in advance and incorporate them appropriately into planning, rather than wait until a conflict arises. The development of innovative ways to assess biodiversity and habitat condition allows us to build a greater understanding of the complex interactions between individual species and the environment in which they live. Utilising parameters for biodiversity mapping, measuring and modelling provides us with the ability to undertake inventory and assessment,

which is essential for the establishment of baseline biological data that will aid in the successful management of our environment.

While undertaking floristic inventory, population mapping and bioprospection of unexplored Kathua district during 2016-2017, one field tour (*w.e.f.* 9th-15th October 2016) was carried out in Billawar region for biodiversity mapping and floristic study, and 58 field numbers comprising of 73 plant specimens were collected along with field notes (date of collection, habit, habitat, ecological notes) from the study area. Collected specimens were processed for identification, authentication and accession in Janaki Ammal Herbarium, IIIM Jammu. Common species were *Eriophorum comosum* (Willd.) Nees, *Aegle marmelos* (L.) Correa, *Vitex negundo* L., *Persicaria glabra* (Willd.) M.Gomez, *Barleria cristata* L., *Boehmeria macrophylla* Hornem., *Marsilea vestita* Hook. Grev., *Bidens biternata* (Lour.) Merr.& Sherff, *Murraya koenigii* (L.) Sprengel, *Spilanthes acamella* Murr., *Physalis minima* L., *Euphorbia hirta* L., *Rubus ellipticus* Sm., *Bambusa bambos* (L.) Voss, *Achyranthes aspera* L., *Pinus roxburghii* Sarg., *Gymnema sylvestre* R.Br, *Cannabis sativa* L., *Aerva sanguinolenta* (L.) Blume, *Persicaria maculosa* Gray, *Amaranthus virdis* L., *Morus alba* L., *Justicia adhatoda* L., *Acorus calamus* L.

Another field tour (*w.e.f.* 15th-21st March 2017) was undertaken for survey and plant collection in Bani, Malhar and Sarthal forest range for floristic inventory, population mapping and bio-prospection. Total 32 field numbers comprising 51 specimens of plants were collected along with field notes (date of collection, habit, habitat, peculiar characters) from Kakunu forest and other adjoining areas of Bani valley, and processed as per Jain & Rao herbarium technique. Commonly known species were *Onychium japonicum* (Thunb.) Kunze, *Rubus idaeus* L., *Galium aparine* L., *Asplenium alternans* Wall., *Dryopteris dilatata* (Hoffm.) A.Gray, *Polystichum polyblepharum* (Roem ex Kunze) C.Presl, *Valeriana jatamansi* D.Don, *Berberis aristata* DC., *Viola odorata* L., *Cedrus deodara* (Roxb.) G.Don, *Prinsepia utilis* Royle, *Zanthoxylum armatum* DC., *Rabdosia rugosa* (Wall. ex Benth.) H.Hara, *Rhododendron arboreum* Sm., and *Pteris cretica* L.

Fig. 1.9.1 Floristic inventory, population mapping and bioprospection of unexplored in Kathua district

1.10. New Discovery of Plant Species from Indian Himalaya: *Laportea stolonifera* B.L.Bhellum & B.Singh, *sp. nov.* (Urticaceae)

BL Bhellum, Bikarma Singh

The genus *Laportea* Gaudich. (1826: 498) is an annual herb, occasionally the habit becomes under-shrubs or shrubs, similar to that of the genus *Urtica* L. (1753: 983) and *Nanocnide* Blume (1856:

154), but differs from these genera by the presence of alternate leaves and compressed-asymmetric achenes with a filiform eccentric stigma. The genus represents 25 accepted names of species, chiefly distributed in Africa and Madagascar with a few pantropic species. Currently, 4 species of *Laportea* (*L. aestuans* (L.) Chew, *L. bulbifera* (Siebold & Zucc.) Wedd., *L. interrupta* (L.) Chew and *L. stolonifera* B.L.Bhellum & B.Singh, *sp. nov.*), including the new species, are known from India. However, most of the *Laportea* species are confined to Northeast India, Northwest Himalaya and South India.

A new herb species of Urticaceae, *Laportea stolonifera* B.L.Bhellum & B.Singh, is described and illustrated from a restricted habitat of subtropical forest of Northwest Himalaya, India. The new taxon is vegetatively similar to *Laportea ovalifolia* (Schumach. & Thonn.) Chew, an African endemic species and *Laportea interrupta* (L.) Chew but differs by phenotypic characters such as cordate leaves, unbranched inflorescence, stem hairs types, linear cystoliths with varying shapes, and presence of 2 to 3 stolons arising from basal node of stems. The similarity with the allied species is due to similar habitats occupancy, but isolated geographically from each other. *Laportea stolonifera* is assessed as Endangered, and the population data, ecological parameters and associated taxa are also presented.

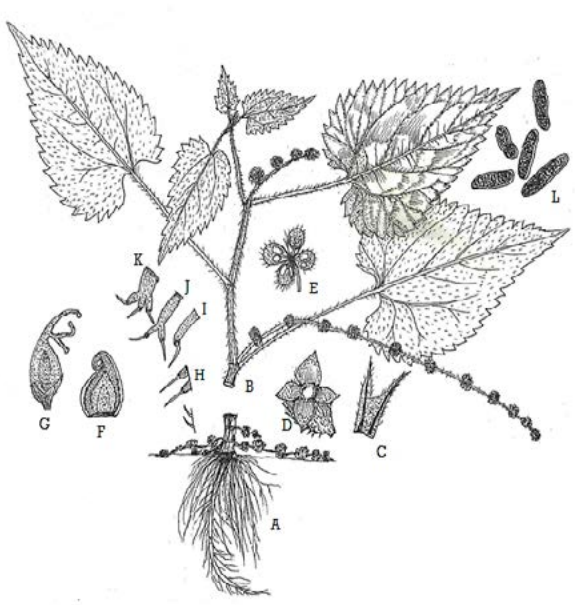


Fig 1.10.1 Morphology and illustration of *Laportea stolonifera* sp. nova

Table 1.10.1 Population data of *Laportea stolonifera* employed for classification of threatened categories of species as per IUCN 2001, Version 4.0.

Criterion A. Population reduction	A1. ≥20% decline per generation (a) Direct observation: very less occurrence, only 3 population observed (b) Density per 10 m^2 : 7-9 individual (c) Quality of habitat: fragmented forest, disturbed (d) Exploitation: exposed to habitat loss due to clearing of forests for timber and NTFP, land use for construction of roads, and extraction of firewood
Criterion B. Restricted geographic range and fragmentation	B2. Area of occupancy (AOO): < 500 km^2 (a) Severely fragmented, 2 locations (b) Continuing decline, (i) extent of occurrence: <5000 km (ii) area of occupancy: 700 m (iv) number of locations: 2 places, 1 place virgin; less expose to habitat loss (v) number of matured individuals: 1196
Criterion C. Small population size and decline	Number of matured individuals in each sub population: <250 C2. estimated continuing decline, (a.i) Number of mature individuals in each sub population: ≤ 250 (a.ii) % of matured individuals in one subpopulation: 95-100%

1.11. New Record for India: *Lepidium didymum* L. (Brassicaceae) from Jammu & Kashmir State

Maridul Kundan, Bikarma Singh

Tribal communities have 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 folk are knowledge passed down from one generation to next generation by the way of living. While inventorying and studying the biodiversity and traditional knowledge associated with Gujjar and Bakarwal tribes of J&K state, an interesting herb plant of the genus *Lepidium* L. was collected from the hill top, the road running to Patnitop-Sanasar route (33º05'09.8''N, 75º19'33.9''E, 2114m asl) of Udhampur district. The vouchers were carefully identified with the help of deposited herbarium specimens of RRLH, JU.

Lepidium is an important economic genus placed under the family Brassicaceae (or Cruciferae) of flowering plants that comprises of 234 species distributed in Africa, America, Asia, Australia and Europe. Mining of published literatures reveals 14 species of this genus (*L. africanum* (Burm.f.) DC., *L. apetallum* Willd., *L. aucheri* Boiss, *L. capitatum* Hook.f. & Thomson, *L. cartilagineum* (J. Mayer) Thell., *L. draba* L., *L. didymum* L.(Present study), *L. latifolium* L., *L. obtusum* Basiner, *L. perfoliatum* L., *L. pinnatifidum* Ledeb, *L. ruderale* L., *L. sativum* L. and *L. virginicum* L.) in India growing at different altitudes in different agro-climatic zones.

Lepidium didymum was collected and taxonomically enumerated for the first time from India in Western Himalaya of Jammu and Kashmir State. This contribution is important for India from biodiversity richness point of view as this contribution increases the floristic data about the angiosperm diversity of the country, as well as it adds knowledge about the genus *Lepidium* distribution at regional and global scenario.

Fig. 1.11.1. Mapping and habit characterization of *Lepidium didymum*

Herbaceous annual herbs, upto 25 cm high, with simple trichomes; roots slightly whitish, 10-15 cm deep penetrated. Stems branched from base, decumbent, often somewhat foetid, glabrous or hairy. Leaves two types: radical leaves, short, 1 or 2-pinnatisect, stalked petioled, 0.5-4.5 cm long petiole, leaves entire; cauline leaves pinnatifid, 1.5-3 cm x 0.5-1.2 cm, sessile or subsessile, lobes sinuate toothed, usually only on one side. Racemes elongated in matured plants, dense, ebracteate, 3- 8 cm long, 30-60 flowered. Flowers minute, usually white in colour, slightly greenish below; sepals ovate, 0.5-0.8 mm; petals ovate to lanceolate, smaller than sepals, 0.3-0.4 mm long; stamens 2; filaments 0.3-0.4 mm; anthers whitish, minute. Fruiting pedicels short, 3-4 mm long, filiform. Fruits didymous, 1-2 mm long, 2-3 mm broad, looks broader than long, bilobed; valves globose, reticulately rugose; septum narrowly thin, inconspicuous; seeds ovate, 1-2 mm long, reddish-brown.

1.12 New Record for State: *Elaeagnus umbellata* Thunb., a new plant species record for Meghalaya State

Bikarma Singh

The family Elaeagnaceae, so called, Oleaster fruits, represented by four genera, viz.: *Elaeagnus* L., *Hippophae* L., *Lepargyrea* Raf. and *Shepherdia* L., widely reported distribution from Eurasia, Northeast Australia and North America. The genus *Elaeagnus* comprised of 50 species, *Hippophae* with 15 species, *Lepargyrea* is monotypic, and *Shepherdia* with 3 species. All these species within the respective genera have nitrogen-fixing bacteria called *Frankia* (Actinomycetes) in their root nodules making them useful for soil reclamation. The reproductive biology of the species varies between genera to genera. The three genera (*Hippophae*, *Lepargyrea*, *Shepherdia*), have male and female reproductive organs in separate individuals (dioecious), while *Elaeagnus* is monoecious. The species within the family shows xerophytic (tolerance to dry) and halophytic habitats (tolerating high levels of soil salinity). While studying the floristic composition of Himalaya, one species of the genus *Elaeagnus* was collected on way to Cherrapunjee (GPS point: latitude 25˚33´53.88”N, longitude 91˚51´21.30”E, elevation 1606 m). Critical studies were done by comparing and evaluating the herbarium with that of the different herbarium specimens housed at different Herbarium. After complete scrutiny, the identity of the species was confirmed as *Elaeagnus umbellata* Thunb., which was first published by Carl Peter Thunberg in J.A.Murray’s edition ‘Systema Vegetabilium’ in 1784 (May-June). Earlier, this species was reported from the United States in 1830. Taylor (1914) reported the same species from Northern India and adjoining countries viz. Afghanistan, China and Japan. This species was not reported before from Meghalaya in the relevant literature of this region, therefore, it was recorded here for the first time from Meghalaya State and rediscovered from Northeastern states (coming under Himalaya belts) after a gap of 75 years.

Fig. 1.12.1. Taxonomical enumeration of *Elaeagnus umbellata***,** a wild edible plant of Himalaya

Elaeagnus umbellata is a scandent, deciduous shrub upto 4 m high; branches slender and spreading, spiny, young branches and buds covered with silvery scales. Bark brown or slightly yellowish brown, smooth in young branches, scaly in old ones. Leaves alternate, variable, usually elliptic to oblong-lanceolate, 1.6-6.2 cm long, 0.6-2.6 cm broad, cuneate at base, obtuse or acute at apex, papery, dull green above, with sparsely white lepidote, lower surface densely white lepidote; petioles 0.2-0.5 cm long. Inflorescence axillary, clusters of 2-7 flowers along twigs, densely white lepidote. Flowers small, silvery white; pedicel 0.3-0.5 cm long, elongating 1-1.2 cm long in fruit. Perianth tube 0.8-1 cm long, tubular, gradually narrowed at base. Style 0.6-0.7 cm long, stellately hairy; stigma ca 0.1 cm across, hairy. Fruit drupaceous, subglobose to broadly ellipsoid, 0.6-0.9 cm across, green and covered with scales when young, red to slightly pink when ripe; endocarp not hard, 8-ribbed. Seeds 0.5-0.6 cm long.

1.13. Rediscovery of plant species after a Century: *Haematocarpus validus* Bakh.f. ex Forman (Menispermaceae) from Indo-Myanmar biodiversity hotspot

Bikarma Singh, Yashbir Singh Bedi

During the decades of 18th and 19th Century, the English botanists' viz., Robert Kyd (1746–1963), William Roxburgh (1751–1815), William Griffith (1810–1845) and Robert Wight (1796–1872) collected numerous plant species and made significant contributions to the knowledge of the plant diversity of India. Joseph Dalton Hooker (1817–1918), one of the greatest British botanist and explorer for British India assisted by several workers published '*The Flora of British India*' in 7 volumes [1] and contributed the most reliable reference book for India even till to-date. The U.N. Kanjilal along with several botanists of 20th century published the '*Flora of Assam*' in 5 volumes between 1934 and 1940, and is the most referral books for Northeast India. During explorations, these botanists collected and published several species, subspecies and variety new to science and new records for country, some of which are still known only from their type locality. *Haematocarpus validus* Bakh.f. ex Forman (Menispermaceae), a species critically endangered, was rediscovered after a gap of 100 years from India, and add new location to Indo-Myanmar biodiversity hotspot province. After critical scrutiny of herbarium and review of published literature on its distribution, its natural occurrence was known only from Borail Reserve Forest (Assam) for this species from India and the recent discovery of its habitats in Mawlakhieng village (Meghalaya) add new locality.

Taxonomy elumeration

Large woody climber, perennial, leave deciduous, 15–50 m long, spreads on tall trees; bark somewhat rough, pale grey when living, brown or slightly black when dried, slightly fissured; stem 3–6.6 cm diam, glabrous,; branches glabrous, stout, pale to grey, usually branched; wood with consecutive layers of thin radiating plates. Leave 7.3–10.2 cm long, 3.4–5.2 cm wide, oblong or oblong-elliptic, rigidly coriaceous, pale glabrous beneath, dull green when living, pale grey or slightly whitish and shining when dried, margin entire, base rounded or slightly peltate or acute, apex bluntly acuminate; basal nerve 3, 1 on each side of the midrib, prominent, slightly raised beneath, running nearly to the apex; secondary nerves slender, reticulate, spreads at nearly right angle, conspicuous; petioles 0.7–2 cm long, 0.2–0.3 mm diam, slender, pale grey when dried. Inflorescence axillary or supra-axillary, branched; staminate inflorescence 3.5–7.5 cm long, axillary, solitary, fascicled racemes, slender, branched; pistillate inflorescence not seen. Flower minute, dioecious; male flower 3–6 mm diam, pale white to yellow; pedicel, 2–4 mm long, slender; sepals 12 with 3 bracts, 3 outer ones less than 4 mm long, 3 middle ones 4–5 mm long, 6 inner ones 5–6 mm long, all broadly ovate and obtuse depending on size, margin of all ciliate; petals 6, thicker than sepal, 3–5 mm long, concave, base auricled; stamens 6, all free, 1–1.2 mm long filament, broadly ovate 2-celled anthers; rudimentary carpels 3, very minute; female flowers not seen. Fruit in woody racemes, 8–30 cm long, stout; torus slightly globose, scars 4–6; drupes 2–6 together, 0.4–0.6 cm long and stout stalk; drupes 2.3–3.6 cm long, 1.6–2.1 cm diam, oblong or oblique, fleshy, yellowish to slightly pink or red when mature living, dark brown when dried, full of copious blood-red juice when ripe, style scar about half way down the drupe, endocarp fibrous, adherent; seeds 2–3 cm long, somewhat inflaxed, oblong, albumen absent, cotyledons fleshy, thick, curved.

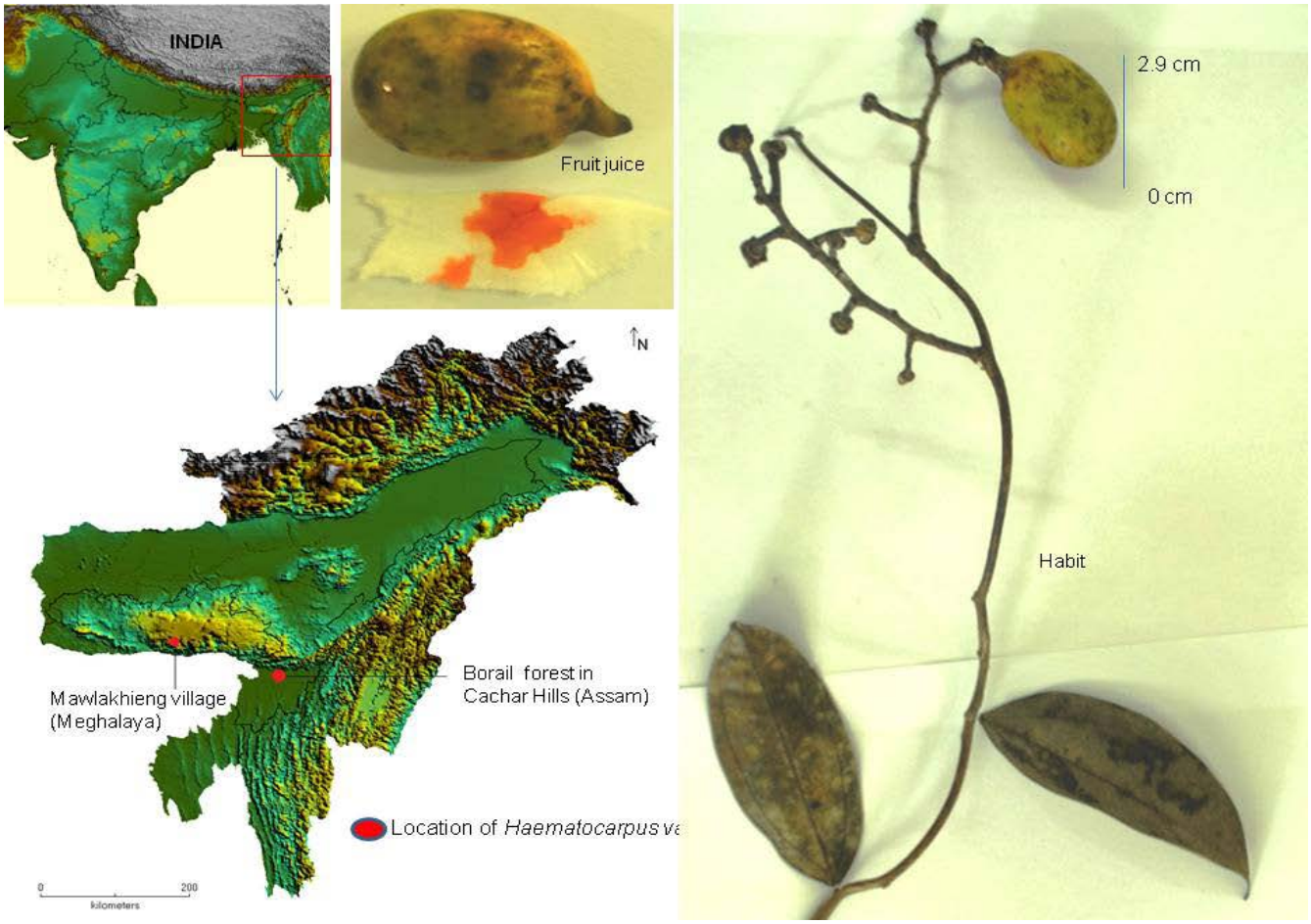


Fig. 1.13.1. Mapping and rediscovery of *Haematocarpus validus*, a critically endangered species of India

1.14 Agrotechnology transfer and thymol crystal from Jammu Monarda

S.R. Meena, Divya Dheer, Jyoti, Bikarma Singh, Rajendra Bhanwaria, Sabha Jeet, V.P. Rahul, Kushal Bindu, M.K. Verma, Ravi Shankar, Suresh Chandra, Ram Vishawakrma.

Jammu monarda is an annual herbaceous plant. This plant species is suitable for subtropical climatic conditions of Jammu and temperate climatic conditions of Kashmir, and has potential for large-scale production of essential oil (Fig. 1.141). The essential oil possesses high level of antifungal activity against common post-harvest fungal pathogens of the variety of crops both by direct contact and in the vapor phase.

Four week plant under nursery

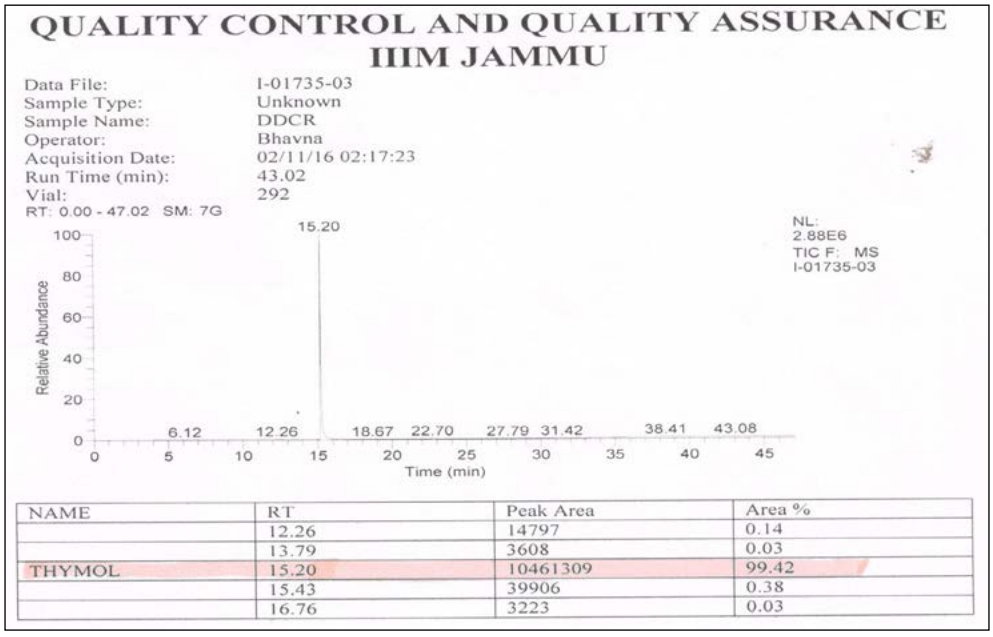
Fig 1.14.1 Monarda plant at nursery stage for societal development.

The essential oil contains high amount of thymol (70-85%) and carvacrol. The demand of thymol containing essential oils is increasing every year. Essential oil of Jammu monarda has been accepted by pharmaceutical houses as an additional and alternative source of thymol. This plant species is suitable for subtropical climatic conditions of Jammu and temperate climatic conditions of Kashmir, and has potential for large-scale production of essential oil. The essential oil contains high amount of thymol (70-85%). The present studies will deliver the new knowledge of cultivation, optimized harvesting time and post-harvest processing of Jammu monarda in different location and improved technology will be useful for farmers to cultivation the crop in scientific manner and higher yield with quality to get the higher economic return. Agrotechnology has been developed under good agricultural practices and large scale cultivation of Jammu Monarda initiated further preparing seed under nursery and transplant in farmer's field at second fortnight in November (Fig.1.14.2)

Fig 1.14.2. Monarda plant at field scale at IIIM farm Chatha, Jammu.

The prevailing price of the oil in Indian market is 1500 rupees / kg. Large-scale cultivation of this crop will produce tonnage of thymol rich essential oil for fulfill the industrial demand of natural thymol crystals. Thymol (2-iso-propyl-5-methylphenol) is a naturally occurring monoterpene phenol which is isomeric with carvacrol and has shown antibacterial, antifungal, antitumor and anti-inflammatory activities. It also acts as an antioxidant, free radical scavenger and antilipid peroxidative agent. Thymol is obtained from both synthetic and natural sources. In addition, it is a valuable intermediate in the production of synthetic menthol by catalytic hydrogenation. At laboratory scale (Fig 3), to recover thymol in maximum quantity from Jammu Monarda oil 8 experiments carried out with 1 litre scale and recovered thymol with 99% purity (Purity was monitored by GCMS, Fig 4), at various temperatures still standardization in progress. It has been observed many essential oil tend to change their chemical properties at heating therefore, we are trying to standardize procedure to get pure thymol in maximum at cooling condition with highest purity.

Fig 1.14.3. Essential oil extraction from aromatic plant at lab scale.



NAME	RT	Peak Area	Area %
	12.26	14797	0.14
	13.79	3608	0.03
THYMOL	15.20	10461309	99.42
	15.43	39906	0.38
	16.76	3223	0.03

Fig 1.14.3. GCMS of Recovered thymol from Jammu monarda oil

2.0 VALUE ADDITION

2.1 Value Addition of Aroma Bearing Crops

Bikarma Singh, Kiran Koul, S.R. Meena, Rajendra Gochar, Chandra Pal, Vijay Kumar, Kushal Bindu, M.K. Verma, Phalisteen Sultan, Suphla Gupta, A.K. Katare, Q.P. Hussan, Ravi Shankar, Vikash Babu, Rajendra Bhanwaria, V.P. Rahul, Sabhajeet, Rajneesh Anand, Ram A. Vishwakarma, Suresh Chandra

Aromatic plants have been used for centuries in cosmetic, medicine, perfumery, and have been added as a source of value added component to food as part of herbs or spices. Essential oils are aromatic and volatile liquids extracted from plant material, such as from whole plant samples, woods, barks, leaves, flowers, roots, fruits, and seeds. These volatile liquids are considered to be secondary metabolites, such as alcohols, hydrocarbons, phenols, aldehydes, esters, ketones, and also constituents of hundreds of organic components, including hormones, vitamins and other natural elements. These secondary metabolites produced by plants are important for plant defence as they possess antimicrobial properties and act as a defence mechanism against insects, infections, as well as attract pollinators. Aroma bearing crops have added lots of value to the growth of flavor and fragrance industries as well as boasted sectors agriculture. Essential oils are backbone in the process of globalization, which started about a decade before, and is now growing rapidly. Industrial data indicates that essential oils of Tulsi, Citronella, Lemongrass, Lavender, Palmarosa, Patchouli, Sandalwood, Geranium and various varieties of Mints are finding increasing use in formulations of aroma value added products, and also act as a roadway therapeutically in aromatherapy. It is believed that the herbal aromatherapy can give good effect to body without causing side effects to human's life. Besides, the usage of aromatic plants in various sector have supported the economy of the country. Perfumes, essential oils and aroma are some of the products which indicate religious values, living standards, personality development for personal use and adornment from years back. Currently, CSIR-Indian Institute of Integrative Medicine, Jammu has developed agrotechnology of high yielding varieties of aroma bearing crops, and involved in captive cultivation and extension of these crops in J&K state and elsewhere in various states of India. Keeping the pre-historic importance of aroma bearing crops, Scientists of IIIM Jammu has prepared aroma value added product entitled "Nature Fresh...Aroma Value Kit....sense of living". Prepared aroma kits are of two types: 6 ml capacity and 3 ml capacity. The 6 ml capacity aroma kit contains five types of essential oils, viz., Mint oil, Lavender oil, Lemongrass oil, Himros oil and Jammu Monarda oil. The 3 ml capacity aroma kit has six types of essential oils, such as Rosemary oil, Mint oil, Lavender oil, Lemongrass oil, Himros oil and Jammu Monarda oil. The oil of the essential oils bears the name of the plant from which it was derived. The crop lavender and rosemary are high altitude high value crops, where as Mint, Lemongrass, Himrose and Jammu Monarda crops are usually cultivated in tropical and sub-tropical belts only. The details of crops used in the preparation of aroma value kit is given below:

1. Jammu Monarda (Monarda citriodora Cerv. ex Lag. [IIIM(J)MC-02]: Developed and released for commercial cultivation on the occasion of Foundation day on 1st December 2010.

   Characteristics: A rich source of thymol (about 60-75%) and better economic returns (100-125 kg/ha). Essential oil active against cancerous cell line (HL60), acceptability by flavour and pharmaceutical industries. It is also used as an antiseptic, expectorant and cough medication, to treat nail fungus infection.

2. Himrosa [Cymbopogon khasianus Bor IIIM (J) CK-10]: Developed and released by CSIR-IIIM Jammu on 1st December, 2012 on the occasion of IIIM(J) Foundation day 2012

   Characteristics: Having high drought and salt tolerance ability, and is a rich source of Geraniol (75-85 %). The oil is extensively used as perfumery raw material in soaps, "oral rose-like perfumes, cosmetics preparations, and in the manufacture of mosquito repellent products. The essential oil has a scent similar to that of rose oil, and named Himrosa.

3. Anant carvomint [Mentha longifolia (L) Hudson var. incana (Willd) Dinson RRL(J)ML-4]: Released for commercial cultivation on 30th January, 2007

Characteristics: Hyper productive strain developed though clonel multiplication, wider adaptability (Kashmir to Kanya Kumari). It is in rich in ℓ-carvone 67±5 %). It has essential oil content (0.5 to 0.9%w/w FWB) depending on season to season. It has wider acceptability shown by perfume, flavour & pharmaceutical industries.

4. Lemon grass (Cymbopogon khasianus x C. pendulus) [CKP-25]: Released in 2002

   Characteristics: It is an interspecific hybrid and the oil contents are 0.5%. Its main constituents are citral (80-85%). It is very useful in perfumery, flavoring & pharmaceutical industry.

5. Lavender (Lavandula officinales) [RRL 12]: Released in 1972

   Characteristics: Lavender is high altitude high value crop and is an incredible and much sought aromatic plant having significant position in trade all over the world due to its essential oil which has multifarious uses and market outlets. Main constituents are Linalool, Linalyl acetate, 1,8 cineole, borneol, caryophyllene, terpineol, ocimenes, Lavandulyl acetate. It is useful in perfumery, flavor and cosmetic industry.

6. Rose Mary (Rosmarinus officinalis L.)

   Characteristics: Rose Mary is yet another high value crops and its main constituents are p-cymene (40-44.02%), linalool (18-20.5%), gamma-terpinene (14-16.62%), thymol (1-1.81%), beta-pinene (2-3.61%), alpha-pinene (1-2.83%) and eucalyptol (1-2.64%), which is useful in perfumery, flavor and cosmetic industry.

Fig. 2.1.1: CSIR-IIIM developed Aroma Kit from essential oils

2.2. Exotic Plants as a Source of Nutraceutical Values

Bikarma Singh, Sumit Singh, Surrinder Kitchlu, Kiran Koul, A.K. Katare, Suresh Chandra

Nutraceuticals are food or part of food that provides medicine or health benefits including the prevention and/or treatment of a disease. It has advantages over the medicine because they avoid side effect, easily available, economically affordable and have composition of naturally dietary supplement. Herbal nutraceuticals used as a powerful instrument in maintaining health and to act against nutritionally induced acute and chronic diseases, thereby promoting optimal health, longevity, and quality of life. The food sources used as nutraceuticals are all natural and can be dietary fibers, probiotics, prebiotics, polyunsaturated fatty acids, antioxidant vitamins, polyphenols and spices. While studying different parameters on nutraceuticals and potential value added plants, R&D on following plants are underway:

Fig. 2.2.1: Exotic Plants as a Source of Nutraceutical Values growing in IIIM Jammu campus, (a) Passiflora incarnate, (b) Symphytum officinale, (c) Echinacea purpurea, (d) Rosmarinus officinalis, (e) Nasturtium officinale, (f) Lepidium sativum

1. Passiflora incarnata L. (Passifloraceae): The genus Passiflora L. is represented by ca 500 taxa and most of the species are Pantropical in distribution. Wide distribution of the species reported from Australia, South America, Eastern Asia, New Zealand, Southern Asia and New Guinea. The habit of almost all species within the genus is vine. In India, 23 species reported from different regions. Passiflora incarnata L. is an important species and is a fast growing perennial vine with climbing or trailing stems. It is native to North America. It flowers in April-May. Medicinally, the plant is used in anxiety disorders. Flavonoid group of compounds are its components and it is represented by chrysin, apigenin, luteolin, quercetin, kaempferol and isovitexin.

2. Symphytum officinale L. (Boraginaceae): Commonly known as Comphery, the genus Symphytum L. is native to Europe. It is represented by ca 35 species.

The habit of all species is perennial herb. Symphytum officinale L. well known species in the above genus is a perennial herb native to Europe and also occurs in North America. Flowering time is generally May-June. Medicinally, the plant is used in folk medicine as a poultice for treating wounds and burns. Major compounds isolated from this plant are pyrrolizidine alkaloids, symlandine, symphytine, echimidine, riddelliine, senecionine N-Oxide, seneciphylline, retrosine, heliotrine etc.

3. Echinacea purpurea (L.) Moench. (Asteraceae): The genus Echinacea Moench. Is comprised of ca 9 species. Plants are generally perennial herbs. Distribution ranges from eastern to southern North America. Echinacea purpurea (L.) Moench. a native species to North America is a perennial herb. Flowering time is generally early july to August. Medicinally, it is oftenly used externally for wounds, insect bites, stomach pain, toothace, throat infections. Phenolic compound are the main constituent of this plant represent by cynarin, cichoric acid, caftaric, chlorogenic and isochlorogenic acids. Major flavonoids is Rutoside.

4. Nasturtium officinale W.T.Aiton. (Brassicaceae): The genus Nasturtium L. is represented by roughly 80 species. Habit of the species mostly perennial herbs. Genus is widely distributed in south and central America. Nasturtium officinale W.T.Aiton. is an important species and aquatic or semi aquatic in habit native to Europe and Asia. Flowering is generally in April to June. Plant has very nutrition value and consumed as food rich in vitamin K, also contain significant amount of Vitamin A, C, calcium, manganese. Medicinally, used as an antiscorbutic, depurative, diuretic, hypoglycemic, stimulant,tonic etc. Phenols and flavnoids are the major compounds present in the plant.

5. Rosmarinus officinalis L. (Lamiaceae): The genus Rosmarinus L.represented by 40 species. They are mostly Perennial herbs. It is native to the Mediterranean basin. Rosmarinus officinalis an important species in the above genus is a Perennial herb. Flowering time is March-October. It is used majorly in traditional medicine, extracts and essential oils from leaves are used for various disorders. Major compound isolated from this plant are rosmarinic acid, camphor, caffeic acid, ursolic acid, betulinic acid, carnosic acid and carnosol. As a nutritive point of view, leaves are used as flavouring agents. Herbal tea can be made from leaves.

6. Lepidium sativum L. (Brassicaceae): The genus Lepidium L. is comprised of ca 175 to 220 species. The genus is widely distributed in Americas, Africa, Asia, Europe, and Australia. Nearly all species are herbaceous in nature. Lepidium sativum L. is a widely distributed species under this nature. Plant is a fast growing annual herb. Flowering time is generally June-July. Medicinally, it is very effective Ayurvedic herb. Its seeds are useful in bloating, irregular periods, Estrogen deficiency etc. Plant is rich in nutritional value and consumed as salads, as cooked food. Major compounds isolated from this plant

2.3 Scientist-Farmer-Industry Interaction National Seminar on Aroma Bearing Crops

Bikarma Singh, S.R. Meena, Suphla Gupta, A.K. Katare, Q.P. Hussan, Ravi Shankar, Rajendra Bhanwaria, V.P. Rahul, Sabhajeet, Ram A. Vishwakarma, Suresh Chandra

A One Day National Seminar on Aroma Bearing Crops was organized in CSIR-IIIM, Jammu on 4th March, 2017 in collaboration with International Congress Of Essential Oils, Fragrances And Flavours - 1989 (ICEOFF-1989). This one day seminar was attended by fifty advanced farmers of Jammu region, twenty five industrialists from aroma industry and twenty scientists of CSIR-IIIM Jammu.

- The inaugural lecture was presented by Sh. Vinod Seth, President ICEOFF-1989 emphasizing the need for interaction between research industry and farmers. The meeting included eight presentations on aroma bearing crops by the researchers of the Institute.
- Dr. Ram Vishwakarma, Director, CSIR-IIIM Jammu welcomed the delegates and highlighted the work done by the Institute in the related area. He invited the Industrialist and the farmers to come to a common platform for mutual interaction and benefit.

The farmers and the Industrialists shared their problems and expectations, respectively. Several farmers were encouraged and got sensitized after the meet to cultivate the aromatic crops. It was decided after the meeting that CSIR-IIIM will act as a facilitator between farmers and Industrialist in procurement of certified essential oil. This will ensure quality of the oil and benefit farmers at large.

Fig. 2.3.1: Glimpse of Value Addition National Seminar Held at IIIM Jammu

3.0 MICROBIAL BIOTECHNOLOGY

Discovery of Notch pathway modulators: Aberrant Notch pathway is implicated in process of oncogenesis with leukemia associated with down regulated notch signalling whereas breast cancers are associated with elevated notch signalling. We have discovered IS00676, a pyrimidyl-aza-indole based lead derived from Meriolin as a potent inhibitor of γ-secretase with an IC_{50} value of 3nM. It was found to decrease the cleavage of full length Notch1 to NICD. The protein levels of γ -secretase complex components including Nicastrin and Presenilin were found unchanged. The levels of Notch regulated gene Hes1 were found reduced by the treatment of compound IS00676 in cell based assay. This compound was also found to inhibit the growth and proliferation of MCF breast cancer cell lines. Similarly we have discovered IIIM-8, a derivative of Mahanambine isolated from Murraya koenigii as an activator of Notch signaling pathway with an EC_{50} value equal to 0.85 μM. It also inhibited the cell proliferation and colony formation of the K562 human leukaemia cell line.

4.0 DISCOVERY INFORMATICS

4.1 Identification of a novel Mtb-SK inhibitor and its allosteric mode of action

Rukmankesh Mehra, Amit Nargotra, Vikrant Rajput, Inshad Ali Khan.

Mycobacterium tuberculosis shikimate kinase (Mtb-SK) is a key enzyme involved in the biosynthesis of aromatic amino acids through shikimate pathway. It is a promising target for anti-TB drug discovery as it is proven to be essential for the survival of the microbe and moreover it is absent in mammals. In this study, a combined approach of *in silico* similarity search and pharmacophore building using already reported inhibitors was used to screen a procured library of 20,000 compounds of commercially available ChemBridge database. By applying similarity search technique, 50 hits were retrieved from the 20,000 compound library that followed 0.6 Tanimoto coefficient criterion. Since, similarity search cannot be the only possible criterion for the compounds to be active, pharmacophore modeling was also carried out, which included a set of common pharmacophoric features a compound should possess for being active against a biological target. By applying pharmacophore based screening, top 500 hits were selected from the library based on the fitness score. In order to find the compounds from the similarity search hits that possessed common pharmacophoric features, common hits were identified between similarity search hits and pharmacophore hits. This ensured that no active compound was missed from the compound library from similarity and pharmacophoric point of view. There were 15 compounds found to be common between similarity search hits and pharmacophore hits, which were then carried forward for *in vitro* screening for Mtb-SK enzyme inhibition. Two compounds presented significant enzyme inhibition with IC50 values of 10.69 ± 0.9 µM and 46.22 ± 1.2 µM. Both these compounds successfully passed through the PAINS filter, which showed that the identified inhibitors were not PAINS compounds. The identified inhibitors were also searched through SciFinder, which is an online scientific information retrieval system. It was revealed that these compounds were structurally novel as Mtb-SK inhibitors. The best hit "5489375" was reported to be the un-competitive and non-competitive inhibitor of SKM and ATP respectively thereby, suggesting the presence of an allosteric site. This allosteric site was identified in the Mtb-SK crystal structures, where the identified inhibitor (5489375) binds in the presence of both the substrates (ATP and SKM). Binding site prediction using SiteMap revealed the presence of only one binding site, apart from ATP and SKM binding sites, in all the three complexes (Figure 4.1.1). This showed revealed the presence of an allosteric site in Mtb-SK where the inhibitor could effectively bind with high affinity. The binding cavity of Mtb-SK was found to be L-shaped, where long arm of the L represented ATP site and the short arm represented SKM site.

