CSIR-IIIM

द्विवार्षिक प्रतिवेदन

Biennial Report

2013-2015

सीएसआइआर–भारतीय समवेत औषध संस्थान, जम्मू–180001 (भारत)

CSIR-Indian Institute of Integrative Medicine

(Council of Scientific and Industrial Research)

JAMMU-180001 (INDIA)

CONTENTS

CONTENTS

DIRECTORS REPORT

I have pleasure in presenting the Biennial Report of CSIR-Indian Institute of Integrative Medicine, Jammu which covers the major highlights of the work done during 2013-15. So far as R&D activities are concerned, in my opinion, this period has been highly exciting as IIIM, Jammu filed 14 patents both in India and in Foreign countries. Nine PCT patent applications were also granted to IIIM during this period. IIIM, Jammu published 290 quality research papers with an average impact factor significantly increasing from 2.54 to 3.552 over these years.

Earlier two patents entitled, "A process of isolation of novel compound 2,6-Dihydroxy-2-(P-Hydroxybenzyl)-3(2h)-Benzofuranone-7-C-*Pterocarpus marsupium"* and *"A process for extraction of antidiabetic formulation mainly containing flavonoid glycosides",* were filed by our institute under a project sponsored by Indian Council of Medical Research, New Delhi. A Bangalore based pharmaceutical company M/s Sami Labs got interested in these patents and under a tripartite agreement between ICMR, IIIM and M/s Sami Labs, both these patents were licensed to the Bangalore based Sami Labs Limited on non-exclusive basis.

This period has also been significant as IIIM completed the project of creating a State of the Art current Good Manufacturing Practices (cGMP) facility for extraction, formulation and packaging of herbal drugs which shall be used for developing novel herbal products for clinical and marketing trials. It shall also be used by small and medium scale herbal and pharma units for manufacturing herbal products under strict quality control and cGMP certification. IIIM has already received letters of intent from herbal drug companies for regular use of this modern facility.

Under Societal mission, IIIM Jammu contracted a project from State Innovation Fund for demonstration of "End to end technology on Phalsa cultivation and its products". Phalsa (*Grewia asiatica*) was abundantly available in dry land/ Kandi belt of Jammu but over a period of time it disappeared from market. Having very high nutritional value IIIM Jammu launched a drive for extensive cultivation of Phalsa plants in Jammu region and also demonstrate innovative products obtained from this fruit. IIIM manufactured more than one lakh tetrapacks of 200 ml capacity health drink from its fruit and presented the same at various public and social meetings for public awareness.

I am sure the research work carried and presented in this Biennial Report shall be even more exciting to you as you go through the same.

(Ram Vishwakarma)

1. BIODIVERSITY AND APPLIED BOTANY

1.1 Disruption of the PI3K/AKT/mTOR signaling cascade and induction of apoptosis in HL-60 cells by an essential oil from *Monarda citriodora*

Anup Singh Pathania, Santosh Kumar Guru, M.K. Verma, Chetna Sharma, Sheikh Tasduq Abdullah, Fayaz Malik, Suresh Chandra, Meenu Katoch, Shashi Bhushan

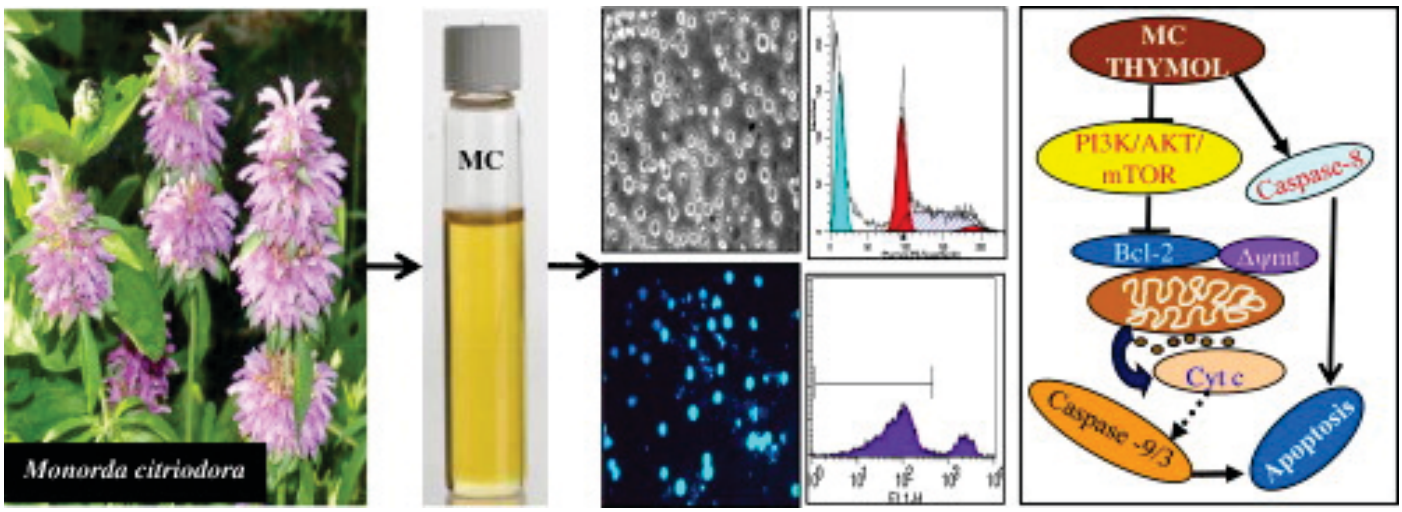


Figure 1.1. Isolation Process of an Essential oil from *Monarda citriodora*

Isolated an essential oil from *Monarda citriodora* (MC) and characterized its 22 chemical constituents with thymol (82%), carvacrol (4.82%), β-myrcene (3.45%), terpinen-4-ol (2.78%) and p-cymene (1.53%) representing the major constituents. We have reported for the first time the chemotherapeutic potential of MC in human promyelocytic leukemia HL-60 cells by means of apoptosis and disruption of the PI3K/AKT/mTOR signaling cascade. MC and its major constituent, thymol, inhibit the cell proliferation in different types of cancer cell lines like HL-60, MCF-7, PC-3, A-549 and MDAMB-231. MC was found to be more cytotoxic than thymol in HL-60 cells with an IC_{50} value of 22 µg/ml versus 45 µg/ml for thymol. Both MC and thymol induce apoptosis in HL-60 cells, which is evident by Hoechst staining, cell cycle analysis and immuno-expression of Bcl-xL, caspase-3,-8,-9 and PARP-1 cleavage. Both induce apoptosis by extrinsic and intrinsic apoptotic pathways that were confirmed by enhanced expression of death receptors (TNF-R1, Fas), caspase-9, loss of mitochondrial membrane potential and regression of Bcl-2/Bax ratio. Interestingly, both MC and thymol inhibit the downstream and upstream signaling of PI3K/AKT/mTOR pathway. The degree of apoptosis induction and disruption of the PI3K signaling cascade by MC was significantly higher when compared to thymol.

1.2 Comparative analysis of the aroma chemicals of Melissa *officinalis* using hydrodistillation and HS-SPME techniques

Shakeel-u-Rehman, Romaisa Latief, Khursheed A. Bhat, Mohammad A. Khuroo, Abdul S. Shawl, Suresh Chandra

Headspace solid-phase micro extraction (HS-SPME) coupled with gas chromatography– mass spectromety (GC–MS) has been used for the chemical analysis of Melissa officinalis (leaves) cultivated in Institute Germplasm. The HS-SPME analysis led to the identification of 22 compo- nents constituting 99.1% of the total volatile constituents present in the leaves whereas its hydro- distillate led to the identification of 24 volatile constituents constituting 98.1% of the volatile material. The chemical

composition of the SPME and hydrodistilled extract of M. officinalis leaves comprised mainly of oxygenated monoterpenes (78.5% and 57.8% respectively) and sesquiterpene hydrocarbons (14.9% and 29.7% respectively). The major components identified in the HS-SPME extract were citronellal (31.1%), citronellol (18.3%), b-caryophyllene (12.0%), (E)-citral (11.9%), (Z)-citral (9.6%), geraniol (3.6%), (Z)-b-ocimene (3.1%) and 1-octen-3-ol (2.0%) whereas hydro- distilled essential oil was rich in (Z)-citral (19.6%), b-caryophyllene (13.2%), (E)-citral (11.2%), citronellal (10.2%), germacrene-D (8.3%), d-3-carene (5.0%), 6-methyl-5-hepten-2-one (3.7%) and citronellyl acetate (3.7%). The comparative analysis of volatile constituents of M. officinalis leaf extract using HS-SPME and hydrodistillation techniques shows both qualitative as well as quantitative differences. The current study is the first report involving rapid analysis of volatile compo- nents of M. officinalis by HS-SPME.

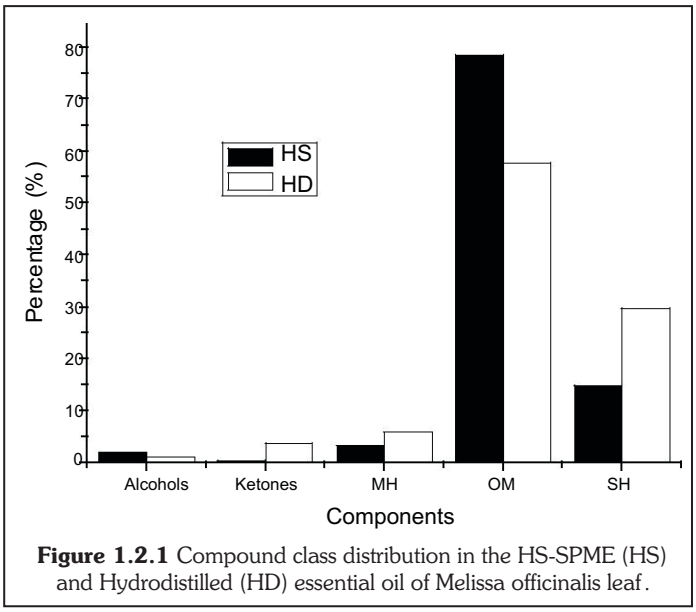


Figure 1.2.1 Compound class distribution in the HS-SPME (HS) and Hydrodistilled (HD) essential oil of Melissa officinalis leaf.

Table 1.2.1 Essential oil composition of *Melissa officinalis*.

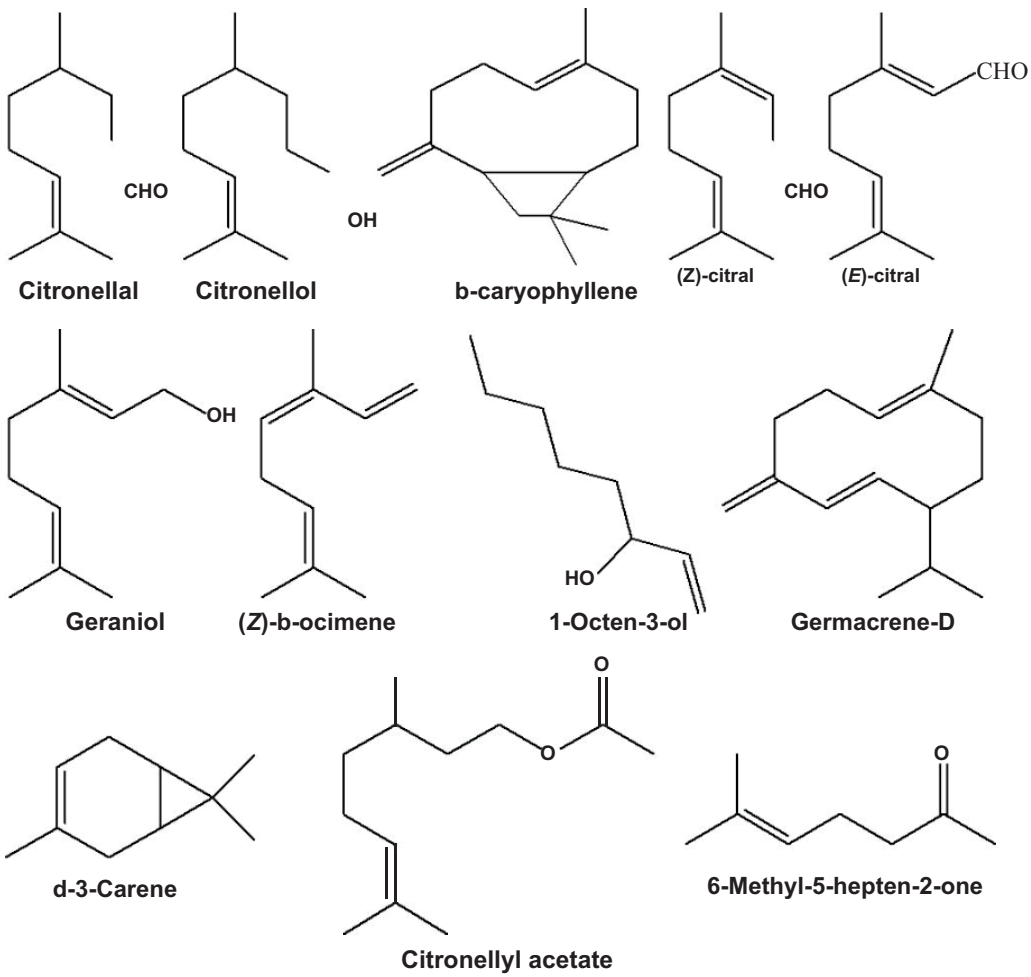
S. N.	Compound	RI a, b	Peak area % (HS-SPME)	Peak area % (HD)	Methods of identification
1	b-Pinene	974	0.2	0.2	MS, RI
2	Artemiseole	976	1.0	1.0	MS, RI
3	1-Octen-3-ol	979	2.0	0.9	MS, RI
4	3-Octanol	991	–	0.2	MS, RI
5	6-Methyl-5-hepten-2-one	995	0.4	3.7	MS, RI
6	d-3-Carene	1011	–	5.0	MS, RI
7	(Z)-b-Ocimene	1032	3.1	0.6	MS, RI, Std
8	Linalool	1095	0.5	2.7	MS, RI
9	Cis-rose oxide	1106	1.2	0.5	MS, RI
10	Trans-rose oxide	1125	0.6	–	MS, RI
11	Cis-verbenol	1141	–	0.7	MS, RI
12	Limonene oxide	1142	0.7	–	MS, RI
13	Citronellal	1148	31.1	10.2	MS, RI, Std
14	Isopulegone	1149	0.3	–	MS, RI
15	Myrtenol	1195	–	2.8	MS, RI
16	Citronellol	1225	18.3	–	MS, RI, Std
17	Geraniol	1252	3.6	1.9	MS, RI, Std
18	(Z)-Citral	1316	9.6	19.6	MS, RI, Std
19	Methyl geranate	1324	0.3	1.3	MS, RI
20	(E)-Citral	1338	11.2	11.2	MS, RI, Std
21	Citronellyl acetate	1352	0.1	3.7	MS, RI
22	a-Copaene	1376	–	1.4	MS, RI
23	Geranyl acetate	1379	–	2.2	MS, RI
24	b-Caryophyllene	1417	12.0	13.2	MS, RI, Std
25	a-Bergamotene	1434	0.4	–	MS, RI, Std
26	a-Humulene	1452	0.9	1.9	MS, RI, Std
27	Germacrene-D	1484	1.4	8.3	MS, RI, Std
29	a-Farnesene	1505	0.2	2.3	MS, RI, Std
30	d-Cadinene	1523	–	2.6	MS, RI
	Total (%)		99.1	98.1	