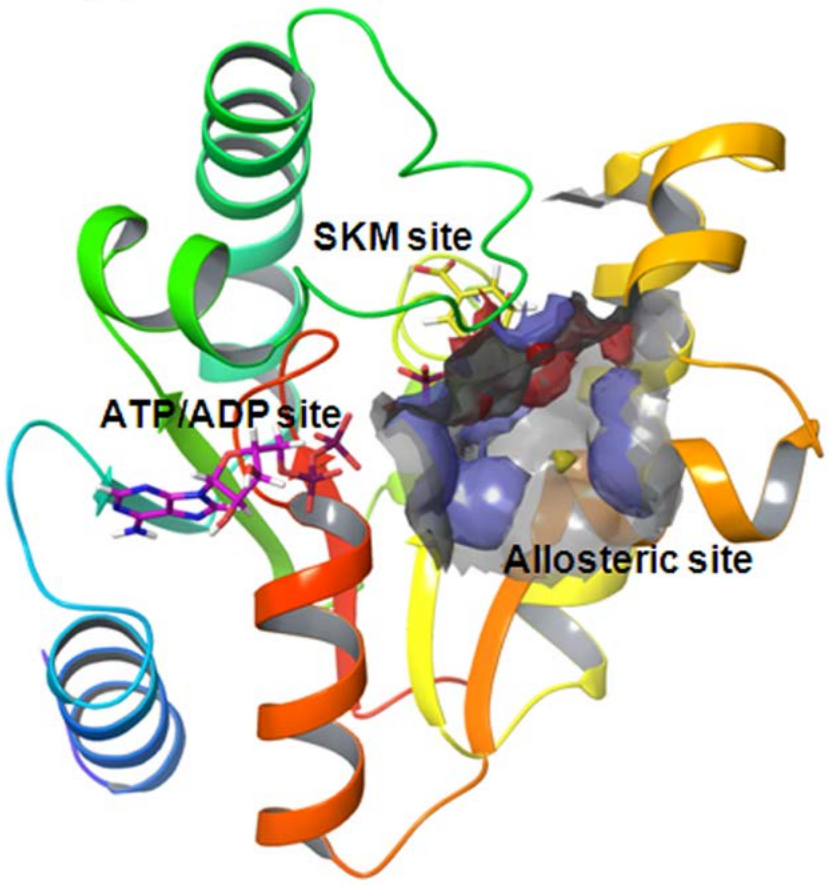


Fig. 4.1.1 Allosteric binding site of Mtb-SK predicted by SiteMap.

To further study the mode of inhibition of the best hit ("5489375"), three different protein complexes viz: substrate complex, intermediate

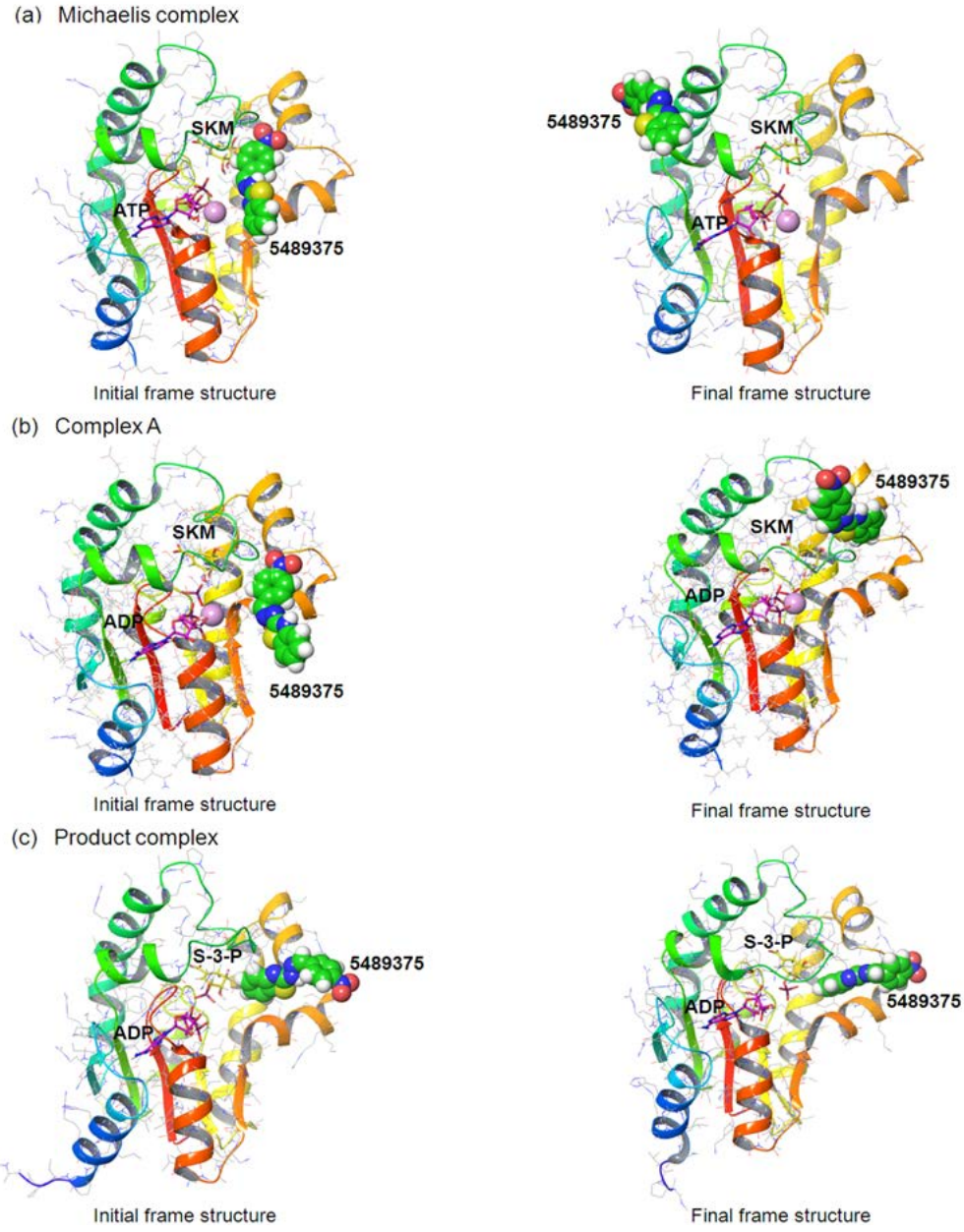


Fig. 4.1.2. Initial and final frame structures of the three complexes obtained from MD simulations.

complex and product complex were studied. The substrate complex comprised of the shikimate kinase bound with ATP/Mg2+/SKM. Whereas, shikimate kinase bound with ADP/Mg2+/PO3-/SKM and ADP/S-3-P were taken as the intermediate and product complexes respectively (figure 4.1.2). Docking simulations of the inhibitor was carried out on the predicted allosteric binding site of all the three complexes.

Analysis of the binding mode using docking and MD simulation studies revealed that "5489375" has high probability of binding to the allosteric site of Mtb-SK after the products are formed but are not released. The inhibitor was mainly bound to the residues of the SB domain and formed crucial interactions with the residues ARG43, ILE45 and PHE57. The binding of "5489375" prevented the formation of strong salt bridge interaction between the guanidinium group of ARG117 and phosphate group of S-3-P, thus inhibiting the force required for the product release. The binding of the inhibitor to the allosteric site of Mtb-SK, which is the first report so far, indicates its higher selectivity for Mtb-SK as compared to other mammalian kinases. The site thus identified will help in designing more selective inhibitors for this important target.

4.2 Further computational studies on EGFR

Priya Mahajan, Amit Nargotra, Nitasha Suri, Shashank K Singh.

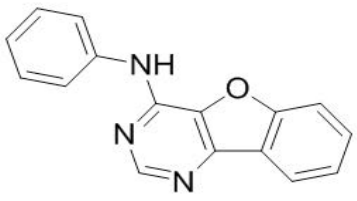
In continuation to our earlier work on molecular modeling of EGFR, in vitro studies and molecular dynamics simulation was carried out of the best inhibitor identified.

i) IC50 determination of ID-5934507 against EGFR

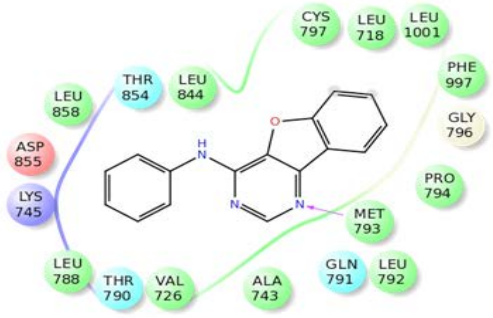
Clinically validated FDA approved drug Erlotinib, a small molecule inhibitor of EGFR was taken asthereference standard, and it showed IC50 of 7.1nM, IC50 of ID-5934507 was determined at varying concentrations ranging from 10 to 4000nM given in figure 5. IC50 of ID-5934507 was 3.483µM and other 4 molecules showed negligible anti-cancer EGFR kinase activity but can be active for inflammation caused by EGFR (Fang Q et al., 2016).

ii) Molecular dynamics simulation

MD studies were carried out on molecule ID 5934507 showing anti-cancer activity for EGFR enzyme in invitro studies to know the stability of complex. On analysing the MD simulation run, it was identified that the Lys745 and Thr854 amino acid residues were indirectly interacting with the molecule via forming H-bonding with the water residues, these interactions persists for 33% and 93% respectively during the simulation run of 20ns. Met793 was the only amino acid residue which forms direct H-bonding with the N-atom of the aromatic ring for 42% while the simulation. The RMSD plot of protein ligand complex showed that the RMSD of protein was 2.7A° greater than that of ligand ~2 A° thus forms a stable complex. From viewing the interaction between protein-ligand complex before and after the MD simulation it was identified that Met793 showed interaction in both case whereas two more interactions were seen after MD with Lys745 and Thr854. These H-bonding interactions with lesser RMSD of ligand with protein prove the stability of the protein-ligand complex depicted in figure 4.2.1. As this moiety was already reported for anti EGFR inhibition but for the first time we are providing the stability of this molecule in complex with EGFR proteinand the suggested lead optimization studies gives the rational to medicinal chemistry to design better inhibitors with higher potency for EGFR.



a)



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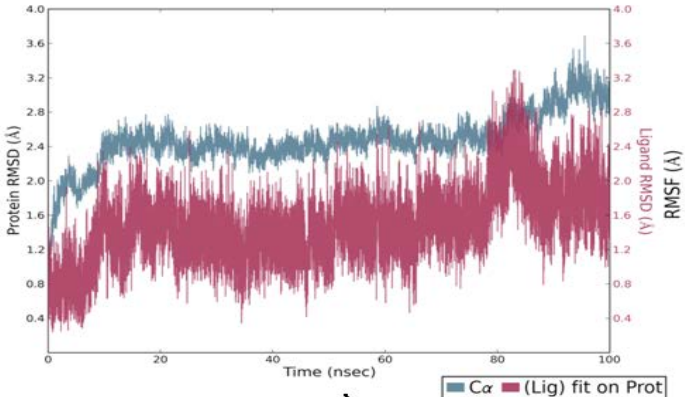

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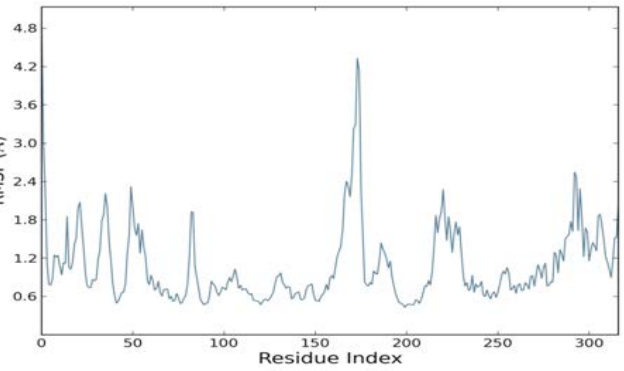

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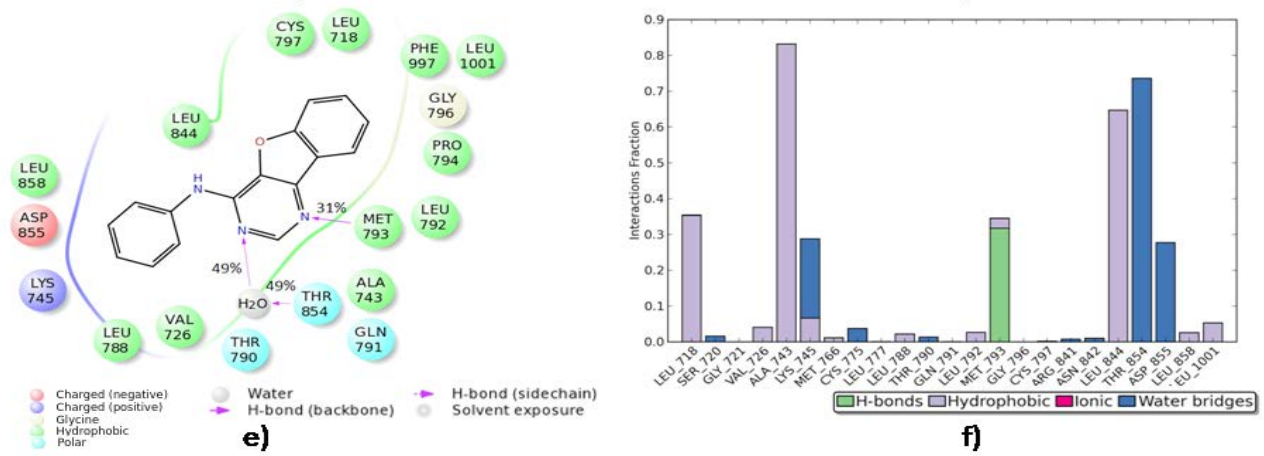


Figure 4.2.1. MD simulation studies on Id 5934507 a) 2D structure of molecule Id 5934507, b) protein-ligand interaction diagram before MD run, c) RMSD plot of protein backbone and ligand, d) RMSF plot of protein backbone, e) A detailed protein-ligand interaction diagram after MD run with protein residues interacting more than 30% during the simulation and f) Interaction plot of contacts occurs between protein and ligand during the simulation run of 100ns.

4.3 Updation of Stem cell database (MedchemDB)

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

In continuation to our earlier efforts towards the development of MedchemDB, which is a systematic compilation of various pathways, crystal structures and target details related to the stem cell research, further activities have been carried out for improving the database. During the reporting period, 51 new crystal structures of various targets, and 89 new scaffolds of reported inhibitors have been added and the database is being regularly updated which is available at http://medchemdb.iiim.res.in/.

4.4 Repository database updation and compound flow management

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

During the reporting period 40 Natural Products and 79 new chemical entities from the med chem projects have been added to the repository along with the HPLC/HPTLC profile. All these compounds are also incorporated into the database for sub-structural search. The outcome of this compound repository in various Institutional discovery activities is highlighted in figure 4. A total of 1471 compounds were issued for biological evaluation within the Institute.

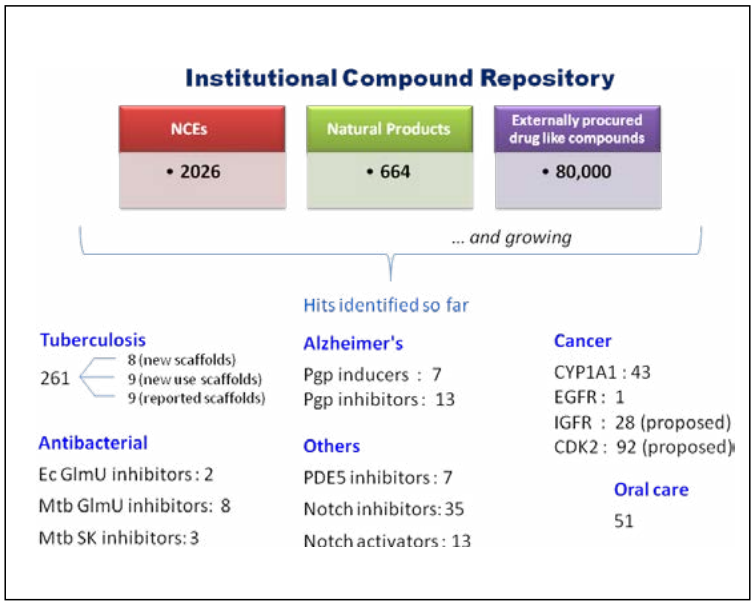


Figure 4.4.1. Discovery outcome of the Institutional compound repository

5.0 BIOORGANIC CHEMISTRY

5.1 Novel xanthones and biologically active secondary metabolites from *Codonopsis ovata*

A. A. Dara, N. A. Dangroo, A. Raina, A. Qayum, S. K. Singh, P. L. Sangwan

Codonopsis ovata Benth., locally known as 'Ludut", is an important medicinal plant native to Asia, typically found at an altitude of 3000-4200 m in the Western Himalayan region (Dar et al., 2014). The roots and leaves of this plant are used for the treatment of wounds, poultice for bruises, ulcers, and skin disinfectants by the Indian System of Medicine (ISM) (Varma and Tandon, 1989; Chopra et al., 1986). The alcoholic extract of this plant is reported to possess significant oxytocic and antifertility properties (Varma and Tandon, 1989). Recently, we reported quantitative analysis of eight secondary metabolites and their antioxidant profile by HPTLC (Dar et al., 2014). The traditional folklore applications of *C. ovata* and our preliminary work prompted us to perform a thorough chemical investigation of the whole plant. Therefore, systematic studies of the chemical constituents of the whole *C. ovata* plant and their cytotoxic activity against six human cancer cell lines were performed. Herein, the isolation, structural elucidation and cytotoxic activity of five new xanthones (1-5) together with 21 known secondary metabolites (6-26) (Dar et al., 2014) (Fig. 5.1.1) from the CH2Cl2-MeOH extract of *C. ovata* are reported. All isolated metabolites were screened for cytotoxic activity against six human cancer cell lines by SRB assay.

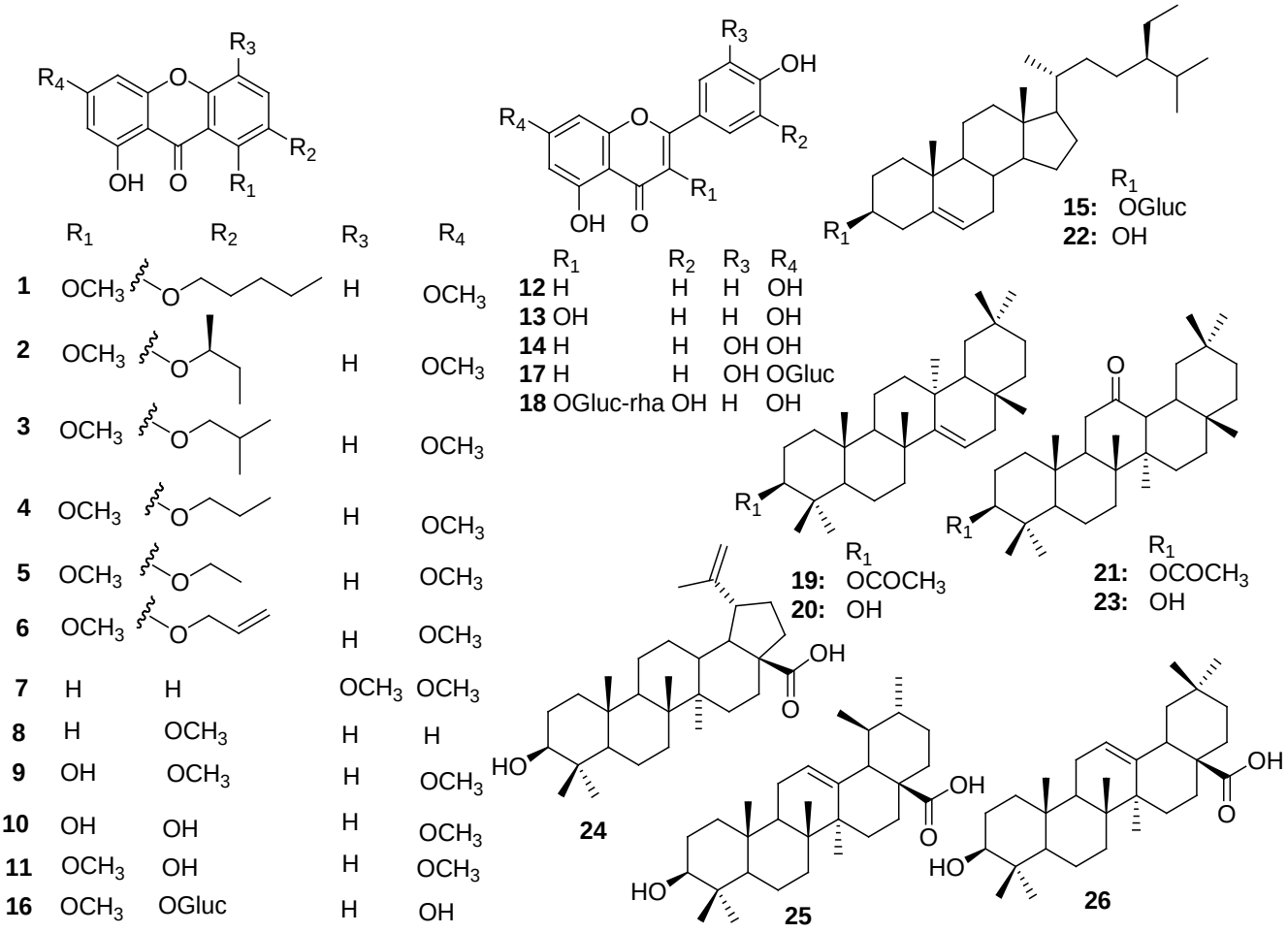


Fig. 5.1.1 Structures of compounds 1-26

Five new xanthones, named coxanthones A-E (1-5), together with 21 known secondary metabolites (6-26) that include seven xanthones, five flavonoids, two steroids and seven triterpenoids were isolated from the chemically unexplored whole plant Codonopsis ovata. The structures of new metabolites were elucidated by HRMS, interpretation of NMR spectra and other spectroscopic techniques. The absolute configuration of the stereogenic centre of coxanthone B (2) was determined by electronic circular dichroism (ECD) spectroscopy. This is the first report of xanthones from the genus Codonopsis. All isolated metabolites were evaluated for

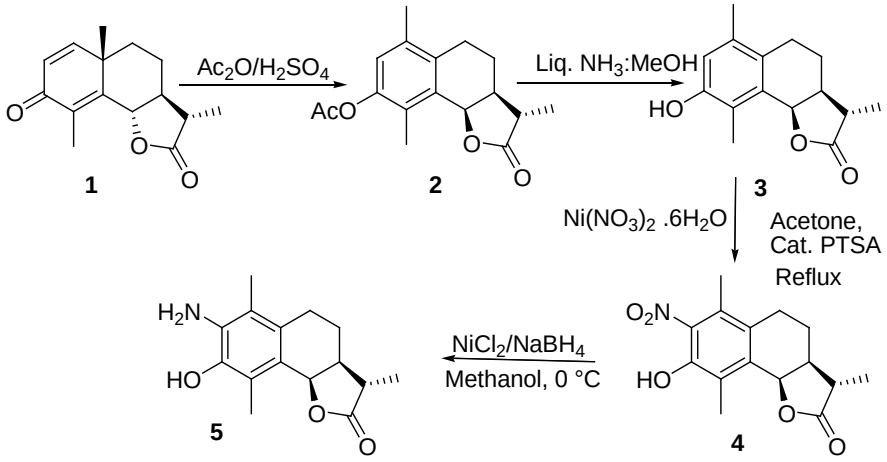
cytotoxic activity by SRB assay against six human cancer cell lines A549 (lung), PC-3 (prostate), HCT-116 (colon), MCF-7 (breast), SF-295 (CNS), and MDAMB-435 (melanoma). Among the new compounds, coxanthone B (2) exhibited significant inhibitory activity against SF-295 and MDAMB-435 with IC50 values of 7.0 and 15.0 µM, respectively. Coxanthone A (1) displayed cytotoxicity against A549 cell line at IC50 value of 22.5 µM. Cytotoxic activity of 1-hydroxy-3,5-dimethoxyxanthone (7), swertiperenine (9) and 1,7,8-trihydroxy-3-methoxyxanthone (10) are reported here first time that exhibited the IC50 values of 3.0, 5.0 and 21.0 µM against A549, MDAMB-435, and A549 cell lines, respectively. Kaempferol (13) showed most potent cytotoxic activity with an IC50 values in the 1.0-2.3 µM range against all tested cancer cell lines.

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

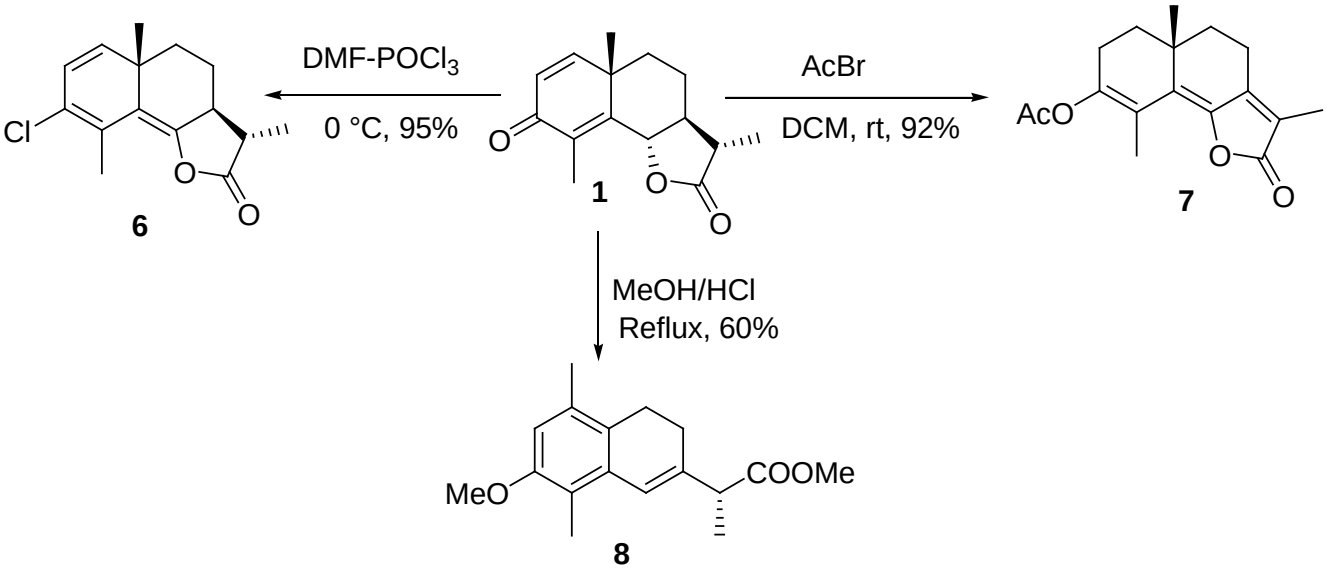
P. K. Chinthakindi, Jasvinder Singh, Shilpa Gupta, Amit Nargotra, Priya Mahajan, Anupurna Kaul, Zabeer Ahmed, Surrinder Koul, P. L. Sangwan

α-Santonin 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 was subjected to Thiele reaction (rearrangement) with Ac2O/H2SO4 to get acetyl α-desmotroposantonin which on deacetylation afforded α-desmotroposantonin, the latter on nitration using nickel nitrate (II) hexahydrate in acetone/p-TSA resulted in the formation of 2-nitro α-desmotroposantonin (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 NiCl2/NaBH4 afforded 2-amino-α-desmotroposantonin 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.

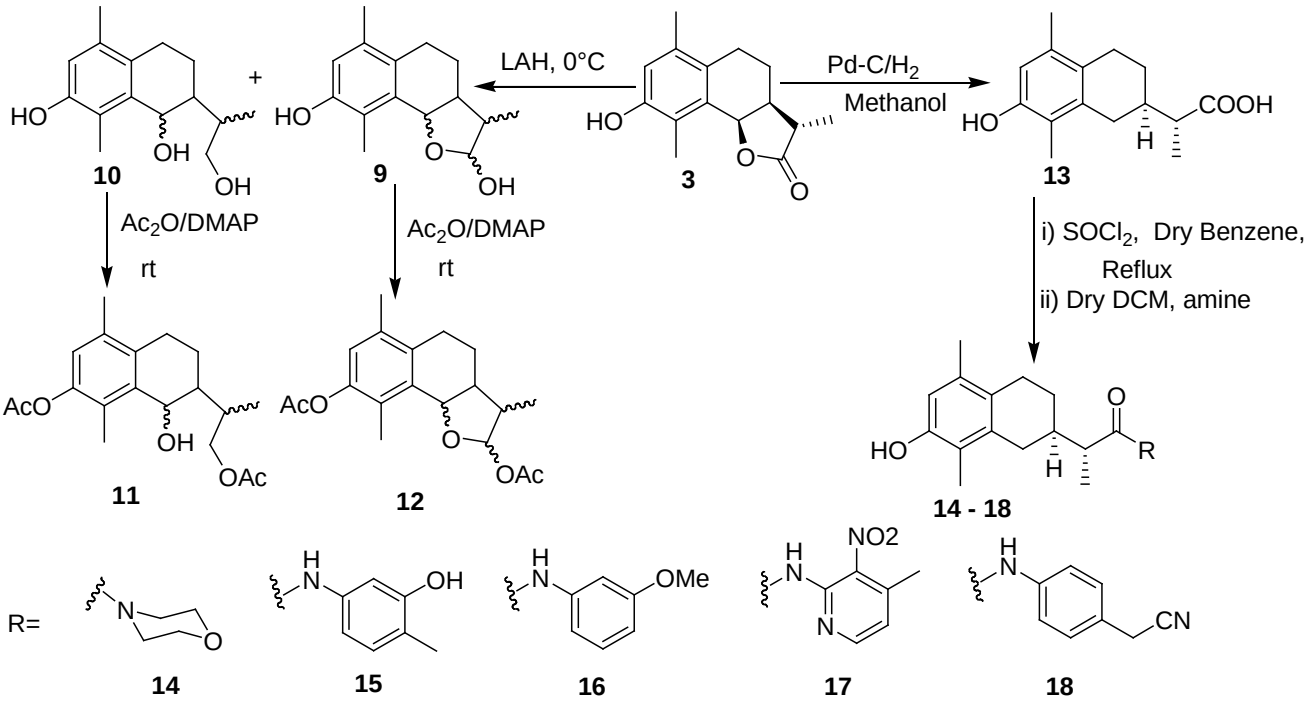
DMF-POCl3 reaction of 1 at 0°C resulted in the formation of 8-chloro-3, 5, 9-trimethyl-tetrahydronaphtho furan-2(3H)-one involving modification in the ring A and B of α-santonin. 1H NMR of 6 showed signals for olefinic proton at δ 5.81 along with disappearance of typical IR band at 1680 cm-1 for enone carbonyl group of 1. Further confirmation was obtained by mass spectrum showing m/z [M+] at 265 and 267. Reaction of α-santonin with acetyl bromide in DCM resulted in the formation of a rearranged product 3,5,9-trimethyl-2-oxo-hexahydronaphtho-furan-8-yl acetate. Compound 7 showed signals for three methyl groups as singlet at δ 2.0, 1.89 and 1.15 respectively in 1H NMR spectrum and disappearance of band due to enone carbonyl in ring A and observance of band at 1753 cm-1 for carbonyl group of –O-CO-CH3 in IR spectrum. Further, [M+] m/z at 289 in mass spectrum and carbon signals in 13C NMR supported the assigned structure of 7. The reaction sequence for the preparation of 6 and 7 is shown in Scheme-2. Modification was carried out in the lactone part (ring C) of compound 1 by refluxing α-santonin with HCl/MeOH which led to the formation of 8 (Scheme 2). The product 8 in its 1H NMR spectrum showed signal for olefinic proton at δ 6.47, in IR spectrum a band for ester carbonyl at 1725 cm-1 and in mass spectrum [M+] m/z at 274. Spectral data including 13C NMR confirmed the assigned structure of 8 as methyl-2-(7-methoxy-5,8-dimethyl-3,4-dihydronaphthalen-2-yl) propanoate. The product was identified as 2-(aryl) propanoic acid and belongs to the NSAID group of compounds.



Scheme 5.2.1. Structural modification of ring A: Preparation of α-santonin derivatives 2-5.

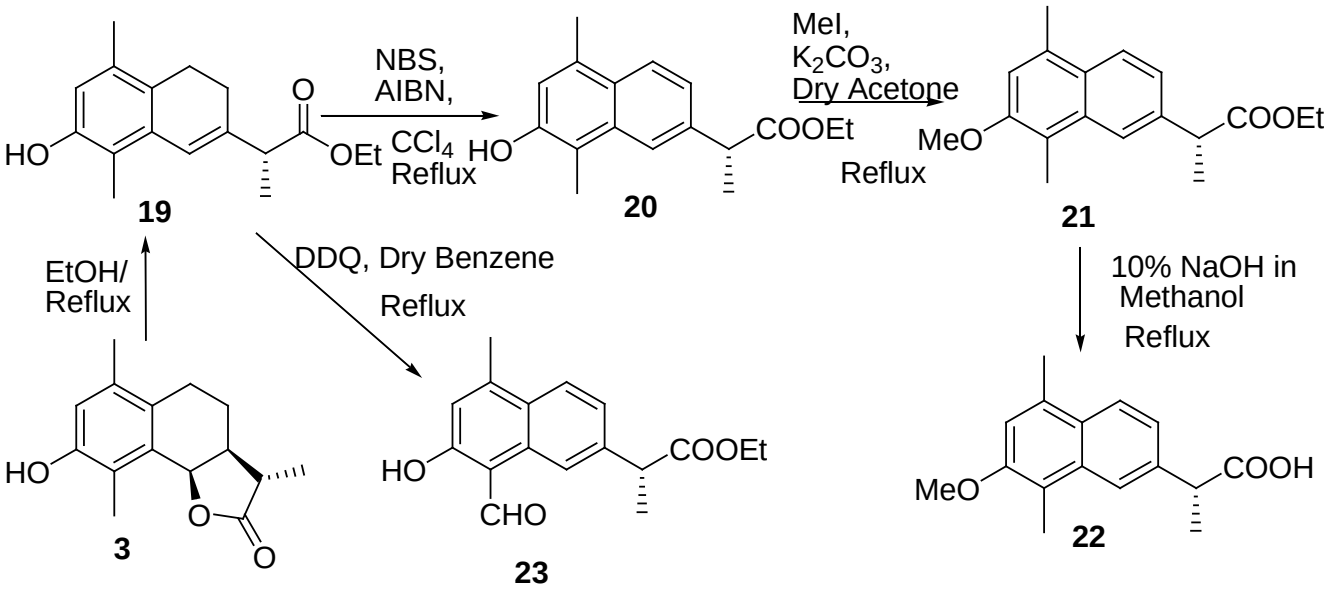


Scheme 5.2.2 Structural modification at ring-A, B and C: Preparation of α-santonin derivatives 6–8. Further structural modification of compound 3 was carried out by LAH reduction to afford a mixture of 9 (diol) and 10 (triol) (Scheme 3) which after purification and subsequent acetylation afforded respective di- and tri-acetylated derivatives 11 and 12. The structure of products (9-12) was confirmed by IR, 1H, 13C NMR and mass spectral data. Hydrogenation of α-desmotroposantonin (3) in methanol-Pd/C resulted in the formation of product 13, identified as 2-(7-hydroxy-tetrahydronaphthalen-2-yl) propanoic acid. Treatment of 13 with thionyl chloride in dry benzene followed by coupling with appropriate amines in dry DCM, afforded the respective amides (14-18) (Scheme 3). The structures of the resulting amides were confirmed by IR (bands for amide carbonyl observed at 1685-1660 cm-1), NMR and mass spectra.



Scheme 5.2.3. Structural modification in lactone ring of α-desmotroposantonin (3): Preparation of compounds 9-18. Refluxing of 3 in ethanolic hydrochloric acid solution after usual workup afforded ethyl (7-hydroxy-dihydronaphthalen-2-yl) propanoate (19). The structure of the product was confirmed by spectral data and X-ray crystallography. To find out the role of saturation/ unsaturation in ring B of the 2-(tetrahydro naphthalene) propanoic acid (13), unsaturated 2-(substituted naphthyl) propanoic acids/esters (19-23) were prepared by following Scheme 4. Reaction of 19 with NBS in CCl4 using AIBN as a radical initiator afforded ethyl 2-[7-(hydroxy-dimethylnaphth-2-yl)] propanoate (20), and its methylated product (21). The latter on saponification and subsequent acidification afforded [2-(7-methoxy-5,8-dimethyl-1-napthyl)] propanoic acid (22) which is dimethyl substituted positional isomer of naproxen [26] and in true sense a mimic of NSAID drug naproxen. The structure of 22 was confirmed by 1H NMR where four aromatic proton signals were observed at δ 7.9, 7.84, 7.35 and 7.08. Bands for carbonyl group (COOH) observed at 1675 and 1257 cm-1 in IR spectrum and M+ m/z at 260 in its mass spectrum.

Reaction of 19 with DDQ in dry benzene afforded ethyl (5-formyl-hydroxy-methylnaphth-2-yl) propanoate (23). In 1H NMR spectrum, four aromatic proton signals were observed at δ 8.26, 7.93, 7.43, 6.98 and a signal for aldehyde proton at δ 10.76. In IR spectrum, bands for phenolic OH and carbonyl group (CHO) observed at 3391 and 1705 cm-1 respectively. Observance of [M+] m/z at 287 further confirmed the assigned structure.

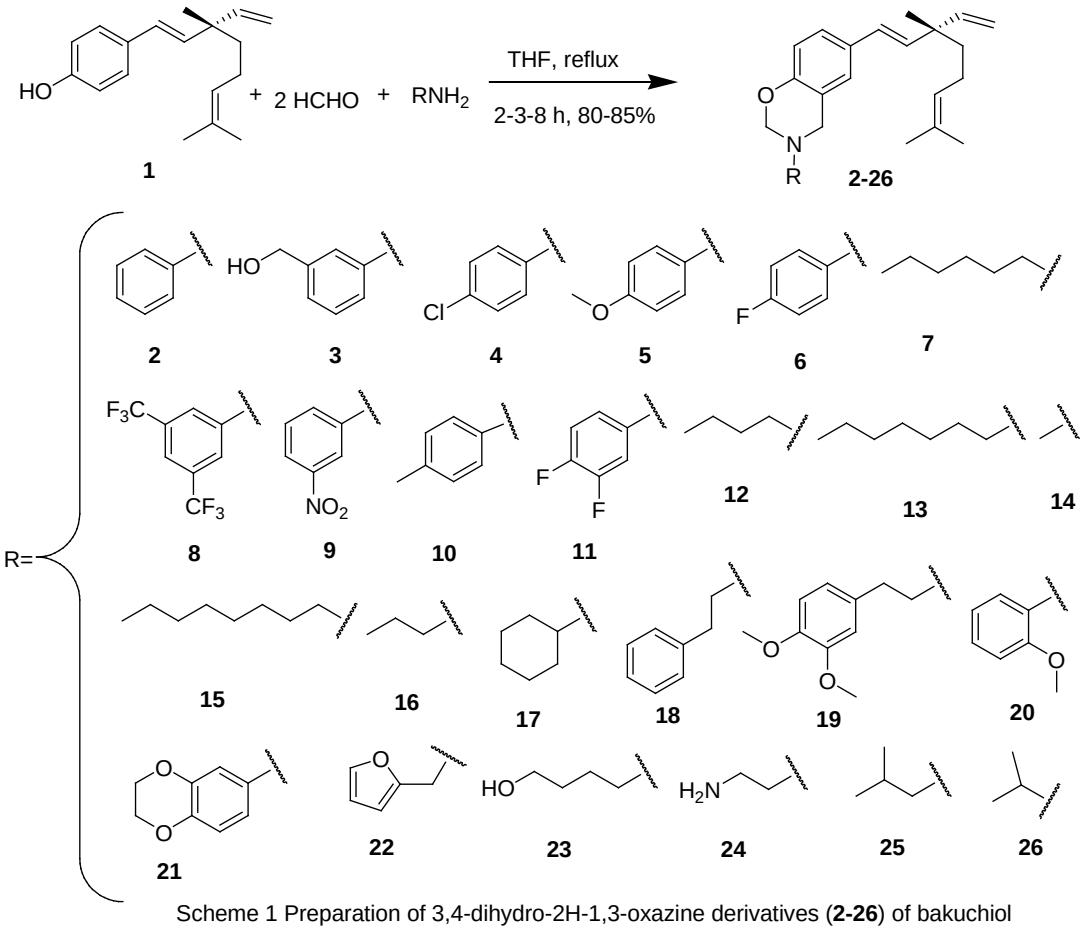


Scheme 5.2.4 Structural modification of α-desmotroposantonin (3): Preparation of compounds 19-23 The compounds from α-santonin was synthesized and tested against Con-A induced T-cell proliferation and LPSinduce B-cell proliferation via MTT assay. The study resulted in the identification of potent immunosuppressant molecules, which were further screened along with α-santonin for Tumor Necrosis Factor Alpha (TNF-α) inhibitory activity. One of the molecules (7) at 10 µM showed equipotency to that of dexamethasone (1 µM conc.) used as a standard. Structure activity relationships of the synthesised compounds along with our earlier reported α-santonin derivatives have been studied. Inferences from the modifications carried out at all the three sites of α-santonin have been elaborated. Computational study of the active compounds shows TNF-α protein as its preferable target rather than Inosine Monophosphate Dehydrogenase (IMPDH).

5.3 Synthesis and anti-proliferative evaluation of novel3,4-dihydro-2H-1,3-oxazine derivatives of bakuchiol

Nidhi Gupta, Sonia Sharma, Arun Raina, N. A. Dangroo, Shashi Bhushan, P. L. Sangwan

Bakuchiol 1 was isolated in preparative scale from seeds of *Psoralea corylifolia* and taken for structural modification. The 3,4-dihydro-2H-benzo[e] [1,3]oxazines analogs (2-26) were prepared by treatment of 1 with 37% formaldehyde (w/v) and respective primary amines in tetrahydrofuran (THF) via Mannich type condensation-cyclization reaction (scheme 1) in good to excellent yields. Structures of all the derivatives were confirmed by spectroscopic techniques (1H NMR, 13C NMR, IR and HRMS). In 1H NMR, characteristic singlet of two methylene protons of 1, 3-oxazine ring appeared in the range of δ 3.8-4.6 and δ 4.6-5.3 correspond to Ar–CH2–N and O–CH2–N groups respectively. In 13C NMR, Ar–CH2–N carbon appeared at δ 51 and O–CH2–N carbon appeared at δ 81. The IR spectrum showed the characteristic absorption peaks of benzoxazine ring structure at 1230 cm-1 correspond to asymmetric stretching of C-O-C and at 1018 cm-1 correspond to symmetric stretching of C-O-C. Also, C-N stretching absorptions were observed in the range of 1200-1400cm-1 with aromatic C-N absorptions at higher frequency than aliphatic. Further confirmation for the formation of derivatives 2-26 was also done by HRMS data.



Scheme 1 Preparation of 3,4-dihydro-2H-1,3-oxazine derivatives (**2-26**) of bakuchiol

Cell growth inhibition: Based on the % growth inhibition. The IC50 of selected compounds are calculated and provided in Table 2. The promising IC50values (2.0 to 7.0 µM) were observed for compounds 7, 12-19 and 23-26 against all the cell lines examined (HL-60, MIA-Pa-Ca-2, MCF-7 and HCT-116). The compound 15 showed better cytotoxic profile (2.0 to 3.0 µM) against all the selected cell lines. The pancreatic cell line (MIA-Pa-Ca-2) proved most sensitive (2.0 to 3.0 µM) towards semi-synthetic analogs in particular compound 15 exhibited maximum cytotoxic effect with IC50 value 2.0 µM and hence chosen for further cell death mechanistic study. Compound 15 increases sub-G1 (G0) apoptotic population in MIA-Pa-Ca-2 cellsThe extent of apoptotic cell death in MIA-Pa-Ca-2 cells was assessed using flow cytometry through determination of sub-G1 cell population by propidium iodide (PI) staining. As depicted in Fig.1, the percentage of apoptotic cells exposed to compound 15 increased in a concentration-dependent manner after 24 h of incubation. The sub-G1 (G0) apoptotic population was found to be 3, 4 and 25% following 1, 3 and 10 µM concentration of compound 15 treatment compared to control (untreated cells- 2%).

Table 5.3.1. Ic50 values in µM of bakuchiol and its selected analogs on selected human cancer cell lines.

Compound	Breast MCF-7	Pancreatic MIA-Pa-Ca-2	Colon HCT-116	Leukemia HL-60
1	>10	>10	>10	>10
7	3	3	3.6	6
12	3.6	3	5.5	5
13	3	2.5	2.5	6
14	6	3	6.5	7
15	2.4	2	2	3
16	5.2	3	4	6
17	3.6	3	3	3
18	5	3	3.7	3
19	3.2	3	2.5	3
23	6	3	6	3
24	6	3	3.7	4
25	6	3	3.8	5
26	3	3	4	6

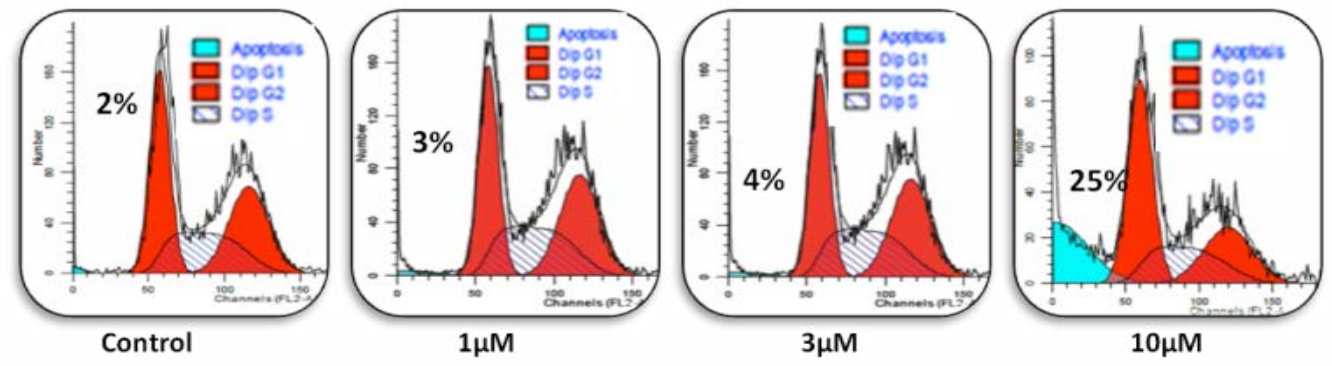


Figure 5.3.1 MIA-Pa-Ca-2 cells (2 × 106) were seeded in 6-well plates and treated with different concentrations of compound 15 (1µM, 3 µM, and 10 µM) for 24 h to determine DNA fluorescence and cell cycle phase distribution as described in experimental section. Data were analyzed by Modfit software (Verity Software House Inc., Topsham, ME) for the proportions of different cell cycle phases. The fraction of cells from apoptos s, G1, S and G2 phases analyzed from FL2- A vs. cell counts are shown in %. Data are representative of one of three similar experiments.

Compound 15 induces apoptotic bodies

The pancreatic cancer cells (MIA-Pa-Ca-2) were treated with compound 15 at 1, 3 and 10 µM concentrations for 24 h and observed under microscope for any morphological changes that occur during apoptosis. Simultaneously, nuclear morphology was analyzed through Hoechst staining. Characteristic changes of apoptosis such as nuclear condensation, membrane blebbing and formation of apoptotic bodies were observed in the morphology of treated cells in a concentration-dependent manner, whereas the nuclei of untreated cells were found to be of normal intact morphology (Fig. 5.3.2). The results suggested that compound 15 was able to induce apoptotic cell morphology in MIA-Pa-Ca-2 cells

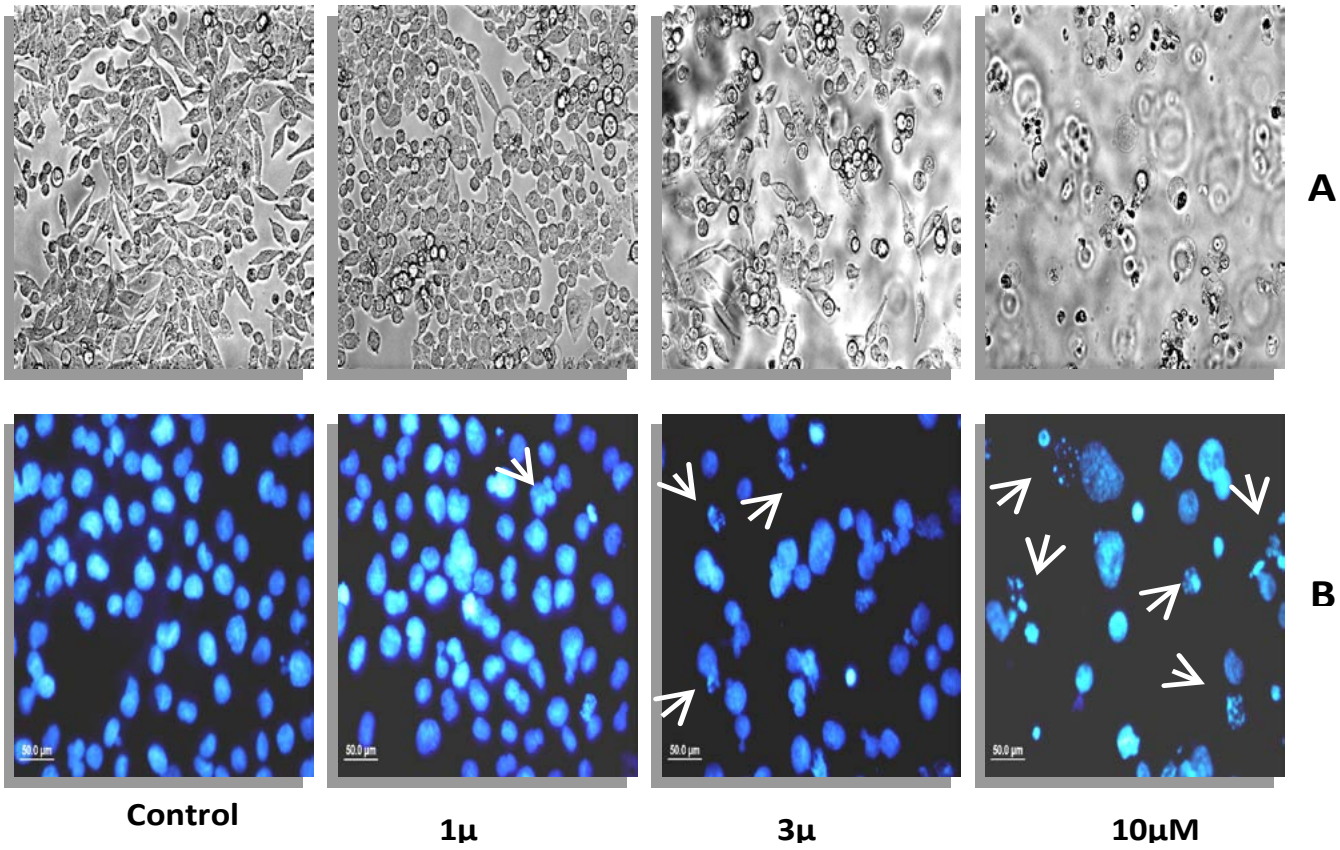


Fig. 5.3.2 Effect of compound 15 on cellular and nuclear morphology of MIA-Pa-Ca-2 cells. Cells were visualized for cellular and nuclear morphology as described in experimental section. Condense nuclei and the apoptotic bodies are indicated by white arrows. Data are representative of one of three similar experiments and magnification of the pictures was 30X on Olympus 1X 70 inverted microscopes.

Compound 15 triggers mitochondrial membrane potential loss

Mitochondrial membrane potential (MMP) loss is a key step in the induction of apoptosis in cancer cells. Loss of MMP leads to depolarization of mitochondrial membrane resulting in mitochondrial dysfunctioning and ultimately a cell death. Disruption of mitochondrial membrane releases a variety of proteins that activates procaspase cascade inside the cells and triggers apoptosis.21 The MMP loss in treated and untreated cells is measured by rhodamine-123 dye (Rh-123) which is reduced by healthy mitochondria into fluorescent probe whose fluorescence is measured by flow cytometer in FL-1 channel. Compound 15 caused MMP loss in concentration dependent manner (Fig.3). At 1 and 3 µM concentrations, it caused 4% and 9% loss of mitochondrial membrane potential respectively while at 10 µM concentration, it caused 94% loss in mitochondrial membrane potential.

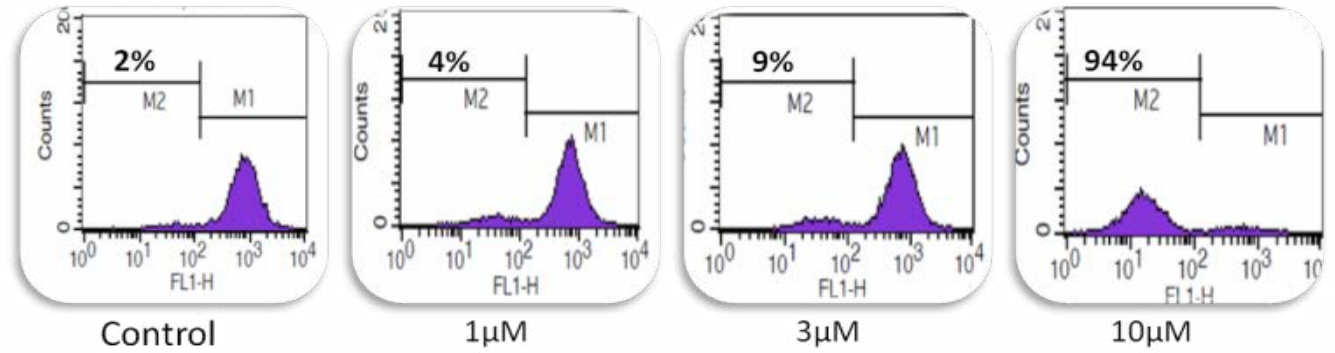


Fig. 5.3.3. Compound 15 induced mitochondrial potential loss in pancreatic cancer MIA-Pa-Ca-2 cells. Cells were treated with compound 15 at 1, 3, and 10 µM concentration for 24 h time period. Thereafter, cells were stained with Rhodamine-123 (200 nM), added 40 min before experiment termination and analyzed in FL-1 channel of flow cytometer. Data are representative of one of three similar experiments

Compound 15 triggers extrinsic and intrinsic apoptosis in MIA-Pa-Ca-2 cells

Compound 15 caused mitochondrial membrane potential loss. Damaged mitochondria relay signals to downstream elements that further initiate intrinsic apoptotic signals. During apoptosis, cytochrome c is released from the mitochondria which form an essential part of apoptosome. This results in the activation of caspase-9 which then processes and activates other caspases.22 Role of caspases (family of intracellular cysteine proteases) in apoptosis is well known and active caspase-8 or -9 activate various effector caspases -3, -6 and -7 which cleaves the several key proteins required for cellular functioning and survival and PARP-1 is one of the several known substrates of caspases. Cleavage of PARP-1 by caspases is considered as a hallmark of apoptosis.23 Compound 15 activated these caspases and PARP-1 cleavage. It inhibited both procaspase-9 and procaspase-8, which indicates that compound 15 triggers apoptosis via both extrinsic and intrinsic pathways in MIA-Pa-Ca-2 cells (Fig. 5.3.4).

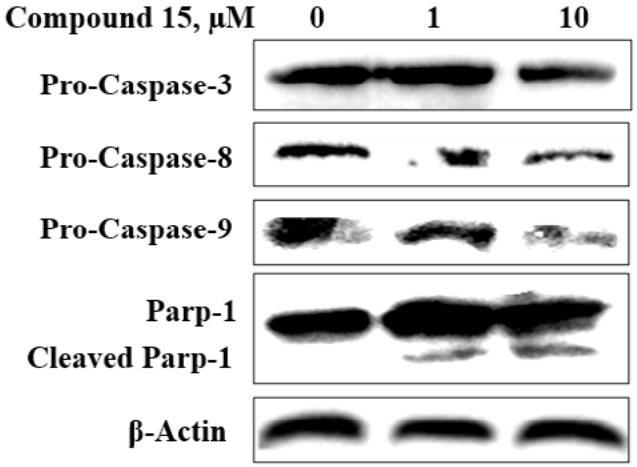
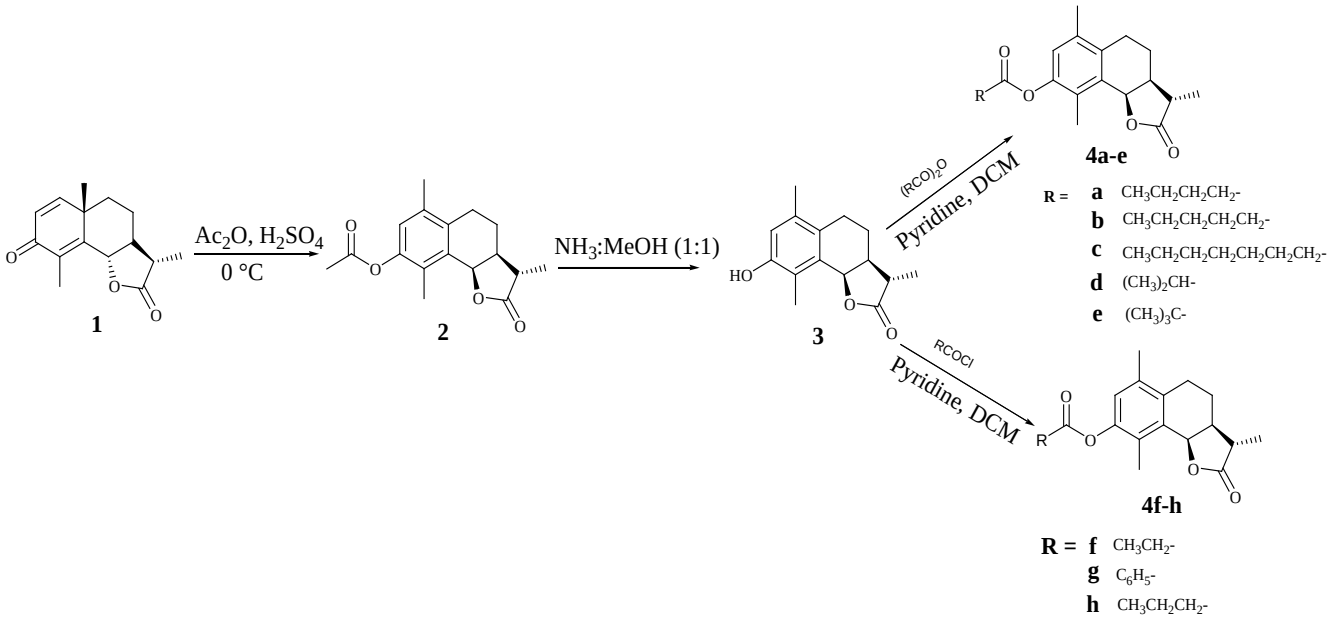


Fig. 5.3.4. Influence of compound 15 on the expression of important proteins involved in the initiation of apoptosis. Cells were treated with 1 and 10 µM concentrations of compound 15 for 24 h. Protein lysates were prepared and electrophoresis as described in Experimental section. β-actin was used as an internal control to represent the same amount of proteins applied for SDS-PAGE. Western blot analyses of the indicated proteins were performed in the whole cell lysate. Data are representative of one of three similar experiments.

5.5 T- and B-cell immunosuppressive activity of novel α-santonin analogs with humoral and cellular immune response in Balb/c mice

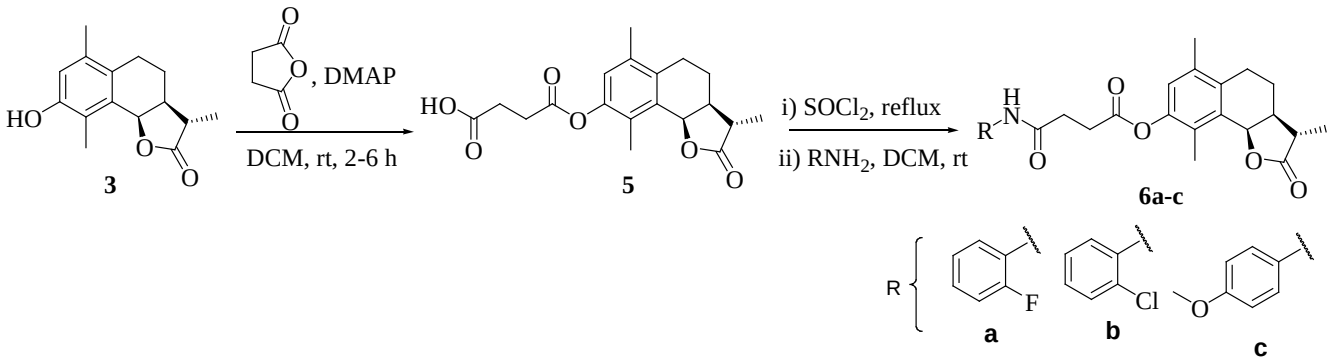
N. A. Dangroo, Jasvinder Singh, Nidhi Gupta, Shashank Singh, A. Kaul, P. L. Sangwan

NP santonin 1 was subjected to dienone phenone type reaction using Ac2O/H2SO4 to get acetyl α-desmotroposantonin 2, which on deacetylation in NH3: MeOH furnished α-desmotroposantonin 3. The ester analogs 4a-e were prepared by treating 3 with appropriate anhydride in dry dichloromethane (DCM) in presence of pyridine at room while analogs 4f-h were synthesized by treatment of 3 with appropriate acid chloride in dry dichloromethane in good to excellent yields (scheme 5.5.1).



Scheme 5.5.1 Synthetic route for compounds 4a-h

Compound 5 was prepared by reacting 3 with succinic anhydride in dry DCM by employing different bases like NaHCO3, K2CO3, pyridine, Et3N, dimethyl amino pyridine (DMAP) and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU). However, best results were obtained in DMAP. Compound 5 on reaction with SOCl2 in dry DCM at refluxing resulted in situ generation of acid chloride, followed by the addition of appropriate amine afforded compounds 6a-c (scheme 5.5.2).

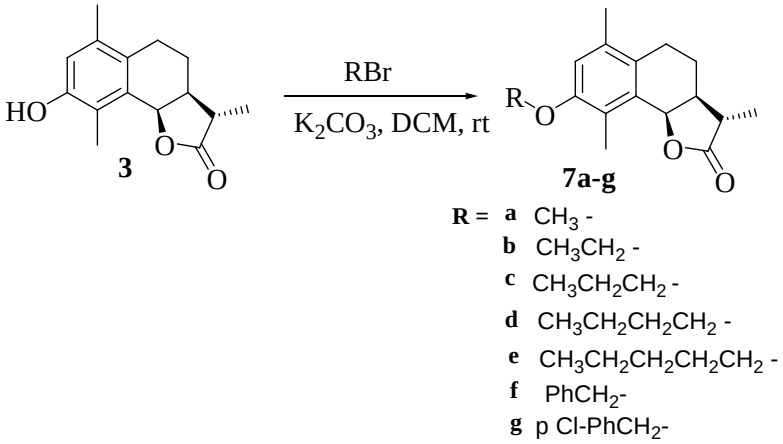


Scheme 5.5.2 Synthetic route for compounds 6a-c

Ether analogs were synthesised by the treatment of 3 with different alkyl halides in DCM in the presence of pyridine at room temperature to afford 7a-g (scheme 3). All the analogs were characterized by 1H NMR, 13C NMR and HRESIMS.

In summary, a series of new α-santonin derived O-aryl/ aliphatic ether, ester and amide derivatives were synthesised. All the compounds were investigated for their in vitro immunosuppressive effect on T- and B-lymphocyte of BALB/c mice. Many analogs showed strong inhibition against Con-A and LPS stimulated T-cell and B-cell proliferation in a dose

dependent manner. The screening data revealed that the presence of carbonyl group and appropriate aliphatic side chain play important factors toward contribution of high immunosuppressive potency in these analogs. More interestingly, compounds 4c, 4d, 4e and 4h exhibited potent in vitro activity and the compound 4e revealed the most immunosuppressive effects. Further, compound 4e was investigated for in vivo delayed-type hypersensitivity (DTH) reaction and antibody production in BALB/c mice models. The in vitro and in vivo immunosuppressive activity suggested that compound 4e suppressed both humoral and cell mediated immunity.

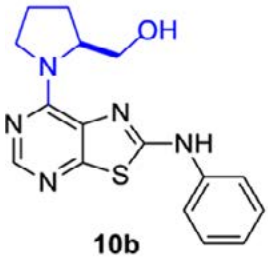


Scheme 5.5.3 Synthetic route for compounds 7a-g

6.0 MEDICINAL CHEMISTRY

6.1 Discovery of 7-(prolinol-N-yl)-2-phenylamino-thiazolo[5,4-d]pyrimidines as novel non-nucleoside partial agonists for the A2A adenosine receptor

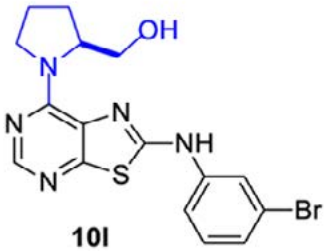
Bharate SB, Singh B, Kachler S, Oliveira A, Kumar V, Bharate SS, Vishwakarma RA, Klotz KN, Gutiérrez de Terán H. J. Med. Chem. 2016, 59, 5922-5928



10b

A_{2A}: *Ki* = 200 nM
A_1: *Ki* = 555 nM
A_3: *Ki* = 978 nM

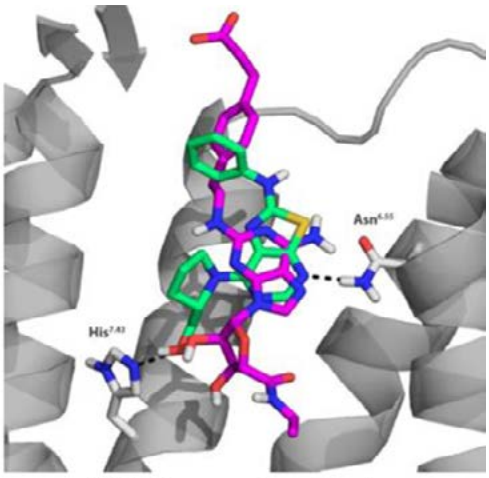
S_{water} = 4.3 mg/ml
CLogP: 3.21



10l

A_{2A}: *Ki* = 153 nM
A_1: *Ki* = 530 nM
A_3: *Ki* = 1070 nM

S_{water} = 0.16 mg/ml
CLogP: 4.08



10b (green) with A_{2A}

We describe the identification of 7-(prolinol-Nyl)-2-phenylamino-thiazolo[5,4-d]pyrimidines as a novel chemotype of non-nucleoside partial agonists for the A2A adenosine receptor (A2AAR). Molecular-modeling indicated that the (S)-2-hydroxymethylene-pyrrolidine could mimic the interactions of agonists' ribose, suggesting that this class of compounds could have agonistic properties. This was confirmed by functional assays on the A2AAR, where their efficacy could be associated with the presence of the 2-hydroxymethylene moiety. Additionally, the best compound displays promising affinity, selectivity profile, and physicochemical properties.

6.2 A chromatography-free isolation of rohitukine from leaves of *Dysoxylum binectariferum*

Kumar, Vikas; Guru, S.K.; Jain. S.K.; Joshi, P.; Gandhi, S.G.; Bharate, S.B.; Bhushan, S.; Bharate, S.S.; Vishwakarma, R.A. Bioorg. Med. Chem. Lett. 2016, 26, 3457-3463

Rohitukine is a chromone alkaloid isolated from an Indian medicinal plant *Dysoxylum binectariferum*. This natural product has led to the discovery of two clinical candidates (flavopiridol and P276-00) for the treatment of cancer. Herein, for the first time we report an efficient protocol for isolation and purification of this precious natural product in a bulk-quantity from leaves (a renewable source) of *D. binectariferum* (>98% purity) without use of chromatography or any acid–base treatment.

6.3. Identification of tetraethyl-2-phenylethene-1,1-diyldiphosphonate as an orally bioavailable P-gp inducer

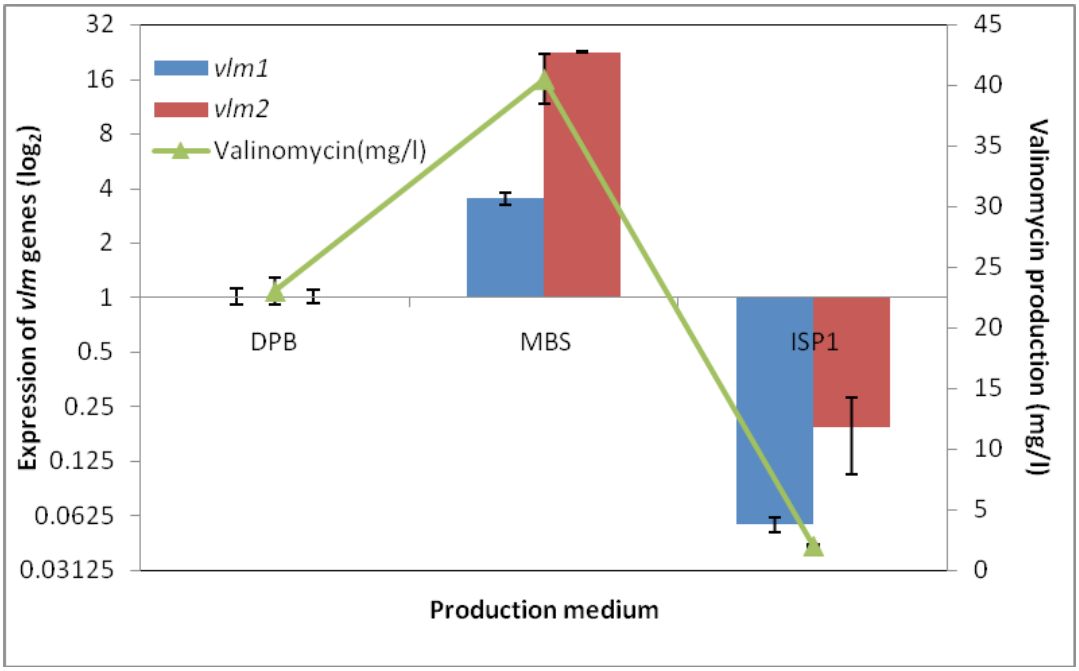
Manda, S.; Wani, A.; Bharate, S.S.; Vishwakarma, R.A.; Kumar, A.; Bharate, S.B. Med. Chem. Commun. 2016, 7, 1910-1915

N-(2,2,2-Trifluoroethyl)-N-[4-[2,2,2-trifluoro-1-hydroxy-1-(trifluoromethyl)ethyl]phenyl]-benzenesulfonamide (T0901317) is a potent activator of pregnane-X-receptor (PXR), which is a nuclear receptor controlling P-gp expression. Herein, we aimed to investigate P-gp induction activity of T0901317 and establish its structure-activity relationship. T0901317 along with a series of N-triazolyl-methylene-linked benzenesulfonamides were synthesized and screened for P-gp induction activity using a rhodamine-123 based efflux assay in the P-gp overexpressing human adenocarcinoma LS-180 cells, wherein several compounds showed potent P-gp induction activity at 5 uM. Treatment with benzene sulphonamides led to the decrease in intracellular accumulation of a fluorescent P-gp substrate rhodamine-123 up to 48% (control 100%). In the western-blot studies, T0901317 and its triazole linked analog 26e at 5 uM displayed induction of P-gp expression in LS180 cells. These compounds were non-toxic in LS-180 and human neuroblastoma SH-SY5Y cells (IC50 > 50 uM). The compound 26e showed significant P-gp induction even at 0.3 mM, indicating an excellent therapeutic window. These results clearly indicate promise of this class of compounds as potential agents to enhance amyloid-beta clearance in Alzheimers patients.

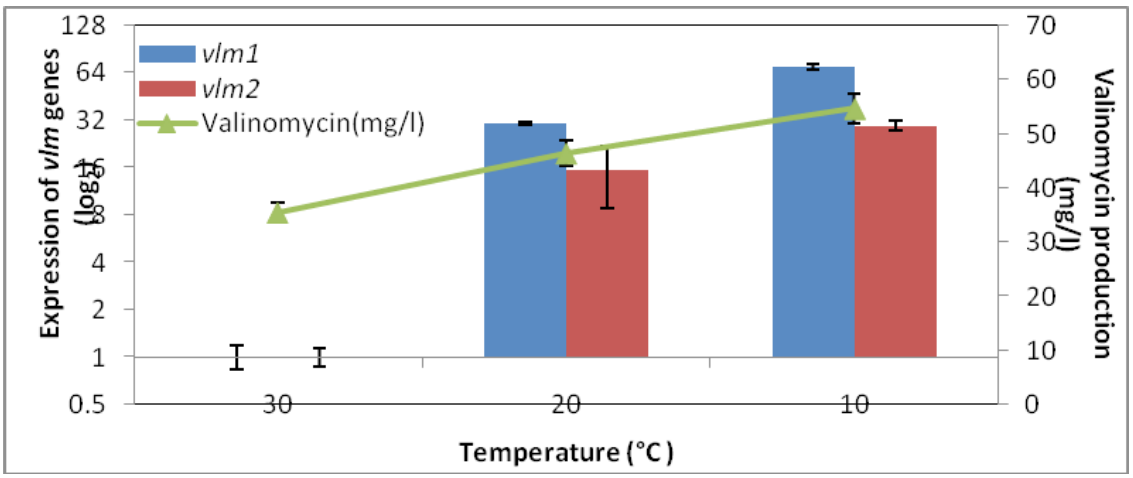
7.0 FERMENTATION

7.1 Revelation and cloning of Valinomycin synthetase genes in *Streptomyces lavendulae* ACR-DA1 and their expression analysis under different fermentation conditions

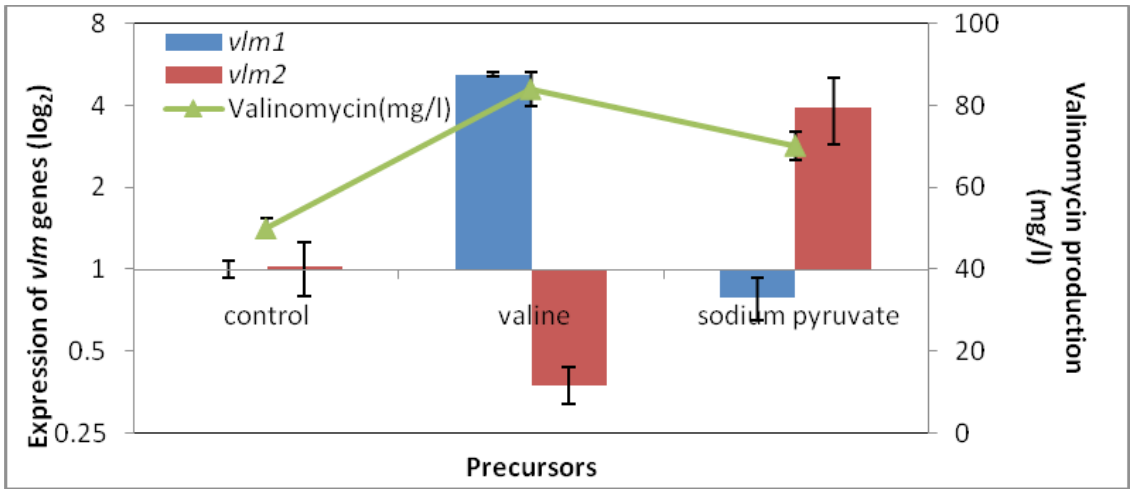
Streptomyces species are amongst the most exploited microorganisms due to their ability to produce a plethora of secondary metabolites with bioactive potential, including several well known drugs. They are endowed with immense unexplored potential and substantial efforts are required for their isolation as well as characterization of their bioactive potential. Unexplored niches and extreme environment are host for diverse microbial species. In this study we report *Streptomyces lavendulae* ACR-DA1, isolated from extreme cold desert of the North Western Himalayas, which produces a macrolactone antibiotic, valinomycin. Valinomycin is a K+ ionophoric non ribosomal cyclodepsipeptide with a broad range of bioactivities including antibacterial, antifungal, antiviral and cytotoxic/anticancer activities. The strain ACR-DA1 was optimized for the production of valinomycin under different fermentation conditions like fermentation medium, temperature and addition of biosynthetic precursors. Synthetic medium at 10°C in the presence of precursors i.e. valine and pyruvate showed enhanced valinomycin production. In order to assess impact of various elicitors, the expression of the two genes viz. vlm1 and vlm2 that encode components of heterodimeric valinomycin synthetase, was analyzed using real time RT-PCR and correlated with quantity of valinomycin using LC-MS/MS.



A



B



C

Fig. 7.1.1: Graphs depicting the valinomycin production in relation to expression levels of vlm1 and vlm2 genes in S. lavendulae ACR-DA1 (a) different production media (b) different temperatures (c) different precursors

7.2. Expression of Fumiquinazoline biosynthetic genes in *Aspergillus fumigatus* (GA-L7) in presence of epigenetic modifier

Formation of fumiquinazoline C involves one unit of L-tryptophan, two units of L-alanine and one non proteinogenic amino acid i.e. L-anthranilate as precursors. As shown in Fig.1 all the precursors are assembled by a trimodular NRPS Afua_6g 12080 to form fumiquinazoline F which further converts to Fumiquinazoline A by the coordinated action of Afua_6g 12060 and Afua_6g 12050. Conversion of Fumiquinazoline A to fumiquinazoline C is finally mediated by a mono-covalent flavoprotein Afua_6g 12070 . Therefore, in order to study, how valproic acid affects fumiquinazoline C biosynthetic genes, their expression profiles were studied in valproic acid treated culture vis-à-vis under normal cultivation conditions.

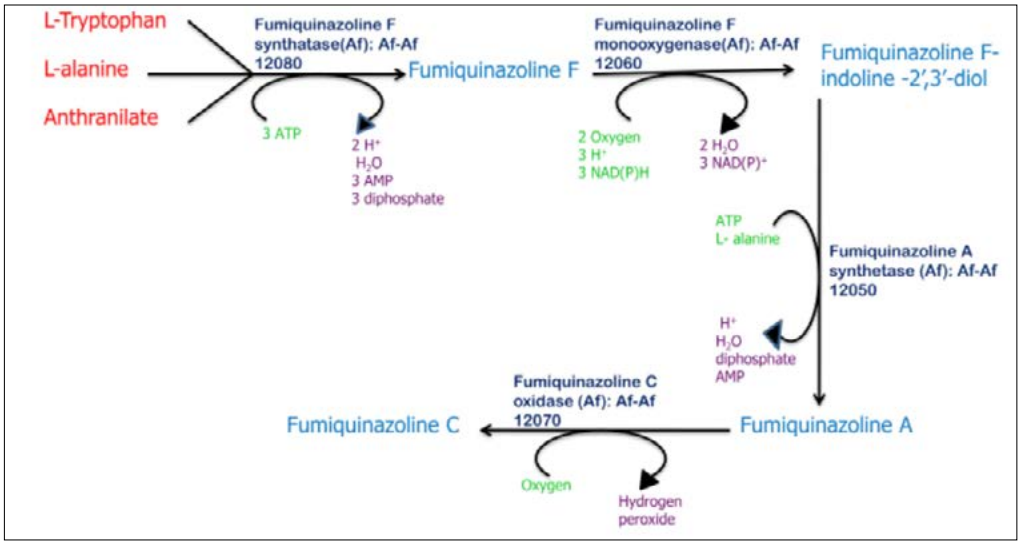


Fig. 7.2.1: Schematic representation of the genes involved in the biosynthesis of fumiquinazoline C

Addition of valproic acid in the growth medium resulted in the alteration of secondary metabolic profile with an enhanced production of a metabolite i.e. fumiquinazoline C by 10 folds. In order to assess the effect of valproic acid on the biosynthetic pthway of fumiquinazoline C, we studied the expression of the genes involved in its biosynthesis, both in the valproic acid treated and untreated control culture. Our results revealed that all the genes i.e. Afua_6g 12040, Afua_6g 12050, Afua_6g 12060, Afua_6g 12070 and Afua_6g 12080, involved in the biosynthesis of fumiquinazoline C were overexpressed significantly by 7.5, 8.8, 3.4, 5.6 and 2.1 folds respectively resulting in overall enhancement of fumiquinazoline C production by about 10 folds.

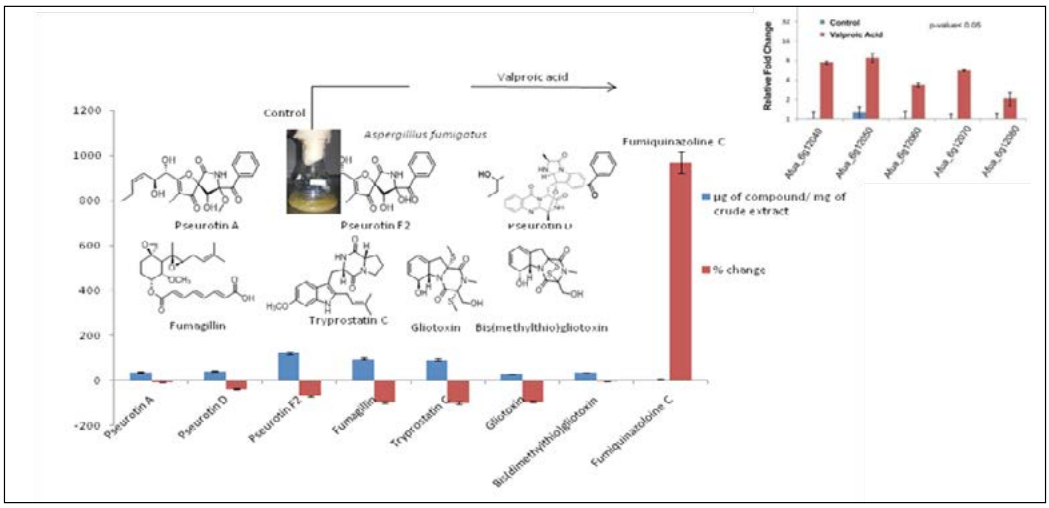


Fig. 7.2.2 Expression profiling of the genes involved in fumiquinazoilne C biosynthesis in *Aspergillus fumigatus* (GAL7), an endophyte from Grewia asiatica. All the genes exhibited significant upregulation in valproic acid treated culture compared to that of untreated control culture.