RI, retention index.
[a] As identified by GC–MS software; names according to NIST mass spectral library, and by comparing their Kovats retention indices. [b] Kovats retention indices of each component were collected from the literature for column RTX-5.

Table 1.2.2 Compound class composition in the HS-SPME (HS) and Hydrodistilled (HD) essential oil of *Melissa officinalis* leaf.

S. No.	Class of compounds	Peak area % (HS-SPME)	Peak area% (HD)
1	Alcohols	2.0	1.1
2	Ketones	0.4	3.7
3	Monoterpene hydrocarbons	3.3	5.8
4	Oxygenated monoterpenes	78.5	57.8
5	Sesquiterpene hydrocarbons	14.9	29.7
6	Total (%)	99.1	98.1

Figure 1.2.2 Structures of the major essential oil constituents.



In conclusion, the present report of the chemical profile of the essential oil of M. officinalis provides further indepth informa- tion about the chemo diversity in the chemical composition of the essential oil of the genus Melissa. Also the HS-SPME is a ra- pid, simple and eco-friendly method for the essential oil screening of aromatic plants. This novel process can produce essential oil in concentrate form, free from any residual solvents, con- taminants, or artefacts. A study of the application of this new method for the quantitative determination of volatile constitu- ents from food, cosmetics and medicine is under way.

2. PLANT BIOTECHNOLOGY AND DIVERSITY

2.1 Molecular cloning and functional characterization of an antifungal PR-5 protein from *Ocimum basilicum*

Irshad Ahmad Rather, Praveen Awasthi, Vidushi Mahajan, Yashbir S. Bedi, Ram A. Vishwakarma & Sumit G. Gandhi

Pathogenesis-related (PR) proteins are involved in biotic and abiotic stress responses of plants and are grouped into 17 families (PR-1 to PR-17). PR-5 family includes proteins related to thaumatin and osmotin, with several members possessing antimicrobial properties. In this study, a PR-5 gene showing a high degree of homology with osmotin-like protein was isolated from sweet basil (*Ocimum basilicum* L.). A complete open reading frame consisting of 675 nucleotides, coding for a precursor protein, was obtained by PCR amplification. Based on sequence comparisons with tobacco osmotin and other osmotin-like proteins (OLPs), this protein was named *ObOLP*. The predicted mature protein is 225 amino acids in length and contains 16 cysteine residues that may potentially form eight disulfide bonds, a signature common to most PR-5 proteins. Among the various abiotic stress treatments tested, including high salt, mechanical wounding and exogenous phytohormone/ elicitor treatments; methyl jasmonate (MeJA) and mechanical wounding significantly induced the expression of *ObOLP* gene. The coding sequence of *ObOLP* was cloned and expressed in a bacterial host resulting in a 25 kDa recombinant-HIS tagged protein, displaying antifungal activity. The *ObOLP* protein sequence appears to contain an N-terminal signal peptide with signatures of secretory pathway. Further, our experimental data shows that *ObOLP* expression is regulated transcriptionally and *in silico* analysis suggests that it may be post-transcriptionally and post-translationally regulated through microRNAs and post-translational protein modifications, respectively. This study appears to be the first report of isolation and characterization of osmotin-like protein gene from *Ocimum basilicum* (Figures 1-8).

Figure -1

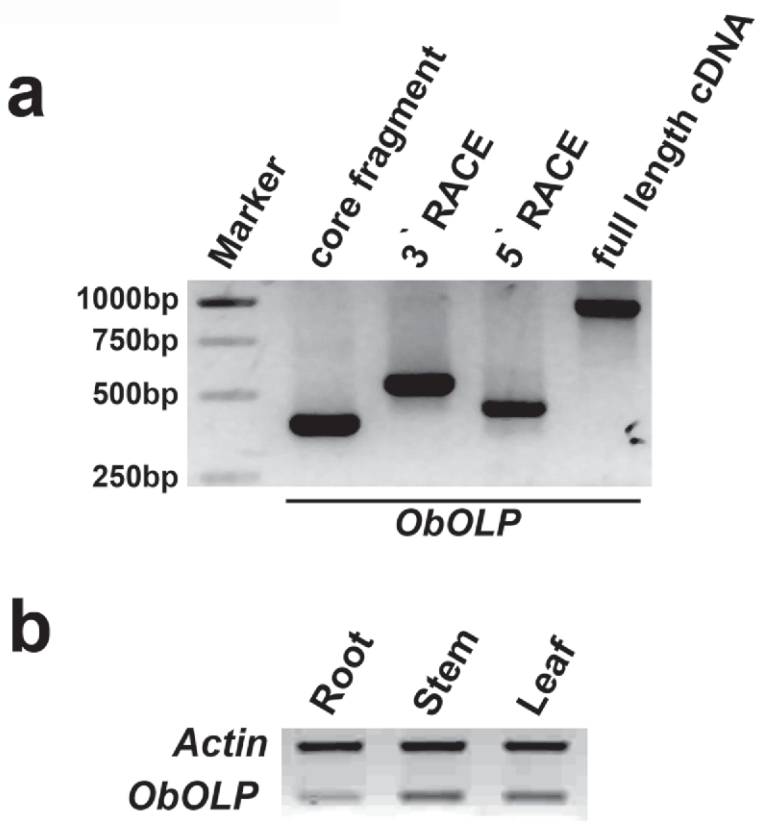


Figure-1: Cloning of *ObOLP* and tissue expression profile of *ObOLP* mRNA. 1a. Cloning of the *ObOLP* gene from *O. basilicum*. Gel picture shows the PCR amplicons of core fragment, 5' and 3' RACE PCR fragments and full length *ObOLP* gene. 1b. Expression profile of *ObOLP* gene in root, stem and leaves of adult *O. basilicum* plants, assessed with RT-PCR. *Actin* was used as housekeeping internal control.

Figure -2

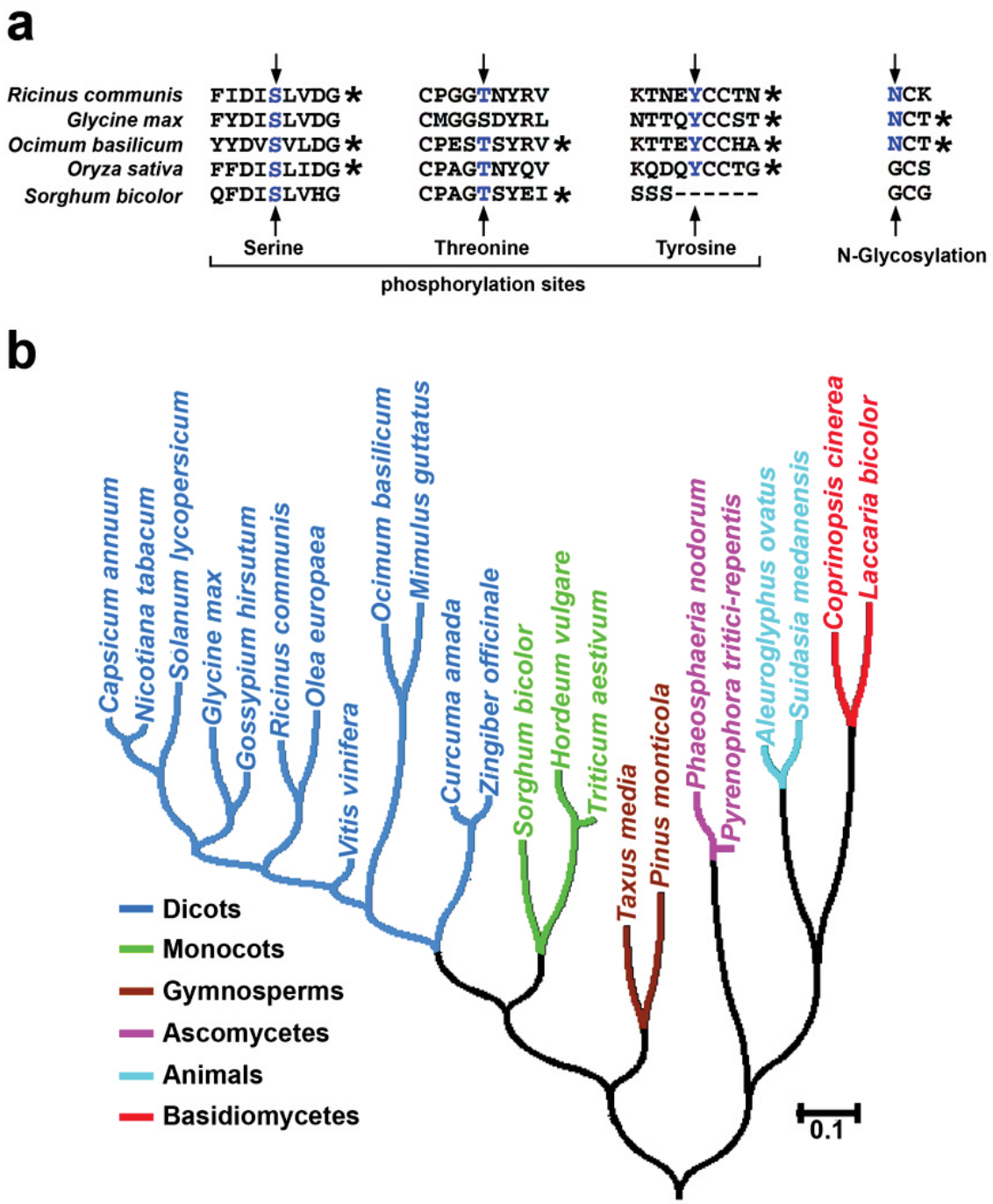


Figure-2: Prediction of post-translational modifications and construction of phylogenetic tree of ObOLP and other PR-5 proteins. 2a. Prediction of Phosphorylation and N- Glycosylation post-translational modification sites in ObOLP and its homologs from other plant species. Conserved target residues are shown in blue color and star indicates a positive prediction of post-translational modification in the protein sequence. 2b. Molecular phylogenetic tree of osmotin related proteins showing clustering of sequences from different taxonomic groups of plants, fungi and animals. ObOLP clusters with related sequences from dicotyledonous plants.