7.3. Production of kojic acid from *Aspergillus sojae*

A high kojic acid producing fungus has been isolated from rice husk using glucose-peptone medium. The pure strain was obtained through several steps of monospore isolation procedures using spread plate technique and later identified as *Aspergillus sojae*. Optimization of medium composition and cultural conditions for kojic acid production by this fungus were carried out in shake flask. This strain was able to grow and produce kojic acid in various carbon and nitrogen sourses. Using this optimal medium the maximum kojic acid production in batch fermentation using shake flask was 17 g/L. This fermentation gave yield and productivity of 0.04 g/g and 0.07 g/L/h, respectively and is comparable to that reported in the literature for industrial strain.

7.4 Application of amidase for production of benzohydroxamic acids

Amidase or amidohydrolase is an enzyme that catalyzes the hydrolysis of amides to release free carboxylic acids and ammonia. In recent years, amidases have gained considerable interest in industries for the synthesis of wide variety of carboxylic acids which find applications in commodity chemicals synthesis, pharmaceuticals agrochemicals, and waste water treatments, etc. Apart from amide hydrolysis activity, some amidases also exhibit an acyl transferase activity which leads to the formation of pharmaceutically important hydroxamic acids according to the following reaction:

RCONH2 + NH2OH → RCONHOH + NH3

An amidase producing culture has been isolated from soil sample of hot water springs of Himachal Pradesh. On the basis of 16S r DNA, isolated culture has been designated as Bacillus sp. IIIMB2907. It has been found that amidase from the isolated strain is exhibiting amide hydrolase as well as acyl-transferase activity with benzamide (as shown in figure). Therefore, currently this enzyme is being used in the synthesis of benzohydroxamic acid and other pharmaceutically important aromatic hydroxamic acids

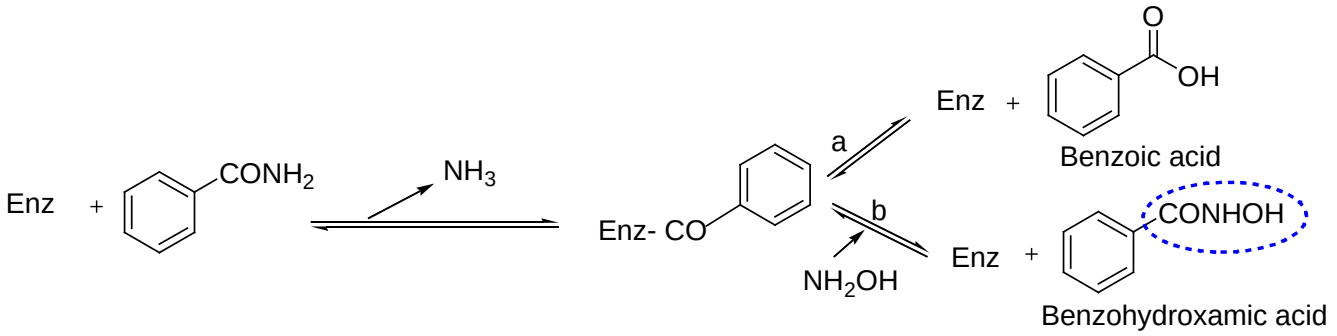


Fig. 7.4.1: Reaction of amidase (Enz) with benzamide Pathway (a), amidase catalyzes the hydrolysis of benzamide to the corresponding benzohydroxamic acid. Pathway (b) acyltransferase activity of amidase (in presence of hydroxylamine) for the synthesis of benzohydroxamic acid

8.0 CANCER PHARMACOLOGY

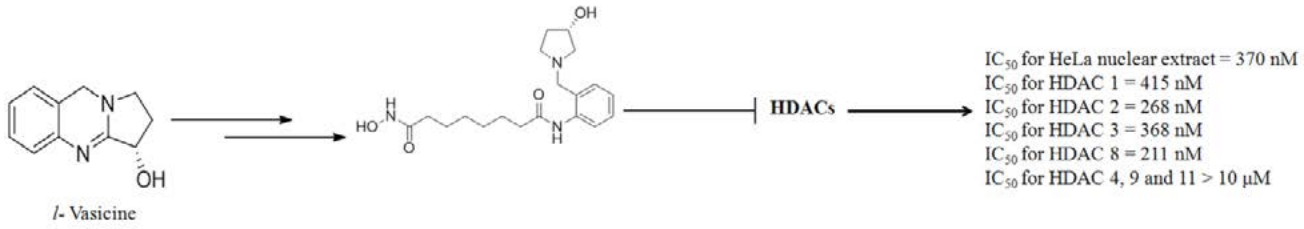
8.1 Chromatin & novel antitumor histone deacetylase inhibitor(s)interaction: relevance in cancer epigenetic therapeutics

Mudassier Ahmad, Javeed Ahmad Bhat, Abid Hamid

In cancer, epigenetics has been found to play an important role in the origin, development and metastasis. Last decade has also witnessed clinical applications of epigenetics in cancer. Epigenetic writer and reader enzymes like histone deacetylases (HDACs), DNA methyl transferases (DNMTs), histone methyl transferases (HMTs) are being increasingly used as targets for chemotherapeutic intervention in cancer and other diseases like diabetes and neuro-degenerative disorders. Acetylation of histones is the common epigenetic mechanism used by cells for regulating the cellular processes like gene expression, cell growth, cell death etc. Dysregulation of the acetylation has been associated with diverse cellular events in the cancer pathologies. Global hypoacetylation of H4 is the common feature of human tumours. Acetylation of histones and other proteins is maintained by two antagonistic families of enzymes, histone deacetylases (HDACs) and histone acetyl transferases (HATs). Due to its reversible nature, acetylation has been harnessed for cancer chemotherapy. So far, two HDAC inhibitors suberoylanalide hydroxamic acid (SAHA) and romidepsin have already been approved by the FDA as drugs against Chronic T Cell Lymphoma (CTCL). Besides, there are tens of HDAC inhibitors at various stages of clinical trials against different cancers. HDAC inhibitors increase the acetylation level of histones and have been chiefly found to reactivate the expression of numerous silenced genes that promotes cell death. HDAC inhibitors also lead to cell growth arrest, cell differentiation and angiogenesis inhibition which are important biological processes for suppression of cancers.

Taking into account the potential therapeutic efficacy of HDAC inhibitors, several classes of HDAC inhibitors have been designed. However in spite of large efforts the clinical potential of HDACs has not been realized yet. Natural products offer a good opportunity for the design of new HDAC inhibitors. One of the important classes of bioactive natural products is quinazolines. Quinazolines show potent anticancer, anti-microbial and anti-inflammatory activities. We in our current study explored the possibility of using derivatives of quinazoline alkaloid l-vasicine in the design of natural product based HDAC inhibitors. l-vasicine is a unique molecule with electron dense ring system and additional functionalities in its structure, we hypothesized that these structural features may be used to design new HDAC inhibitors with l-vasicine derivatives as cap groups. Using in silico approach, target oriented synthesis (TOS) and biological studies, l-vasicine derivative 3-hyroxypyrrolidine was found to act as a suitable cap group in the design of a novel HDAC inhibitor (S)-N1-hydroxy-N^8-(2-((3-hydroxypyrrolidin-1-yl) methyl) phenyl) octanediamide (4a).

IC50 (nM)									
Molecule	Class I				Class IIa			Class IIb	Class IV
	HDAC 1	HDAC 2	HDAC 3	HDAC 8	HDAC 4	HDAC 5	HDAC 9	HDAC 10	HDAC 11
4a	415	268	368	211	7120	5391	>10000	>10000	>10000
SAHA	150	454	261	300	>10000	2180	>10000	982	>10000



l- Vasicine

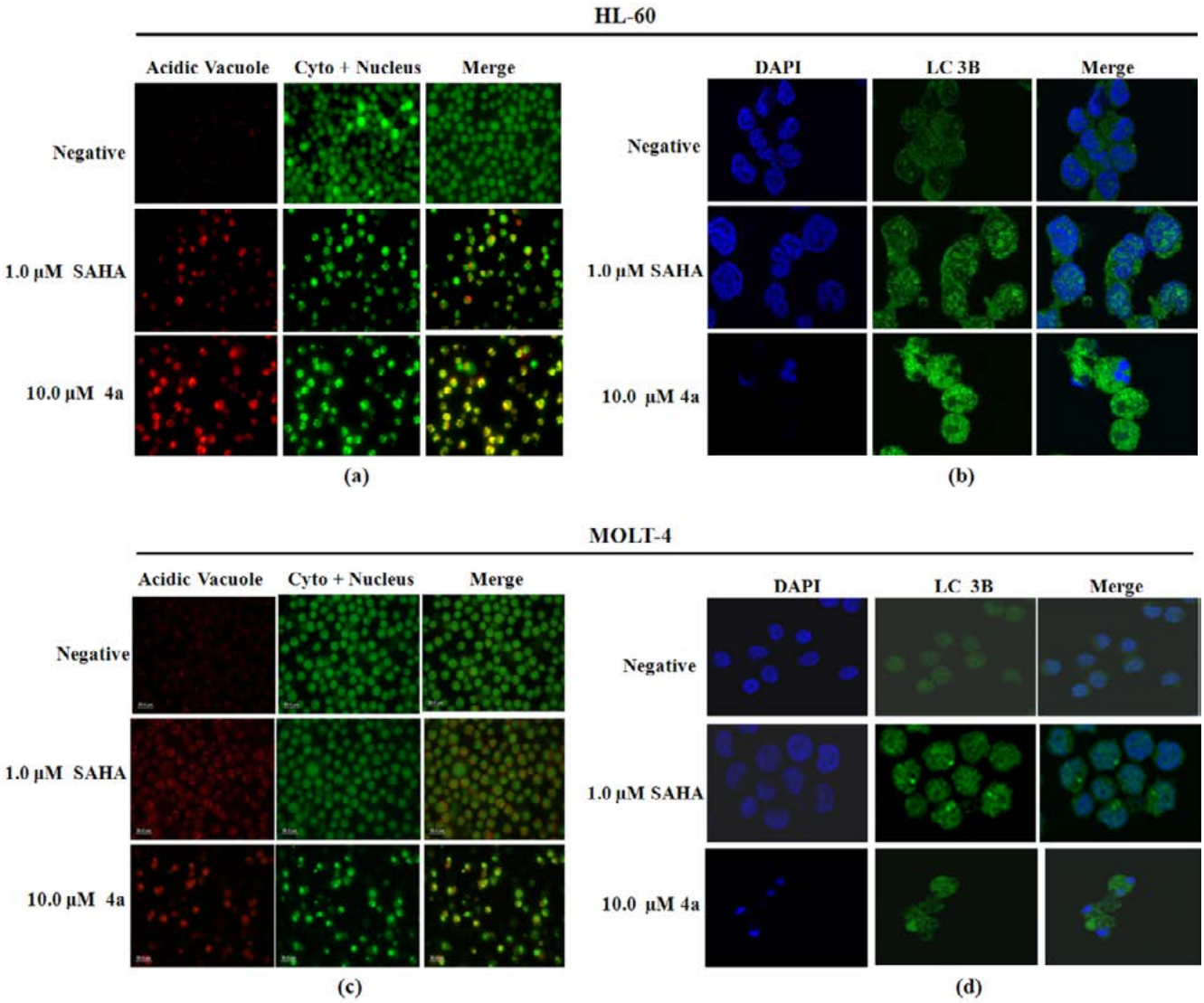


Fig. 8.1.1 Cells treated with novel inhibitor were stained with acridine orange dye and examined under florescent microscope for formation of acidic vacuoles occurs in cytoplasm.

We in our current study report the designing of a novel HDAC inhibitor (S)-N1-hydroxy-N8-(2-((3-hydroxypyrrolidin-1-yl) methyl (phenyl) octanediamide (4a) containing l-vasicine derivative 3-hydroxypyrrolidine as a cap group. This is the first time that l-vasicine has been used in the synthesis of HDAC inhibitors. Our hypothesis was that l-vasicine has essential structural features which may be employed in the designing of novel HDAC inhibitors. During in silico studies, molecules containing various derivatives of l-vasicine as caps and aliphatic linkers of various lengths showed significant docking scores. Three schemes of target oriented synthesis were framed to synthesise these probable HDAC inhibitors. Interestingly, 3-hydroxypyrrolidine cap based molecule 4a with linker length equal to six carbons was found to significantly inhibit enzyme activity of HDACs and induce cell death in different cancer cell lines. 4a was found to be more specific towards class I HDAC isoforms. HDAC inhibition activity of 4a was also confirmed by increase in acetylation level of histones in 4a treated HL-60 and MOLT-4 cells. 3-hydroxypyrrolidine cap was found to be highly sensitive to linker length and any change in linker length rendered molecule inactive. Importantly, 4a showed several fold higher IC50 value against non-cancerous normal cell line fR-2 and MCF 10A as compared to most cancer cell lines, thus indicating that 4a induced cancer specific cell death. Moreover, unlike many other natural product based HDAC inhibitors 4a was found to be non-toxic during in vivo studies on P388 lymphocytic model. Mechanistic studies revealed that 4a facilitated cell death by several pathways. 4a

promoted cell death by inducing mitochondrial membrane potential loss and autophagy in HL-60 and MOLT-4 cells. However unlike many HDAC inhibitors 4a treatment did not lead to accumulation of ROS in HL-60 cells thus inducing ROS independent cell death. Importantly, 4a showed DNA damage which is an important event in initiating cell death in cancer cells and serves as a key marker for cell death detection. In addition, migration assay showed that 4a induces localization in THP-1 cells and decreased their ability to migrate to the wound induced in the THP-1 monolayer, thus indicating anti-metastatic potential of 4a. Moreover, molecular modeling studies revealed that 4a that cap, linker and chelator of 4a interact with the different amino acids in the binding pockets of HDACs 2 and 8. However, the hydrophobic cleft formed by Met274, Cys275 and Phe207 provides an additional stability to 4a for HDAC8 which is not seen in HDAC-2. From this analysis it was concluded that the molecule 4a has more potency for HDAC-8.

Thus our results indicate designing of a novel HDAC inhibitor (4a) employing 3-hydroxypyrrolidine derivative of quinazoline alkaloid l-vasicine as the cap group. Moreover, the cytotoxicity of 4a against spectrum of cancer cells of different tissue origins and significantly high specificity against cancer cell lines are scientifically valuable results which warrants further exploration. 4a is thus a lead candidate with a therapeutic potential. Moreover, importance of 4a also lies in understanding its unique mechanism of action essentially the fact that unlike other HDAC inhibitors it does not produce ROS and is non-toxic to in vivo models unlike many natural product based HDAC inhibitors. Furthermore, it will be interesting to evaluate the applicability of 3-hydroxypyrrolidine cap in HDAC inhibitors containing chelators other than hydroxamic acid. Also the effect of 3-hydroxypyrrolidine cap on bioavailability of 4a may be studied.

8.2. Aberrant methylation of human trophoblastic stem cell origin in the pathogenesis, prognosis and diagnosis of embryonic developmental disorders.

Beenish Rahat, Rauf Ahamd Najar, Rashmi Bagga, Jyotdeep Kaur, Abid Hamid

The proper development of fetus throughout pregnancy is regulated by efficient placental growth. Similar to cancer metastasis, placental development involves proliferation and invasion of placental trophoblasts into normal maternal uterus and hence display a phenotype resembling cancerous cells. There are many shared molecular mechanisms between invasive placentation and metastasis, especially in terms of the factors which enhance growth. These similarities also appear at key epigenetic mechanisms. Additionally the placental growth seems to be enhanced by paternally expressed genes, which are known to show growth promoting phenotype. Studies have suggested major influence of paternal genome in placental development and higher occurrence of paternally expressed genes in placenta. These genes are generally regulated by cis-acting differentially methylated regions (DMRs). These regions are usually also associated with differential histone marks. Such differential epigenetic marks at DMRs of these genes lead to their differential expression via a complex sequence of events, however, if the DMR is also the promoter of that specific gene it directly silences the methylated allele. Disruption of these epigenetic marks at DMRs result in abnormal gene expression leading to major phenotypic changes, associated with developmental deformities, placental disorders and malignancies. Considering the similarity between cancer and placentation, it is likely that placental epigenome too is liable to alterations during advancing gestation, pathological conditions and external factors like availability of nutrients etc.

Disease pathologies associated with inappropriate gene expression are quite often related to aberrantly functioning placenta. Preeclampsia, which is associated with placental dysfunction, is one such pathology which might be associated with defective gene expression, leading to poor invasion of endovascular trophoblasts and abnormal remodeling of maternal spiral arteries. Paternally expressed genes have also been recently reported to play an important role in the pathogenesis of preeclampsia. These genes might be of special importance in the development of preeclampsia as these genes are known to control trophoblastic invasion and placental growth. Folic acid being a key source of the one carbon group required to methylate DNA, is generally recommended preconceptionally during early pregnancy. DNA methylation is an epigenetic modification critical to normal development of placenta and regulation of gene expression. Therefore, folate supplementation can directly affect gene expression, which emphasizes the importance of the analysis of the effect of folic acid supplementation on expression of these genes.

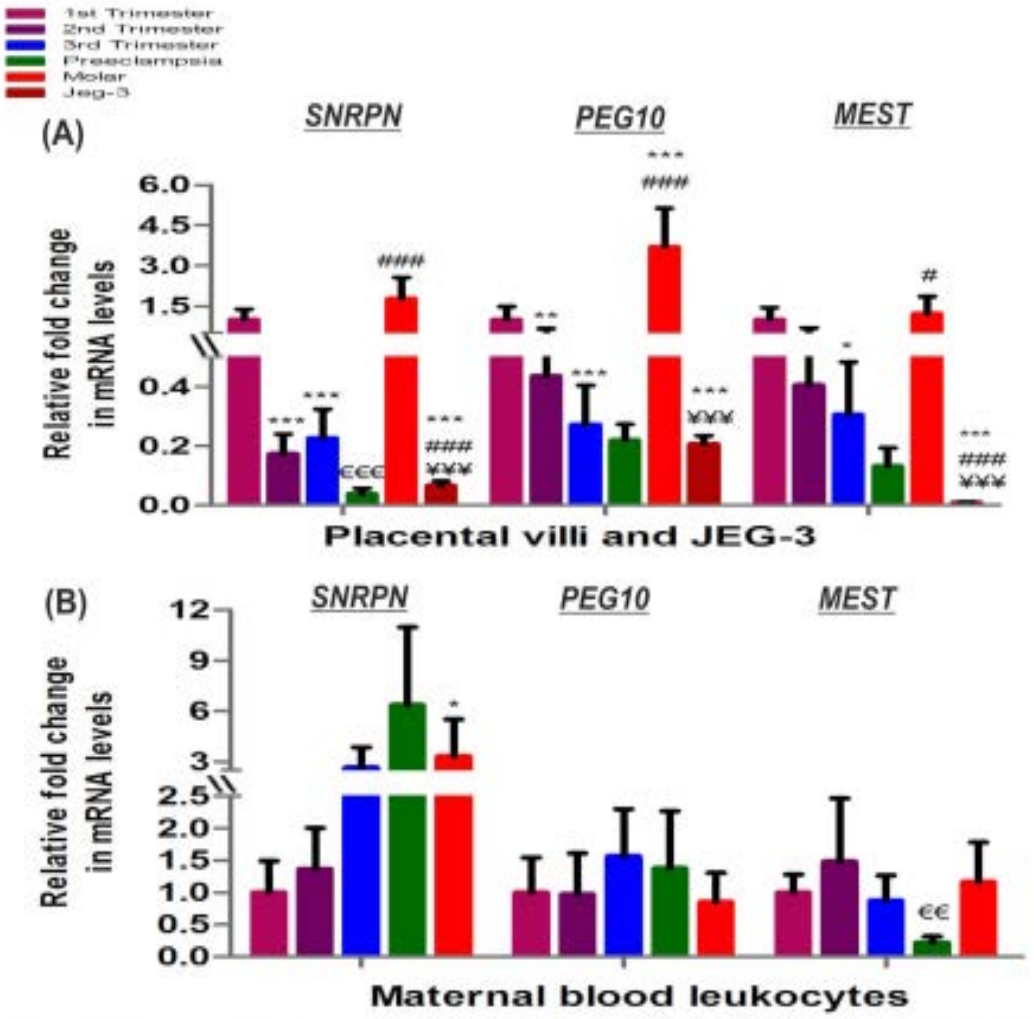


Figure 1. Relative fold change in mRNA of imprinting genes normalized with GAPDH. Relative mRNA expression among (**A**) placental villous samples and JEG-3 cells (**B**) maternal blood leukocytes [$^{*}p<0.05$, $^{**}p<0.01$, $^{***}p<0.001$ *vs* 1st trimester, $^{\#}p<0.05$, $^{\#\#\#}p<0.001$ *vs* 2nd trimester, $^{€€}p<0.01$, $^{€€€}p<0.001$ *vs* 3rd trimester and $^{¥¥¥}p<0.001$ *vs* molar]. The data is presented as mean of the observed fold change ± SEM, n = 30 per group.

Invasive placentation and cancer development shares many similar molecular and epigenetic pathways. Paternally expressed, growth promoting genes (SNRPN, PEG10 and MEST) which are known to play crucial role in tumorogenesis, are not well studied during placentation. This study reports for the first time of the impact of gestational-age, pathological conditions and folic acid supplementation on dynamic nature of DNA and histone methylation present at their differentially methylated regions (DMRs). Here, we reported the association between low DNA methylation/H3K27me3 and higher expression of SNRPN, PEG10 and MEST in highly proliferating normal early gestational placenta. Molar and preeclamptic placental villi, exhibited aberrant changes in methylation levels at DMRs of these genes, leading to higher and lower expression of these genes, respectively, in reference to their respective control groups. Moreover, folate supplementation could induce gene specific changes in mRNA expression in placental cell lines. Further, MEST and SNRPN DMRs were observed to show the potential to act as novel fetal DNA markers in maternal plasma. Thus, variation in methylation levels at these DMRs regulates normal placentation and placental disorders. Additionally, the methylation at these DMRs might also be susceptible to folic acid supplementation and has the potential to be utilized in clinical diagnosis.

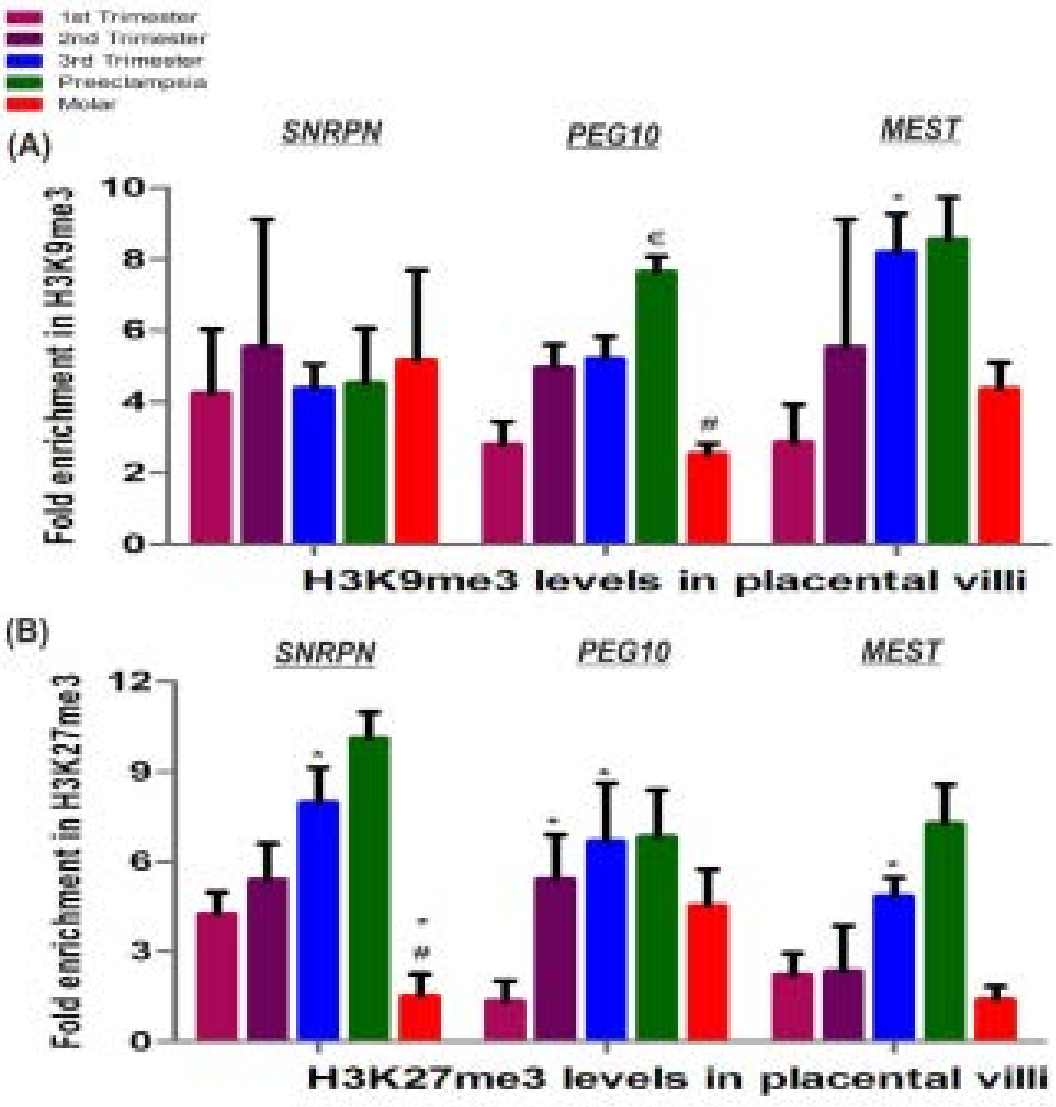


Fig. 8.2.2 Quantification of histone trimethylation at DMRs of imprinting genes among placental villous groups. Fold enrichment relative to non-specific IgG acting as negative control and normalized with input DNA in (A) H3K9me3 and (B) H3K27me3. The data is presented as mean of the observed fold change±SEM; n=4 per group.

8.3 Modulation of glycolysis and lipogenesis by inhibition of kinase signaling for checking the tumor growth

Aashiq Hussain, Abid Hamid

An alteration in the metabolism of cancer cells is considered to be fundamentally connected to the transformation of a normal cell to a cancerous cell. Unlike the normal cells, cancer cells exhibit glycolysis even in the presence of oxygen. This aerobic glycolysis or Warburg effect may be the result of abnormalities like mitochondrial damage, adaptation to hypoxia within tumors, oncogenic stimuli and particularly over-expression of glycolytic enzymes. Glycolysis in cancer cells produces only 2 molecules of ATP per molecule of glucose, therefore to compensate for this energy deficiency, the cancer cells upregulate glucose transporters which increase the uptake of glucose. The glycolytic enzymes are also over-expressed to drive glycolysis at a higher rate and support cancer cell survival and proliferation. In addition, the cancer cells also differ from normal cells in the way it processes pyruvate- the end product of glycolysis. Conversion of pyruvate to lactate is a preferred reaction in the cancer cells and helps to accelerate glycolysis further by regenerating NADH. Lactate induces certain metabolic changes in the cancer cells which are significant for the survival, invasion and proliferation

of the tumors. Lactate secreted into the tumor microenvironment helps to fuel other cells which, otherwise, do not have access to nutrients from the blood stream. Lactate also promotes the survival of a tumor cell by eating up the reactive oxygen species which decreases the oxidative stress. The extracellular lactate decreases the pH which aids in the breakdown of extracellular matrix facilitating the spread of cancer to other healthy cells [8]. Glycolysis not only benefits the cancer cell in terms of energy but also provides it with the necessary precursors for biosynthesis of important macromolecules. Glycolytic metabolites enter into other metabolic pathways to regulate the synthesis of such products that help in the tumor progression. For instance, glycolysis promotes the occurrence of lipogenesis via dihyroxyacetone phosphate (DHAP) and latter is considered to be an important hallmark of cancer cells. Also, it has been established that there is a relation between de novo endogenous lipid synthesis and glycolysis in tumor cells as glycolysis makes available energy and important precursors for fatty acid synthesis. In cancer cells lipogenesis, like glycolysis is also regulated by oncogenic pathways and is considered to be responsible for tumor survival, initiation, progression and aggressiveness.

Phosphatidylinositol 3-kinase (PI3K) pathway drives cancer progression through direct regulation of most oncogenic properties. Here, we report that PI3K pathway signaling up-regulates cancer cell proliferation, metastasis and angiogenesis through modulation of cancer metabolism. These oncogenic metabolic processes were disrupted, by a novel PI3K inhibitor, 3-Dihydro-2-(naphthalene-1-yl) quinazolin-4(1H)-one (DHNQ) in colon cancer cells. DHNQ inhibited the Warburg effect and lipid synthesis by reducing gene expression of glycolytic and lipogenesis regulatory enzymes. This downregulation at gene level by DHNQ inhibited metabolic flux to repress proliferation, migration and invasion characteristics of colon cancer. Furthermore, the metabolic attenuation caused repression of in vitro/in vivo angiogenesis providing new insights in PI3K regulated angiogenesis via metabolic alterations. Our results suggest that multifaceted targeting of oncogenic metabolism by their upstream PI3K regulatory signaling may be an effective cancer treatment approach.

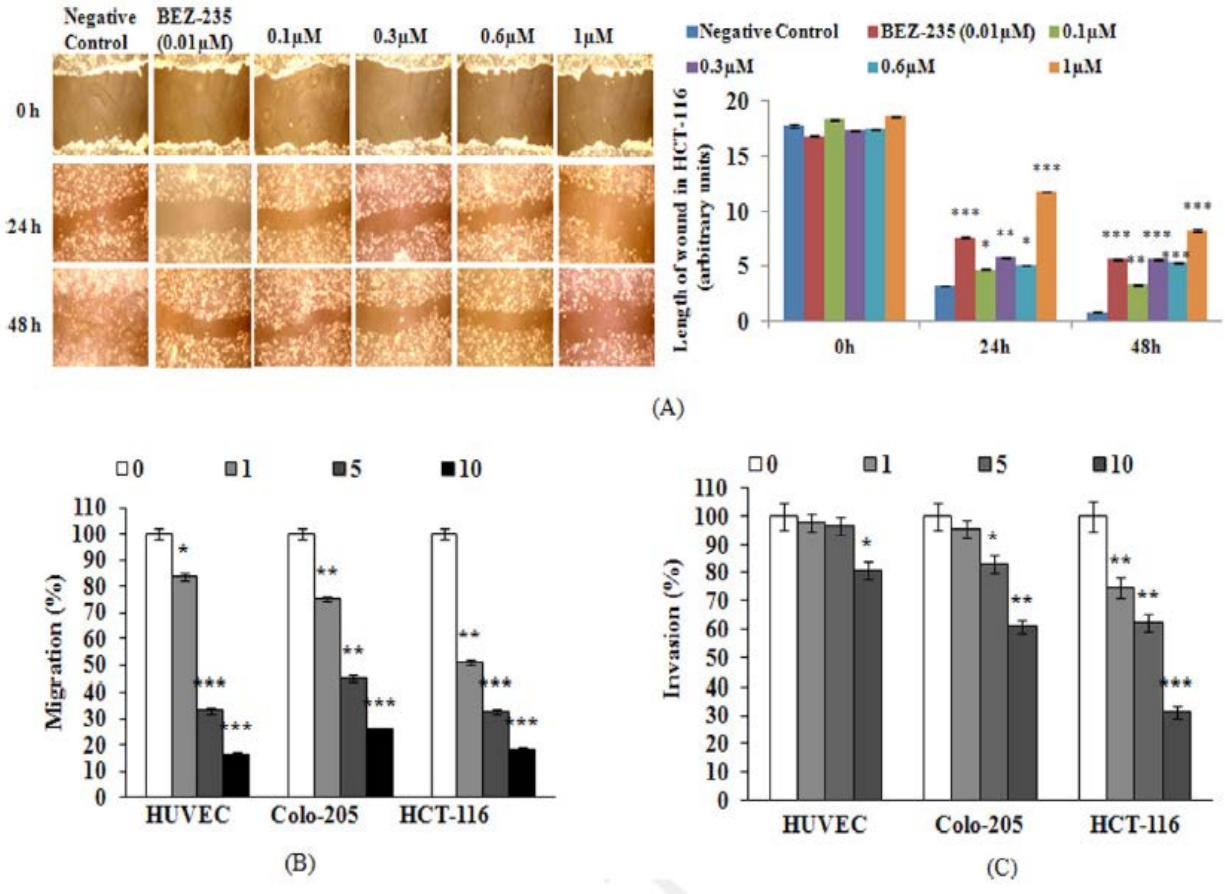


Fig. 8.3.1 Inhibition of Chemotaxis cell migration and invasion.

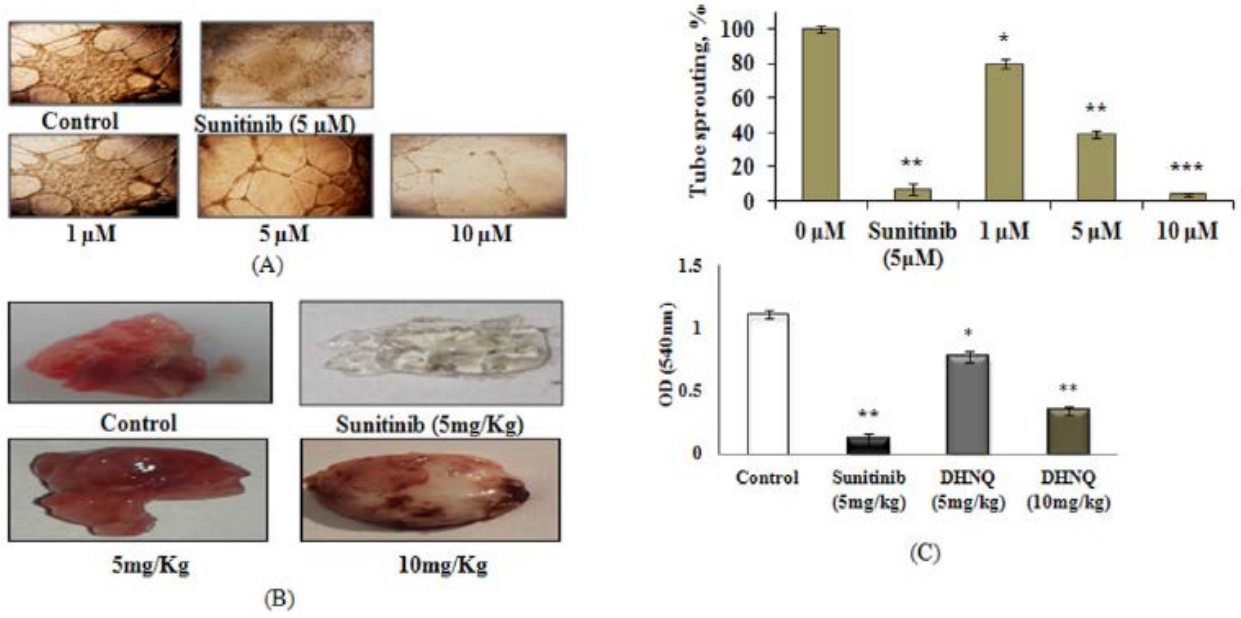


Fig. 8.3.2 VEGF mediated angiogenesis via PI3K mediated attenuation of glycolysis and lipogenesis.

8.4 Neuroprotection against NMDA-induced excitotoxicity in model systems by metabolites from *Withania somnifera*

Nawab John Dar, Abid Hamid, Muzamil Ahmad

Glutamate is the primary excitatory neurotransmitter in mammalian central nervous system (CNS). Under physiological conditions, it plays a vital role in neural development, synaptic plasticity, transmission, learning and memory. Under pathologic conditions, there is an excessive release and accumulation of glutamate in extracellular space which in-turn activates the ionotropic N-methyl-D-aspartate (NMDA), α-amino-3-hydroxy-5-methyl-4-isoxazoleproprionate (AMPA) and Kainate as well as metabotropic classes of postsynaptic receptors resulting in the neuronal death. This process is commonly known as excitotoxicity. Excitotoxicity is the underlying mechanism of most of neurodegenerative disorders, including Parkinson's disease, Alzheimer's disease, Huntington's disease, amyotrophic lateral sclerosis and other acute insults such as stroke and trauma. NMDA receptors (NMDARs) are major excitotoxic receptors distributed throughout cerebral cortex and hippocampus. NMDARs act via receptor-gated ion channels and are highly permeable to calcium ions and their persistent opening triggers Ca2+ influx. The calcium influx in turn results in activation of a number of enzymes that damage cellular architecture through collapse of the mitochondrial membrane, increased formation of reactive oxygen species (ROS) and reactive nitrogen species (RNS), nitric oxide (NO) lipid peroxidation and DNA damage. Depending upon the extent of stimulation, NMDARs promote cell survival or cell death under in vitro as well as in vivo conditions. NMDAR stimulation with a low dose of NMDA has shown neuronal survival in cerebellar granule cell cultures while as high dose of NMDA induces neuronal death. Stereotactic injections of NMDA into rodent brain have produced lesions identical to damage caused by cerebral ischemia.

Withania somnifera has immense pharmacologic and clinical uses. Owing to its similar pharmacologic activity as that of Korean Ginseng tea, it is popularly called as Indian ginseng. In most cases, extracts of this plant have been evaluated against various diseases or models of disease. However, little efforts have been made to evaluate individual constituents of this plant for neurodegenerative disorders. Present study was carried out to evaluateWithanone, one of the active constituents of *Withania somnifera* against NMDA-induced excitotoxicity in retinoic acid, differentiated Neuro2a cells. Cells were pre-treated with 5, 10 and 20 µM doses of Withanone and then exposed to 3-mM NMDA for 1 h. MK801, a specific NMDA receptor antagonist, were used as positive control. The results indicated that NMDA induces significant death of cells by accumulation of intracellular Ca2+, generation of reactive oxygen species (ROS), loss of mitochondrial membrane potential, crashing of Bax/Bcl-2 ratio, release of cytochrome c, increased caspase expression, induction of lipid peroxidation as measured by malondialdehyde levels and cleavage of poly(ADP-ribose) polymerase-1 (Parp-1), which is

indicative of DNA damage. All these parameters were attenuated with various doses of Withanone pre-treatment. These results suggest that Withanone may serve as potential neuroprotective agent.

Also, the present study was carried out to investigate withanolide-A, one of the active constituents of *Withania somnifera* against glutamate-induced excitotoxicity in retinoic acid differentiated Neuro2a neuroblastoma cells. The results indicated that glutamate treatment for 2 h induced death in cells that was significantly attenuated by pre-treatment with MK-801 (specific NMDA receptor antagonist) and different concentrations of withanolide-A. Withanolide-A abated the glutamate-induced influx of intracellular calcium and excessive ROS production significantly. Further on, glutamate treatment resulted in increased levels of pro-apoptotic and decreased levels of anti-apoptotic proteins, and these protein levels were normalized by various doses of withanolide-A. All of these protective effects were partly due to inhibition of MAPK family proteins and activation of PI3K/Akt signaling. Thus, our results suggest that withanolide-A may serve as potential neuroprotective agent.

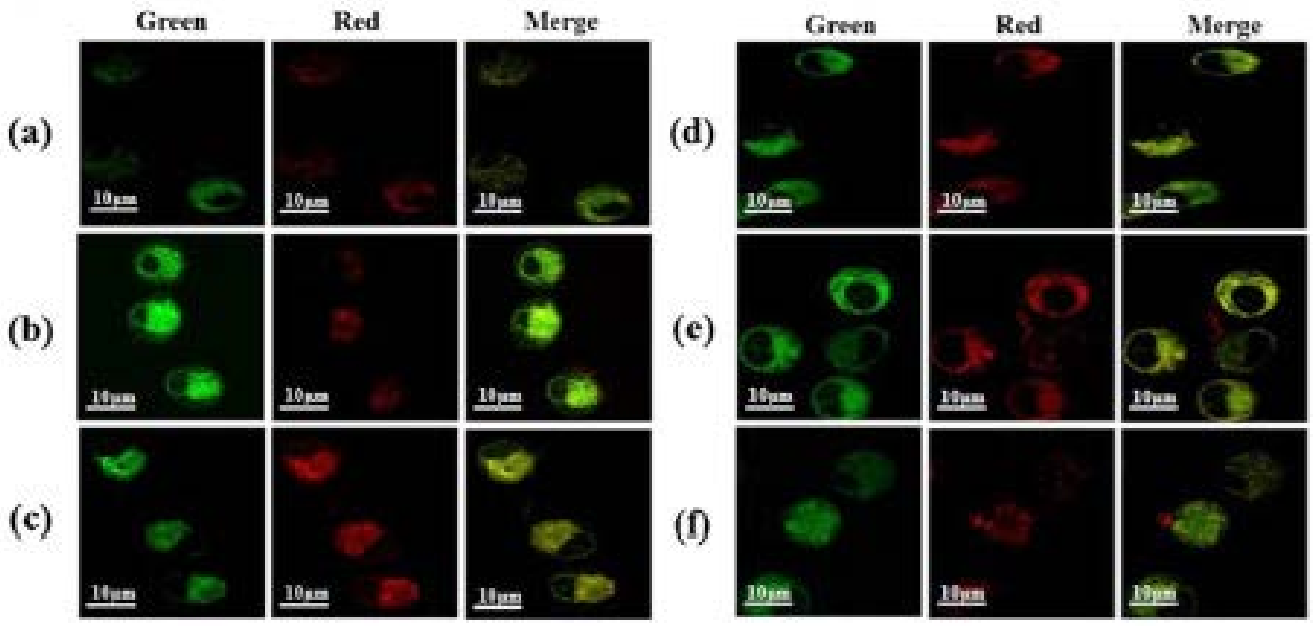


Fig. 8.4.1 Neuroprotection measurements

8.5 Nuclear activities of GFP-fusion p110α and p110β isoforms of PI3K signaling pathway in MCF-7 and HCT-116 cancer cells

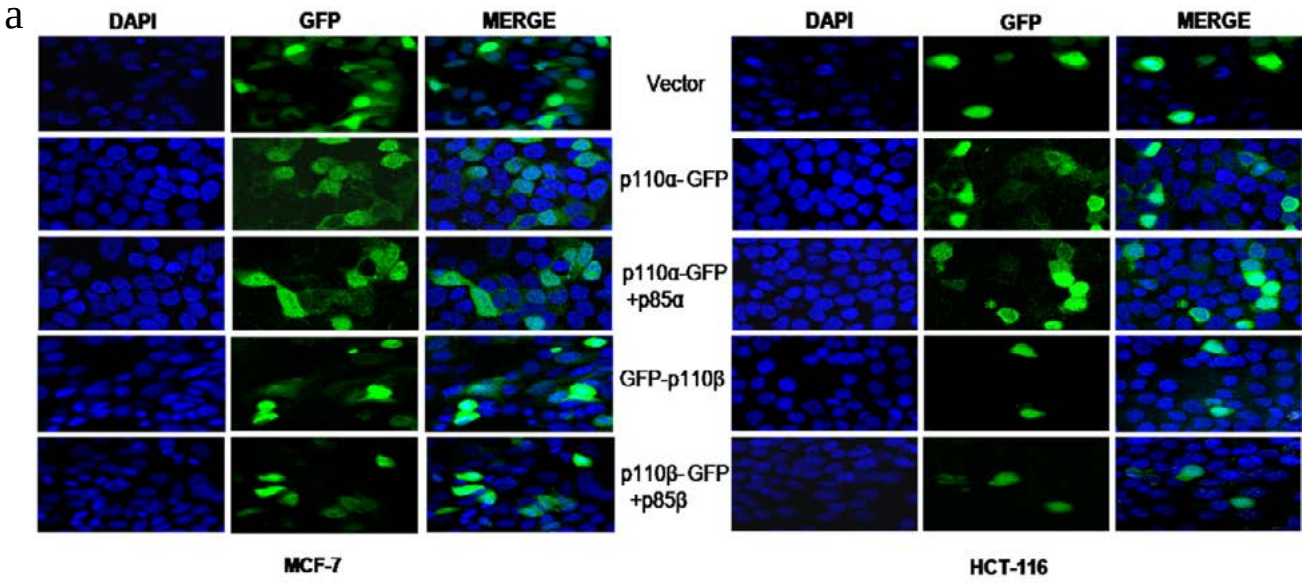
ParamjeetSingh,Mohd SaleemDar andMohd Jamal Dar

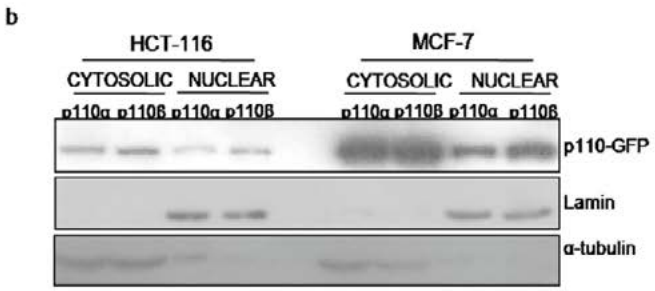
Nuclear functions of p110α and p110β isoforms of PI3K signaling pathway: The phosphoinositide 3-kinase (PI3K) signaling pathway has received a great deal of attention for the last few decades because this pathway is one of the major pathways hijacked by the cancer cells to proliferate in an uncontrolled fashion. The PI3K pathways are typically divided into 3 classes; class-I, class-II and class-III. The majority of research has focused on the class-I PI3Ks, arguably the most important PI3K signaling pathway, which has the best characterized role in human cancer.

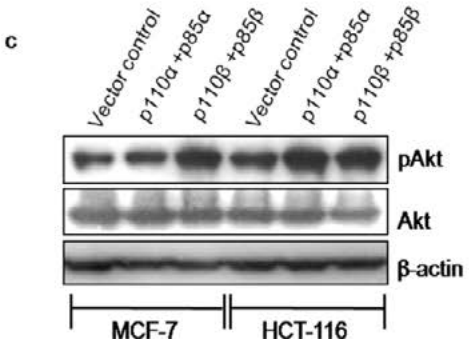
These class-I PI3Ks are well known lipid kinases whose primary biochemical function is to phosphorylate the 3-hydroxyl group of phosphoinositides (PIP2) that results in generation of second messengers (PIP3). Once generated, this lipid molecule, PIP3, binds to serine/threonine kinase Akt resulting in the activation of Akt in order to initiates a vast array of signaling events that are critical for controlling cell growth, metabolism, apoptosis and cell survival.The class-1A PI3-kinases are heterodimers consisting of a catalytic subunit p110 (p110α, p110β, or p110δ are its various isoforms) in complex with regulatory subunit p85. There are five regulatory subunits p85α, p55α, p50α splice variants of p85α p85β and p55γ. PI3K isoforms p110α and p110β are commonly expressed in all tissues whileas the expression of p110δ is largely restricted to the immune system and is highly enriched in leukocytes and to a lesser extent

in neurons. When PI3K signaling fails to function properly, cells grow in an unregulated manner. For this reason, PI3K isoforms are validated drug targets for cancer chemotherapy. Many small molecule inhibitors designed to inhibit PI3K isoforms p110α and p110β are in various phases of clinical trials. However, there are few challenges faced in targeting these isoforms which include the conserved nature of kinase binding sites. Moreover, p110α and p110β soforms have recently been shown to translocate into the nucleus of normal cancer cells which adds another level of complexity to design small molecules for blocking the nuclear activities of p110α and p110β isoforms.

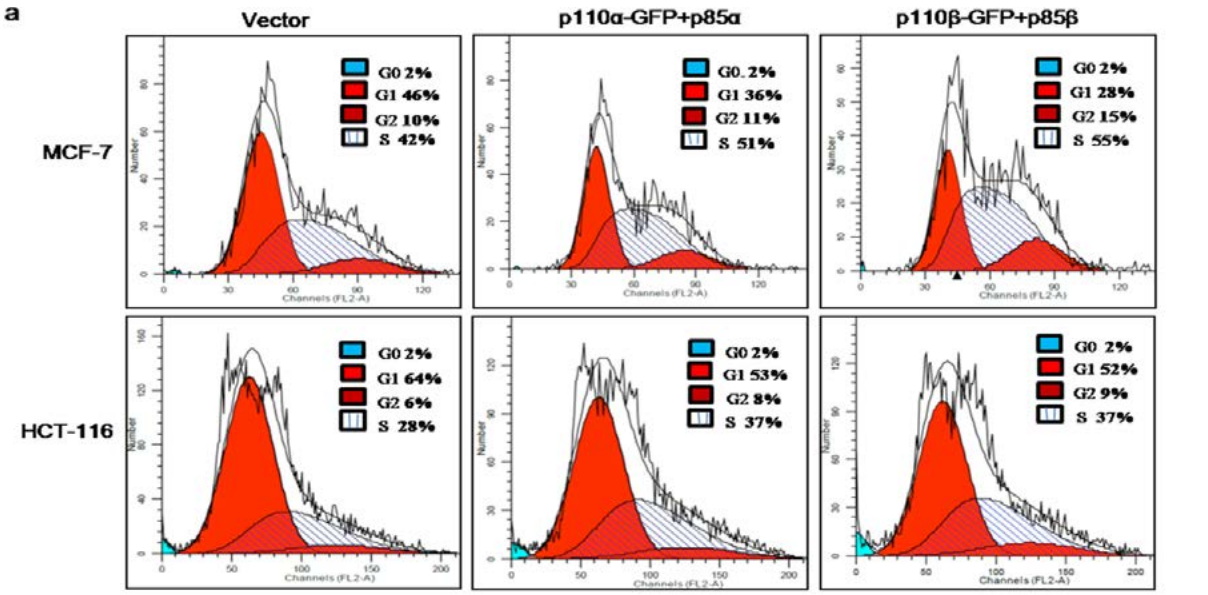
In this study, we have tagged the C-terminus of human p110α and p110β with green fluorescent protein (GFP) to analyze their subcellular distribution and to investigate the impact of their subcellular localization on cell signaling in various cell lines. We provide substantial evidence that p110α and p110β translocate into the nucleus of MCF-7 and HCT-116 cancer cells and have variable expression and activities. We carried out cytoplasmic and nuclear fractionation in MCF-7 and HCT-116 cells. After 24 h of transfection p110α-GFP and p110β-GFP were measured in both fractions using GFP-tag specific antibody. Interestingly, p110β as well as p110α were detected in substantial amount in both cytosolic and nuclear fractions of these two cell lines We then examined whether overexpression of p110α and p110β GFP fusion proteins in MCF-7 and HCT-116 cells is upregulating pAkt levels and observed a marked increase in the pAkt levels in these cells in comparision to vector control. Moreover, we show that both p110α and p110β are involved in the regulation of cell growth in these cells, although the level of progression differed slightly in two cell lines. The population of cells in S-phase was more in MCF-7 than in HCT-116 cells in comparison to vector controls cells.

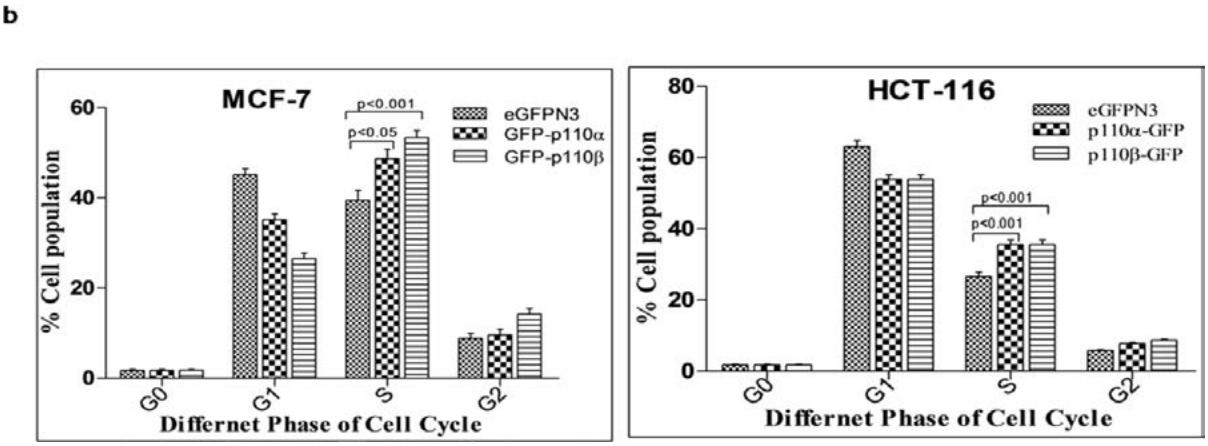






Nuclear localization of p110α-GFP and p110β-GFP in MCF-7 and HCT-116 cells. (a) MCF-7 and HCT-116 cells were transfected with p110α-GFP and p110β-GFP alone or in combination with p85. Fixed cells were stained with DAPI, and images were visualized by confocal microscopy. GFP, vector control, was seen to be equally expressed in all the cell lines. (b) Cell fractionation of p110α and p110β in MCF-7 and HCT-116 cells. Cytosolic and nuclear fractions were resolved and immunoblotted with GFP antibody. anti-lamin and anti-tublin antibodies were used as nuclear and cytosolic controls respectively. (c) MCF-7 and HCT-116 cells were transfected with vector alone, p110α-GFP or p110β-GFP in combination with p85 and probed for pAkt levels.





Cell cycle analysis upon recombinant p110α and p110β overexpression in MCF-7 and HCT-116 cells. (a) shows the propidium iodide assay of MCF-7 and HCT-116 cells after recombinant overexpression of p110α and p110β by flow cytometry. It represents the percent population of cells in a different phases. (b) Data analysis of flow cytometry results by using graphpad prism software. The data represents a significant increase in S-phase sub-population in both the cell lines. Results shown are mean±s.d.

8.6. Elucidating mechanism how β-catenin switches between being a proto-oncogene or an oncogene (cancer causing gene)

Wnt/β-catenin signaling plays critical roles in many biological processes like stem cell maintenance, embryonic development and in cancer. β-Catenin, the central molecule of canonical *Wnt* signaling pathway, has multiple binding partners and performs many roles in the cell. There are two pools of β-catenin within the cell which are required for its two principal roles that include its involvement in cell-

cell adhesion at the cell membrane and its transcriptional functions in the nucleus. Any imbalance in the structural and signalling properties of β-catenin causes dysregulated growth often resulting in cancer. β-Catenin is composed of three domains: N-terminal domain, C-terminal domain and a central armadillo repeat domain. Since almost all of the cancer causing mutations are present at the N-terminal domain of this protein, deciphering its critical structural and functional roles harbors great potential in cancer diagnostics, development, and therapy. Thus, a thorough understanding of the interactions between β-catenin and its N-terminal domain variants with its binding partners is crucial for analyzing the mechanism(s) of cell-cell adhesion, signaling as well as for the designing small molecules as chemotherapeutic agents. In this study we have created a library of β-catenin deletion and point mutants in order to identify minimum structural entity required for β-catenin nuclear localization and to understand the role played by the terminal unstructured regions of this protein in cell-cell adhesion, transcription and carcinogenesis. Shown in Fig 1.0 is the schematics of various β-catenin variants generated (left panel) and the subcellular localization of wildtype, cancer specific point mutant (S45Y) and TM. HepG2 cells, a liver specific cancer cell line, harbour a deletion in β-catenin which results in the removal of its 25-140 amino acids at the N-terminal end. We generated a similar construct of β-catenin for its structural and functions studies hereupon called TM. While the wildtype β-catenin was seen to be present at the membrane and cytoplasm, TM and S45Y showed predominant nuclear localization (right panel). Vector (eGFP-N3) and EGFR were used as controls for subcellular localization.

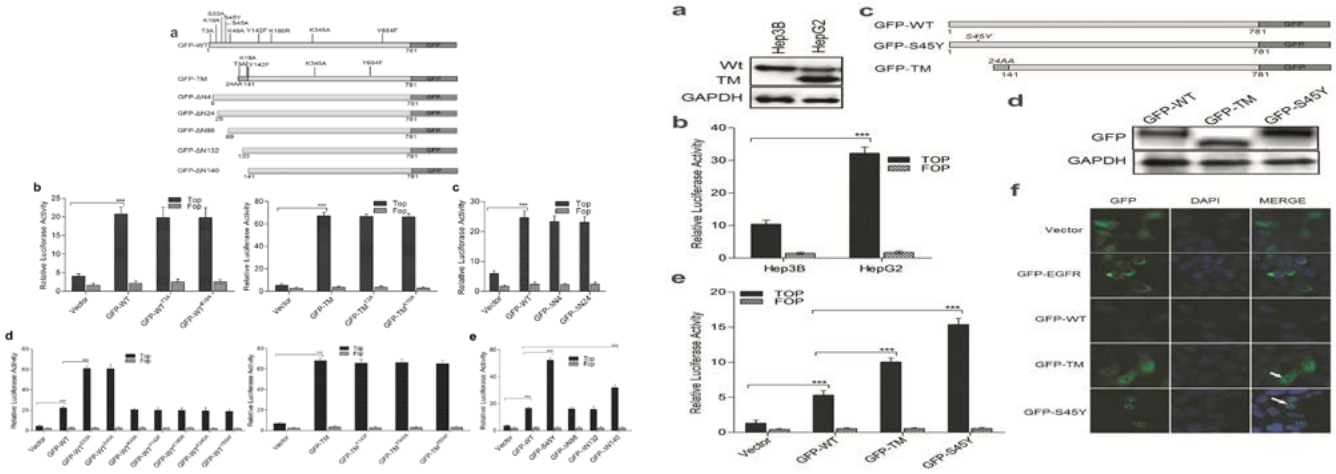


Fig. 8.6.1 Schematics of N-terminal substitution and deletion mutants of β-catenin used in the study. Left panel-Schematics of various beta-catenin constructs generated . Right Panel- Subcellular localization of selected variants as visualized by confocal microscopy. Since TM and S45Y variants of β-catenin showed predominant nuclear localization, we analyzed the activity selected β-catenin mutants by Top-Flash luciferase reporter assay as shown in Figure 8.6.2.

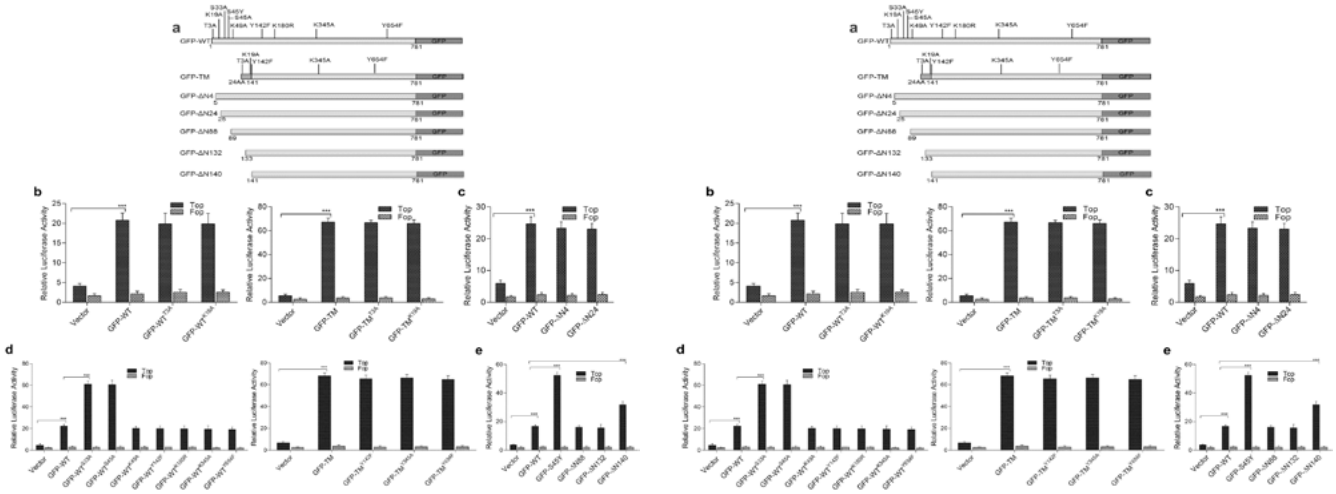


Fig. 8.6.2 Top-Flash activity of various β-catenin mutants. Left panel shows the activity of β-catenin point mutants while as the right panel shows the activity of deletion mutants. All the experiments were done in triplicates in HEK293 cells. For analysis Student's t-test and One-way ANOVA was used, bar graphs are mean±s.e.m. ***P < 0.001.

We observed a robust increase in Top-Flash reporter activity for S33A and S45Y (cancer specific) mutants while as the other point mutants did not had any impact on this activity of β-catenin (Fig Left panel). Among the N-terminal deletion mutants only delta-140 (which is more or less similar toTM) mutant resulted in two fold increase in Top-Flash reporter activity while as d-88 and d-132 had activity equal to wildtype β-catenin. Earlier structural studies of β-catenin have shown that the binding region of alpha-catenin on β-catenin maps to 120-140 amino acids. Since this whole region is missing in delta-140 and TM mutants, as a result these protein fail to interact with alpha-catenin and are free to move into the nucleus (as seen in Fig 8.6.1 above). Moreover, these proteins cannot be recruited into the destruction complex for phosphorylation mediated degradation due to the absence of exon-3 region in these protein. In another set of experiments, we have observed that TM and S45Y show robust clonogenic activity while as no such activity was observed for wildtype and d-88 proteins. Moreover, we carried immune-precipitation assays to show that only wildtype β-catenin protein interacts with alpha-catenin while the TM showed no detectable binding to alpha-catenin (Fig 3.0 Left panel). Finally, we carried out pulldown assays to confirm our results that TM does not interact with alpha-catenin unlike wildtype β-catenin (Fig 8.6.3 right panel). From all these experiments we conclude that failure of TM to interact with alpha-catenin enhances the stability of this protein and also increases the nuclear pool of beta-catenin which causes the upregulation of the activity of β-catenin target genes that promote cell growth and proliferation often resulting in cancer as seen in liver cancer cells- HepG2 cells.

9.0 CHEMICAL ENGINEERING

Current Good Manufacturing Practices (cGMP) Plant facility which has been recently established in Jammu would provide a high level world-class infrastructure for the manufacture of botanical/Phyto-pharmaceutical in a way to ensure their safety, efficacy and quality for global market. The newly built, state-of-the-art Plant for extraction, formulation, packaging of medicinal plant based Phyto-pharmaceutical drugs under internationally accepted GMP guidelines was inaugurated at CSIR-IIIM, in Jammu on October 20. This is the first such national Current Good Manufacturing Practices (cGMP) Plant facility established in the public sector in India. The facility has been issued a manufacturing licence by Drug and Food Control Organisation, Jammu and Kashmir. The establishment of this facility at CSIR-IIIM will also help all CSIR Institutes engaged in drug discovery and development in converting their natural product leads to pre-clinical and clinical development for marketing approvals. It will also 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. The experience, expertise and infrastructure like the state-of-the-art QC/QA division coupled with GLP standard Animal House available with IIIM are suitable to extend incubation ecosystem to entrepreneurs/ SMEs by providing wide range of services available in the Institute as an overall holistic research and development support, mentorship and hand holding in all spheres of phytopharmaceutical product development cycle.

Honourable minister of Science and Technology, Dr. Harsh Vardhan, inaugurated cGMP facility with Dr. Jitender Singh Minister of State (MoS) (Independent Charge) with Director General of Council of Scientific and Industrial Technology, Dr. Girish Sahni along with Director IIIM Jammu; Dr. Ram A.Vishwakarma

Institute has developed health drink from the Hippophae (*sea buckthorn)* fruit keeping medicinally important properties of the fruit in view to boost economic growth of the Ladakh region where this plant grow in wild in abundance. After a detailed study IIIM has developed a product trade named as **INDUS BERRY (**HEALTH DRINK) from Sea buckthorn pulp, filled in tetra packs of 200ml capacity which is under Beta testing of the one of the leading company in ISM in India for commercial launch. Sea Buckthorn is a super fruit full of all the Omegas – 3, 6, 9 and the rare 7, as well as a host of antioxidants and other healing nutrients. It has been used to heal psoriasis and to make skin glow, boost immunity, slow aging, and lower cholesterol, but it also has numerous other qualities that make it a superior source of vitamins and minerals we all need

The main health benefits of the fruit are the following:-

1. Treating gastrointestinal ulcers.
2. Reducing skin marking, rashes and infection, increase skin glow.
3. Improves sight and colon health
4. Anti aging and hepato-protective

CSIR-INDIAN INSTITUTE OF INTEGRATIVE MEDICINE

Canal Road, Jammu - 180001

CSIR-IIIM

INDUS BERRY

A Health Drink Developed from Sea buckthorn fruit

A new product developed by CSIR-IIIM, Jammu

- Quite rich in three Omega oils, such as omega 6, 9 and the rare 7.
- Host of antioxidants and other nutrients.
- Increases skin glow, boosts immunity, slows aging and lower cholesterol levels.
- Rich source of vitamins and minerals.
- Improves sight and colon health and is hepato-protective.
- Sea buckthorn products have the advantage of having protein building amino acids such as Vitamin A, B1, B2, C, E and K.
- The fruit also helps in treating gastro intestinal ulcer, reducing skin marking, rashes and infection.

Nutraceutical values

Components	Contents
Energy	63.375 k.cal/100ml
Carbohydrate	15.438%
Added sugar	12.5 g
Fruit sugar	2.5 g
Fat	0.112 g
Malic acid	0.452

Vitamin (per 100 g)	
A	1.64 mg
B1	0.63 mg
B2	1 mg
B6	2.1 mg
B9	4.6 mg
B12	0.48 mg
C	0.27 mg
E	9.75 mg
K	5.1 mg

About 60,000 tetra packs of 200ml capacity of the health drink were prepared for market evaluation and pubic awareness.

- Raw material: Sea buckthorn fruit obtained from Ladakh region of J&K
- Initially 400 kgs of sea buckthorn pulp was obtained from Ladakh for Lab scale experiments for the production of health drink
- Based on the results obtained in laboratory scale experiment, 12 quintals of sea buckthorn pulp were procured from Ladakh region and processed, as per the protocol finalized in the laboratory scale experiments, in an automatic plant.

Sea buckthorn (*Hippophae rhamnoides* L.) is one of the most important medicinal value fruit. It is abundantly distributed in the Himalyan regions of Leh, Ladakh and its adjoining areas of J&K. It has been used in China for quite sometimes to heal various ailments. It is a part of many modern day Allopathic and Ayurvedic formulations.

Technology / Process / Product development

9.1 Development of Standardized extract of *Woodfordia fruticosa*

Woodfordia fruticosa

Dhataki

Extract

Figure 1: *Woodfordia fruticosa* (shade dried flowers)

Introduction

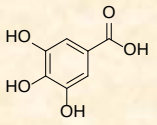
Dry Extract powder consists of *Woodfordia fruticosa* (Linn.) Kurz. (Part used: Flowers), (Fam. Lythraceae): much branched, semi deciduous, undershrub or shrub, 1-3 m high, rarely upto 3m, found throughout India, ascending to 1500 m in Himalayas and also in the Gangetic plains, also cultivated in gardens.

SYNONYMS - Sanskrit : Bahupuspi, English : Fire flame bush, Hindi : Dhai. Dhataki.

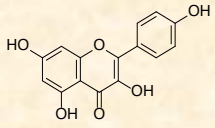
CHEMICAL CONSTITUENTS - Gallic acid, Kaempferol, Quercetin and Oenothein C.

THERAPEUTIC USES - Anti-ulcer, diarrhoea, dysentery

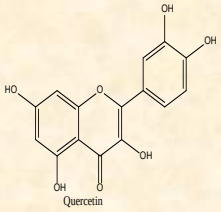
EXTRACTION PROCESS – Hydroalcoholic extraction.



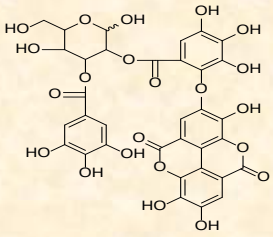
Gallic acid



Kaempferol



Quercetin

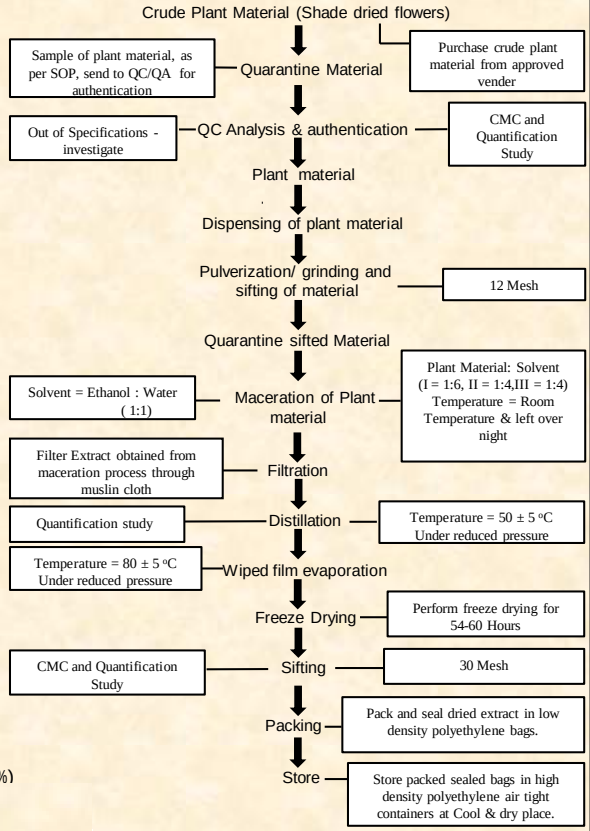


Oenothein C

Figure 2: Markers (Chemical constituents)

Figure 3: Lyophilized dry extract powder (Extractive value 25-35%)

Process flow chart of *Woodfordia fruticosa* extract powder



9.2 Development of Standardized extract of *Colebrookea oppositifolia*

Colebrookea oppositifolia

Binda

Extract

Figure 1: *Colebrookea oppositifolia* (shade dried leaves)

Introduction

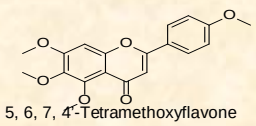
Dry Extract powder consists of *Colebrookea oppositifolia* (Part used: Leaves), Sm.(Family: Lamiaceae). Colebrookea oppositifolia is a branched shrub, growing to 1-3 m tall. Light colored stems are stout. The leaves are oblong, lancelike, finely serrated, 10-15 cm long, darkish green above, whitish hairy below. Numerous tiny white flowers occur in panicles of upright spikes, 5-10 cm long. The flower spikes look hairy, and resemble squirrel's tail. Indian Squirrel Tail is found in the Himalayas, from Kashmir to Bhutan, Punjab, Western Ghats, and many other parts of India, at altitudes of 250-1700 m.

SYNONYMS - Hindi: Binda, Marathi: Bhaman, Dasai, Konkani: Bhamini

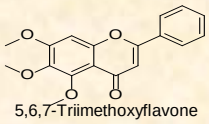
CHEMICAL CONSTITUENTS - Acteoside, CO-1, CO-3 and CO-4.

THERAPEUTIC USES – Liver fibrosis (Hepatoprotective), Cough, Antiseptic, haemostatic,dysentery.

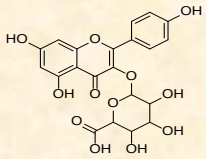
EXTRACTION PROCESS – Alcoholic extraction.



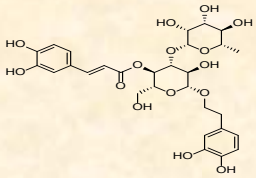
5, 6, 7, 4'-Tetramethoxyflavone (CO-4)



5,6,7-Triimethoxyflavone (CO-3)



5,7,4'-Trihydroxyflavone-3-O-glucuronide (CO-1)

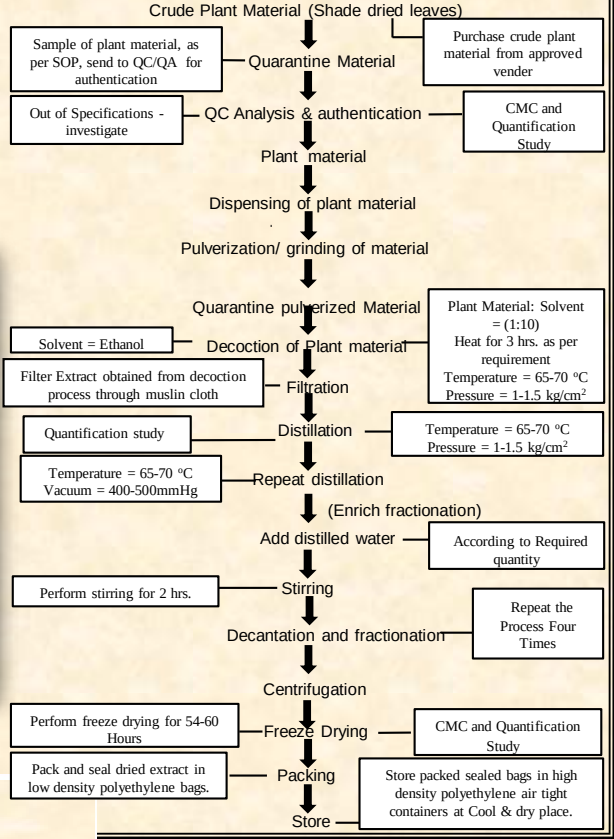


Acteoside

Figure 2: Markers (Chemical constituents)

Figure 3: Lyophilized dry extract powder (Extractive value 10-15%)

Process flow chart of *Colebrookea oppositifolia* extract powder



9.3 Development of Standardized extract of *Bergenia ciliate*

Bergenia ciliata

Pasanabheda

Extract

Figure 1: *Bergenia ciliata* (shade dried rhizome)

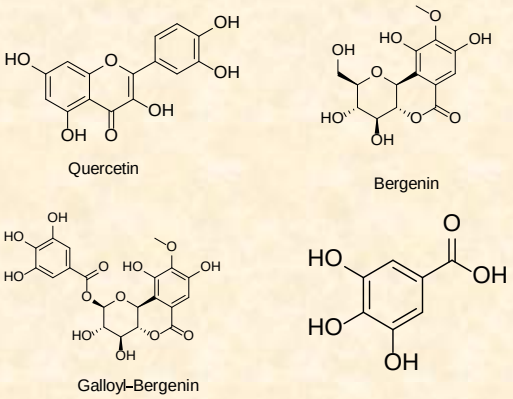


Figure 2: Markers (Chemical constituents)

Figure 3: Lyophilized dry extract powder (Extractive val

Introduction

Dry extract powder consists of *Bergenia ciliata* (Haw.) Sternb., Syn. Bergenia ligulata (Wall.) Engl. (Part used: Rhizome), (Fam. Saxifragaceae), a small perennial herb found throughout temperate Himalayas from Bhutan to Kashmir at an altitude between 2000-3000 m and in Khasia hills up-to 1200 m altitude.

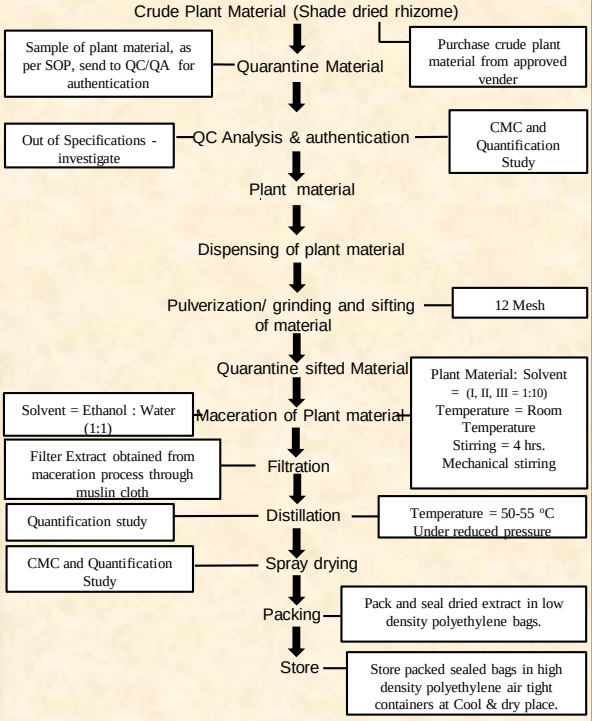
SYNONYMS - Sanskrit: Silabheda**,** Hindi: Silphara, Kashmiri: Pashanbhed

CHEMICAL CONSTITUENTS - Gallic acid, Bergenin, Quercetin and Galloyl-Bergenin.

THERAPEUTIC USES - Rheumatoid arthritis, Antidiabetic, Antibacterial and Anticancer.

EXTRACTION PROCESS – Hydroalcoholic extraction.

Process flow chart of *Bergenia ciliata* extract powder



9.4 Development of Standardized extract of *Withania somnifera*

ASHWAGANDHA

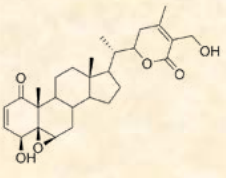
Withania somnifera

Extract

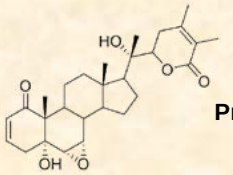
Saving Biodiversity Saving Life

CSIR-IIIM

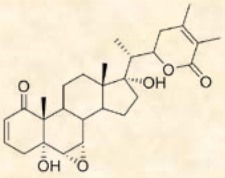
Figure 1: *Withania somnifera* (shade dried roots)



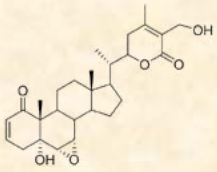
Withaferin-A



Withanolide-A



Withanone



12- deoxy withastramonolide

Figure 2: Markers (Chemical constituents)

Figure 3: Lyophilized dry extract powder (Extractive value 10-20%)

Introduction

Dry extract powder consists of *Withania somnifera* Dunal. (Part used: Roots), (Fam. Solanaceae), a perennial shrub, found in waste land, cultivated field and open grounds throughout India, widely cultivated in certain areas of Madhya Pradesh and Rajasthan, roots collected in winter, washed and cut into short pieces

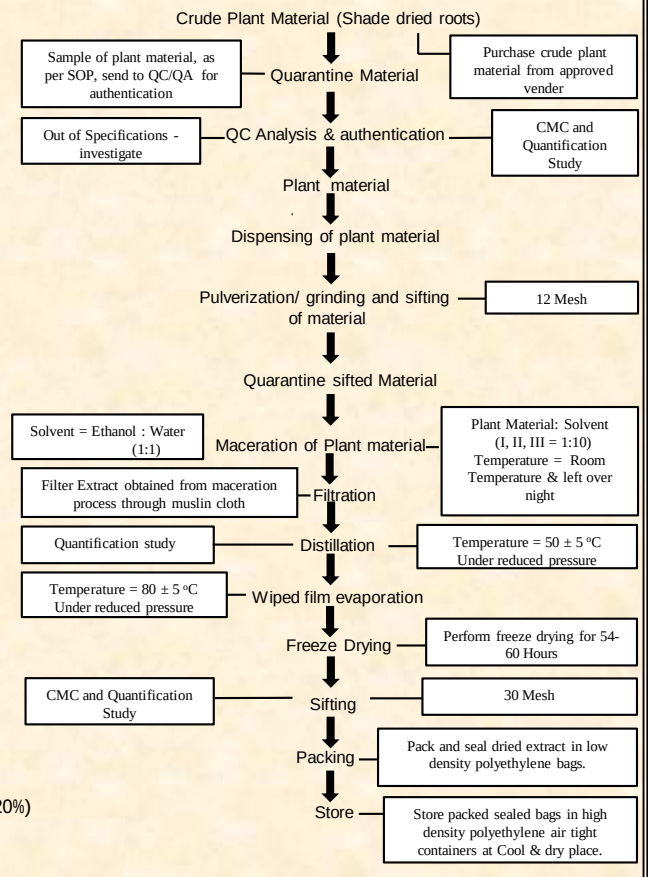
SYNONYMS - Sanskrit: Hayagandha, Hindi: Asgandh

CHEMICAL CONSTITUENTS –Withaferin-A, Withanolide -A, Withanone and 12-deoxy - withastramonolide.

THERAPEUTIC USES - Antiadipogenic, anxiety, insomnia,Immunosuppressive,, tumors

EXTRACTION PROCESS – Hydroalcoholic extraction.

Process flow chart of *Withania somnifera* extract powder



9.5 Development of Standardized extract of *Berberies Asiatica*

Berberis asiatica

Daruharidra

Extract

Saving Biodiversity Saving Life

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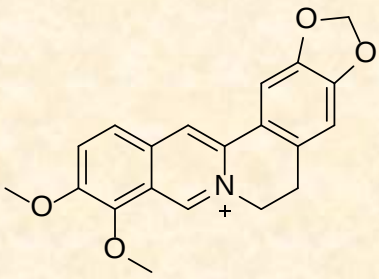
Figure 1: *Berberis asiatica* (shade dried roots)



Berberine

Figure 2: Marker (Chemical constituents)

Figure 3: Lyophilized dry extract powder (Extractive value 15-20%)

Introduction

Dry extract powder consists of *Berberis asiatica* Roxb. ex DC., (Part used: Roots), (Fam. Berberidaceae); an erect, spinous, deciduous shrub, usually 1.8-3.6 m in height found in the Himalayan ranges at an elevation of 1000-3000 m, and in the Nilgiri hills in South India.