Figure -3

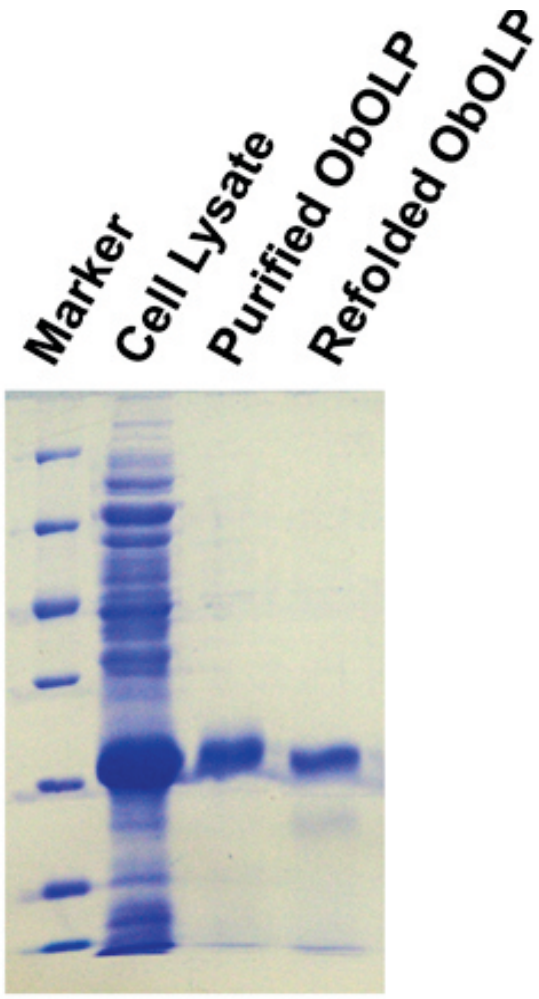


Figure-3: Heterologous expression of ObOLP protein. A truncated form of ObOLP (designated ObOLP) was expressed using a cold inducible promotor in *Escherichia coli*. Recombinant HIS tagged ObOLP lacks the N-terminal secretory signal sequence. It was purified using Ni-NTA chromatography. Purified protein was refolded to yield a functional, soluble protein.

Figure -4

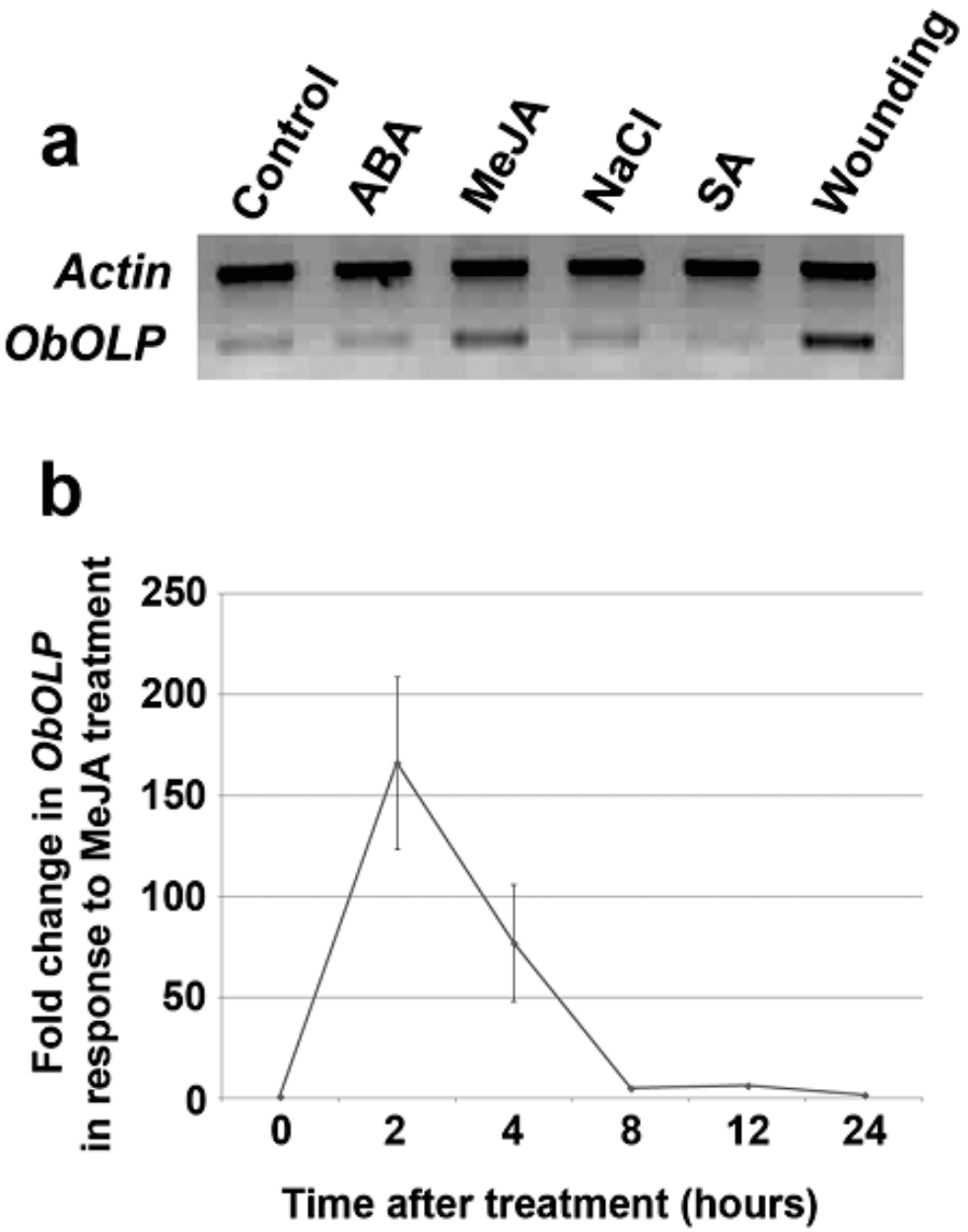


Figure-4: Effect of elicitor treatments on expression of *ObOLP* mRNA. 4a. Induction patterns of the *ObOLP* gene after treatment with abscisic acid (ABA), methyl jasmonate (MeJA), NaCl (high salt), salicylic acid (SA) and wounding, as compared to control plants. *Actin* was used as housekeeping internal control. 4b. Expression profile of *ObOLP* in response to MeJA treatment with respect to time post-treatment, as determined by quantitative real-time RT-PCR.

Figure -5

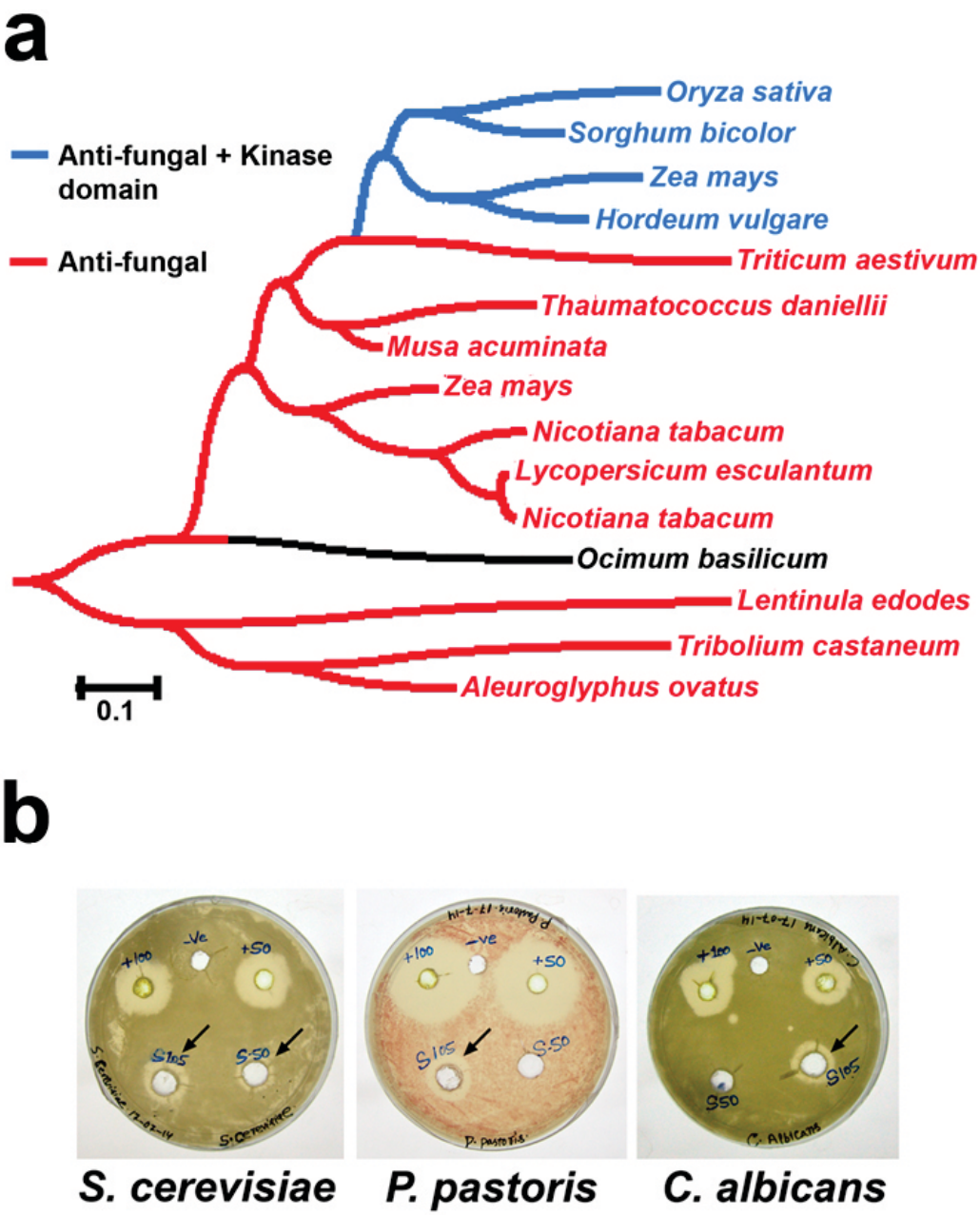


Figure-5: ObOLP exhibits antifungal activity. 5a. Phylogenetic tree of osmotin related proteins with and without kinase domains. ObOLP clusters with osmotin related protein sequences lacking the kinase domain. 5b. Antifungal activity of purified ObOLP protein was tested against *Saccharomyces cerevisiae*, *Pichia pastoris* and *Candida albicans* at 50 µg and 105 µg concentrations. Amphotericin B was used as positive control at 50 µg and 100 µg concentrations.

Figure -6

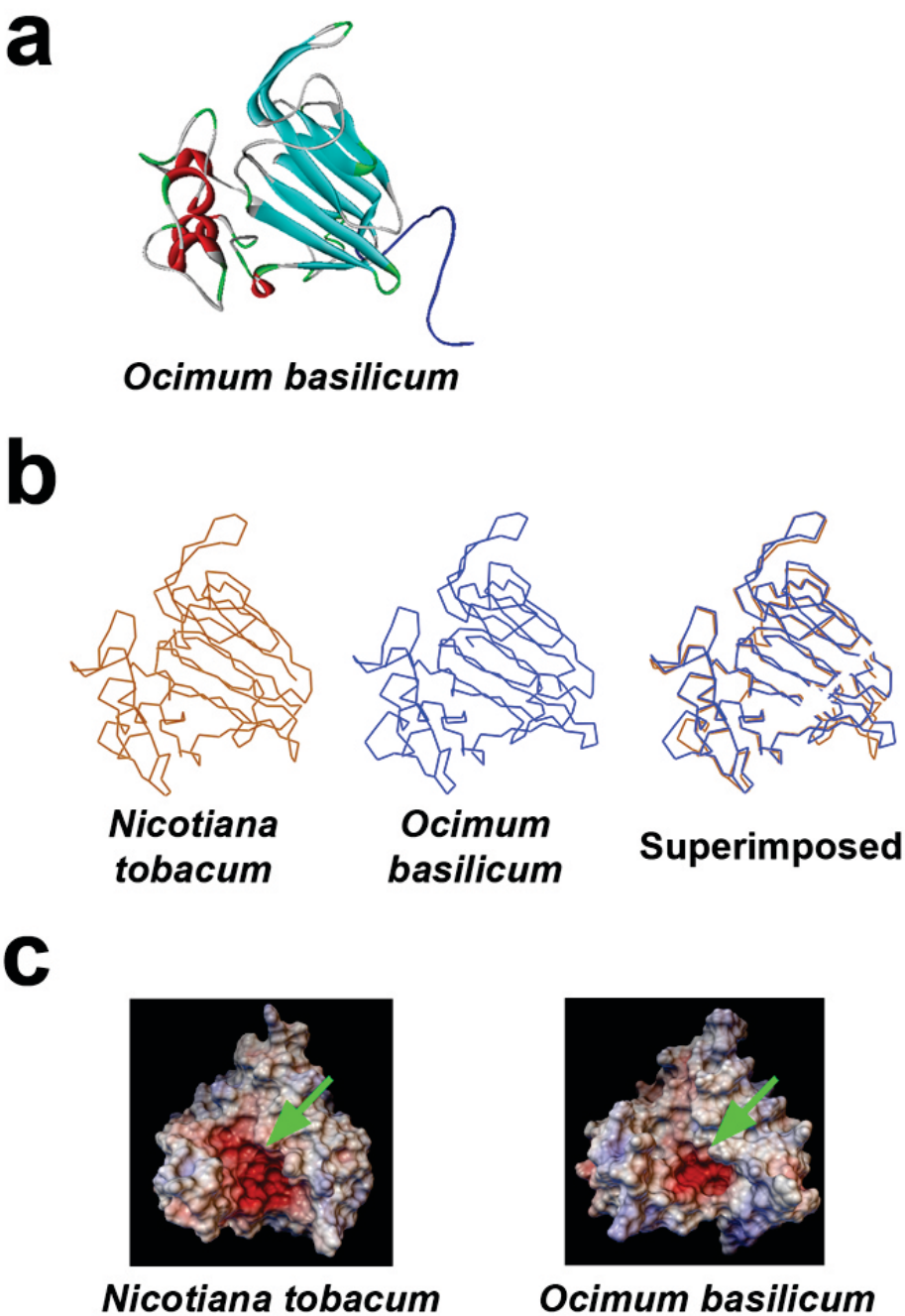


Figure-6: Prediction of 3D structure of ObOLP. 6a-b. Prediction of protein 3D structure of *O. basilicum* and *N. tabacum* and their superimposition. 6c. Conservation of acidic cleft in ObOLP and its homolog from *N. tabacum*.