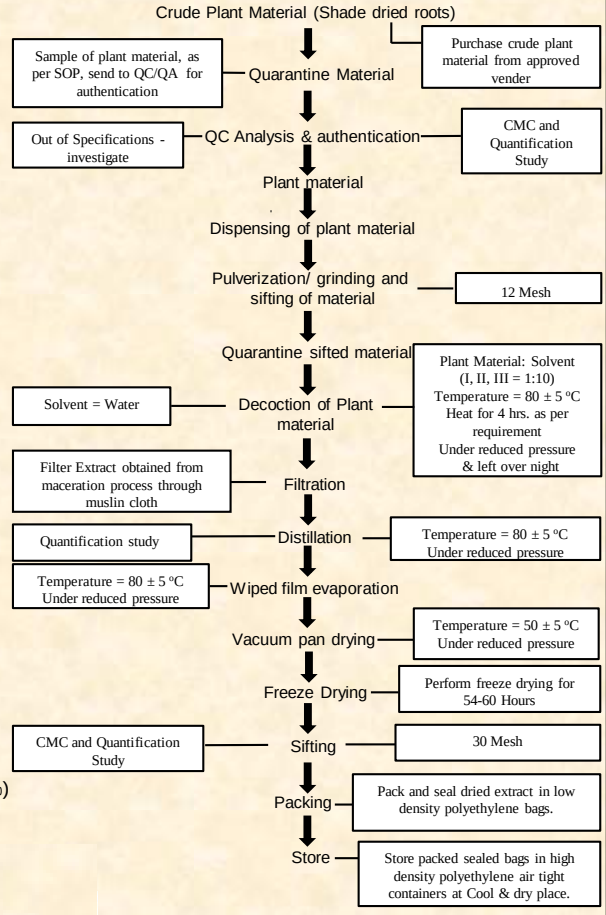
SYNONYMS - Sanskrit : Katamkateri, English : Indian Berberry, Hindi : Daruhaldi, Darhald.

CHEMICAL CONSTITUENTS – Berberine.

THERAPEUTIC USES – Antibacterial, Anticancer, Laxative, Odontalgic and Ophthalmic.

EXTRACTION PROCESS – Aqueous Extraction

Process flow chart of *Berberis lycium* extract powder



Product development of Standardized plant extract in the form of capsule/Tablet/Syrup

IIIM Jammu has created cGMP unit, a state-of-the-art national facility, for small and medium manufacturers to get their products manufactured under GMP conditions besides its use for research purpose in IIIM. Being a unique facility in CSIR, it shall cater to the research and development requirements in the country, in particular to the Northern part of the country. Several botanical leads and drug candidates (besides PHPs, nutraceuticals) have been identified at IIIM Jammu (RJM0862, ICB014, BC A002, DC A002, RJM0001, RJM0010, RJM0024, RJM0035, and RJM1195) for their production and commercialization.

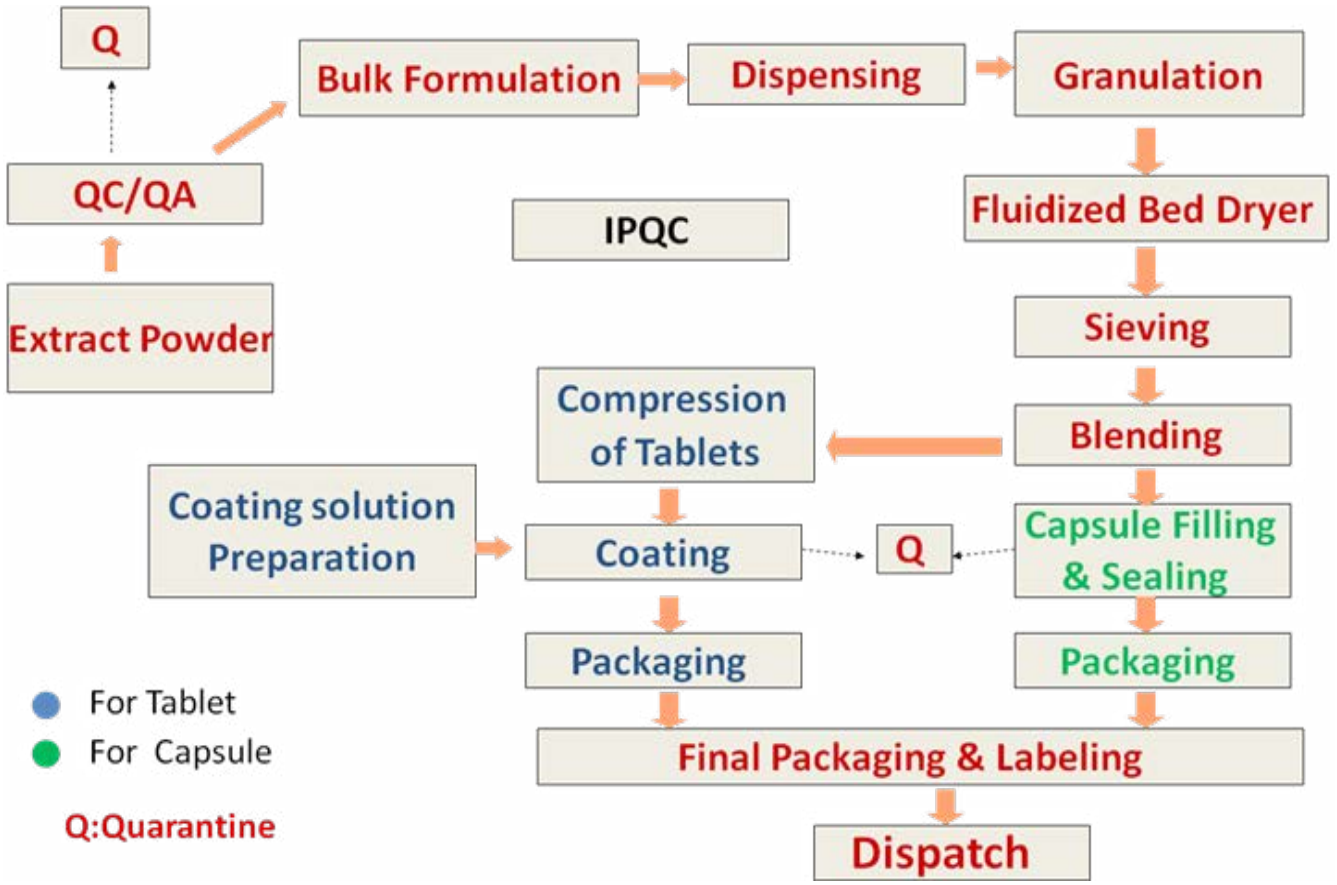
To meet global standards of quality, efficacy, safety and standardization, it requires:

- Clinical proof of efficacy done under GLP conditions using drug material prepared under Good Manufacturing Practices (GMP).
- The plant material selected to be harvested by captive cultivation/Good Agricultural Practices (GAP)

The cGMP unit has been granted license by the state regulatory authority (DFCO) and has got License for the manufacture and commercialization of following botanicals:

Sr. No.	Name of Plant Extract	Theraputic properties	Dosage form
1	*Woodfordia fructicosa*	Anti-ulcer	(Tablet/Capsule)
2	*Bergenia ciliata*	Anti-inflammatory	(Tablet/Capsule)
3	*Colebrookea oppositifolia*	Hepatoprotective	(Tablet/Capsule)

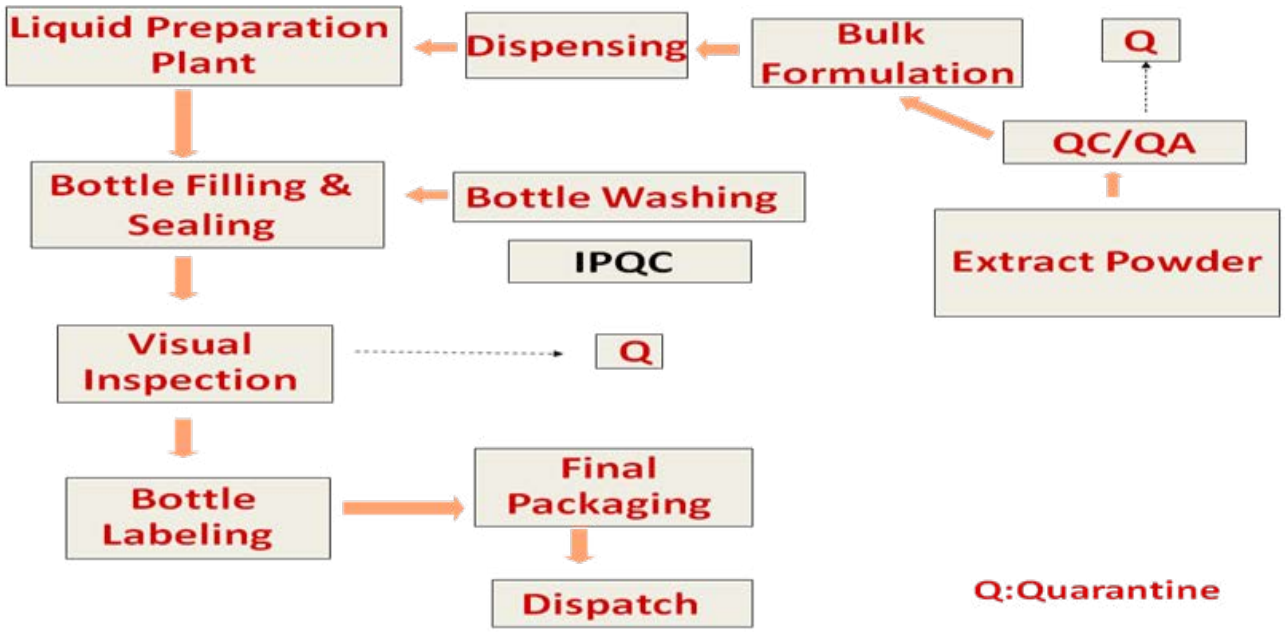
Process flow chart for Tablets & Capsule:





(Final product development in capsule and tablet form)

Process flow chart for Syrups



(Final Product in the form of syrup)

Tapewormin : Novel Herbal Drug for infections caused by Tapeworm

Vidanga consists of dried fruits of *Embelia ribes Burm*.F (Family: Myrsinaceae), large scandent shrub with long slender, flexible branches, distributed throughout hilly parts of India up to 1600 m.

Development of desired formulation by scientific validation, authentication of raw material, chemical fingerprinting, by observing all quality control and quality assurance parameters and Manufacturing its final formulation for commercialization

Brand Name : Tapewormin
Synonymous : Vidanga, Vidang, Babading,
Part used : Fruit
Taste : Slightly aromatic and astringent

This herbal drug is used against "Taeniasis" an intestinal infection caused by two species of tapeworm, namely *Taenia solium* (pork tapeworm), *Taenia saginata* (beef tapeworm), *Diphyllobothrium latum* from fish. Eating undercooked meat from infected animals is the main cause of tapeworm infection in people. When a person is infected with pork tapeworm, its larvae (cysticerci) develop in the muscles, skin, eyes and the central nervous system. When cysts develop in the brain, the condition is referred to as neurocysticercosis which causes severe headaches, blindness, convulsions, and epileptic seizures, and can be fatal.

Product Information:
Each single dose contains powder of Embelia ribes – 5 gms.
Embelia ribes, Churna (Powder)
Ingredients: Added Piper nigrum powder (0.16%w/w) for potentiating activity of active formulation.
Therapeutic activity: Anthelmintic
Manufactured By:
IIIM-CSIR Unit for Manufacturing Herbal Drugs, Jammu -180001
Mfg. License No: JK/01/14-15/AY-UN/216
Storage Condition: Store in cool and dry place away from direct sunlight.

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

Quality Control and Quality assurance Division is a National Accreditation Board for Testing and Calibration Laboratories (NABL) accredited laboratory for chemical testing as per ISO: 17025-2005. Its mission and goals are to deliver basic and applied research outputs of international quality in selected branches of chemical and biological science and to render analytical services of upmost quality associated with high degree of professional satisfaction and confidence to the customer. It is dedicatedly involved in quality control and quality assurance of agricultural and processed foods, nutraceuticals, medicinal and aromatic plants and in Chemistry Manufacturing & Control (CMC) of medicinal plants, herbal extracts and formulations. This division works hand in hand with cGMP pilot plant unit, a state-of-the-art national facility created as per WHO guidelines, for small and medium manufacturers to get their products manufactured under GMP established under Drugs and Pharmaceutical Research Program (DPRP) of DST. QCQA division has been NRL (National Referral Lab) for Honey for export to EU/Non EU and had successfully handled Residue Monitoring Plan (RMP) in project mode from 2008 till 2013.

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

I) Industry

Majorly to food industry viz a) In agricultural and processed products b) Honey and honey products c) Alcoholic drinks and beverages d) Animal feeds e) Spices and condiments. Analysis of heavy metals, pesticides, aflatoxins, various physicochemical parameters like total ash, acid insoluble ash, crude fiber, peroxide value, free fatty acids etc are being carried out. In Nutraceuticals; impurity residual profile of heavy metals, pesticides, total energy, minerals and macronutrients, vitamins analysis are being done. In Drugs and Pharmaceuticals, Quality control and CMC study on herbal extracts and formulations are been studied. In Essential Oil industry, assay, profiling and fingerprinting are done.


Figure: Facilities in QC & QA Division

II) Society

Physiochemical testing and microbial load of water from various public and private schools, universities, hospitals, small and large scale industries across whole J&K and from all parts of India. As a part of Skill Development Program (SDP), trainings are also organized on analytical instruments for postgraduate students giving them hands on experience on modern high end analytical instruments.

Details of samples received from various public, private, industries and other government sectors and analysis performed during March 2016-April 2017

S.No.	Name of the samples & Quantity	Registration No. / Date	Analysis completed
April-2016 to March-2017			
1.	Apricot oil & Apricot cake (02)	C-1718 05-04-2016	Carbohydrates, Crude fat, Energy value, Moisture, Protein, Total Ash,Ca, Cu, Fe, Mg, Mn, Zn, Aflatoxins & Vitamins
2.	Walnut kernels (01)	C-1719 06-04-2016	Moisture, Peroxide value, F.F.A & Microbial load

S.No.	Name of the samples & Quantity	Registration No. / Date	Analysis completed
3.	Water (01)	C-1720 06-04-2016	Physical, Chemical & Microbial load
4.	Water (02)	C-1721 12-04-2016	Physical & Microbial load
5.	Saffron (01)	C-1722 12-04-2016	Colour, Taste & Odor
6.	Mustard oil (01)	C-1723 12-04-2016	Acid Value, Argemone oil, Iodine Value Refractive Index, Saponification Value & Unsaponifiable Matter
7.	Water (01)	C-1724 13-04-2016	Physical
8.	Water (07)	C-1725 13-04-2016	Physical, Chemical, Pesticide & Microbial load
9.	Honey (02)	C-1726 19-04-2016	Sucrose & Fructose glucose ratio
10.	Honey (01)	C-1727 19-04-2016	Sucrose & Fructose glucose ratio
11.	Water (01)	C-1728 21-04-2016	Physical, Chemical & Microbial load
12.	Water (01)	C-1729 25-04-2016	Physical & Microbial load
13.	Water (01)	C-1730 26-04-2016	Microbial load
14.	Water (02)	C-1731 26-04-2016	Oil/grease, pH, Total Suspended Solids & Microbial load
15.	Water (01)	C-1732 28-04-2016	Microbial load
16.	Saffron (01)	C-1733 02-05-2016	Colour, Taste & Odor
17.	Water (01)	C-1734 04-05-2016	Microbial load
18.	Water (01)	C-1735 09-05-2016	Microbial load
19.	Water (01)	C-1736 16-05-2016	Physical, Chemical, Pesticide & Microbial load
20.	Tofu soya paneer (01)	C-1737 16-05-2016	Carbohydrates, Sugar, Energy value & Protein
21.	Essential oil (04)	C-1738 16-05-2016	GCMS
22.	Water (01)	C-1739 23-05-2016	Physical, Chemical, Pesticide & Microbial load
23.	Water (01)	C-1740 23-05-2016	Microbial load
24.	Water (01)	C-1741 24-05-2016	Physical, Chemical & Pesticide

S.No.	Name of the samples & Quantity	Registration No. / Date	Analysis completed
25.	Honey (01)	C-1742 30-05-2016	Fructose glucose ratio, Moisture, Sucrose, Total reducing sugar & Total sugar
26.	AFPS Samples (02)	C-1743 06-06-2016	PT / ILC
27.	Water (01)	C-1744 06-06-2016	Chemical & Microbial load
28.	Water (02)	C-1745 06-06-2016	Microbial load
29.	Water (03)	C-1746 07-06-2016	Microbial load
30.	Honey (01)	C-1747 07-06-2016	Tetracycline & Oxytetracycline
31.	Honey (05)	C-1748 10-06-2016	Sucrose &Fructose glucose ratio
32.	Water (08)	C-1749 13-06-2016	Microbial load
33.	Water (01)	C-1750 17-06-2016	Turbidity
34.	Water (01)	C-1751 20-06-2016	Turbidity
35.	Water (01)	C-1752 23-06-2016	Microbial load
36.	Beer (01)	C-1753 27-06-2016	Ethyl Alcohol, Methyl Alcohol, Carbon dioxide & pH
37.	Beer (01)	C-1754 27-06-2016	Ethyl Alcohol, Methyl Alcohol, Carbon dioxide & pH
38.	Beer (01)	C-1755 27-06-2016	Ethyl Alcohol, Methyl Alcohol, Carbon dioxide & pH
39.	PT-AQ-05G (01)	C-1756 27-06-2016	PT / ILC
40.	Water (01)	C-1757 29-06-2016	Microbial load
41.	Water (01)	C-1758 01-07-2016	Physical, Chemical, Pesticide & Microbial load
42.	Water (02)	C-1759 07-07-2016	Physical, Chemical, Pesticide & Microbial load
43.	Water (01)	C-1760 07-07-2016	Microbial load
44.	Water (01)	C-1761 08-07-2016	Microbial load
45.	Water (01)	C-1762 08-07-2016	Microbial load
46.	Water (01)	C-1763 11-07-2016	Microbial load

S.No.	Name of the samples & Quantity	Registration No. / Date	Analysis completed
47.	Walnut oil (01)	C-1764 22-07-2016	Free fatty acid
48.	Walnut kernels (01)	C-1765 26-07-2016	Moisture, Peroxide value, F.F.A & Microbial load
49.	Water (01)	C-1766 26-07-2016	Chemical & Microbial load
50.	Walnut kernels (01)	C-1767 03-08-2016	Moisture, Peroxide value, F.F.A & Microbial load
51.	Water (01)	C-1768 09-08-2016	Chemical & Microbial load
52.	Pro Life Herbal Mosquito Repellent Spray (01)	C-1769 12-08-2016	GCMS & Specific gravity
53.	Water (01)	C-1770 12-08-2016	Chlorides, Suspended matter, Organic & Inorganic
54.	Water (01)	C-1771 16-08-2016	Microbial load
55.	Water (02)	C-1772 19-08-2016	Microbial load
56.	Water (01)	C-1773 22-08-2016	Microbial load
57.	Water (01)	C-1774 22-08-2016	Chloride, Ph, Total dissolved solids, Total hardness, Total suspended solids & Turbidity
58.	Walnut kernels (01)	C-1775 24-08-2016	Moisture, Peroxide value, F.F.A & Microbial load
59.	Water (04)	C-1776 30-08-2016	Chemical & Microbial load
60.	Water (01)	C-1777 30-08-2016	Microbial load
61.	Water (01)	C-1778 30-08-2016	Microbial load
62.	Garlic (11)	C-1779 31-08-2016	Total sugar
63.	Water (01)	C-1780 05-09-2016	Microbial load
64.	Water (01)	C-1781 06-09-2016	Microbial load
65.	Water (01)	C-1782 07-09-2016	Microbial load
66.	Water (01)	C-1783 08-09-2016	Physical, As, Fe, Pesticide & Microbial load
67.	Walnut oil cake (01)	C-1784 09-09-2016	Oil %
68.	Water (01)	C-1785 15-09-2016	Microbial load

S.No.	Name of the samples & Quantity	Registration No. / Date	Analysis completed
69.	Walnut kernels (01)	C-1786 15-09-2016	Moisture, Peroxide value, F.F.A & Microbial load
70.	Water (01)	C-1787 16-09-2016	Physical, As, Fe, Pesticide & Microbial load
71.	Water (01)	C-1788 19-09-2016	Microbial load
72.	Water (01)	C-1789 27-09-2016	Microbial load
73.	Water (04)	C-1790 27-09-2016	Microbial load
74.	Water (01)	C-1791 27-09-2016	Microbial load
75.	Water (01)	C-1792 27-09-2016	Microbial load
76.	Water (01)	C-1793 03-10-2016	Microbial load
77.	Water (01)	C-1794 04-10-2016	Calcium, Chloride, Total dissolved solids, Iron & Zinc
78.	Water (01)	C-1795 04-10-2016	Microbial load
79.	Peacannuts (05)	C-1796 06-10-2016	Oil content, Copper, Manganese, Zinc & GCMS
80.	Water (01)	C-1797 07-10-2016	Microbial load
81.	Beer (01)	C-1798 14-10-2016	Ethyl Alcohol, Methyl Alcohol, Carbon dioxide & pH
82.	Water (01)	C-1799 17-10-2016	Microbial load
83.	Water (01)	C-1800 17-10-2016	Microbial load & pH
84.	Water (01)	C-1801 17-10-2016	Physical
85.	Water (01)	C-1802 19-10-2016	Physical & Microbial load
86.	Walnut kernel (02) & Oil (01)	C-1803 19-10-2016	Moisture, Peroxide value, F.F.A & Microbial load
87.	Water (01)	C-1804 19-10-2016	Chemical & Microbial load
88.	Water (01)	C-1805 19-10-2016	Chemical & Microbial load
89.	Water (01)	C-1806 24-10-2016	Microbial load
90.	Water (01)	C-1807 25-10-2016	Microbial load

S.No.	Name of the samples & Quantity	Registration No. / Date	Analysis completed
91.	Water (02)	C-1808 25-10-2016	COD, Oil & grease, pH & Total suspended solids
92.	Herbal extract (04)	C-1809 31-10-2016	HPTLC
93.	Water (01)	C-1810 02-11-2016	COD, pH, Free chlorine & Microbial load
94.	Agricultural products (31)	C-1811 02-11-2016	Ash, Citric acid, Heavy metals, Minerals, Plant extract, Total dissolved solids, Vitamins & Water content
95.	Walnut kernels (01)	C-1812 08-11-2016	Moisture, Peroxide value, F.F.A & Microbial load
96.	Water (01)	C-1813 15-11-2016	Microbial load
97.	Peach juice (01)	C-1814 18-11-2016	Total soluble solids
98.	Water (01)	C-1815 22-11-2016	Physical & Microbial load
99.	Mango juice (01)	C-1816 28-11-2016	Total soluble solids
100.	Water (02)	C-1817 01-12-2016	Physical, Chemical, Pesticide & Microbial load
101.	Water (01)	C-1818 08-12-2016	Total Hardness
102.	Water (01)	C-1819 13-12-2016	Chemical & Microbial load
103.	Water (01)	C-1820 15-12-2016	Physical & Microbial load
104.	Water (03)	C-1821 16-12-2016	COD, pH & Microbial load
105.	Water (03)	C-1822 19-12-2016	Physical, Chemical, Pesticide & Microbial load
106.	Water (01)	C-1823 20-12-2016	Microbial load
107.	Water (01)	C-1824 20-12-2016	Microbial load
108.	Water (01)	C-1825 28-12-2016	Microbial load
109.	Ayurvedic medicine (66)	C-1826 28-12-2016	Description, Heavy metals, Aflatoxins, Microbial load, Ph, L.O.D, Total ash, Acid insoluble ash, Alcohol soluble extractive & Water soluble extractive
110.	Agricultural products (09)	C-1827 28-12-2016	Heavy metals
111.	Water (03)	C-1828 04-01-2017	pH, Total hardness, Turbidity, Iron & Microbial load

S.No.	Name of the samples & Quantity	Registration No. / Date	Analysis completed
112.	Water (02)	C-1829 04-01-2017	Physical, Chemical, Pesticide & Microbial load
113.	Water (04)	C-1830 05-01-2017	Microbial load
114.	Water (01)	C-1831 10-01-2017	Microbial load
115.	Water (01)	C-1832 10-01-2017	Chemical & Microbial load
116.	Water (01)	C-1833 11-01-2017	Chemical & Physical
117.	Water (04)	C-1834 17-01-2017	Total dissolved solids
118.	Water (01)	C-1835 31-01-2017	Chemical & Microbial load
119.	Water (01)	C-1836 02-02-2017	Microbial load
120.	Water (01)	C-1837 06-02-2017	Physical
121.	Water (02)	C-1838 06-02-2017	pH, Total dissolved solids & Total hardness
122.	Water (01)	C-1839 13-02-2017	Microbial load
123.	Water (01)	C-1840 13-02-2017	Microbial load
124.	Water (03)	C-1841 20-02-2017	Arsenic
125.	Water (01)	C-1842 20-02-2017	Total dissolved solids, Total hardness & Microbial load
126.	Water (01)	C-1843 20-02-2017	Microbial load
127.	Water (01)	C-1844 20-02-2017	Microbial load

Internal samples with registration record and analysis performed in 2016-2017

S.No.	Name & No. of samples	Registration No. / Date	Analysis completed
April-2016 to March-2017			
1.	Lyophilized powder (02)	I-1755 04-04-2016	Microbial load, lactobacillus Moisture & Hygroscopicity
2.	Water (01)	I-1756 04-04-2016	Microbial load
3.	Endophytes (01)	I-1758 08-04-2016	GCMS

S.No.	Name & No. of samples	Registration No. / Date	Analysis completed
4.	Purified fractions of an extract (04)	I-1761 11-04-2016	GCMS
5.	Purified fractions of Plant extract (13)	I-1762 11-04-2016	GCMS
6.	Lyophilized powder (01)	I-1763 21-04-2016	Microbial load, lactobacillus Moisture & Hygroscopicity
7.	Sea buckthorn juice (01)	I-1765 25-04-2016	Acidity, Calorific value, Carbohydrate, Fat, Malic acid, pH, Protein, Total soluble solids & Vitamins
8.	Dry leaves (10)	I-1767 28-04-2016	Pesticide Residues, Solvent residues, Heavy Metals, Aflatoxins, Microbial load & Hygroscopicity
9.	Purified fractions from Natural product (7)	I-1768 28-04-2016	GCMS
10.	Liquid (1)	I-1769 28-04-2016	GCMS
11.	Dried wild rose fruits (3)	I-1770 28-04-2016	Vitamins, Fat, Protein & Carbohydrates
12.	Extracts (3)	I-1772 04-05-2016	Metals (Cu & Mn)
13.	Sea buckthorn oil (03)	I-1774 05-05-2016	GCMS
14.	Salt (02)	I-1775 05-05-2016	Na, Fe, K, Mg & Iodine
15.	Essential oil (01)	I-1776 09-05-2016	GCMS
16.	Dry leaf powder (10)	I-1778 19-05-2016	Protein, Carbohydrates, Sugar, Cr, Cu, Fe, K, Mg, Mn, Se, Zn & Vitamins
17.	Lyophilized powder (02)	I-1791 14-06-2016	Protein, Fat, Total solid, Sugar, Calcium & Iron
18.	Lyophilized powder (02)	I-1792 14-06-2016	Microbial load
19.	Water (01)	I-1796 20-06-2016	Microbial, Chemical & Physical
20.	Liquid (03)	I-1798 22-06-2016	Microbial, Chemical & Physical
21.	Aloe drink juice (01)	I-1806 01-07-2016	Microbial Load, Vitamins, Energy value, pH, Heavy metals & Pesticide residues
22.	Powder (01)	I-1807 05-07-2016	Moisture, Protein, Sugar & Dissolved solids
23.	Essential oil (01)	I-1809 14-07-2016	GC
24.	Churan powder (03)	I-1812 20-07-2016	Pesticide residues
25.	Nasturtium officinale (fixed oil) (01)	I-1813 20-07-2016	Minerals, Vitamins, Fatty acid profile & Nutritional profile

S.No.	Name & No. of samples	Registration No. / Date	Analysis completed
26.	Alcoholic ext. (03)	I-1817 28-07-2016	Vitamins, Protein, Sugar & Carbohydrates
27.	DHA (01)	I-1818 29-07-2016	GCMS
28.	DHA (02)	I-1819 03-08-2016	GCMS
29.	Capsule (Sailin-Hbs) (01)	I-1822 23-08-2016	HPLC Quantification, Aflatoxin, Heavy metals & Microbial load
30.	Fermented material (02)	I-1823 26-08-2016	% of alcohol ethanol
31.	Plant material (01)	I-1824 02-09-2016	GCMS
32.	F-1 liquid (01)	I-1825 02-09-2016	Microbial load & Total Sugar
33.	Plant ext. (01)	I-1827 05-09-2016	GCMS
34.	*Colebrookea* (01)	I-1828 05-09-2016	Aflatoxin & Microbial load
35.	Watercress Kale (03)	I-1829 07-09-2016	GCMS
36.	*Bergenia ciliate* extract(03)	I-1832 22-09-2016	Hygroscopicity & Microbial Load
37.	Pinole (01)	I-1833 29-09-2016	GCMS
38.	Extracts (06)	I-1834 29-09-2016	HPLC Quantification
39.	*Colebrookea & Bergenia ciliate* extracts (02)	I-1835 05-10-2016	Moisture, Hygroscopicity, Aflatoxins & Microbial Load
40.	Plant ext. (04)	I-1837 25-10-2016	Heavy metals
41.	RJM-0862 (01)	I-1840 04-11-2016	Aflatoxin & Microbial load
42.	Solid (01)	I-1842 09-11-2016	Minerals and Heavy Metals
43.	Distilled water/RJMAEF/ *Colebrookea* (03)	I-1844 22-11-2016	Aflatoxin & Microbial load
44.	Lemon grass oil/Volatile oil (02)	I-1845 23-11-2016	GCMS
45.	Water (01)	I-1846 25-11-2016	Microbial, Chemical & Physical
46.	Soil (03)	I-1847 25-11-2016	As, Cd, Cu, Fe, Pb, Mn, Hg, K, Zn & Pesticide residues
47.	Apricot oil (01)	I-1848 29-11-2016	GC/MS, F.F.A, Iodine value, Peroxide value, Saponification value & Heavy metals

QCQA Services delivered to cGMP plant in 2016-17

S.No.	Name of the Plant / Extract & No. of samples	Registration No. / Date	Analysis completed
2016			
1.	Plant material (02)	I-1757 05-04-2016	Heavy metals, Quantification by HPLC, Microbial load & Moisture content
2.	*Bergenia ciliata* (Hydroalcoholic extract) (03)	I-1759 11-04-2016	Microbial load
3.	*Bergenia ciliata* (Hydroalcoholic extract) (03)	I-1760 11-04-2016	Aflatoxins
4.	Distillated alcohol	I-1766 26-04-2016	% of alcohol
5.	*Colebrookea oppositifolia* Extract (03)	I-1771 26-04-2016	Quantification by HPLC
6.	Crude Plant Material (02)	I-1777 20-05-2016	Aflatoxins, Pesticide and foreign matter
7.	Extracts CEXTD (04)	I-1779 24-05-2016	% of alcohol
8.	Extracts CEXTD (01)	I-1780 24-05-2016	Extractive value
9.	*Woodfordia fruticosa* extract (Stability samples) (05)	I-1781 24-05-2016	Description, HPLC Quantification, Hygroscopicity & Microbial load
10.	USP PW RO water (15)	I-1781 24-05-2016	Total viable aerobic count, pathogens and TBC
11.	USP PW RO water (15)	I-1783 25-05-2016	pH, conductivity, acidity and alkalinity, Calcium and Magnesium, chloride and heavy metals
12.	RJM Syrup and Extract	I-1784 30-05-2016	pH, Specific gravity, assay by HPLC
13.	CG/T (03)	I-1786 31-05-2016	% of alcohol
14.	*Bergenia ciliata* Plant material (01)	I-1787 08-06-2016	Acid insoluble ash, Total ash, Alcohol soluble & water soluble extractive, LOD Moisture, Pesticides, Aflatoxins, Heavy metals, Hygroscopicity, pH, HPLC Quantification, Microbial load & Density/Bulk density test
15.	*Bergenia ciliata* Hydroalcoholic extract (01)	I-1788 08-06-2016	Acid insoluble ash, Total ash, Alcohol soluble & water soluble extractive, LOD Moisture, Pesticides, Aflatoxins, Heavy metals, Hygroscopicity, pH, HPLC Quantification, Microbial load & Density/ Bulk density test
16.	*Colebrookea oppositifolia* Extract (01)	I-1789 09-06-2016	Acid insoluble ash, Total ash, Alcohol soluble & water soluble extractive, Pesticides, Aflatoxins, Heavy metals, Hygroscopicity, pH, HPLC Quantification, Microbial load & Density/Bulk density test

S.No.	Name of the Plant / Extract & No. of samples	Registration No. / Date	Analysis completed
17.	RA/ after (03)	I-1790 10-06-2016	% of water
18.	*Bergenia ciliata* Extract (01)	I-1793 14-06-2016	Acid insoluble ash, Total ash, Alcohol soluble & water soluble extractive, LOD Moisture, Pesticides, Aflatoxins, Heavy metals, Hygroscopicity, pH, HPLC Quantification, Microbial load & Density/ Bulk density test
19.	*Colebrookea oppositifolia* Alcoholic extract (01)	I-1794 15-06-2016	Acid insoluble ash, Total ash, Alcohol soluble & water soluble extractive, Pesticides, Aflatoxins, Heavy metals, Hygroscopicity, pH, HPLC Quantification, Microbial load & Density/Bulk density test
20.	*Woodfordia fruticosa* Extract (02)	I-1795 15-06-2016	Quantification by HPLC
21.	Phalsa pulp (04)	I-1797 17-06-2016	Pesticides, aflatoxins, heavy metals, pH, microbial load & calories, fat, carbohydrates, proteins & vitamins estimation
22.	*Bergenia ciliata* (01)	I-1801 24-06-2016	Acid insoluble ash, Total ash, Alcohol soluble & water soluble extractive, LOD Moisture, Pesticides, Aflatoxins, Heavy metals, Hygroscopicity, pH, HPLC Quantification, Microbial load & Density/ Bulk density test
23.	RA / after (03)	I-1802 28-06-2016	% of water
24.	CO Rinse water	I-1803 28-06-2016	pH, microbial load
25.	BC Rinse water	I-1804 29-06-2016	pH, microbial load
26.	*Woodfordia fruticosa* Hydroalcoholic Extract	I-1805 01-07-2016	HPLC Quantification & Microbial load
27.	*Colebrookea oppositifolia* leaves (01)	I-1810 19-07-2016	Description, Acid insoluble ash, Total ash, Alcohol soluble & water soluble extractive, LOD, Pesticides, Aflatoxins, Heavy metals, Hygroscopicity, pH, HPLC Quantification, Microbial load
28.	BC Rinse water	I-1811 19-07-2016	pH, microbial load
29.	*Colebrookea oppositifolia* Plant material (03)	I-1815 26-07-2016	Microbial load
30.	Sea buck thorn (01)	I-1820 05-08-2016	Microbial load
31.	Water (06)	I-1821 10-08-2016	Microbial load, Heavy metals & Physical
32.	*Woodfordia fruticosa* Hydroalcoholic Extract (03)	I-1826 30-08-2016	Extractive value & pH

S.No.	Name of the Plant / Extract & No. of samples	Registration No. / Date	Analysis completed
33.	Bergenia Capsules (01)	I-1830 14-09-2016	Disintegration test
34.	Woodfordia fruticosa Hydroalcoholic Extract Stability studies(05)	I-1831 14-09-2016	LCMS Quantification, Microbial load, Description & Hygroscopicity
35.	CBOF Hepatocole (02)	I-1836 24-10-2016	Chemical analysis by LCMS
36.	CETD extract (003-005)	I-1838 31-10-2016	Hygroscopicity
37.	Starch inactive powder (01)	I-1839 28-10-2016	pH, L.O.D, Moisture & Microbial
38.	Bergenia Capsules (06) Stability samples	I-1841 07-11-2016	Description, Disintegration test HPLC quantification & Microbial load
39.	Tapewormin powder form churna (1)	I-1843 17-11-2016	Description, pH, ash, L.O.D, Acid insoluble ash, Aflatoxins, Water & Alcohol soluble extractive, Heavy metals, Pesticide & Microbial load
40.	Cassia Grinded plant (1)	I-1849 02-12-2016	Description, pH, ash, L.O.D, Acid insoluble ash Aflatoxins, Water & Alcohol soluble extractive, Heavy metals, Pesticide & Microbial load
41.	Crude plant materials WS, GG, BS (03)	I-1851 19-12-2016	Description, pH, ash, L.O.D, Acid insoluble ash Aflatoxins, Water & Alcohol soluble extractive, Heavy metals, Pesticide & Microbial load
42.	Sailin Hbs Capsules (02) & Extract (01)	I-1853 21-12-2016	Description, pH, ash, L.O.D, Acid insoluble ash Aflatoxins, Water & Alcohol soluble extractive, Heavy metals, Pesticide & Microbial load
43.	Woodfordia Extract (01)	I-1854 23-12-2016	Description, pH, ash, L.O.D, Acid insoluble ash Aflatoxins, Water & Alcohol soluble extractive, Heavy metals, Pesticide & Microbial load

QCQA Services delivered to cGMP plant in 2017

S.No.	Name of the Plant / Extract & No. of samples	Registration No. / Date	Analysis completed
1.	WF/B-4, Long term stability study	I-1855 03-01-2017	Hygroscopicity, Microbial load & LCMS Quantification
2.	CA-OC Rinse water (02)	I-1860 05-01-2017	Traces of previous material by LCMS Quantification
3.	ER Powder form (01)	I-1861 05-01-2017	HPLC Quantification
4.	*Woodfordia fruticosa* / Plant material (01)	I-1863 10-01-2017	Microbial load
5.	CG/Alcohol	I-1864 10-01-2017	% age of alcohol
6.	PW/Before/WF-06	I-1866 10-01-2017	pH, Conductivity & Microbial load

S.No.	Name of the Plant / Extract & No. of samples	Registration No. / Date	Analysis completed
7.	Cassia Alcoholic extract (03)	I-1867 12-01-2017	LCMS Quantification
8.	Cassia Alcoholic extract (03)	I-1868 12-01-2017	LCMS Quantification
9.	Cassia Alcoholic extract (03)	I-1869 12-01-2017	LCMS Quantification
10.	Cassia Alcoholic extract (03)	I-1870 12-01-2017	LCMS Quantification
11.	Cassia Alcoholic extract (03)	I-1871 12-01-2017	LCMS Quantification
12.	Cassia Alcoholic extract (03)	I-1872 12-01-2017	LCMS Quantification
13.	Cassia Alcoholic extract (03)	I-1874 19-01-2017	LCMS Quantification
14.	PW/Before/WF-07	I-1876 19-01-2017	pH & Conductivity
15.	WF-07/Rinse water	I-1878 24-01-2017	Description and traces of previous product by LCMS
16.	*Cassia occidentalis* extract (01)	I-1877 20-01-2017	Description, Aflatoxin, Heavy metals, Acid insoluble ash, Total ash, Loss on drying, Alcohol soluble extractive, Water soluble extractive, Hygroscopicity, pH, Pesticide residue & Microbial load
17.	Rinse water (01)	I-1878 24-01-2017	Description & LCMS Quantification
18.	DEXTD (WF/CMC/B-06)	I-1879 25-01-2017	Description, HPLC Quantification, Aflatoxin, Heavy metals, Acid insoluble ash, Total ash, Loss on drying, Alcohol soluble extractive, Water soluble extractive, Pesticide residue & Microbial load
19.	PW/ Before/ WS-01	I-1880 25-01-2017	Microbial load
20.	*Cassia occidentalis* Grinded plant (01)	I-1881 30-01-2017	Microbial load
21.	*Colebrookea oppositifolia* / Lyophilized powder (01)	I-1882 30-01-2017	LCMS Quantification
22.	*Colebrookea oppositifolia* Crude plant material	I-1886 07-02-2017	Description, HPLC Quantification, Aflatoxin, Heavy metals, Acid insoluble ash, Total ash, LO.D, Alcohol soluble extractive, Water soluble extractive, Pesticide residue & Microbial load
23.	CO/Liquid Rinse water (01)	I-1888 14-02-2017	Description & Quantification by HPLC
24.	PW/Before/WS-02	I-1889 14-02-2017	Conductivity, pH & Microbial load
25.	*Woodfordia fruticosa* capsules (03)	I-1890 14-02-2017	Description, Disintegration test, Quantification by HPLC & Microbial load

S.No.	Name of the Plant / Extract & No. of samples	Registration No. / Date	Analysis completed
26.	Woodfordia Capsules (03)	I-1891 14-02-2017	Description, Disintegration test, Quantification by HPLC & Microbial load
27.	PW/Before/WS DEXTD-006 Water	I-1894 22-02-2017	Conductivity, pH & Microbial load
28.	CO/ CMC/B-01 Lyophilized powder (01)	I-1896 03-03-2017	Description & Quantification by HPLC
29.	PW/Before/WS-04	I-1899 07-03-2017	Conductivity, pH & Microbial load
30.	*Colebrookea oppositifolia* Recovered alcohol	I-1900 08-03-2017	% of Alcohol & traces of previous product
31.	PW/Before/GG-01	I-1901 08-03-2017	Conductivity, pH & Microbial load
32.	*Colebrookea oppositifolia* / Dried extract powder (02)	I-1902 10-03-2017	Description, HPLC Quantification, Aflatoxin, Heavy metals, Acid insoluble ash, Alcohol soluble extractive, Hygroscopicity, L.O.D, pH, Total ash, Water soluble extractive, Pesticide residue & Microbial load
33.	*Colebrookea oppositifolia* Recovered alcohol	I-1903 15-03-2017	%age of Alcohol and water & Traces of previous product by LCMS Quantification
34.	WS-04 Rinse water DEXTD-007	I-1904 15-03-2017	Description & Traces of previous product by LCMS Quantification
35.	Woodfordia Hydroalcolic extract stability studies (04)	I-1907 21-03-2017	Description & HPLC Quantification Study & microbial load
36.	BC Extract tablets Solid dosage form (03)	I-1908 21-03-2017	Description, HPLC Quantification, Aflatoxin, Heavy metals, Acid insoluble ash, Alcohol soluble extractive, Hygroscopicity, L.O.D, pH, Total ash, Water soluble extractive, Pesticide residue, Weight variation, Disintegration test, Size diameter, Hardness, Average weight, Friability test & Microbial load
37.	Raw Water	I-1909 28-03-2017	Microbial load
38.	CG/Alcohol/cGMP	I-1910 30-03-2017	Total Acidity as Tartaric Acid, Ethyl Alcohol, Volatile acidity as acetic acid, Methyl Alcohol, Total solids, Esters as ethyl acetate, Aldehydes as acetaldehyde
39.	Rinse Water (01)	I-1911 30-03-2017	Description & HPLC Quantification Study

11.0 KNOWLEDGE RESOURCE CENTRE (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 them 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:

11a) 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 Agro-technology & Cultivation of Medicinal and Aromatic plants.

During financial year 2016-17, IIIM KRC purchased 205 document including books (both in Hindi & English Language), Standards and other reference resource in its collection.

The present holding status is as under:

i. Purchased documents: 27640
ii. Periodicals Bound Volumes: 17187
iii. Doctoral Thesis: 62
iv. Standards: 1089
v. Photocopies (Bound): 2129
vi. Gratis and Pamphlets - 773

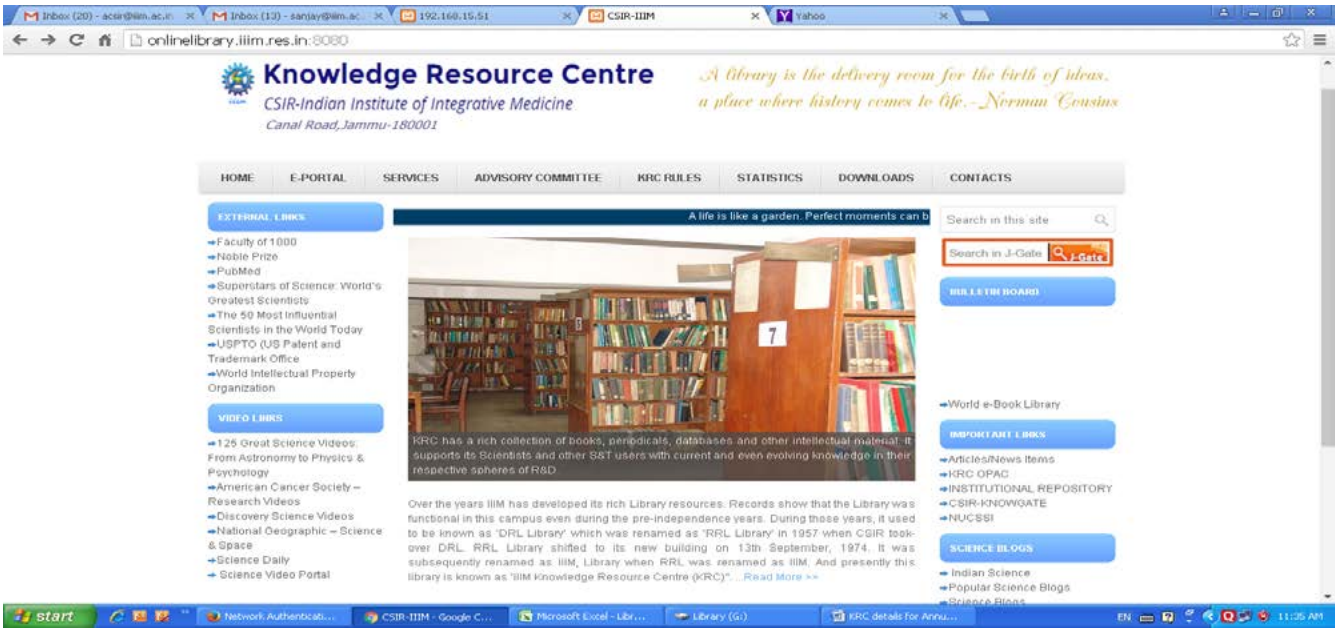
11b) E-Resources:

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. Presently, a total of 26 online e-Journals and six online databases are being subscribed.

The total budget allocation during the financial year 2016-17 was Rs.1.25 crore.

It has computerized all its in-house activities which are being maintained and updated on a regular basis. KRC 'Online Public Access Catalogue (OPAC)' link has been provided on KRC Website.



A screenshot of Homepage of IIIM Library (KRC) website.

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.

Key initiatives:

1. KRC has developed its website with the help of IIIM-IT Cell (URL: www.onlinelibrary.iiim.res.in/). Besides other useful information and links, links to all the subscribed e-resources; NKRC resources, etc. are available through this website.

2. The Institute organised a two week's training programme on "Tools and Techniques in Chemical Ecology" (A DBT's Chemical Ecology Network Programme – National Centre for Biological Science (TIFR), Bangaluru). During this training programme a presentation cum live demo of "Library e-Resources and their applications at IIIM" was given to the participants.

3. Training programmes on online databases being subscribed by the Institutes were organized for the benefit of internal Researchers, Scientists and other Technical Staff.

12.0 Academy of Scientific and Innovative Research (AcSIR) activities at CSIR-IIIM, Jammu during 2016-17

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, 2016 session a total of ten (10) PhD Students got themselves registered at IIIM, Jammu. Similarly, in January, 2017 session twenty four (24) Students were selected for admission to PhD programme.

As course curriculum, a student has the choice to select his/her Course Work topics 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. The Comprehensive Examination and Viva Voce (OEB) of the student involve at least one 'External Expert Member'.

A total of 24 Comprehensive Examination Meetings were conducted during the period. Also, 26 AcSIR students successfully defended their PhD viva voice (OEB) examination. The list of successful candidates is as under:

S. No.	Name & Enrollment No. of Scholar	Supervisor/ Co-Supervisor	Title of Thesis	Month & Year
1.	Mr. Deepak Kumar (10CC11J37022)	Dr. Debaraj Mukherjee	Target based synthesis of medicinally important compounds inspired from microbial natural product scaffold	April, 2016
2.	Mr. Yempalla Kushalva Reddy (10CC11J37046)	Dr. Parvinder Pal Singh	Design and Synthesis of Novel Anti-TB Leads	April, 2016
3.	Mr. Reddy G. Lakashma (10CC11J37036)	Dr. S.D. Sawant	Synthesis and biological evaluation of analogs of pyrazolopyrimidine scaffold	April, 2016
4.	Mr. Bilal Ahmad Rah (10BB11J37009)	Dr. Anindya Goswami	Molecular Signaling Based Study of a Novel 3-azido-withaferin A for Anticancer Therapeutic Potential	April, 2016
5.	Mr. Baljinder Singh (10CC11J37018)	Dr. Ram Vishwakarma / Dr. Sandip B. Bharate	Exploring the Medicinal Potential of High Altitude Plants and Microbes: Synthesis and Biological Evaluation of Natural Products and Their Analogs	May, 2016
6.	Mr. Madhubabu Tatina (10CC11J37027)	Dr. Debaraj Mukherjee	Development of novel methods for C-glycosylation and synthesis of sugar derived versatile building blocks	May, 2016
7.	Mr. Rammohan R. Yadav (10CC11J37035)	Dr. Sandip B. Bharate	Medicinal chemistry of indole and quinazoline class of marine natural products to explore their biological potential	June, 2016
8.	Mr. Sudhakar Manda (10CC11J37040)	Dr. Sandip B. Bharate	Medicinal chemistry of indole alkaloids and alkylidene phosphonates to explore their biological potential	June, 2016
9.	Mr. Sravan Kumar Aithagani (10CC11J37037)	Dr. Parvinder Pal Singh	Development of New Synthetic Methods: Functionalization of Electron-Deficient Heteroarenes and Arynes	June, 2016
10.	Mr. Arvind Kumar (10CC13J37010)	Dr. Bhahwal Ali Shah	Synthesis of Natural Products Inspired Bioactive Molecules and Development of New Synthetic Methods	July, 2016

S. No.	Name & Enrollment No. of Scholar	Supervisor/ Co-Supervisor	Title of Thesis	Month & Year
11.	Mr. Nagaraju Mupparapu (10CC11J37033)	Dr. Qazi Naveed Ahmed	2- Oxoiminium promoted oxidative cross coupling reactions to different exigent C-X(X=C, N & S) bonds and medicinal chemistry of 2-3 dihydroquinazolin-4(1H)-ones for generation of anti-cancer agents	July, 2016
12.	Mr. Nalli Yedukondalu (10CC11J37045)	Dr. Asif Ali	Chemical Investigation of Medicinal Plants, Microbes and Synthetic modification of bioactive metabolite to achieve new biological knowledge	August, 2016
13.	Mr. Zila Mahesh Kumar (10CC11A37009)	Dr. Asif Ali	Isolation, synthetic modification of natural products to develop lead molecules and development of new synthetic methodologies for the preparation of biologically active molecules	August, 2016
14.	Mr. Srinivas Maheshuri (10CC11J37039)	Dr. S.D. Sawant	Synthesis and Biological Evaluation of Quinazolinone and ET743 Anlogs for Discovery of Anticancer Agents and Development of New Synthetic Methods	Sept., 2016
15.	Mr. Satyanarayan Battula (10CC11J37020)	Dr. Qazi Naveed Ahmad	Studies on Reactions of Selective Nucleophiles at Key Aldehyde Electrophilic Centers and Development of β–Carbolines as Antimalarial Agents	Sept., 2016
16.	Mr. Anup Singh Pathania (10BB11J37007)	Dr. Fayaz Malik	Exploring molecular mechanisms associated with the cancer cell death induced by plant based natural product	Oct., 2016
17.	Mr. Narsiah Battini (10CC11J37019)	Dr. Qazi Naveed Ahmad	2-Oxo Driven Novel Reactions and Medicinal Chemistry of β-carbolines for the Generation of Anti-malarial Candidates	Dec., 2016
18.	Ms. Chitra Rani (10BB11J37010)	Dr. Inshad Ali Khan	Identification of small molecule inhibitors of the N-acetylglucosamine-1-phosphate uridyltransferase in *Mycobacterium tuberculosis*	Dec., 2016
19.	Ms. Rashmi Sharma(10BB11J37013)	Dr. Inshad Ali Khan	Identification of small molecule inhibitors of the acetyltransferase domain of N acetylglucosamine-1-phosphate-uridyltransferase/ glucosamine-1-phosphate acetyltransferase (GlmU) in Escherichia coli	Dec., 2016
20.	Mr. Vikrant Singh Rajput(10BB11A37002)	Dr. Inshad Ali Khan	Identification of inhibitors of Shikimate kinase of Mycobacterium tuberculosis	Dec., 2016
21.	Mr. Desaboini Nageshwara Rao(10CC11J37023)	Dr. Parthasarthi Das	Studies Directed Towards the formation of C-N and C-C Bonds for the Synthesis of Nitrogenated Heterocycles	January, 2017
22.	Mr. Anil Kumar Pagadala(10CC11J37017)	Dr. Qazi Naveed Ahmed	Development of Different Exigent Carbon-Heteroatom Bonds Employing Aldehydes & Acids and Medicinal Chemsitry of T0901317 for the Generation of P- glycoprotein	February, 2017
23.	Mr. Anil Kumar Kusunuru (10CC11A37010)	Dr. Debaraj Mukherjee	Development of novel methods for C-glycosylation	February, 2017

S. No.	Name & Enrollment No. of Scholar	Supervisor/ Co-Supervisor	Title of Thesis	Month & Year
24.	Mr. Jaideep. B. Bharate (10CC12A37032)	Dr. Ram Vishwakarma	Metal-Free and Metal – Mediated Domino One-Pot Synthesis of Medicinally Important Scaffolds and Screening of Molecular Libraries as Potential Modulators of P-glycoprotein Efflux Pump	February, 2017
25.	Ms Rajni Sharma (10CC11J37034)	Dr. Ram Vishwakarma / Dr. Sandip B. Bharate	Discovery of natural products based leads for cancer chemoprevention and anticancer therapy via semi-synthetic modifications	March, 2017
26.	Mr. Thanusha Thatikonda (10CC11J37042)	Dr. Parvinder Pal Singh	Design and synthesis of 1,3,5-triazine based PI3K inhibitors and development of novel synthetic methodologies	March, 2017

The AcSIR Cell at IIIM is taking necessary initiatives to ensure smooth functioning of all 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 Coordination office, AcSIR-Coordinator, Ph. D Supervisors, Students, DAC Members & other External Experts.

It is taking utmost care in proper record-keeping; to ensure that AcSIR 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 2016)

S.No.	Title	Author	Impact Factor
1	Glycyrrhiza glabra extract and quercetin reverses cisplatin resistance in triple-negative MDA-MB-468 breast cancer cells via inhibition of cytochrome P450 1B1 enzyme. Bioorganic & Medicinal Chemistry Letters (2017), 27(24), 5400-5403, DOI:10.1016/j.bmcl.2017.11.013	Sharma, Rajni; Gatchie, Linda; Williams, Ibidapo S.; Jain, Shreyans K.; Vishwakarma, Ram A.; Chaudhuri, Bhabatosh; Bharate, Sandip B.	2.454
2	(E)-3-(3,4,5-Trimethoxyphenyl)-1-(pyridin-4-yl)prop-2-en-1-one, a heterocyclic chalcone is a potent and selective CYP1A1 inhibitor and cancer chemopreventive agent. Bioorganic & medicinal chemistry letters (2017), 27(24), 5409-5414.	Horley Neill J; Beresford Kenneth J M; Kaduskar Supriya; McCann Glen J P; Ruparelia Ketan C; Sonawane Vinay R; Joshi Prashant; Williams Ibidapo S; Gatchie Linda; Bharate Sandip B; et al	2.454
3	Phytochemical evaluation of major bioactive compounds in different cytotypes of five species of Rumex L. Industrial Crops and Products (2017), 109, 897-904. DOI:10.1016/j.indcrop.2017.09.015	Jeelani, Syed Mudassir; Farooq, Umer; Gupta, Ajai Prakash; Lattoo, Surrinder K.	3.181
4	Design of Novel 3-Pyrimidinylazaindole CDK2/9 Inhibitors with Potent In Vitro and In Vivo Antitumor Efficacy in a Triple-Negative Breast Cancer Model. Journal of Medicinal Chemistry (2017), 60(23), 9470-9489, DOI:10.1021/acs.jmedchem.7b00663	Singh, Umed; Chashoo, Gousia; Khan, Sameer U.; Mahajan, Priya; Nargotra, Amit; Mahajan, Girish; Singh, Amarinder; Sharma, Anjna; Mintoo, Mubashir J.; Guru, Santosh Kumar; et al	6.259
5	Synthesis of Tetrahydroquinoline-Embedded Bridged Benzothiaoxazepine-1,1-dioxides. European Journal Of Organic Chemistry (2017), (45), 6671-6679.	Borgohain, H; Devi, R; Dheer, D; Borah, BJ; Shankar, R; Das, SK	2.834
6	Design and synthesis of indolopyridone hybrids as new antituberculosis agents. Microbial Pathogenesis (2017), 113, 330-334. DOI:10.1016/j.micpath.2017.10.045	Rather, Muzafar Ahmad; Rasool, Faheem; Bhat, Zubair Shanib; Dar, Hafiz- Ullah; Maqbool, Mubashir; Amin, Shajrul; Yousuf, Syed Khalid; Ahmad, Zahoor	2.009
7	The Ritter Reaction of 2-Oxoaldehydes at Room Temperature: Divergent Behaviour towards Acid Strength. ChemistrySelect (2017), 2(34), 11336-11340, DOI:10.1002/slct.201701862	Khan, Shahnawaz; Kumar, Atul; Gupta, Raman; Ahmed, Qazi N.	YET TO COME
8	Pharmacokinetics, pharmacodynamics and safety profiling of IS01957, a preclinical candidate possessing dual activity against inflammation and nociception. Regulatory Toxicology and Pharmacology (2017), 91, 216-225, DOI:10.1016/j.yrtph.2017.10.033	Sharma, A; Magotra, A; Dogra, A; Rath, SK; Rayees, S; Wazir, P; Sharma, S; Sangwan, PL; Singh, S; Singh, G; Nandi, U	2.221
9	Preparation, characterization and cytotoxic evaluation of bovine serum albumin nanoparticles encapsulating 5-methylmellein: A secondary metabolite isolated from Xylaria psidii. Bioorganic & Medicinal Chemistry Letters (2017), 27(23), 5126-5130, DOI:10.1016/j.bmcl.2017.10.064	Arora, D; Kumar, A; Gupta, P; Chashoo, G; Jaglan, S	2.454

S.No.	Title	Author	Impact Factor
10	Antagonistic potential of a psychrotrophic fungus: &ITTrichoderma velutinum&IT ACR-P1. Biological Control(2017), 115, 12-17.	Sharma, R; Magotra, A; Manhas, RS; Chaubey, A	2.307
11	Synthesis of 2-amino-4H-chromen-4-ylphosphonates and beta- phosphonomalonates via tandem Knoevenagel-Phospha-Michael reaction and antimicrobial. Research On Chemical Intermediates (2017), 43(12), 7319-7329.	Kour, P; Kumar, A; Sharma, R; Chib, R; Khan, IA; Rai, VK	1.369
12	. Development and characterization of hyaluronic acid modified PLGA based nanoparticles for improved efficacy of cisplatin in solid tumor. Biomedicine & Pharmacotherapy (2017), 95, 856-864, DOI:10.1016/j.biopha.2017.08.108	Alam, Noor; Koul, Mytre; Mintoo, Mubashir J.; Khare, Vaibhav; Gupta, Rahul; Rawat, Neha; Sharma, Parduman Raj; Singh, Shashank K.; Mondhe, Dilip M.; Gupta, Prem N.	2.759
13	Cell wall: A versatile fountain of drug targets in Mycobacterium tuberculosis. Biomedicine & Pharmacotherapy (2017), 95, 1520-1534, DOI:10.1016/j.biopha.2017.09.036	Bhat, Zubair Shanib; Rather, Muzafar Ahmad; Maqbool, Mubashir; Ul Lah, Hafiz; Yousuf, Syed Khalid; Ahmad, Zahoor	2.759
14	Synthetic and medicinal perspective of thiazolidinones: A review. Bioorganic chemistry (2017), 75406-423	Kaur Manjal Sundeep; Kaur Ramandeep; Bhatia Rohit; Kumar Kapil; Kaur Rupinder; Singh Virender; Shankar Ravi; Rawal Ravindra K	3.231
15	Bioactive and biocontrol potential of endophytic fungi associated with Brugmansia aurea Lagerh. FEMS microbiology letters (2017), 364(21)	Singh Gurpreet; Razak Mod; Katoch Meenu; Singh Gurpreet; Katoch Archana; Goswami Anindya; Katoch Meenu; Katoch Archana; Goswami Anindya; Kitchlu Surinder	1.765
16	α-pyrones and their hydroxylated analogs as promising scaffolds against Mycobacterium tuberculosis. Future Medicinal Chemistry (2017), 9(17), 2053-2067, DOI:10.4155/fmc- 2017-0116	By Bhat, Zubair Shanib; Rather, Muzafar Ahmad; Syed, Khalid Yousuf; Ahmad, Zahoor	3.556
17	Alkyne-azide cycloaddition analogues of dehydrozingerone as potential anti-prostate cancer inhibitors via the PI3K/Akt/NF-kappa B pathway. MedChemComm(2017), 8(11), 2115-2124.	Kumar, C; Rasool, RU; Iqra, Z; Nalli, Y; Dutt, P; Satti, NK; Sharma, N; Gandhi, SG; Goswami, A; Ali, A	2.608
18	The synthesis, biological evaluation and structure-activity relationship of 2-phenylaminomethylene-cyclohexane-1,3-diones as specific anti-tuberculosis agents. MedChemComm (2017), 8(11), 2133-2141, DOI:10.1039/C7MD00350A	Rather, Muzafar Ahmad; Lone, Ali Mohd; Teli, Bisma; Bhat, Zubair Shanib; Singh, Paramjeet; Maqbool, Mubashir; Shairgojray, Bashir Ahmad; Dar, Mohd Jamal; Amin, Shajrul; Yousuf, Syed Khalid; etal	2.608
19	Isolation of three new metabolites and intervention of diazomethane led to separation of compound 1 & 2 from an endophytic fungus, Cryptosporiopsis sp. depicting cytotoxic activity. Medicinal Chemistry Research (2017), 26(11), 2900-2908, DOI:10.1007/s00044-017-1989-4	Kumar, Sunil; Nalli, Yedukondalu; Qadri, Masroor; Riyaz-Ul- Hassan, Syed; Satti, Naresh K.; Gupta, Vivek; Bhushan, Shashi; Ali, Asif	1.277
20	Short hybrid peptides incorporating β- and γ- amino acids as antimicrobial agents. Peptides (2017), 97, 46-53. DOI:10.1016/j.peptides.2017.09.016	Wani, Naiem Ahmad; Singh, Gurpreet; Shankar, Sudha; Sharma, Arushi; Katoch, Meenu; Rai, Rajkishor	2.778

S.No.	Title	Author	Impact Factor
21	New Semi-Synthetic Rosmarinic Acid-Based Amide Derivatives as Effective Antioxidants. CHEMISTRYSELECT (2017), 2(31), 10153-10156	Ayoob, I; Lone, SH; Masood-ur-Rahman; Zargar, OA; Bashir, R; hakeel-u-Rehman; Khuroo, MA; Bhat, KA	YET TO COME
22	Regiospecific Synthesis of Ring A Fused Withaferin A Isoxazoline Analogues: Induction of Premature Senescence by W-2b in Proliferating Cancer Cells. Scientific reports (2017), 7(1), 13749	Rasool Faheem; Nayak Debasis; Katoch Archana; Faheem Mir Mohd; Yousuf Syed Khalid; Hussain Nazar; Goswami Anindya; Mukherjee Debaraj; Rasool Faheem; Hussain Nazar; et al	4.259
23	Anti-inflammatory chromone alkaloids and glycoside from Dysoxylum binectariferum. Tetrahedron Letters (2017), 58(42), 3974-3978. DOI:10.1016/j.tetlet.2017.09.005	Kumar, Vikas; Gupta, Mehak; Gandhi, Sumit G.; Bharate, Sonali S.; Kumar, Ajay; Vishwakarma, Ram A.; Bharate, Sandip B.	2.193
24	Synthesis, pH dependent, plasma and enzymatic stability of bergenin prodrugs for potential use against rheumatoid arthritis. Bioorganic & Medicinal Chemistry (2017), 25(20), 5513-5521, DOI:10.1016/j.bmc.2017.08.011	Singh, Rohit; Kumar, Vikas; Bharate, Sonali S.; Vishwakarma, Ram A.	2.93
25	Development and evaluation of long- circulating nanoparticles loaded with betulinic acid for improved anti-tumor efficacy. International Journal of Pharmaceutics (Amsterdam, Netherlands) (2017), 531(1), 153-166, DOI:10.1016/j.ijpharm.2017.08.076	Saneja, Ankit; Kumar, Robin; Singh, Amarinder; Dhar Dubey, Ravindra; Mintoo, Mubashir J.; Singh, Gurdarshan; Mondhe, Dilip M.; Panda, Amulya K.; Gupta, Prem N	3.649
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30	Isolation of isoxanthanol and synthesis of novel derivatives as potential cytotoxic agents. Medicinal Chemistry Research (2017), 26(10), 2499-2513, DOI:10.1007/s00044-017-1949-z	Chinthakindi, Praveen K.; Rath, Santosh K.; Singh, Jasvinder; Singh, Shashank; Koul, Surrinder; Sangwan, Payare L.	1.277
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51	Dendrimer encapsulated and conjugated delivery of berberine: A novel approach mitigating toxicity and improving in vivo pharmacokinetics. International journal of pharmaceutics (2017), 528(1-2), 88-99	Gupta Lokesh; Sharma Ashok Kumar; Gothwal Avinash; Khan Mohammed Shahid; Khinchi Mahaveer Prasad; Qayum Arem; Singh Shashank Kumar; Gupta Umesh	3.649

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56	Anti-inflammatory potential of hentriacontane in LPS stimulated RAW 264.7 cells and mice model. Biomedicine & Pharmacotherapy (2017), 92, 175-186, DOI:10.1016/j.biopha.2017.05.063	Khajuria, Vidushi; Gupta, Shilpa; Sharma, Neha; Kumar, Ashok; Lone, Nazir A.; Khullar, Mowkshi; Dutt, Prabhu; Sharma, Parduman Raj; Bhagat, Asha; Ahmed, Zabeer	2.759
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66	α-pyrones: Small molecules with versatile structural diversity reflected in multiple pharmacological activities-an update. Biomedicine & Pharmacotherapy (2017), 91, 265-277, DOI:10.1016/j.biopha.2017.04.012	Bhat, Zubair Shanib; Rather, Muzafar Ahmad; Maqbool, Mubashir; Lah, Hafiz U. L.; Yousuf, Syed Khalid; Ahmad, Zahoor	2.932
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177	Identification, isolation, and synthesis of seven novel impurities of anti-diabetic drug Repaglinide. Drug testing and analysis (2017).	Kancherla Prasad; Alegete Pallavi; Khagga Mukkanti; Kancherla Prasad; Keesari Srinivas; Alegete Pallavi; Das Parthasarathi	3.469

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- **Bhellum BL**, Bikarma Singh (2016). A new species of Laportea Gaudich. (Urticaceae) from Himalaya, India. Bangladesh Journal of Plant Taxonomy 23(2): 189-194. DOI:10.3329/bjpt.v23i2.30849. [Print ISSN 1028-2092, Online ISSN 2224-7279; Impact factor: 0.6]. (Publisher: Bangladesh Association of Plant Taxonomist)
- **Maridul Kundan**, Bikarma Singh (2016). Lepidium didymium Linnaeus (Brassicaceae)-a new record for India from Jammu and Kashmir State. Pleione 10(2):383-387. [ISSN: 0973-9467]. (Publisher: East Himalayan Society for Spermatophyte Taxonomy).
- **Bikarma Singh**, P Sultan, QP Hassan, S Gairola, YS Bedi (2016) Ethnobotany, Traditional Knowledge, and Diversity of Wild Edible Plants and Fungi: A Case Study in the Bandipora District of Kashmir Himalaya, India. Journal of Herbs, Spices & Medicinal Plants 22(3): 247-278. DOI: 10.1080/10496475.2016.1193833 [Print ISSN: 1049-6475, Online: 1540-3580]. (Publisher: Taylor & Francis)
- **Bikarma Singh**, YS Bedi (2016). Rediscovery, taxonomic history and extended enumeration of Haematocarpus validus Bakh.f. ex Forman (Menispermaceae) to Indo-Myanmar biodiversity hotspot. National Academy Science Letter 39(5): 383-387. DOI: 10.1007/s40009-016-0483-8 [Print ISSN: 0250-541X, Online ISSN: 2250-1754; NAAS Rating: 6.24; Impact factor: 0.345]. (Publisher: Springer)
- **Bikarma Singh**, B Singh (2016). Fagaceae Contribution to Floral Wealth of Himalaya: Checklist on Diversity and Distribution in North-Eastern States of India. Current Life Sciences 2(3): 72-83. 10.5281/zenodo.57840. [ISSN: 2449-8866].
- **Bikarma Singh** (2017). Elaeagnus umbellata Thunb.: New Record for Meghalaya State. Indian Forester 143(3): 288-289 [Online ISSN: 2321-094X, Print ISSN: 0019-4816; NAAS Rating: 4.27].

LIST OF PATENTS (2016-2017)

a) Patents filed in India

S.No	NFNO	Lab	Title	Inventors	Prov. Filing Date	Comp. Filing Date	Application No.	Patent No.
1	0218NF2015/IN	IGIB + IIIM	Synthetic melanin nanoparticles for skin pigmentation	Manika Vij, Ritika Grover, Vishwabandhu Gotherwal, Naiem Ahmad Wani, Prashant Joshi, Munia Ganguli, Rajkishor Rai, Vivek Tirunelveli Natrajan, Rajesh Sudhir Gokhale	29-Apr-16	---	2.01611E +11	---
2	0294NF2015/IN	IIIM	FURANOCHALCONES AS INHIBITORS OF CYP1A1, CYP1A2 AND CYP1B1 FOR CANCER CHEMOPREVENTION	BHARATE SANDIP BIBISHAN, SHARMA RAJNI, JOSHI PRASHANT, VISHWAKARMA RAM, CHAUDHURI BHABATOSH	---	12-Aug-16	2.01611E +11	--

b) Patents filed in Foreign

SNo	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Status	Patent No.
1	0225NF2012/JP	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	01-Apr-16	2016-520053	PP	---
2	0225NF2012/US	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	04-Apr-16	15/027,137	PP	---

SNo	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Status	Patent No.
3	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-16	14725544.2	PP	---
4	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-16	15/115573	PP	---
5	0106NF2013/EP	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-16	14824549.1	PP	---
6	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-16	15/121328	PP	---
7	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-16	15720483.5	PP	---

SNo	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Status	Patent No.
8	0222NF2015/ WO	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	21-Nov-16	PCT/ IN2016/ 050416	PP	---
9	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-17	15/509183	PP	---
10	0036NF2014/ CA	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-17	2960455	PP	---
11	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-17	15807704	PP	---
12	0058NF2014/ CA	ALKYLIDENE PHOSPHONATE ESTERS AS P-GLYCOPROTEIN INDUCERS	BHARATE SANDIP, KUMAR AJAY, MANDA SUDHAKAR, JOSHI PRASHANT, BHARATE SONALI, WANI ABUBAKAR, SHARMA SADHANA, VISHWAKARMA RAM	13-Mar-17	---	PP	---
13	0058NF2014/US	ALKYLIDENE PHOSPHONATE ESTERS AS P-GLYCOPROTEIN INDUCERS	BHARATE SANDIP, KUMAR AJAY, MANDA SUDHAKAR, JOSHI PRASHANT, BHARATE SONALI, WANI ABUBAKAR, SHARMA SADHANA, VISHWAKARMA RAM	13-Mar-17	15/510952	PP	---

SNo	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Status	Patent No.
14	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-17	15787031.2	PP	---
15	0060NF2014/CA	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	27-Mar-17	---	PP	-

c) Patents granted in India

SNo	NFNO	Title	Inventors	Prov. Filing Date	Comp. Filing Date	Application No.	Status	Grant Date	Patent No.
1	0159NF2008/IN	A PROCESS FOR THE PREPARATION OF OPTICALLY ACTIVE N-BENZYL-3-HYDROXYPYRROLIDINES	SUBHASH CHANDRA TANEJA, MUSHTAQ AHMAD AGA, BRIJESH KUMAR, VIJAY KUMAR SETHI, SAMAR SINGH ANDOTRA, GHULAM NABI QAZI	24-Nov-08	23-Nov-09	2648DEL2008	IF/2017	04-Apr-16	272479
2	0042NF2009/IN	NOVEL HYBRIDS OF PERFUMERY MOLECULES WITH EXTREMOLYTES, HUMECTANTS AND EXFOLIATING AGENTS FOR THE DEVELOPMENT OF NEW GENERATION MULTIPLE ACTION SKIN/BEAUTY CARE BIOCONJUGATES	QAZI GHULAM NABI, HALMUTHUR MAHABALARAO SAMPATH KUMAR, SAWANT SANGHAPAL DAMODHAR, REDDY DOMA MAHENDER, BANDAY ABID HUSSAIN	31-Mar-09	31-Mar-10	0656DEL2009	IF/2018	11-Aug-16	274883

d) Patents granted in Foreign

SNo	NFNO	Title	Inventors	Comp. Filing Date	Application No.	Grant Date	Patent No.
1	0195NF2011/CN	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	19-Nov-14	2.0138E+11	07-Dec-16	ZL2013800262915

BOOK CHAPTERS

- Suphla Gupta, Saima Khan, Malik Muzafar, Manoj Kushwaha, Arvind Kumar Yadav and Ajai Prakash Gupta, "Encapsulation: Entrapping essential oil/flavours/aromas in food", Encapsulations Volume 2 of the Nanotechnology in the Agri-Food Industry series Edited by Alexandru Grumezescu, Elsevier, 2016.
- Saima Khan, Pankaj Pandotra, Asif Khan, Sajad A Lone, Malik Muzafar, Ajai Prakash Gupta and Suphla Gupta, "Medicinal and nutritional qualities of Zingiber officinale. In: Health Fruits, Vegetables, and Herbs: Bioactive Foods in Promoting", Edited by Ronald Watson and Victor Preedy. Elsevier, The Boulevard, Langford Lane, Kidlington, Oxford, OX5 1GB, United Kingdom, Registration No. 1982084, Registered in England and Wales. Chapter 25(2016).
- Saima Adeeb, Pankaj Pandotra, Ajai Prakash Gupta, R K Salgotra, M Muzaffar, Suphla Gupta. Plant Molecular Breeding: war forward through Next Generation Sequencing (Chapter 7). In: Plant Omics and Crop breeding. Dr. Sajad majeed Zargar & Dr. Vandna Rai (Eds) . Apple Academic Press, Inc. ISBN: 9781771884556. (2016).
- Ajai Prakash Gupta, Saima Adeeb, M Muzaffar, Gourav Sharma, Rajneesh Anand & Suphla Gupta, "Anticancer Spice Curcuma: Analogues And Structure-Activity Relationship", In: Studies in Natural Product Chemistry (Bioactive Natural Products) , PROF. ATTA-UR- RAHMAN, FRS (Editor), Elsevier Science Publishers – Amsterdam, Netherlands. Volume ; 341-445. ISBN: 978-0-444-63462-7, 2016.
- Saima Khan, Pankaj Pandotra, Asif Khan, Sajad A Lone, Malik Muzafar, Ajai P Gupta and Suphla Gupta. Medicinal and nutritional qualities of Zingiber officinale. In: Health Fruits, Vegetables, and Herbs: Bioactive Foods in Promoting. Edited by Ronald Watson and Victor Preedy. Elsevier, The Boulevard, Langford Lane, Kidlington, Oxford, OX5 1GB, United Kingdom, Registration No. 1982084, Registered in England and Wales. Chapter 25(2016); 525- 543.
- Saima Adeeb, Pankaj Pandotra, Ajai Prakash Gupta, R K Salgotra, M Muzaffar, Suphla Gupta. Plant Molecular Breeding: war forward through Next Generation Sequencing (Chapter 7). In: Plant Omics and Crop breeding. Dr. Sajad majeed Zargar & Dr. Vandna Rai (Eds) . Apple Academic Press, Inc. ISBN: 9781771884556. In production (2016);
- Pankaj Pandotra & Suphla Gupta. Biotechnological Approaches for Conservation of Plant Genetic Resources and Traditional Knowledge. In : Plant Genetic Resources and Traditional Knowledge for Food

Security 2015. R.K. Salgotra & B.B.Gupta (Eds).121-135. DOI.10.1007/978-981-10-0060-7_7. Springer. ISBN: 978-981-10-0058-4

- Biopesticide: Ecofriendly Approach. Saima Khan, Malik Muzafar Manzoor, Manoj Kushwaha, Mohd. Arif, Arvind Kumar Yadav, Ajai Prakash Gupta,* and Suphla Gupta. In: Environmental Sci. & Engg. Vol. 1: Sustainable Development

Hindi Article

- Bikarma Singh (2016). Kashmir Himalaya Mee Gurez Ghaati Ki Jaiw Vividhata: Eek Paricheyee. Gyanvarta 7: 8-11 (Hindi Journal) [ISSN: 2320-2998]. Gyanvarta 6(6): 1-4 [Print ISSN: 2320-2998].

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

- Delivered Lecture on the topic Biotechnological Intervention in the Aroma Bearing Crops in the One Day Programme jointly organised by CSIR-IIIM, Jammu & International Congress of Essential Oils, Fragrances and Flavours'89 (ICEOFF89) on 4th of March, 2017 (Dr. Suphla Gupta).
- Invited Lecture on 'Biodiversity and Conservation', at 4th J&K Women Science Congress at Govt. College for Women Science Congress on 1-3rd Sept. 2016 (Dr. Suphla Gupta).
- Deliver an expert lecture on the topic Role of molecular markers in establishing genetic fidelity of in vitro regenerated clonal plants National Training Programme on Plant Tissue Culture Techniques for Quality Planting Material Production and Crop Improvement from 1- 10 Sept. 2016 at School of Biotechnology, Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, Jammu (J&K), (Dr. Suphla Gupta).
- Poster Presentation on understanding the Role of Cell Differentiation in Glycyrrhizin Biosynthesis. presentation in the 3rd International Conference on Recent Trends and Advancements in Engineering and Technology (ICRTAET) held at Shri Mata Vaishno Devi University, Katra, India from 17-18 November 2016.
- Oral Presentation on ISSR Fingerprinting Analysis and Phytochemical Characterization of Epimedium elatum (Morr & Decne) ─A Monotypic and Rare Medicinal Plant from Kashmir Himalayas in India. presentation in the 3rd International Conference on Recent Trends and Advancements in Engineering and Technology (ICRTAET) to be held at Shri Mata Vaishno Devi University, Katra, India from 17-18 November 2016.
- Poster Presentation on Epimedium elatum: A potential anti-osteoporotic medicinal herb from Northwestern Himalayas. Sajjad A Lone, Saima Khan, Manoj Kushwaha, Mohd. Arif, Pervaiz Qazi, Suresh Chandra, Y S Bedi, Suphla Gupta*, Ajai P Gupta. International Conference on Medicinal Plants: Resource for Affordable New Generation Healthcare @ CIMAP, Lucknow 2-21 MARCH , 2015
- Radio talk on क्लोनिंग- संभावन्य और चुनौतियान--- All India Radio, Jammu & Kashmir on 3 Feb 2016
- Radio talk on पेडो से जुड कुछ रोचक रहस्य --- All India Radio, Jammu & Kashmir on 8 sept 2016
- Invited as Expert Member by School of Biotechnology, University of Jammu during UGC- HRDC Refresher Course Organized in collaboration with HRDC entitled "Potential
- Germplasm Resources of Medicinal and Aromatic Plants in Jammu & Kashmir State" on 7th March 2017 (Dr. Bikarma Singh).
- Invited Lecture on, "Determination of adulteration in essential oil using modern tools", in "Training cum Workshop on Essential Oils, Perfumery & Aromatherapy" held at FRI, Dehradun from June 13-17, 2016 (Dr. Ajai P. Gupta).
- Invited Lecture, "Patent, Copyright, Trademark & Infringement", Workshop on "Intellectual Property Right (IPR)", Govt. College for Women, Gandhi Nagar, Jammu, 18th November 2016 (Dr. Ajai P. Gupta).
- Invited Lecture on, "Determination of adulteration in essential oil using modern tools", in "Training cum Workshop on Essential Oils, Perfumery & Aromatherapy" held at FRI, Dehradun from June 13-17, 2016 (Dr. Ajai P. Gupta).