Figure -7

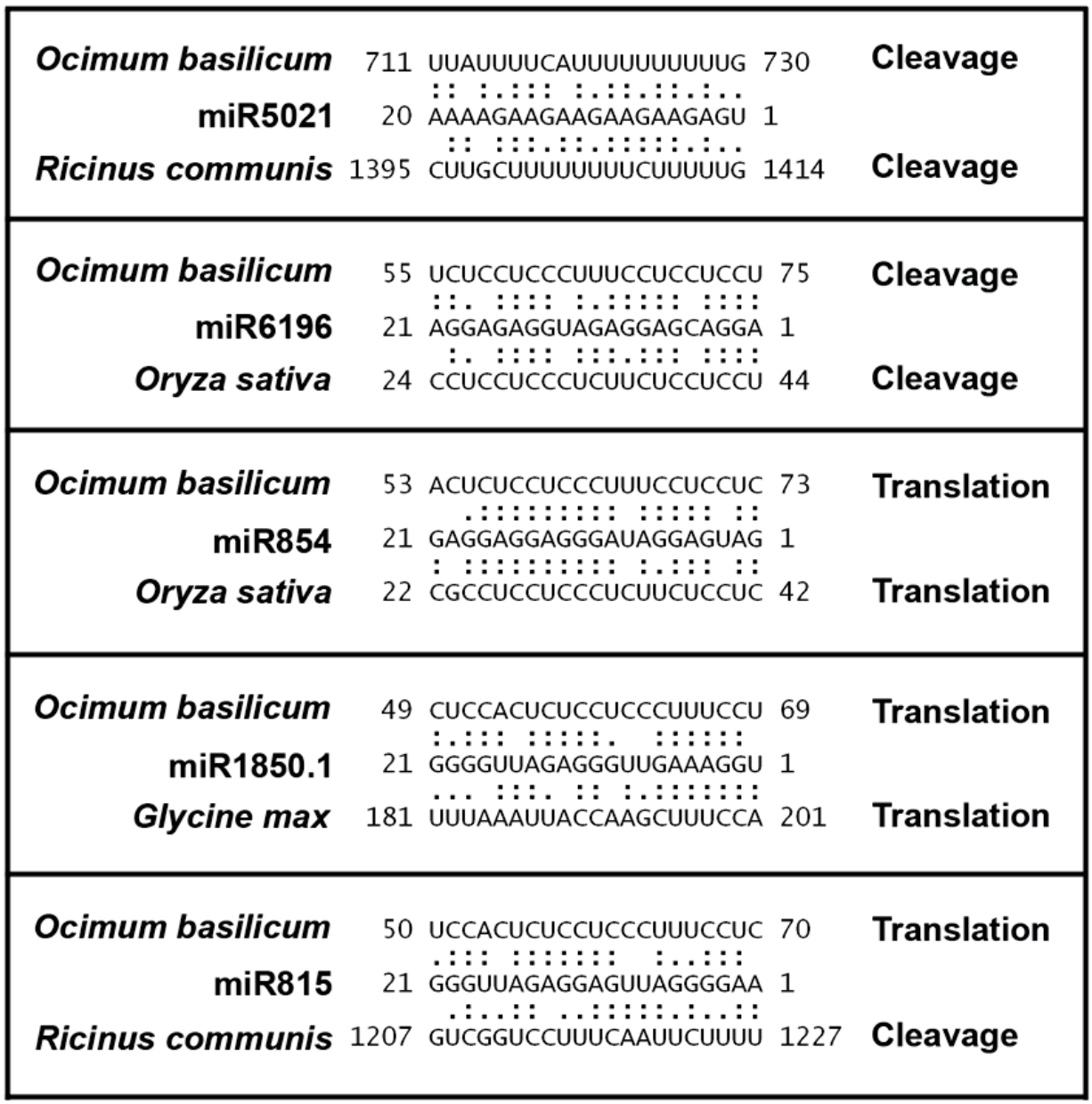
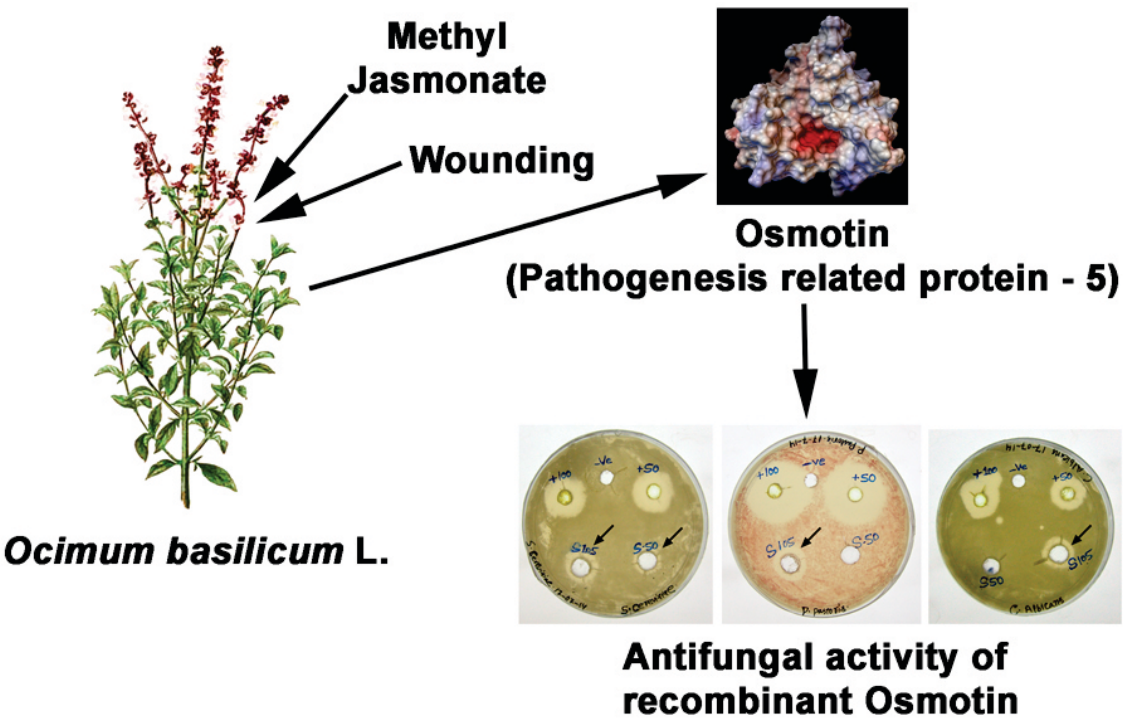


Figure-7: Prediction of miRNAs targeting ObOLP. Picture shows conservation of target sites of predicted miRNAs in ObOLP and related homologs from other plant species, and their possible modes of action (cleavage or inhibition of translation).

Figure8. GRAPHICAL SUMMARY



2.2 Isolation, identification and expression analysis of cytochrome P450 ESTs from *Coleus forskohlii*

Praveen Awasthi, Vidushi Mahajan, Irshad Ahmad Rather, Ajai Prakash Gupta, Yashbir S. Bedi, Ram A. Vishwakarma and Sumit G. Gandhi

Cytochrome P450 genes (CYPs) are one of the largest gene families in plants. They play important roles in biosynthesis of secondary metabolites, odorants, flavors, allelochemicals, defense related compounds, phytohormones as well as in detoxification of harmful chemicals. Degenerate primers, designed from the conserved regions of CYPs, were used to amplify fragments from cDNA of *Coleus forskohlii* (Willd.) Briq. (Lamiaceae), and a library was prepared. *C. forskohlii* is an herb known for production of forskolin, a potent and reversible activator of adenylate cyclase. Forty two sequences homologous to CYPs were isolated from this library (Figure 1, 2 and 3). These sequences were assembled into seven distinct CYP ESTs. Phylogenetic analysis clustered these CYPs into seven families. Expression profiling of CYPs showed that the transcripts of *CfP450C1*, *CfP450C4*, *CfP450C5*, *CfP450C6* and *CfP450C7* were prominent in aerial tissues (flower, young leaf and mature leaf), whereas expression of *CfP450C3* was dominant in root and root tip. *CfP450C2* showed higher expression in flowers and roots as compared to other tissues. Expression profiles of CYPs, in response to different elicitors (abscisic acid, methyl jasmonate, salicylic acid, 2,4-dichloro-phenoxyacetic acid) and stresses (UVA and wounding) were also studied. This study has isolated CYPs from *C. forskohlii*, and may help in understanding their regulation as well as provide clues about their functions (Table 2.1.1 and 2.1.2).

Figure 1: Clustering of *CYP* sequences from *C. forskohlii* and all major plant *CYP* families

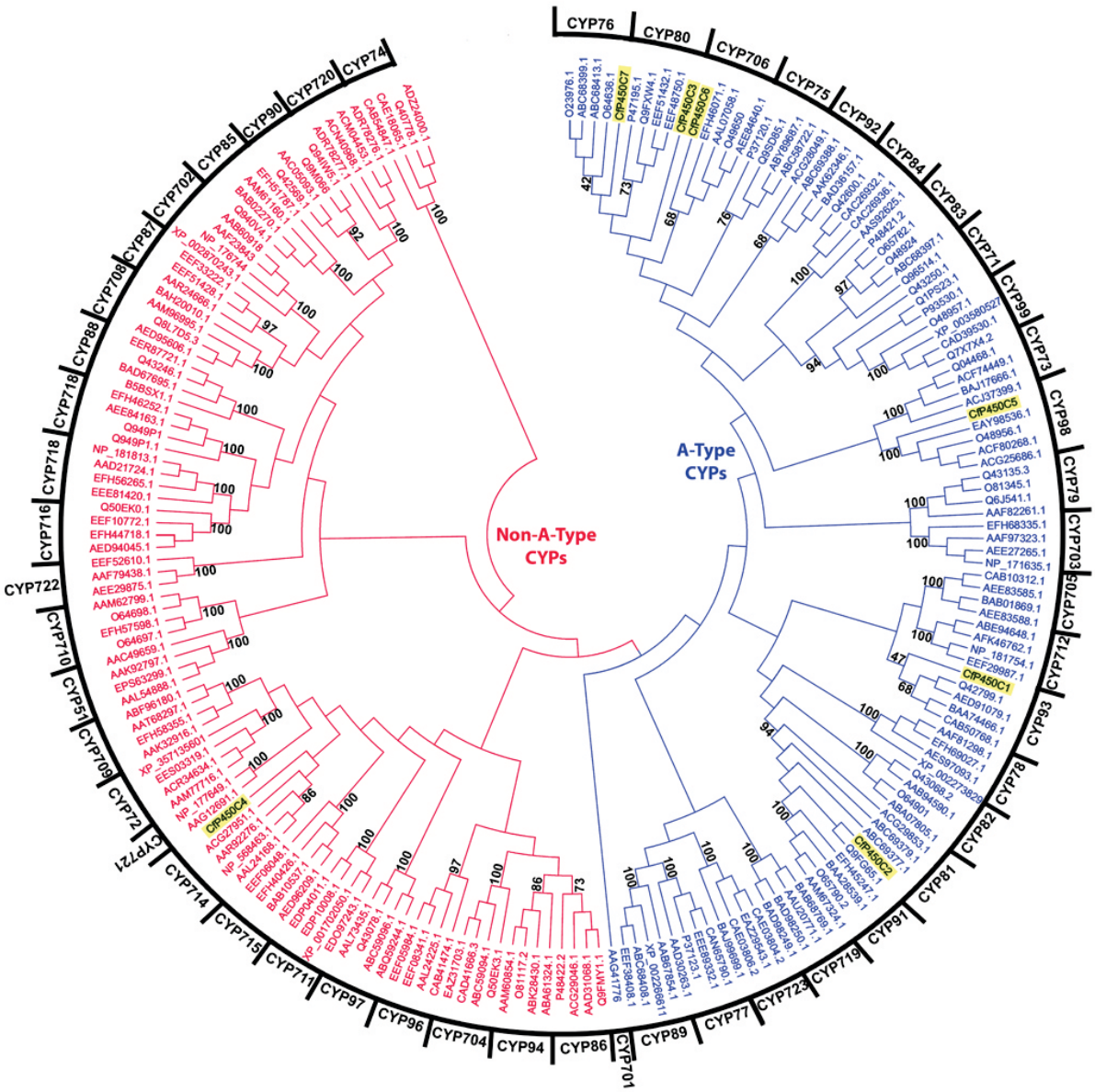


Figure 1: Clustering of *CYP* sequences from *C. forskohlii* and all major plant *CYP* families. *CfP450C1-C3* & *CfP450C5-C7* clustered with A-type *CYP*s, while *CfP450C4* clustered with non-A-type *CYP*s. All the *CYP*s isolated from *C. forskohlii* that clustered with A-type *CYP*s fall into the *CYP71* clan. *CfCYPC4* (non-A-type) fell in the *CYP72* clan. MEGA5 software was used for the analysis. Tree topology support was assessed by bootstrap analysis (100 replicates).