- Invited Lecture on, "Quality Control of MAPs Using Modern Analytical Techniques", One- Day Programme Jointly Organized by ICEOFF-1989, New Delhi & CSIR-IIIM, Jammu, AT IIIM, Jammu on 4th March 2017 (Dr. Ajai P. Gupta).
- Invitation to deliver lecture in refresher course in Biotechnology," Quality-Adulteration- Threats-Innovation-Daily Life Invention", at Biotechnology department, Jammu on 10th March 2017 (Dr. Ajai P. Gupta).
- Invitation to deliver lecture, "Quality Control of MAPS using GCMS", at Govt Women College, Gandhi Nagar, Jammu on 18th March 2017 (Dr. Ajai P. Gupta).
- Organized Workshop on "Bio-Entrepreneurship, Grant Writing and IP Management" 23-24 June 2016, at CSIR-IIIM, Jammu in collaboration with BIRAC, DBT
- Invited Talk on "Fermentation Technology: An integral part of our daily life" on 8 March 2017 in Refresher Course in Biotechnology, organized by School of Biotechnology, University of Jammu (Dr. Asha Chaubey).
- Invited talk on "Human microbiome: prospective source of new drugs" during 4th J&K Women Science Congress from 1-3rd Sep. 2016, held at Govt. College for Women, Gandhi Nagar, Jammu (Dr. Asha Chaubey).
- Delivered a talk on "Biocatalytic synthesis of pharmaceutically important chiral intermediates" in the National Conference on "Bioresources as a Key to Value Added Products" held on 29th & 30th April, 2016.
- Poster presentation during International Conference on Challenges in Drug Discovery and Delivery (ICCD3-2017) Nonribosomal peptides production and its optimization from fungus Trichoderma velutinum 2-4 March, 2017 at BITS Pilani
- CSIR Foundation Day celebrations; 26-27 Sept 2016
- Public Outreach Day; 10 Nov 2016 at CSIR-IIIM
- India International Trade Fair-2016; 14-27 Nov 2017, New Delhi
- India International Science Festival-2016; 7-11 Dec 2016, CSIR-NPL, New Delhi
- National Seminar-cum-exhibition on Kisan Mela, Entrepreneurship Programme and Flower Show-2017; 5 March 2017
- Kisan Mela 17-18 March, 2017 at SKAUST-J

THESIS /AWARDS

- Isolation and characterization of endophytes from Grewia asiatica L. for production of bioactive molecules (Ankita Magotra)
- Isolation and Characterization of microorganisms for production of Non-Ribosomal Peptides (Richa Sharma)
- Best Poster Award to Nahida Rasool in 12th JK Science Congress, University of Jammu, 2-4 March 2017 (Supervisor - PNGupta).

PLANTS VARIETIES RELEASED

1. Jammu Monarda (Monarda citriodora Cerv. ex Lag. [IIIM(J)MC-02]: Developed and released for commercial cultivation on the occasion of Foundation day on 1st December 2010. Characteristics: A rich source of thymol (about 60-75%) and better economic returns (100- 125 kg/ha). Essential oil active against cancerous cell line (HL60), acceptability by flavour and pharmaceutical industries. It is also used as an antiseptic, expectorant and cough medication, to treat nail fungus infection.
2. Himrosa [Cymbopogon khasianus Bor IIIM (J) CK-10]: Developed and released by CSIR- IIIM Jammu on 1st December, 2012 on the occasion of IIIM(J) Foundation day 2012 Characteristics: Having high drought and salt tolerance ability, and is a rich source of Geraniol (75-85 %). The oil is extensively used as perfumery raw material in soaps, "oral rose-like perfumes, cosmetics preparations, and in the manufacture of mosquito repellent products. The essential oil has a scent similar to that of rose oil, and named Himrosa.

3. Anant carvomint [Mentha longifolia (L) Hudson var. incana (Willd) Dinson RRL(J)ML-4]: Released for commercial cultivation on 30th January, 2007 Characteristics: Hyper productive strain developed though clonel multiplication, wider adaptability (Kashmir to Kanya Kumari). It is in rich in ℓ-carvone 67.5 %). It has essential oil content (0.5 to 0.9%w/w FWB) depending on season to season. It has wider acceptability shown by perfume, flavour & pharmaceutical industries.
4. Lemon grass (Cymbopogon khasianus x C. pendulus) [CKP-25]: Released in 2002 Characteristics: It is an interspecific hybrid and the oil contents are 0.5%. Its main constituents are citral (80-85%). It is very useful in perfumery, flavoring & pharmaceutical industry.
5. Lavender (Lavandula officinales) [RRL 12]: Released in 1972 Characteristics: Lavender is high altitude high value crop and is an incredible and much sought aromatic plant having significant position in trade all over the world due to its essential oil which has multifarious uses and market outlets. Main constituents are Linalool, Linalyl acetate, 1,8 cineole, borneol, caryophyllene, terpineol, ocimenes, Lavandulyl acetate. It is useful in perfumery, flavor and cosmetic industry.
6. Rose Mary (Rosmarinus officinalis L.) Characteristics: Rose Mary is yet another high value crops and its main constituents are p- cymene (40-44.02%), linalool (18-20.5%), gamma-terpinene (14-16.62%), thymol (1-1.81%), beta-pinene (2-3.61%), alpha-pinene (1-2.83%) and eucalyptol (1-2.64%), which is useful in perfumery, flavor and cosmetic industry.

RESEARCH COUNCIL 2016-2017

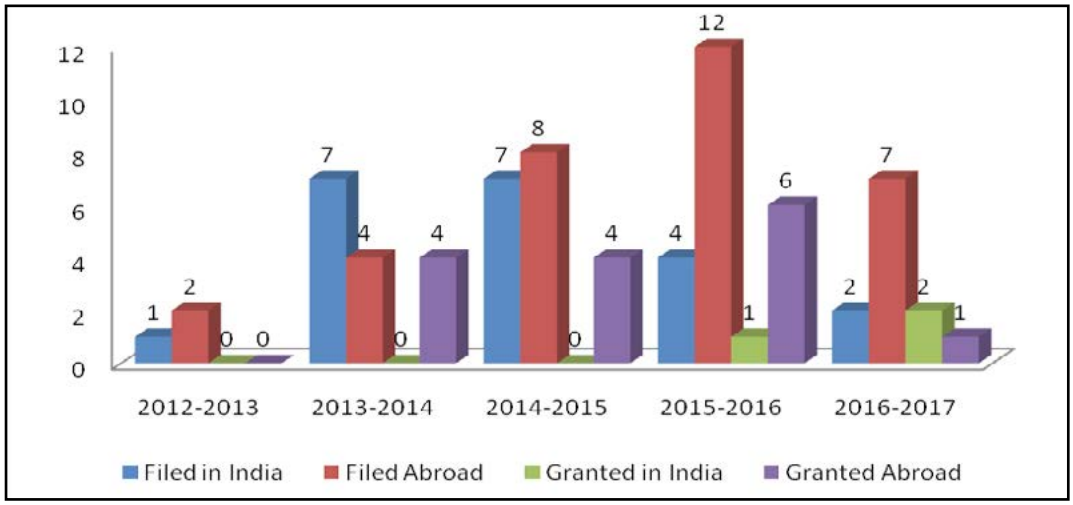
Chariman			
1	Prof. Goverdhan Mehta National Research Proffessor and Lily- Jubilant Chair School of Chemistry University of Hyderabad, Hyderabad – 500046		
External Members			
2	Dr. Rajiv I. Modi Managing Director Cadila Pharmaceuticals Ltd. Cadila Corporate Campus Sarkhej Dhokla Road, Bhat, Ahmedabad - 382210	3	Prof. Sudhir Kumar Sopory Vice Chancellor Jawaharlal Nehru University New Delhi-110067
4	Prof. Satyajit Mayor Professor and Dean National Centre for Biological Sciences (Tata Institute of Fundamental Research) Bellary Road, GKVK Campus Bengaluru-560065	5	Prof. Y.K. Gupta Professor and Head, Department of Pharmacology All India Institute of Medical, New Delhi – 110029
6	Dr. Satyajit Rath Scientist National Institute of Immunology Aruna Asaf Ali Marg, New Delhi – 110067	7	Dr. T.S. Balganesh CSIR Distinguished Scientist CSIR- Fourth Paradigm Institute NAL Belur Campus, Bengaluru - 560037
Agency Representative		**DG Nomiee**	
8	Dr. G . J Samathanam Adviser Department of Science and Technology Technology Bhawan, New Mehrauli Road New Delhi-110016	9	Dr. P . K Biswas Former Adviser (S&T), Planning Commissiong MS-11/905, Kendriya Vihar, Sector-56 Gurgaon-122003
Sister Labrtatory		**Cluster Director**	
10	Dr. Ramesh V.Sonti Scientist CSIR- Center for Cellular and Molecular Biology, Uppal Road, Hyderabad – 500007	11	Dr. P.S. Ahuja Director CSIR- Institute of Himalayan Bioresource Technology Post Box No. 6, Palampur – 176061
Director		**Permanent Invitee**	
12	Dr. Ram Vishwakarma Director CSIR- Indian Institute of Integrative Medicine, Canal Road, Jammu 180001	13	Head or his Nominee Planning & Performance Division Council of Scientific & Iindustrial Research Anusandhan Bhawan, 2, Rafi Marg New Delhi- 110001

MANAGEMENT COUNCIL 2016 – 2017

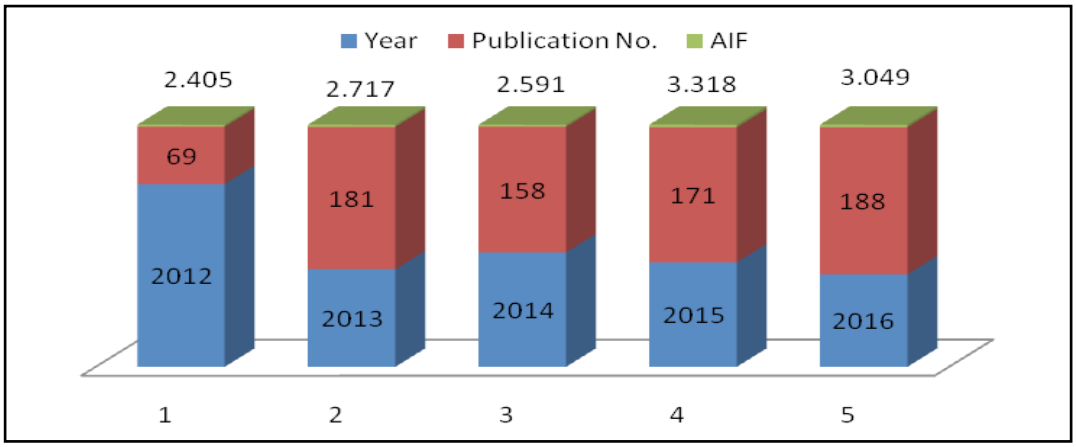
Dr. Ram Vishwakarma Director, Indian Institute of Integrative Medicine Canal Road, Jammu	**Chairman**
Dr. (Ms.) Madhu Dikshit, Director, Central Drug Research Laboratory, Lucknow	**Special Invitee** Ex-officio Member
Dr. Sanjay Kumar Director, Institute of Himalayan Bioresource Technology, Palampur, Himachal Pradesh	**Member**
Dr. Suresh Chandra Chief Scientist, Indian Institute of Integrative Medicine Canal Road, Jammu	**Member**
Dr. Inshad Ali Khan Principal Scientist Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Dr. (Smt.) Suphla Gupta Sr. Scientist Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Dr. Bhahwal Ali Shah Scientist Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Dr. N.K. Satti Principal Technical Officer Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Er. Abdul Rahim Sr. Principal Scientist /Head, PME Division Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Sh. K.C. Paliwal F&AO Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Sh. Pankaj Bahadur, COA Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member-Secretary**

PERFORMANCE PARAMETERS

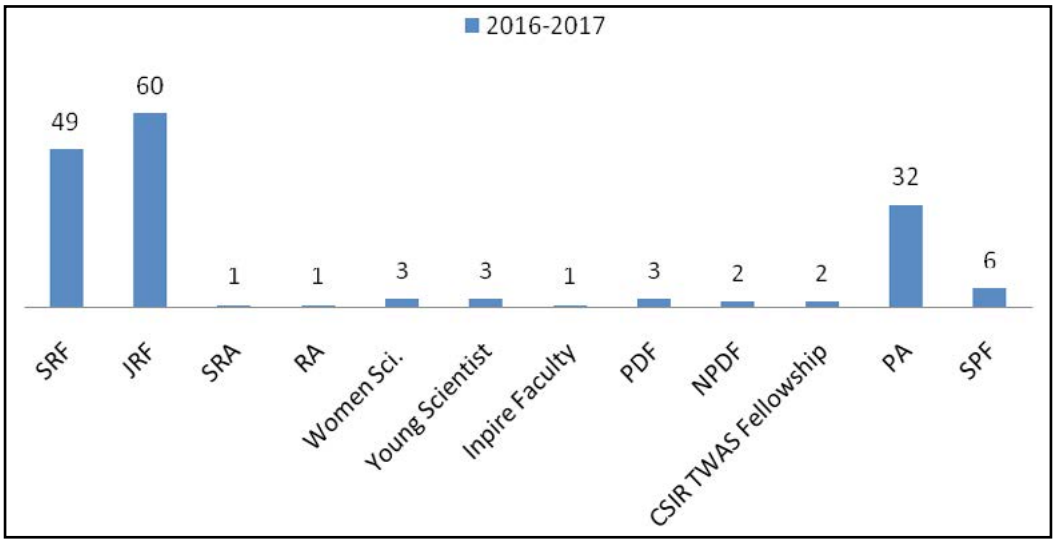
Patents



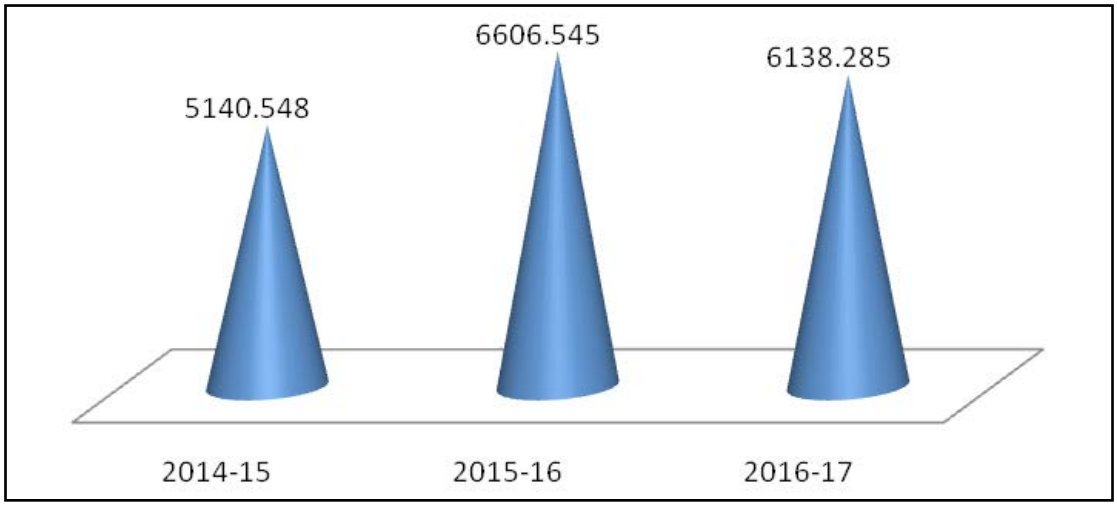
Publications [Calendar Year Wise]



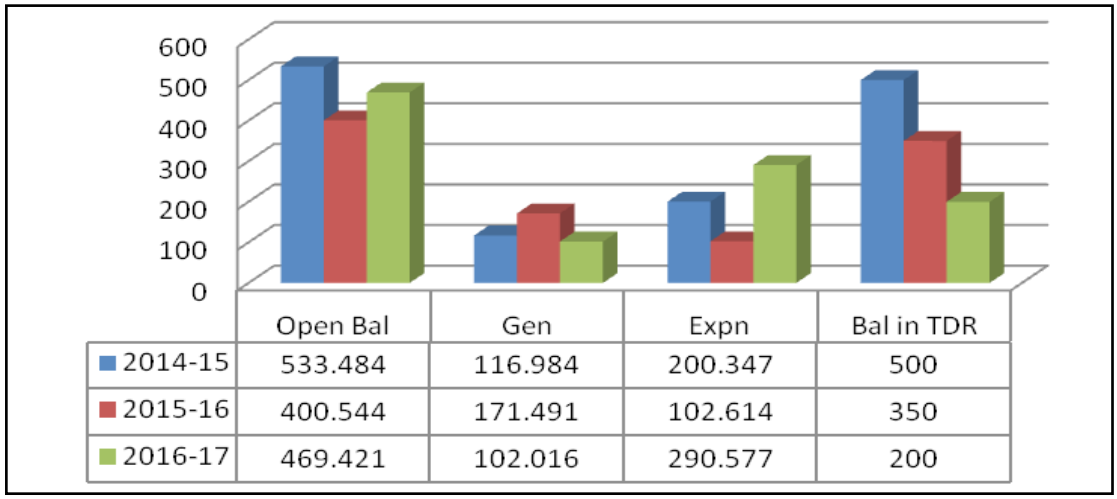
Fellows



Budget (Rs. In Lakhs)

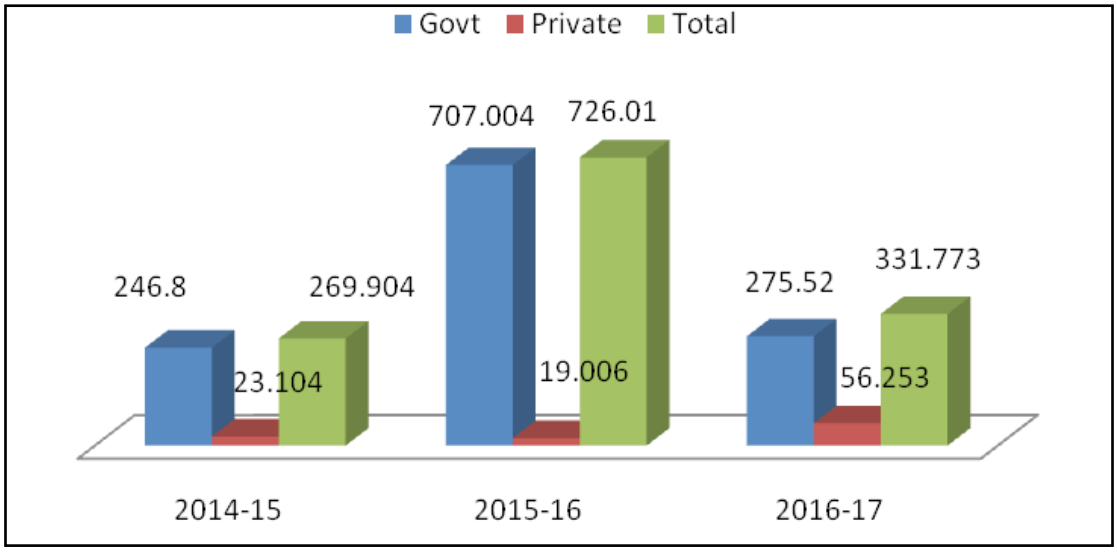


Institute's Reserve (Rs. In Lakhs)



	Open Bal	Gen	Expn	Bal in TDR
2014-15	533.484	116.984	200.347	500
2015-16	400.544	171.491	102.614	350
2016-17	469.421	102.016	290.577	200

External Cash Flow (Rs. In Lakhs)



RURAL DEVELOPMENT AND SOCIETAL ACTIVITIES

PM releases rose scented variety of geranium developed by CSIR-IIIM

Determined to boost the agriculture and allied sectors in the country through revolutionary methods, Prime Minister Narendra Modi interacted with prospective farmers of various States of J&K through Doordarshan live feed to have a feed back about the growing of aromatic plants and urged them to take full advantage of research based crops developed by Council of Scientific & Industrial Research (CSIR).

He sought their views on growing of aromatic plants in their fields. On the occasion, the Prime Minister also released a scented variety of rose developed by CSIR, Jammu. Both the farmers from Jammu informed Modi about the benefits they have got after planting aromatic plants. Bharat Bhushan of Bhaderwah who grows the Lavender an aromatic plant which produces oil that is used for production of cosmetics and perfume, informed the PM that one kg of oil fetches Rs 10,000 for him and per kanal of land gives a yield of two kgs of oil. He has converted all the 20 kanals of land which he possesses for cultivation of aromatic plant. When Prime Minister asked him that the plant is destroyed in case water accumulates around it, Bushan said that the land in Bhaderwah is steep, hence, it has no threat of water stagnation.

Scientist of the Year Award by Essential Oil Association of India, Delhi

eam of scientists & concerned staff members of CSIR-Indian Institute of Integrative Medicine, Jammu has been awarded Scientist of the Year Award by Essential Oil Association of India, Delhi for the extension activities of aromatic crops during Asian Aroma Ingredient Congress Aroma Bearing Sector at Hotel Leela Ambience, Delhi on April 22-24, 2016.

The award was given for diversification of high value aroma bearing Lavender cultivation from Kashmir to Bhaderwah region of District Doda of Jammu & Kashmir state with the maintaining of quality and yield of essential oil.

Secondary CSIR-IIIM has also extended cultivation of Gereniol rich variety RRL-CN-5 successfully in Kutch area of Gujarat under salt affected soil. The essential oil industries highly demanded by essential oil industries for flavour fragrance & pharmaceutical purposes.

The award was given to the dynamic leadership of Dr. Ram Vishwakarma, Director, CSIR-IIIM Jammu with the team leader Dr. Suresh Chandra and team members Dr. Narendra Kumar, Mr. S.R. Meena, Dr. Parvaiz Qazi, Mrs. Kushal Bindu, Dr. M.K. Verma, Dr. Phalisteen Sultan, Mr. Rajendra Gochar, Mr. Chandra Pal Singh, Dr. Shahid Rasool, Mr. Brijendra Koli, Mr. Pratipal Singh, Mr. Vijay Kumar and Dr. A.K. Shahi(Ex-Scientist).

Diwali celebration with CRPF and BSF

As per the directions of our Honorable Prime Minister Sh. Narinder Modhi, IIIM staff on the eve of Diwali celebrated the Diwali function with BSF and CRPF soldiers. There was a very big programme organized by the IIIM staff for the distribution of sweets and lightening of the candles and singing of songs with the Javans of BSF camp palora and CRPF camp Bantalab Jammu in order to boost their moral.

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 2016

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

	Representation of SCs/STs/OBCs (As on 01.01.2017)				Number of appointments made during the calendar year 2016									
					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	100	10	3	10	5	1	-	3	-	-	-	-	-	-
Group B	90	19	2	12	-	-	-	-	-	-	-	-	-	-
Group C	87	35	2	5	-	-	-	-	-	-	-	-	-	-
Group D (Excluding Sweepers)	*													
Group D (Sweepers)	*													
TOTAL	277	67	7	27	5	1	-	3	-	-	-	-	-	-

*shown in Group C Column.

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 2016

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

	Representation of SCs/STs/OBCs (As on 01.01.2017)				Number of appointments made during the calendar year 2016									
					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	6	1	1	-	-	-	-	-	-	-	-	-	-	-
PB-3 Rs.6600	26	7	-	6	5	1	-	3	-	-	-	-	-	-
PB-3 Rs.7600	36	1	-	2	-	-	-	-	-	-	-	-	-	-
PB-4 Rs.8700	27	1	1	-	-	-	-	-	-	-	-	-	-	-
PB-4 Rs.8900	2	-	1	1	-	-	-	-	-	-	-	-	-	-
PB-4 Rs.10,000	2	1	-	-	-	-	-	-	-	-	-	-	-	-
HAG+ Above	1	-	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	100	11	3	9	5	1	-	3	-	-	-	-	-	-

SO (Estb)
O/o Indian Institute of Integrative Medicine, Jammu- 180001

PWD Report I

ANNUAL STATEMENT SHOWING THE REPRESENTATION OF THE PERSONS WITH DISABILITIES IN SERVICES (AS ON 1ST JANUARY 2017)

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	2				2
Group B	1				1
Group C	1				1
Group D					
TOTAL	4				4

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).

SO (Estb)

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

PWD REPORT II

STATEMENT SHOWING THE NUMBER OF PERSONS WITH DISABILITIES APPOINTED DURING THE YEAR
(As on 1st. January 2017)

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

GROUP	DIRECT RECRUITMENT								PROMOTION							
	No. of vacancies reserved			No. of Appointments Made					No. of vacancies reserved			No. of Appointments Made				
	VH	HH	OH	Total	In Identified Posts	VH	HH	OH	VH	HH	OH	Total	In Identified Posts	VH	HH	OH
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Group A	-	1	2	3	3	-	-	2	-	-	-	-	-	-	-	-
Group B	1	1	1	3	3	-	-	2	-	-	-	-	-	-	-	-
Group C&D	-	1	2	3	3	-	-	1	-	-	-	-	-	-	-	-

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).

(iv) There is no reservation for persons with disabilities in case of promotion to Group A and B posts. However, persons with disabilities can be promoted to such posts, provided the concerned post is identified suitable for persons with disabilities.

SO (Estb)
O/o IIIM, Jammu - 180001

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

नगर राजभाषा कार्यान्वयन समिति, जम्मू की अर्द्धवार्षिक बैठक दिनांक 30 जून, 2016 को सायं 3.00 बजे भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में सम्पन्न।

भारत सरकार, गृह मंत्रालय, राजभाषा विभाग के निर्देशानुसार नगर राजभाषा कार्यान्वयन समिति, जम्मू की छमाही बैठक दिनांक 30 जून, 2016 (वृहस्पतिवार) को अपराहन 3.00 बजे भारतीय समवेत औषध संस्थान, जम्मू के कॉन्फ्रेंस हॉल में आयोजित हुई। बैठक की अध्यक्षता संस्थान के निदेशक एवं नराकास अध्यक्ष डॉ. राम विश्वकर्मा ने की। इस अवसर पर श्री प्रमोद कुमार शर्मा, उपनिदेशक (कार्या.), क्षेत्रीय कार्यान्वयन कार्यालय दिल्ली, भारत सरकार, गृह मंत्रालय, राजभाषा विभाग एवं श्रीमती शाश्वती बंद्योपाध्याय, प्रधान रक्षा लेखा नियंत्रक, उत्तरी कमान, जम्मू, सुश्री अंजलि शर्मा, निदेशक दूरदर्शन केन्द्र, जम्मू, डॉ. शरद चन्द्र शर्मा, प्राचार्य, राष्ट्रीय संस्कृत संस्थानम, जम्मू, श्री आर.के.पंडिता, उप महालेखाकार, लेखा व हकदारी, जम्मू, श्री एस.कालगांवकर, कार्यपालक निदेशक, एन.एच.पी.सी., क्षेत्रीय कार्यालय, जम्मू एवं नराकास के केन्द्रीय कार्यालयों/बैंकों/उपक्रमों के सभी कार्यालयाध्यक्ष/गोडल अधिकारी / प्रशासनिक प्रमुख/ राजभाषा अधिकारी/ हिन्दी अधिकारी"हिन्दी अनुवादक/प्रिन्ट व इलैक्ट्रॉनिक मीडिया के संवाददाता तथा अन्य गणमान्य व्यक्ति उपस्थित थे।

सर्वप्रथभ 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 संचस्थ एवं अन्य उपस्थित गणमान्य व्यक्तियों का अभिनंदन किया तथा अध्यक्ष महोदय की अनुमति से बैठक की कार्रवाई आरम्भ की एवं गत बैठक के कार्यवृत्त की सर्वसम्मति से पुष्टि की गई। बैठक में प्रथम अक्टूबर, 2015 से 3 मार्च, 2016 के दौरान सभी सदस्य कार्यालयों के हिन्दी कार्यान्वयन संबंधी प्रगति रिपोर्ट की समीक्षा की। बैठक का मुख्य उद्देश्य केन्द्रीय कार्यालयों/बैंकों/ उपक्रमों में हिन्दी का उत्तरोत्तत विकास करना तथा जम्मू क्षेत्र को राजभाषा की प्रगति की ओर अग्रसर करना है।

तत्पश्चात् बैठक में उपस्थित सदस्यों के परिचय के साथ ही बैठक की कार्वाई आरम्भ हुई। सदस्य-सचिव ने गत बैठक के कार्यवृत्त पर कोई आपत्ति एवं प्रतिक्रिया न मिलने पर सचिव ने अध्यक्ष महोदय के अनुमोदन पर गत बैठक के कार्यवृत्त की पुष्टि की।

इस अवसर पर पी.एन.बी., जम्मू की "त्रिकुटा' तथा पावर ग्रिड कारपोरेशन, जम्मू की "तवी प्रवाह' प्रत्रकाओं का भी इस मंच पर विमोचन किया गया।

संस्थान के निदेशक एवं जज नराकास, अध्यक्ष डॉ. राम विश्वकर्मा ; ने बैठक में उपस्थित केन्द्रीय कार्यालय/ बैंकों/उपक्रमों के. सभी कार्यालय प्रमुखों एवं उपस्थित गणमान्य. व्यक्तियों का अपने अध्यक्षीय.. भाषण में नराकास अध्यक्ष महोदय ने अत्यन्त प्रभावी रूप में कार्यालय-प्रमुखों

से अपने-अपने कार्यालयों में अधिकांशत: सूचना प्रौद्योगिकी के प्रयोग पर बल देते हुए कहा कि जिन कार्यालय के पते में कोई परिवर्तन हो जाए तो वे कार्यालय इसकी सूचना नगर राजभाषा कार्यान्वयन समिति कार्यालय को अवश्य दें ताकि कार्यालयों की सूची समय-समय पर संशोधित कर अद्यतन रखी जा सके।

अन्त में संस्थान के नियंत्रक प्रशासन श्री पंकज बहादुर जी ने धन्यवाद प्रस्ताव ज्ञापित किया तथा बैठक समाप्ति की घोषणा की।

संस्थान में दिनांक 4-29 सितम्बर, 2016 को हिन्दी पखवाड़ा एवं कार्यशाला का आयोजन।

संघ की राजभाषा हिन्दी में सरकारी कामकाज तथा हिन्दी के प्रति रुचि जागृत. करने के उद्देश्य से संस्थान में हा दिनांक 14 सितम्बर, 2016 से 29 सितम्बर, 2016 के दौरान हिन्दी पखवाड़े का आयोजन किया गया। जिसमें हिन्दी कार्यशाला, भाषण प्रतियोगिता, स्लोगन प्रतियोगिता, पोस्टर प्रतियोगिता, अन्तरविभागीय भाषण प्रतियोगिता, शोधलेख प्रतियोगिता, कवि गोष्ठी उमंग कार्यक्रम आदि प्रतियोगिताएं आयोजित की गई, इस दौरान हिन्दी के प्रयोग एवं प्रगति की दिशा में विभिन्न प्रतियोगिताओं में संस्थान के 250 स्टॉफ-सदस्यों ने प्रतियोगी के रूप में प्रतिभागिता दी। इसी दौरान हिन्दी कार्यशाला का आयोजन भी किया गया जिसकी अध्यक्षता संस्थान के वरि. वैज्ञानिक डॉ. रजनीश आनन्द ने की और मुख्य अतिथि के रूप में प्रो./डॉ. प्रतिभा पुरन्धि, जम्मू विश्वविद्यालय, जम्मू ने "देवनागरी लिपि की वैज्ञानिकता' विषय पर व्याख्यान प्रस्तुत किया इस कार्यशाला में संस्थान के श्री पंकज बहादुर, नियंत्रक प्रशासन, वित्त एवं लेखा अधिकारी, श्री प्रफुल्ल कुमार, भण्डार एवं क्रय अधिकारी एवं ध्झ -उा अन्य स्टॉफ सदस्य हिन्दी पखवाड़े के उपलक्ष्य में दिनांक 4 सितम्बर, 2016 को संस्थान के सभी स्टॉफ सदस्यों का स्वागत डॉ. रमा शर्मा, हिन्दी अधिकारी ने किया और। 8 क् हिन्दी पखवाड़े की इस शुभ बेला पर सभी को बधाई दी। डॉ. प्रतिभा जी अनेक विषयों में निष्णात प्रोफेसर तथा बहुत ही जानी-मानी विदुषी हैं तथा इन्हें विदुषी सम्मान से भी अलंकृत किया गया है। हिन्दी पखवाड़े के उद्घाटन अवसर पर आयोजित हिन्दी कार्यशाला में "देवनागरी लिपि की वैज्ञानिकता' विषय पर व्याख्यान देने के लिए संस्थान में आमंत्रित किया गया था। हिन्दी अधिकारी ने स्पष्ट किया कि हम सभी इनके विद्वत्तापूर्ण व्याख्यान से निश्चित् रूप से लाभान्वित हुए हैं।

अंत में, धन्यवाद प्रस्ताव संस्थान के नियंत्रक प्रशासन श्री पंकज बहादुर ने किया।

नगर राजभाषा कार्यान्ववन समिति, जम्मू की अर्द्धवार्षि बैठक दिनांक 30 नवम्बर, 2016 को सायं 3.00 बजे सीएसआईआर-भारतीय समवेत औषध संस्थान, जम्मू के कॉन्फ्रेंस हॉल में सम्पन्न।

भारत सरकार, गृह मंत्रालय, राजभाषा विभाग के निर्देशानुसार नगर राजभाषा कार्यान्वयन समिति, जम्मू की अर्द्धरार्षि बैठक दिनांक 30 नवम्बर, 2016 (बुधवार) को अपराहन 3.00 बजे सीएसआईआर- भारतीय समवेत औषध संस्थान, जम्मू के कॉन्फ्रेंस हॉल में आयोजित हुई। बैठक की अध्यक्षता संस्थान के निदेशक एवं नराकास अध्यक्ष डॉ. राम विश्वकर्मा ने की। इस अवसर पर श्री देवेन्द्र कुमार गौतम, भारतीय विमानपत्तन प्राधिकरण, सिविल एयरपोर्ट, जम्मू, श्री संजय डाबी, श्रमायुक्त, कार्यालय (केन्द्रीय), गांधी नगर, जम्मू, श्रीमती शाश्वती

बंदूयोपाध्याय जी, प्रधान रक्षा लेखा नियंत्रक, उत्तती. कमान, जम्मू एवं नराकास के केन्द्रीय कार्यालयों/बैंका" उपक्रमों के सभी कार्यालयाध्यक्ष/नोडल अधिकारी प्रशासनिक प्रमुख/राजभाषा अधिकारी /हिन्दी अधिकारी /हिन्दी अनुवादक/प्रिन्ट व इलैक्ट्रॉनिक मीडिया के संवाददाता तथा अन्य गणमान्य व्यक्ति उपस्थित थे।

सर्वप्रथभ बैठक में उपस्थित कार्यालयप्रमुखों 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 अभिनन्दन किया तथा अध्यक्ष महोदय की अनुमति से बैठक की कार्रवाई किया एवं गत बैठक के कार्यवृत्त की सर्वसम्मति से पुष्टि की गई। बैठक में प्रथम अप्रैल, 2016 से 30 सितम्बर, 2016 के दौरान सभी सदस्य कार्यालयों के हिन्दी कार्यान्वयन संबंधी प्रगति रिपोर्ट की समीक्षा की। बैठक का मुख्य उद्देश्य केन्द्रीय कार्यालयों/ बैंकों/ उपक्रमों में हिन्दी का उत्तरोत्तत विकास करना तथा अम्मू क्षेत्रओर अग्रसर करने की दिशा में प्रकाश डाला।

तत्पश्चात् बैठक में उपस्थित सदस्यों के परिचय के साथ ही बैठक की कार्रवाई आरम्भ हुई। सदस्य-सचिव ने गत बैठक के कार्यवृत्त पर कोई आपत्ति एवं प्रतिक्रिया न मिलने पर सचिव ने अध्यक्ष महोदय के अनुमोदन पर गत बैठक के कार्यवृत्त की पुष्टि की।

पत्रिकाओं का प्रकाशन- राजभाषा कार्यान्वयन के लिए अधिकारियों/ कर्मचारियों में सृजनात्मकता का विकास करने के लिए पत्रिकाओं के प्रकाशन का अत्यन्त महत्वपूर्ण स्थान है: पी.एन.बी., 2. हे ! जम्मू की "त्रिकुट', आयकर आयुक्त का कार्यालय, जम्मू की नगर राजभाषा कार्यान्वयन समिति "आयकर शिखर' एवं नराकास, जम्मू समिति कार्यान्वयन की जम्मू. 'ज्ञानवार्ता' को सराहा और कहा कि पत्रिकाएं प्रकाशित करने वाले कार्यालयों का यह प्रशंसनीय कार्य है।

वर्ष 2015-16 में जिन कार्यालयों/ बैंकों/उपक्रमों ने हिन्दी में अच्छे कार्य किये हैं उन कार्यालयों के कार्यालयप्रमुखों/राजभाषा अधिकारियों को क्रमशः शील्ड एवं प्रमाण-पत्र भी प्रदान किए गए।

संस्थान के निदेशक एवं नराकास अध्यक्ष डॉ. राम विश्वकर्मा ने अध्यक्षीय भाषण में अत्यन्त प्रभावी रूप में कार्यालय-प्रमुखों से अपने-अपने कार्यालयों में अधिकांशत: सूचना प्रौद्योगिकी के प्रयोग पर बल देते हुए कहा कि हिन्दी के उत्तरोत्तर विकास के लिए समर्पित होने की जरूरत है तथा अनुरोध किया कि जिन कार्यालयों के पते में यदि कोई परिवर्तन हो जाए तो वे कार्यालय इसकी सूचना नगर राजभाषा कार्यान्वयन समिति कार्यलय को अवश्य दें ताकि कार्यालयों की सूची समय-समय पर संशोधित कर अद्यतन रखी जा सके।

अन्त में संस्थान के श्री पंकज बहादुर, नियंत्रक प्रशासन ने धन्यवाद प्रस्ताव ज्ञापित किया और बैठक सम्पन्न हुई।

संस्थान में एकदिवसीय हिन्दी कार्यशाला का आयोजन

राजभाषा हिन्दी में सरकारी कामकाज के अवसर पर हिन्दी कार्यशाला का आयोजन किया गया। जिसमें संस्थान के नियंत्रक प्रशासन श्री पंकज बहादुर, वित्त. एवं लेखा अधिकारी, भण्डार एवं क्रय अधिकारी, वैज्ञानिक, तकनीकी अधिकारी एवं अन्य स्टॉफ सदस्यों ने इस कार्यशाला में उपस्थित थे। कार्यशाला का संचालन डॉ. रमा शर्मा, हिन्दी अधिकारी ने किया। ताकि वैज्ञानिक एवं प्रशासनिक क्षेत्र में हिन्दी की प्रगति सुनिश्चित हो सके। इस दौरान परिषद् मुख्यालय से वरिष्ठ हिन्दी अधिकारी, डॉ. पूरनपाल ने भारतीय समवेत औषध संस्थान, जम्मू का दिनांक 6-8.03.2037 की अवधि के दौरान संस्थान का राजभाषा निरीक्षण किया तथा दिनांक 6.03.207 को 2.00 बजे संस्थान में एक दिवसीय हिन्दी कार्यशाला का आयोजन किया गया और डॉ. पूरनपाल की चिएप्रतीक्षित दक्षता का लाभ हम सब ने उठाया। डॉ. पाल वह शख्सियत हैं जिनके काम से परिषद् मुख्यालय के साथ-साथ परिषद् के सभी संस्थान भिज्ञ हैं। समय-समय पर राजभाषा से जुड़े कार्यो के निष्पादन हेतु परामर्श दाता के रूप में डॉ. पाल एक दीर्घ अवधि से अपनी श्रेष्ठ सेवाएं देते आए हैं। सौभाग्य से राजभाषा निरीक्षण के चलते हमें यह अवसर मिल गया कि संस्थान के समस्त स्टॉफ इनके अनुभवों का प्रत्यक्ष लाभ उठा सकें। हमारे प्रस्ताव पर "राजभाषा नीति कार्यान्वयन में चुनौतियां एवं कठिनाइयां' विषय पर सभी पहलुओं को जैसे प्रशासनिक एवं वैज्ञानिक कार्यो को छूते हुए हमारा मार्गदर्श किया और डॉ. रमा शर्मा ने अपने सदस्यों से भी आग्रह किया कि वे अपनी शंकाओं का समाधान इनके ज्ञान से लेकर पूरा-पूरा लाभ उठाएं।

सभी अनुभागों/प्रभागों में अंग्रेजी/हिन्दी में किए जा रहे कार्यो का प्रत्यक्ष जायजा लेंगे और वरिष्ठ वैज्ञानिकों/अधिकारियों तथा प्रशासन नियंत्रक एवं अन्य अधिकारियों आदि के साथ चर्चा एवं बैठक भी की। कार्यशाला में परिषद् मुख्यालय के डॉ. पूरनपाल ने श्री दुर्गा प्रसाद मिंडाला, तकनीकी सहायक को प्रवेश परीक्षा उत्तीर्ण करने पर प्रमाण-पत्र प्रदान किए।

अन्त में संस्थान के नियंत्रक प्रशासन, श्री पंकज बहादुर ने धन्यवाद किया।

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