Figure 2: Relative tissue expression profiles of CYP sequences

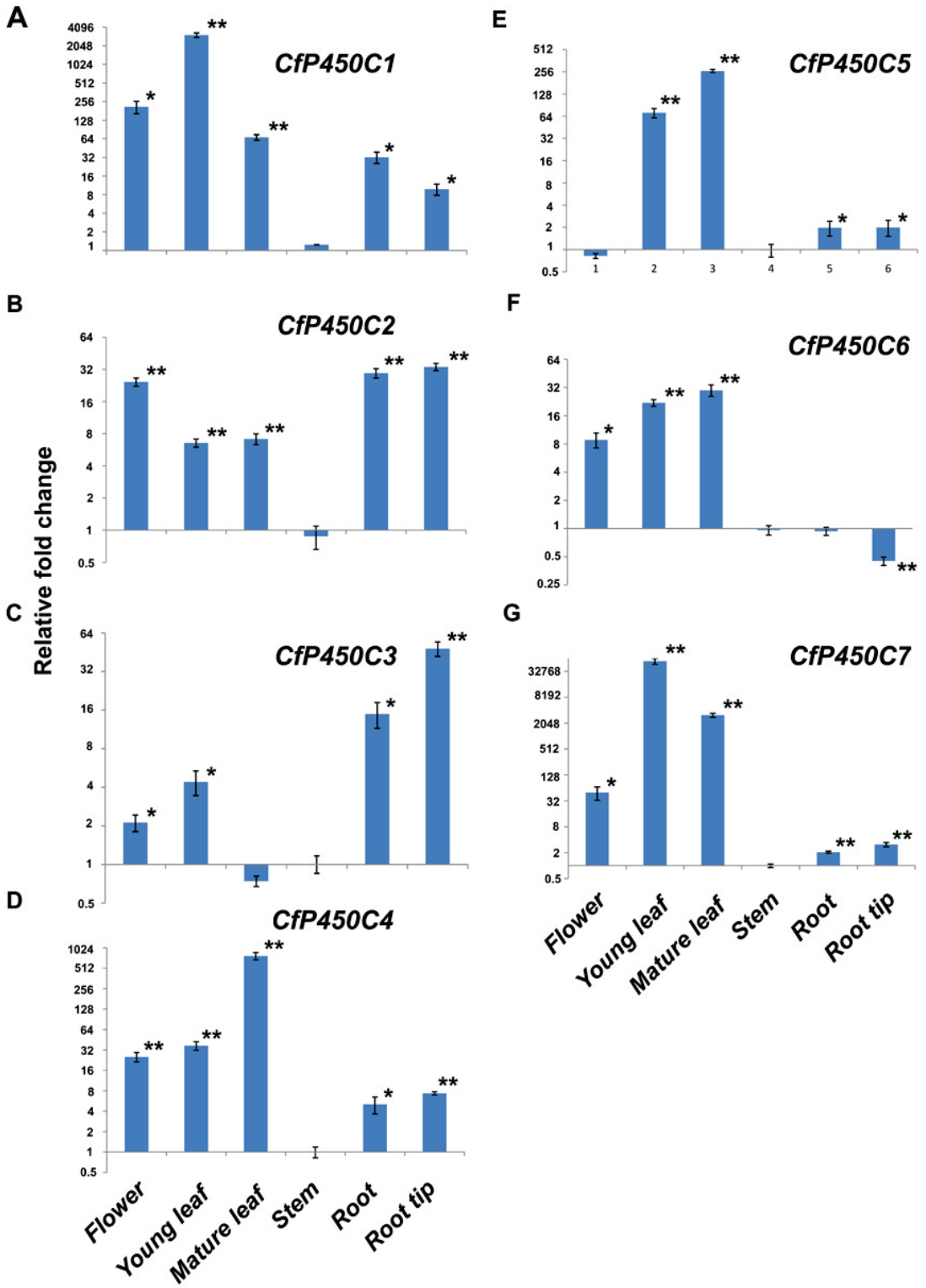


Figure 2: Relative tissue expression profiles of CYP sequences (A) *CfP450C1*, (B) *CfP450C2*, C) *CfP450C3*, (D) *CfP450C4*, (E) *CfP450C5,* (F) *CfP450C6* and (G) *CfP450C7* in flower, young leaf, mature leaf, stem, root and root tip tissues of *C. forskohlii* as determined by quantitative real time RT-PCR (qPCR). Actin was used as housekeeping control and expression of gene-of-interest in stem was used as baseline for calculating fold change. Three replicates were used for analysis.
** indicates p-value <0.01
* indicates p-value <0.05

Figure 3: Expression profiles of CY*P* sequences under different elicitor treatments and stresses

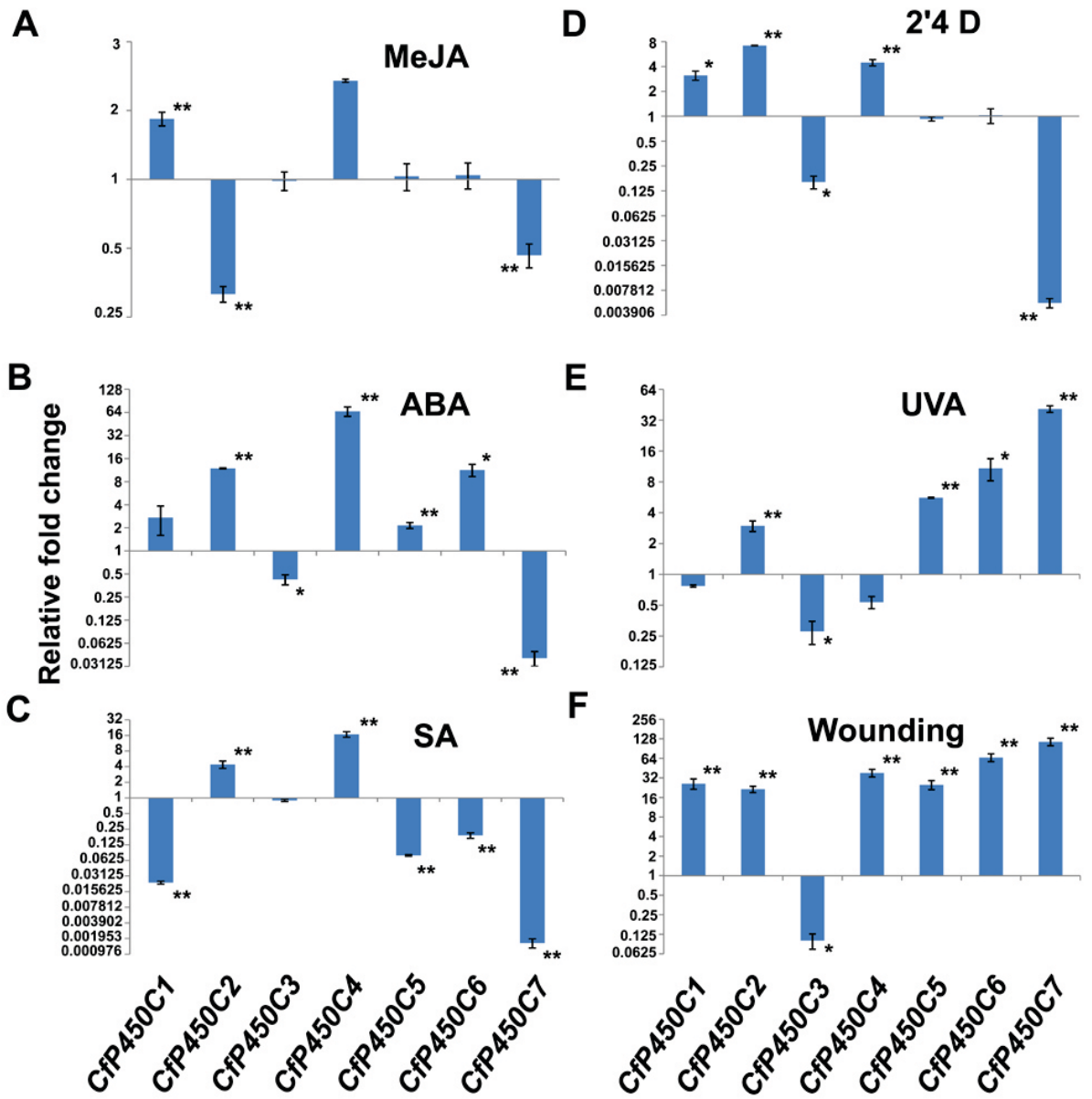


Figure 3: Expression profiles of CYP sequences under different elicitor treatments and stresses (A) MeJA, (B) ABA, (C) SA, (D) 2'4 D, (E) UVA and (F) wounding in *C. forskohlii* (leaves) as determined by quantitative real time RT-PCR (qPCR). *Actin* was used as housekeeping control for normalization and relative quantification was carried out by taking the expression of the gene of interest at 0 h (just before treatment), as baseline for calculating fold change. Three replicates were used for analysis. There was no significant change in expression of *CfP450C1-C7* in control plants.
**indicates p-value <0.01
*indicates p-value <0.05

CYP Name	Genbank Accession no.	Family	Clan	Type	Possible role of members of CYP family in plants
CfP450C1	KF606861	CYP93	CYP71 clan	A-Type CYP	Biosynthesis of flavonoids (Akashi et al. 1999; Ayabe and Akashi 2006; Zhang et al. 2007).
CfP450C2	KF667504	CYP81			Biosynthesis of flavonoids (Ayabe and Akashi 2006; Akashi et al. 1998).
CfP450C3	KF673338	CYP80			Alkaloids biosynthesis (Kraus and Kutchan 1995)
CfP450C5	KF673340	CYP98			Biosynthesis of phenylpropanoids and liginins (Franke et al. 2002; Abdulrazzak et al. 2006; Morant et al. 2007).
CfP450C6	KC307774	CYP706			Terpenoid metabolism (Luo et al. 2001).
CfP450C7	KF673343	CYP76			Biosynthesis of isoprenoids and diterpenoids (Collu et al. 2001; Swaminathan et al. 2009)
CfP450C4	KF673339	CYP714	CYP72 clan	NON-A-Type CYP	Brassinosteroid catabolism, diterpenoid biosynthesis (Bak 2011).

Table 2.1.1: CYP ESTs isolated from *Coleus forskohlii*: CYP sequences were submitted to NCBI GenBank and accession numbers are listed above. These were clustered into CYP families (types and clans) by constructing a phylogenetic tree. Their possible roles in plants are also listed.

Table 2: Expression of the CYP ESTs in response to different elicitors and stresses in *Coleus forskohlii*.

Plant *CYPs*	MeJA		ABA		SA		2'4 D		UVA		Wounding	
	Up	Down	Up	Down	Up	Down	Up	Down	Up	Down	Up	Down
CfP450C1	↑		↔			↓	↑		↔		↑	
CfP450C2		↓	↑		↑		↑		↑		↑	
CfP450C3	↔			↓	↔			↓		↓		↓
CfP450C4	↑		↑		↑		↑		↔		↑	
CfP450C5	↔		↑			↓	↔		↑		↑	
CfP450C6	↔		↑			↓	↔		↑		↑	
CfP450C7		↓		↓		↓		↓	↑		↑	

↑ : upregulated expression level of CYP ESTs.

↓ : downregulated expression level of CYP ESTs.

↔ : no significant change in expression level of CYP ESTs

2.3 Isolation and characterisation of growth promoting endophytic fungi from Artemisia annua L. and its effects on artemisinin biosynthetic pathway genes

Mir Abid Hussain, Vidushi Mahajan, Irshad Ahmad Rather, Yashbir S Bedi, and Sumit G Gandhi

Artemisia annua L. (Asteraceae), a perennial herb commonly known as sweet wormwood, is the primary source of artemisinin, a sesquiterpene lactone having antimalarial activity. It is effectively used worldwide for treatment of cerebral malaria caused by *Plasmodium falciparum*. So far, *A. annua* remains the popular source for artemisinin production throughout the world, but it is in short supply. Total synthesis of artemisinin is economically not viable. Semi-synthetic production of artemisinin from the precursor artemisinic acid produced in engineered strains of *Saccharomyces cerevisiae* has also been demonstrated. Other approaches such as exploiting plant-microbe interactions that affect artemisinin production in *A. annua* are also being explored. Endophytes *Pseudonocardia* sp. and *Colletotrichum* sp. have been reported to stimulate artemisinin production. In this study, endophytic fungi comprising of *Colletotrichum gloeosporioides*, *Cochliobolus lunatus*, *Curvularia pallescens* and *Acremonium persicum*, were isolated from the leaves of *A. annua*. Treatment of potted plants of *A. annua* with elicitor extracts prepared from these endophytic fungi, resulted in an increase in the plant biomass. Effect of these elicitor extracts on transcriptional expression levels of key artemisinin biosynthetic pathway genes, in *A. annua* tissue culture plants, was also determined by semi-quantitative RT PCR. (Figure 1 & 2).

Figure 1: Morphological characterstics of endophytic fungi isolated from *Artemisia annua*

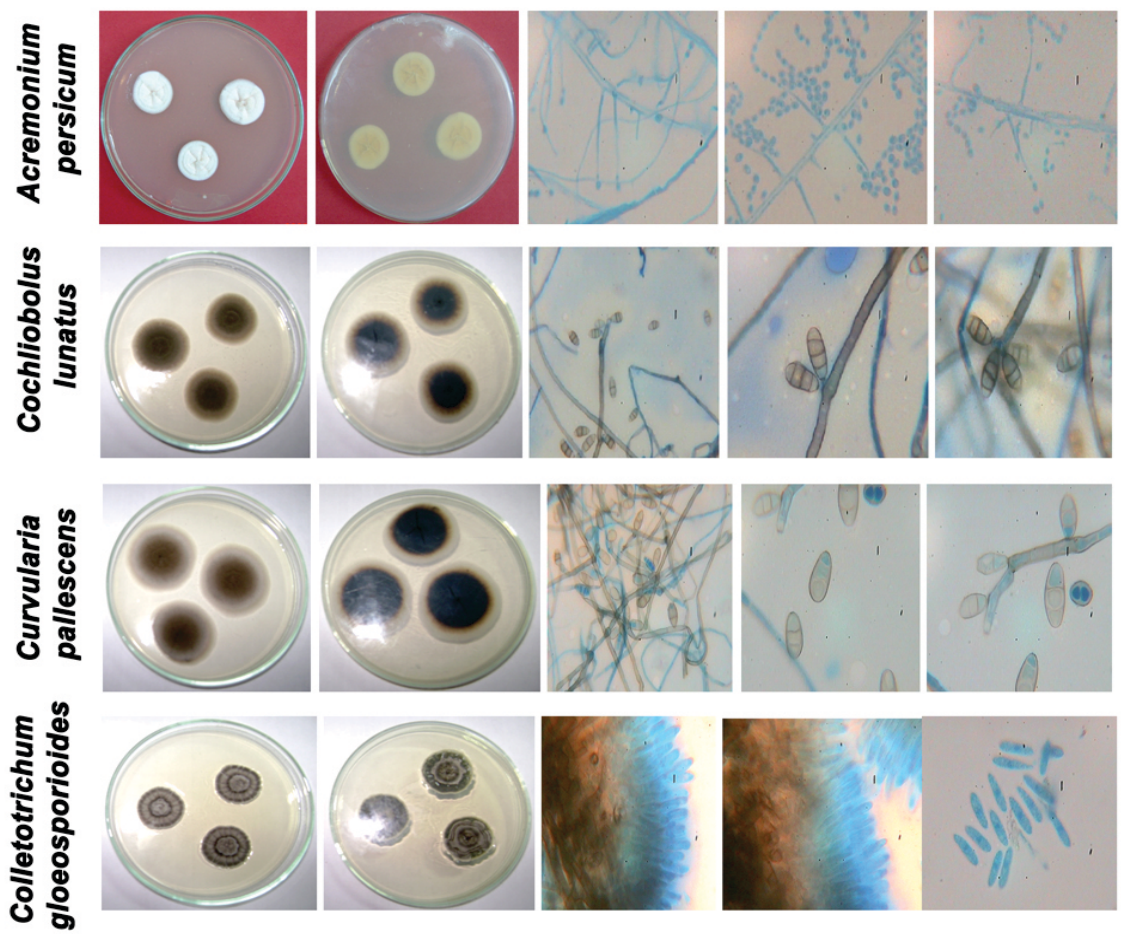


Figure 1: Morphological characterstics of endophytic fungi isolated from *Artemisia annua*. The endophytic fungi were identified on the basis of colony characterstics, hyphal morphology, characterstics of spores and reproductive structures

Figure 2: Effect of endophytic fungal elicitor extract prepared from *Curvularia pallescens* on expression of artemisinin biosynthetic pathway genes in tissue culture *A.annua* plants

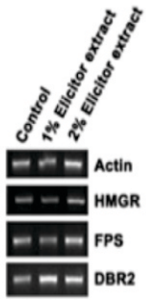


Figure 2: Effect of endophytic fungal elicitor extract prepared from *Curvularia pallescens* on expression of artemisinin biosynthetic pathway genes in tissue culture *A.annua* plants.
Elicitor extract was added at 1% & 2% (w/v) to the tissue culture medium of *A. annua* plants. After 30 days, RNA expression profiles of key artemisinin biosynthetic pathway genes: HMG-CoA reductase (HMGR), Farnesyl pyrophosphate synthase (FPS) and artemisinic aldehyde delta 11(13) reductase (DBR2), were analysed using semi-quantitative RT-PCR.

2.4 Plant survey, collection and documentation-cum-management of biodiversity

Bikarma Singh, Sumeet Gairola, V.K. Gupta, S. Nanda and Yashbir Singh Bedi

Field tours were conducted for plant collection in the interior regions of Jammu province, Kashmir Himalaya, Cold Desert of Ladakh and other parts of Himalayan belt for various Research and Developmental activities undertaken at CSIR-Indian Institute of Integrative Medicine. A brief summary for tours undertaken during 2013-2014 are given in table 2.4.1, figure 2.4.1.

Area surveyed (district)	Objective(s)	Outcome(s)	Period
Pouni Barkh (Reasi district)	Survey and collection of target plant, *Evolvulus alsinoides* L. (Convolvulaceae), for biochemical screening	Chemical evaluation	July 2013
Gurez valley (Bandipora district)	• Floristic composition • Forest mapping • Ethnobotanical documentation on medicinal & aromatic plants • Wild edible plants used by *Sheenas*	Herbarium enrichment, folk knowledge information	September 2013
Vijayapura (Samba district)	Collection of target plant, *Colebrookea oppositifolia* Sm. (Lamiaceae), for biochemical screening	Chemical evaluation	September 2013
Akhnoor (Jammu district)	Collection of target plant, *Abrus precatorius* L. (Fabaceae), for biochemical screening	Chemical evaluation	October 2013

Area surveyed (district)	Objective(s)	Outcome(s)	Period
Shillong (East khasi hills, Meghalaya)	Collection of target plant, *Schima wallichii* (DC.) Korth. (Theaceae), for biochemical screening	Chemical evaluation	March 2014
Uttar Behni area (Samba district)	• Forest mapping and vegetation composition • Ethnobotanical documentation on medicinal & aromatic plants • Wild edible plants used by local people	Herbarium enrichment, folk knowledge information	July 2014
Parmandal area (Samba district)	Collection of medicinal and aromatic plants	Herbarium enrichment, folk knowledge information	July 2014
Jammu area (Jammu district)	Collection of two target plant, *Cleome viscosa* L. (Capparaceae) and *Alternanthera paronychioides* A. St.-Hill (Amaranthaceae), for biochemical screening	Chemical evaluation and herbarium enrichment	August 2014
Uttar Behni area (Samba district)	• Forest mapping and vegetation composition • Ethnobotanical documentation on medicinal & aromatic plants • Wild edible plants used by local people	Herbarium enrichment, folk knowledge information	September 2014
Patnitop and Sanasar areas (Udhampur district)	• Live plant collection for initiation of tissue culture • Live plants for captive cultivation at experimental garden/farm/glasshouse at IIIM	Tissue culture initiated of *Bergenia ciliata*; *Valeriana jatamensis*, *Thymus serpyllum* and *Bergenia ciliate* were initiated for captive cultivation	December2014
Patnitop, Sanasar and adjoining areas (Udhampur district)	Collection of targeted plant samples (*Bergenia ciliata*, *Valeriana jatamensis*, *Berberis lyceum*) for DNA barcoding	Information of wild population, diversity and GPS points taken, and samples handed over to sister division for DNA barcoding	December 2014
Patnitop, Mathatop, Sanasar and adjoining areas (Udhampur district)	Collection of live herbaceous medicinal plant materials and soil samples for microbial evaluation for sister divisions	10 medicinal plants samples collected and supplied for microbial evaluation, microbes extracted and under process of identification	December 2014
Patnitop and Sanasar (Udhampur diostrcit)	• Floristic composition • Forest mapping • Ethnobotanical documentation on medicinal & aromatic plants	Herbarium enrichment, folk knowledge information	December 2014

Figure 2.4.1. Field survey and activities undertaken during plant collection

Plant collection for bioprospection

During the period under review collection or procurement of plant material was undertaken by the group. In all 41 plant species under different genera and families were collected, processed (dried), and supplied to different groups for bioprospection after authentication and accessioning these samples in Institutional Crude Drug Repository. The details of plant collections are given in table 2.4.2.

Table 2.4.2: List of plant species collected and supplied to sister divisions

Botanical name	Parts supplied / CDR Code	Quantity (dried)	Period
Abrus precatorius L.	Aerial Part / P14	1.6 kg	June 2013-May 2014
Acorus calamus L.	Root (Rhizome) /P07: Leaves / P03	1.9 kg:1.1 kg	June 2013-May 2014
Aegle marmelos (L.) Correa	Leaves / P03	200 g	June-December 2014
Ageratum conyzoides (L.) L.	Whole plant / P13	200 g	June-December 2014
Alternanthera paronychioides A. St.-Hil.	Whole plant / P13	2 kg	June-December 2014
Argemone mexicana L.	Seeds / P06	200 g	June-December 2014
Argemone ochroleuca Sweet	Whole plant / P13	200 g	June-December 2014
Boerhavia diffusa L.	Roots/P01: Aerial part/P14	5 kg : 3 kg	June-December 2014
Celastrus paniculatus Willd.	Fruits/P05	1.8 kg	June 2013-May 2014
Cleome viscosa L.(Capparaceae)	Aerial part / P14	1.1 kg	June-December 2014
Colebrookea oppositifolia Sm.	Leaves / P03	200 g	June-December 2014
Colebrookea oppositifolia Sm.	Aerial part /P08	4.5 kg	June 2013-May 2014
Colebrookea oppositifolia Sm.	Stem bark/P10	450 gm	June 2013-May 2014
Cryptolepis buchananii Roem. & Schult.	Roots / P01	50 kg	June-December 2014

Botanical name	Parts supplied / CDR Code	Quantity (dried)	Period
Eclipta alba (L.) L.	Whole Plant/P13	5 kg	June 2013-May 2014
Epimedium elatum C.Morren & Decne.	Whole plant / P13	250 gm	June 2013-May 2014
Evolvulus alsinoides (L.) L.	Whole Plant / P13	700 gm	June 2013-May 2014
Ficus palmata Forssk	Leaves / P03: Stem / P02	0.57 kg:2kg	June-December 2014
Ginkgo biloba L.	Leaves/P03	2.4 kg	June 2013-May 2014
Glycyrrhiza glabra L.	Roots / P01	200 g	June-December 2014
Glycyrrhiza glabra L.	Root/ P01	5 kg	June 2013-May 2014
Hypericum perforatum L.	Whole Plant/P13	7.6 kg	June 2013-May 2014
Kigelia pinnata (Jacq.) DC.	Bark / P10: Fruit / P05	6 kg: 3.8 kg	June-December 2014
Lilium polyphyllum D.Don	Bulb / P17	500 g	June-December 2014
Magnolia grandiflora L.	Leaves / P03	3.1 kg	June-December 2014
Magnolia grandiflora L.	Bark / P 10: Leaves / P03	8 kg:4.1kg	June 2013-May 2014
Malaxis muscifera (Lindley) Kuntze	Whole Plant /P13	25 gm	June 2013-May 2014
Nelumbo nucifera Gaertn.	Root/ P01: Stem / P02	300 gm:5kg	June 2013-May 2014
Nyctanthes arbor-tristis L.	Aerial part/P14	1.9 kg	June 2013-May 2014
Physalia minima L.	Whole plant /P013: Fruits/P05	3.1 kg: 15 kg	June-December 2014
Podophyllum hexandrum Royle	Roots/P01	1.8 kg	June 2013-May 2014
Polygonatum cirrhifolium (Wall.) Royle	Roots & Rhizome/ P07	120 gm	June 2013-May 2014
Polygonatum verticillatum (L.) All.	Roots & Rhizome/ P07	50 gm	June 2013-May 2014
Rheum emodi Wall. ex Meisn.	Rhoot & Rhizome / P07	1.9 kg	June 2013-May 2014
Rhodiola imbricata Edgew	Whole plant / P013	500 gm	June-December 2014
Roscoea purpurea Sm.	Rhizome / P07	500 g	June-December 2014
Schima wallichii (DC.) Korth.	Stem / P02	850 g	June-December 2014
Sphagneticola trilobata (L.) Pruski	Aerial part / P14	4.2 kg	June-December 2014
Syzygium fructicosum Roxb. ex Candolle	Fruit / P05	400 g	June-December 2014
Urtica dioica L.	Aerial part / P14	2 kg	June-December 2014
Valeriana wallichii DC.	Root/P01	5 kg	June 2013-May 2014
Vitex negundo L.	Aerial Part / P14	4.1 kg	June 2013-May 2014
Withania somnifera (L.) Dunal	Root/ P01	2 kg	June 2013-May 2014

Bioresource inventorization with focus on bioprospection of Gurez valley

A field tour to Gurez valley were carried out for inventorization of plant diversity and resource mapping. During surveys, the team visited 22 different localities, collected 206 field numbers comprising of 612 plant samples along with field notes (date of collection, habit, ecological notes, notes on ethnobotany, local name, part used etc.) and GPS points (altitude, longitude and longitude). During tour, a total 700 digital photographs of different plants and their parts were also taken for species authentication and writing description. The team collected 9 live medicinal and aromatic plants viz. *Aconitum violaceum, Pinus wallichii, Taxus baccata, Artemisia meritima, Artemisia vestita, Bergenia ciliata, Podophyllum hexadrum, Epimedium elatum,* and *Juniperus species* for captive plantation and gene pool conservation at Srinagar & Jammu. As many as 312 plant specimens collected from Gurez valley were processed for Herbarium record as per the standard SOP of Jain & Rao (1977) and rest specimens are in process.

Figure 2.4.2.: Bio-resource mapping in the Gurez valley

Biodiversity inventory and bioresource mapping of Ladakh region

Field tour to Cold Desert Ladakh were undertaken for inventorization of plant diversity and resource mapping. During survey, the team collected 402 field numbers comprising of with field notes. All the specimens are under processes of identification.

Figure 2.4.3.: Bio-resource mapping in the Cold Desert of Ladakh

Ethnobotanical studies

While conducting plant survey in different locations of Bandipora district (J & K), *Sheenas* were interviewed and ethnobotanical information associated with the plants used by these folks were recorded.

Detailed information on 41 plants was gathered. These plants used for different diseases. Some medicinal plants include *Bunium persicum, Fagopyrum esculentum, Gentiana tianschanica, Oxyria digyna, Rumex acetosa, Trillium govanianum, Dioscorea deltoidea, Mentha longifolia, Gentianella moorcroftiana, Rubus alceifolius, Rubus niveus, Dipsacus inermis, Persicaria alpine, Potentilla atrosanguinea, Rheum emodi, Alisma plantago-aquatica, Amaranthus caudatus, Salvia moorcroftiana*, etc. Similar studies were also conducted on wild edible plants used by *Sheenas* along LoC border. The ethnobotanical information on 42 raw edible plants used by the local was collected. Most of these species are edible greens, fruits, and tubers. These raw plants are considered as rich source of minerals and vitamins, and also sold by the tribals to supplement their income.

Figure 2.4.4.: Documentation of ethnobotanical plants used by *Sheenas*

Floristic documentation of plants in Parmandal area

In order to document plant species composition of Parmandal area, four field tours undertaken during 2014 and 172 field numbers of plant samples collected. So far a of total 86 plant species under 76 genera and 41 families identified from different locations in the study area. Thirty seven medicinal plants and 10 ethnobotanical plants used by local people in the region were documented. Other activities related to survey and processing of plant samples are under way.

Studies on revision of family Lamiaceae in Himalaya Family Lamiaceae, also called, Labiatae or the mint flowering plants, is one of the largest species comprising family in Angiosperms. It comprises of more than 250 genera representing 7,852 species distributed throughout the world. The plants under this family are important to humans for herb plants useful for flavour, fragrance, or medicinal properties. The family is characterized by square stems; paired, opposite, simple leaves; and two-lipped, open-mouthed, tubular united petals, with five-lobed, bell-like united sepals, and most of them have fragrance quality. Considering this in mint, listing of lamiaceae in Himalaya was undertaken at IIIM.

Under revision of family *Lamiaceae* in Himalayan belts, a checklist of 206 species prepared from scrutiny of two herbaria, viz. Janaki Ammal Herbarium (acronym RRLH) and Botanical Survey of India (acronym ASSAM) and own collection of plants from India Himalaya. The species categorization based on medicinal used, distribution pattern, endemism etc. are under process.

Enrichment of Janaki Ammal Herbarium and Crude Drug Repository

In order to enrich the existing IIIM Janaki Ammal Herbarium, several plant collection tours were carried out during 2013-2014 in different parts of the Himalayas. Approximately more than 1100 voucher specimens including gymnosperms, angiosperms, pteridophytes were collected from different localities and a total of 611 new herbarium samples proceesed and deposited in the herbarium (acronym RRLH) of the institute for reference. Majority of the samples accessioned were from Gurez valley, Uttarakhand and samples from Jammu regions. Forty five herbarium samples new to the herbarium were added. A lectotype of new species *Cleistanthus nokrenis* B.Singh is preserved as new science specimens. Besides this, two specimens of the species recorded for the first time from India, viz. *Juniperus chinensis* L. and *Aglaonema nebulosum* N.E. Br. is also accessioned and maintained in the Janaki Ammal Herbarium. Besides herbarium, a total 428 new drug

Figure 2.4.5 : Documentation and studies on family *Lamiaceae* in Himalaya

samples accessioned to IIIM Crude Drug Repository during 2013-2014, which were collected from different regions of India.

Authentication of Crude Drugs

Authenticity of 22 crude drug plant species collected from market survey and from wild for R&D, was established. The authenticated specimens were processed and deposited in the herbarium of the institute.

2.5 Molecular characterization of two A-type P450s, *WsCYP98A* and *WsCYP76A* from *Withania somnifera* (L.) Dunal: Expression analysis and withanolide accumulation in response to exogenous elicitations

Satiander Rana, Sumeer Razdan, Surrinder K. Lattoo

Pharmacological investigations position withanolides as important bioactive molecules demanding their enhanced production. Therefore, one of the pivotal aims has been to gain knowledge about complete biosynthesis of withanolides in terms of enzymatic and regulatory genes of the pathway. However, the pathway remains elusive at the molecular level. P450s monooxygenases play a crucial role in secondary metabolism and predominantly help in functionalizing molecule core structures including withanolides. Due to diverse versatility of P450 in catalysing the regio and stereo-specific reactions, they are potential targets for industrial biocatalysis. P450s have been applied in industry for the investigation of new drugs, medicine or xenobiotics. Because of the remarkable variety of chemical reactions catalysed and enormous number of substrates attacked, P450s have earned the reputation of "the most versatile biological catalysts in nature".

Identification and characterization of P450s is essential for the elucidation of

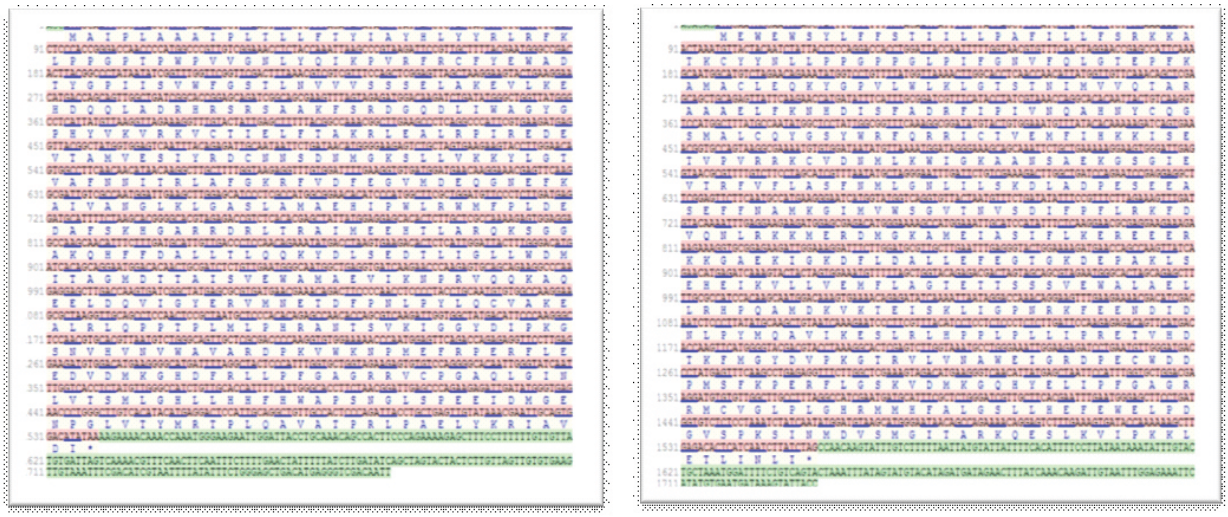


Figure 2.5. 1. A & B. Nucleotide and the deduced amino acid sequence of *WsCYP98A* (A) and *WsCYP76A* (B) from *Withania somnifera*. The start codon (ATG) present at 4th and 7th position whereas stop codons at 1552, 1537 bp, respectively.

various biosynthetic pathways. **A**In an endeavour towards identification and characterization of different P450s, we have cloned and characterized two A-type P450s, *WsCYP98A* and *WsCYP76A* from *Withania somnifera*. Full length cDNAs of reading frames of 1536 and 1545 bp encoding 511 (58.0 kDa) and 515 (58.7 kDa) amino acid residues, respectively (Figure 2.5.1 A &B). To ascertain the degree of evolutionary relatedness, Neighbour-joining phylogenetic tree was constructed with MEGA 6.0 software from the ClustalW alignment of *Ws*CYP98A and *Ws*CYP76A with a number of homologous P450 sequences of different plants retrieved from the NCBI GenBank database. *Ws*CYP98A and *Ws*CYP76A corresponded to two separate phylogenetic clans in accordance with the amino acid similarity among their proteins (Figure 2.5.2). Entire coding sequences of *WsCYP98A* and *WsCYP76A* cDNAs were expressed in

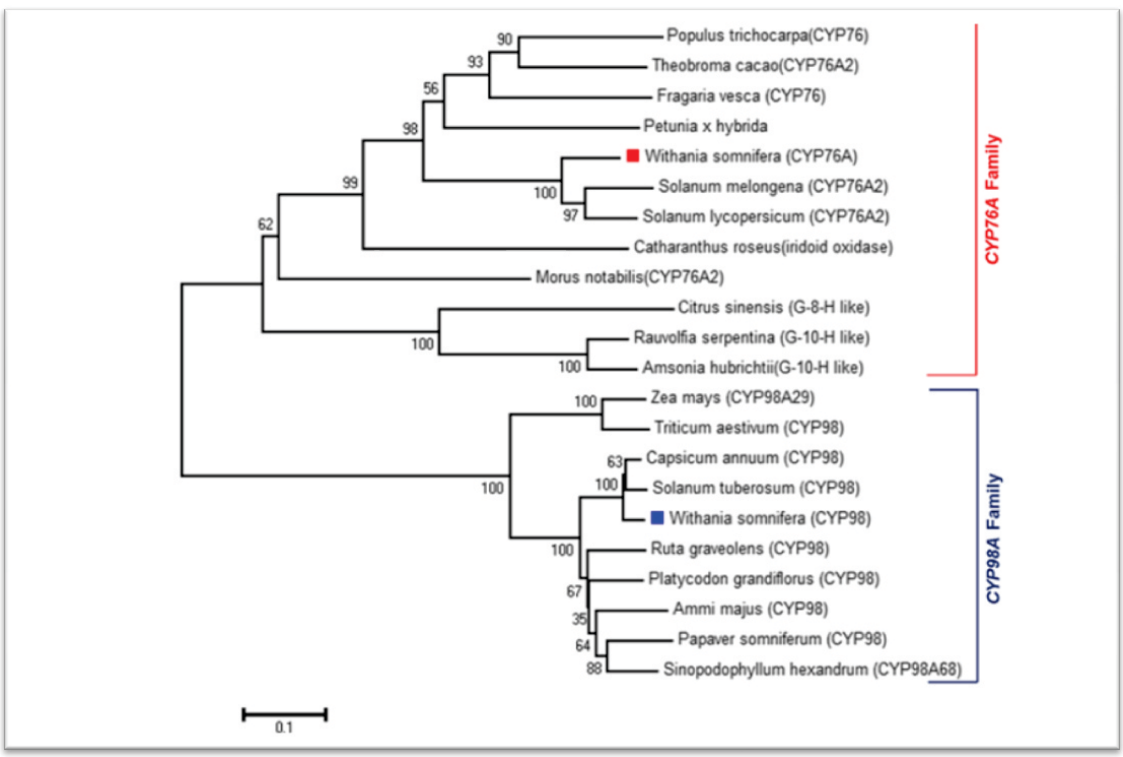


Figure 2.5.2. Phylogenetic analysis of deduced amino acid sequences of WsCYP98A and WsCYP76A was inferred using the Neighbour-joining method employing MEGA 6.0 software. For WsCYP98A total of 10 sequences and for WsCYP76A, 12 sequences including Withania somnifera

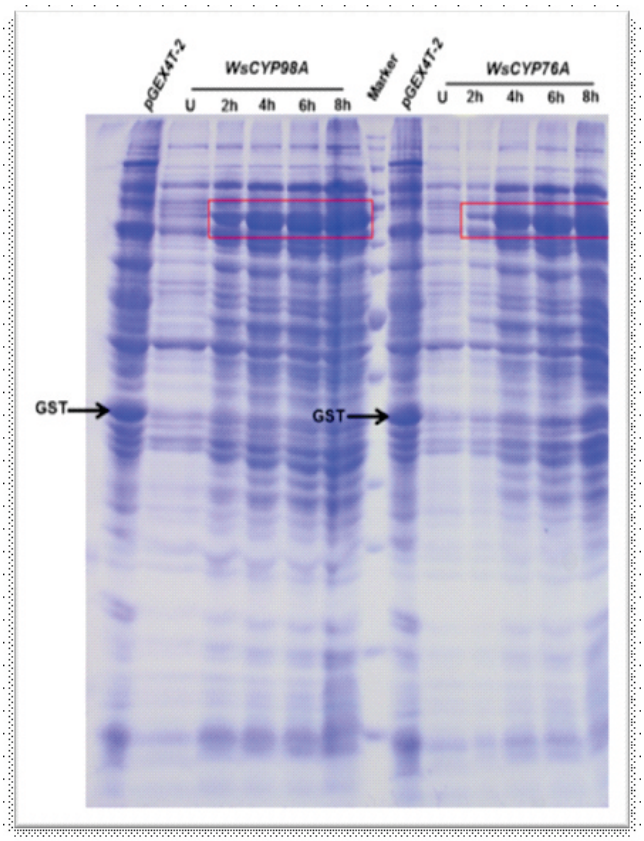


Figure 2.5.3

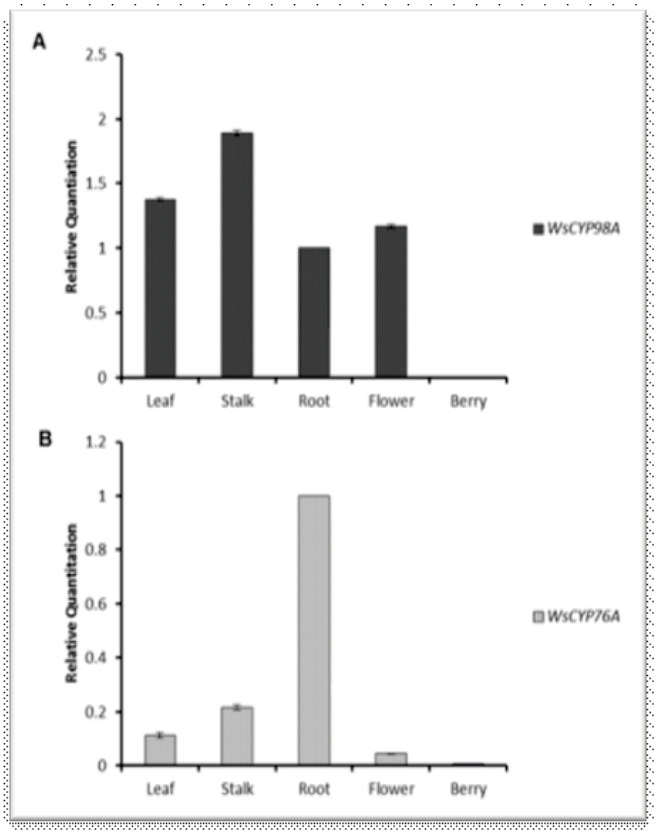


Figure 2.5.4

Figure 2.5.3. Sodium dodecyl sulphate–polyacrylamide gel electrophoresis (SDS-PAGE: 10%) pattern of proteins obtained from E.coli BL21 (DE3) transformed with pGEX-WsCYP98A and pGEX-WsCYP76A

Figure 2.5.4. Quantitative assessment of the expression of (A) *WsCYP98A* and (B) *WsCYP76A* in different tissues of *Withania somnifera.* Data were compared and analysed with analysis of variance (*ANOVA*). Values are means, with standard errors indicated by bars, representing three independent biological samples, each with three technical replicates.

Escherichia coli BL21 (DE3) using pGEX4T-2 expression vector.

The ORFs were released from pJET-*WsCYP98A* and pJET-*WsCYP76A* using *BamH*I/*Sal*I restriction enzymes, and inserted into vector pGEX4T-2. The recombinant expression vectors with the inserted *WsCYP98A* and *WsCYP76A* constructs were identified by PCR analysis and restriction digestion with *BamH*I/*Sal*I. Heterologous expression of proteins was induced with different concentrations of IPTG. SDS-PAGE analysis demonstrated that optimum expression of proteins was observed at 25 °C using 0.8 mM IPTG after 6-8 h of induction. The fusion protein having molecular weight of ~84.06 kDa and ~84.7 kDa appeared in the lysate of recombinant *E. coli* transformed with the expression cassettes pGEX-*WsCYP98A* and pGEX-*WsCYP76A*, respectively (Figure 2.5.3). To study *WsCYP98A* and *WsCYP76A* gene expression pattern in different tissues of *W. somnifera*, cDNA libraries were prepared separately from RNA samples extracted from leaves, stalks, roots, flowers and berries (unripen) of four month old plant. Tissue-specific cDNAs were used as templates for qRT-PCR.

The results obtained showed both genes express widely in leaves, stalks, roots, flowers and berries with higher expression levels of *WsCYP98A* in stalks while *WsCYP76A* transcript levels were more obvious in roots (Figure 2.5.4). The effect of MeJA, SA and GA_3 on expression profile of *WsCYP98A* and *WsCYP76A* was studied using qRT-PCR (Fig. 2.5.5. A,B&C). Exogenous elicitors acted as both positive and negative regulators of mRNA transcripts. Methyl jasmonate and salicylic acid resulted in copious expression of *WsCYP98A* and *WsCYP76A*. Enhanced mRNA levels also corroborated well with the increased accumulation of withanolides in response to elicitations (Figure 2.5.6.A, B&C). The empirical findings suggest that elicitors possibly incite defence or stress responses of the plant by triggering higher accumulation of withanolides.

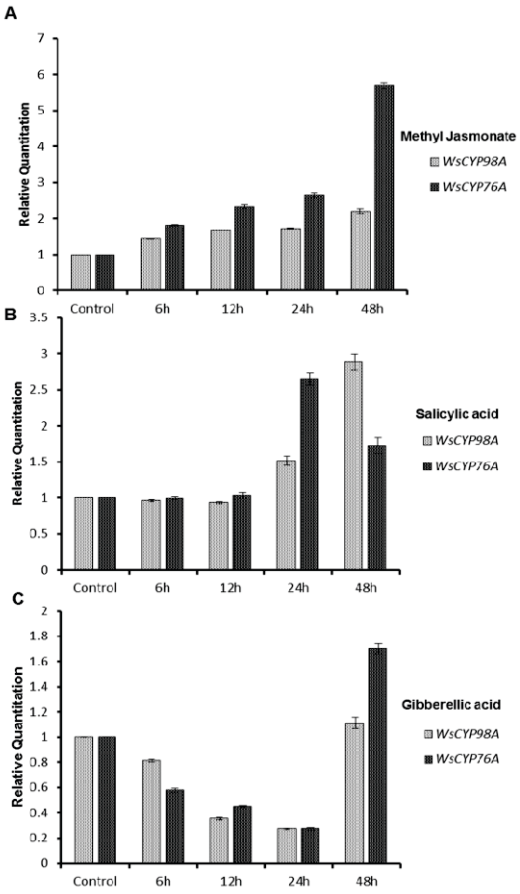


Figure 2.5.5

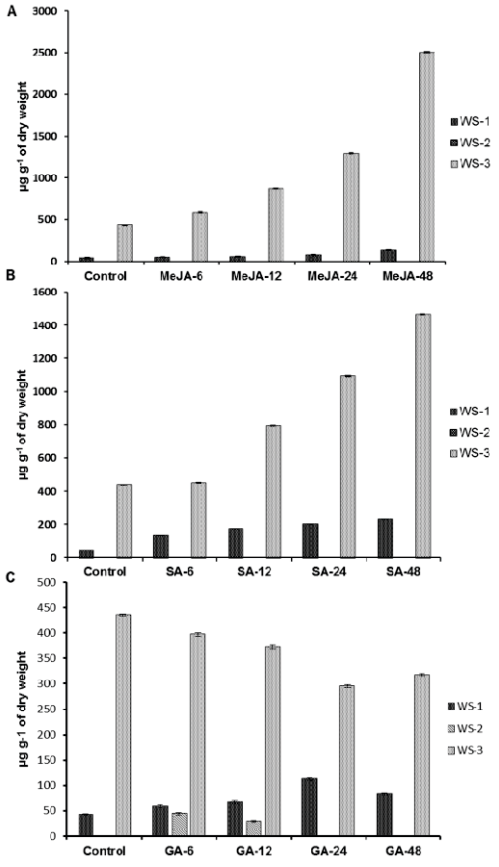


Figure 2.5.6

Figure 2.5.5. Quantitative real-time analysis of *WsCYP98A* and *WsCYP76A* expression in micropropagated *Withania somnifera* induced by (A) methyl jasmonate (MeJA; 0.1 mM), (B) salicylic acid (SA; 0.1 mM) and (C) gibberellic acid (GA_3; 0.1 mM) treatments.

Figure 2.5.6. Time-course effect of elicitor treatments on withanolides accumulation in response to (A) methyl jasmonate (0.1mM), (B) salicylic acid (0.1 mM) and (C) gibberellic acid (0.1 mM) at different time points. Variation in three key withanolides *viz*. withanolide A (WS-1), withanone (WS-2) and withaferine A (WS-3) was confirmed by HPLC analysis at 6, 12, 24 and 48 h.

2.6 Efficient *in vitro* regeneration, analysis of molecular fidelity and *Agrobacterium tumefaciens*-mediated genetic transformation of *Grewia asiatica* L.

Tareq A. Wani, Satiander Rana, Wajid W. Bhat and Surrinder K. Lattoo

Grewia asiatica is a dietotheraphutically important fruit bearing shrub, indigenous to India. It is a rich resource of triterpinoids and flavonoids and is being prescribed in Ayurveda and traditional systems of medicine. The major chemical constituents of Phalsa are grewinol, flavonoids, quercetin and naringenin from flowers; taraxasterol, β-sitosterol, erythrodiol, β- amyrin, lupeol, betulin lupenone, friedelin and α-amyrin from the bark. These constituents have been found to bestow antioxidative, radioprotective, anticancer, antiviral, antidiabetic, anti-inflammatory and antimalarial activities to the plant. Its fruits are claimed to be useful for heart, blood and liver disorders. In spite of the diverse uses, two drawbacks prevent full exploitation of this species. These are short shelf life of its fruits and larger seed volume. Seed abortion or induction of parthenocarpy for developing seedless cultivars through biotechnological interventions is a viable option. One of the prerequisites for such strategy is to develop an efficient plant regeneration and transformation protocols in *G. asiatica*. Against this backdrop multiple shoot induction was achieved from nodal explants with axillary buds, on culturing on Woody Plant medium (WM) fortified with 3% (w/v) sucrose, 2×10^{-5} M Kinetin (Kn) and 1×10^{-5} M indole-3-butyric acid (IBA) giving rise to an average of 4.25 micro-shoots per explant. More than 90% explants formed micro-shoots with mean shoot length of 10.5 cm leading to whole plant regeneration. The varied

Phytohormone combination	Cytokinins/ Auxin molar ratios	Percentage explants producing shoots	Number of shoots/culture	Shoot length (cm)	Internodal length (cm)	Leaves per shoot
MS-Media						
Kn + IBA						
2×10^{-6}M+5×10^{-7}M	4.23:1	23	Profuse	-	-	-
4×10^{-6} M+2×10^{-6}M	2.12:1	26	callusing	-	-	-
1×10^{-5} M + 5×10^{-6} M	2.13:1	31		2.90 ^{c}	1.0 ^{c}	2.25 ^{c}
2×10^{-5} M + 1×10^{-5} M	2.13:1	24	1.31 ^{d}	-	-	-
B_5- Media						
Kn + IBA						
2×10^{-6}M+5×10^{-7}M	4.23:1	46	Callusing			
4×10^{-6} M+2×10^{-6}M	2.12:1	33				
1×10^{-5} M + 5×10^{-6} M	2.13:1	28				
2×10^{-5} M + 1×10^{-5} M	2.13:1	71				
Woody plant Media						
Kn + IBA						
2×10^{-6}M+5×10^{-7}M	4.23:1	76	2.50^{b,c}	8.50^{b}	1.25$^{a, b}$	6.43 ^{b}
4×10^{-6} M+2×10^{-6}M	2.12:1	48	5.78^{c}	10.9$^{a, b}$	2.04^{a}	7.33 $^{a, b}$
1×10^{-5} M + 5×10^{-6} M	2.13:1	63	3.40$^{a, b}$	11.5^{a}	0.90^{b}	6.53 ^{b}
2×10^{-5} M + 1×10^{-5} M	2.13:1	94	4.25^{a}	10.5$^{a, b}$	1.50 $^{a, b}$	8.00 $^{a, b}$
Kn + NAA						
2×10^{-6}M+5×10^{-7}M	4.6:1	59	2.55 $^{b, c}$	12.40 ^{a}	1.50 $^{a, b}$	9.70 ^{a}
4×10^{-6} M+2×10^{-6}M	2.12:1	86	3.24 $^{a, b}$	11.27 ^{a}	1.30 ^{b}	10.20 ^{a}
1×10^{-5} M + 5×10^{-6} M	2.13:1	68	2.00 ^{c}	9.28 $^{a, b}$	2.00 ^{a}	8.50 $^{a, b}$
2×10^{-5} M + 1×10^{-5} M	2.46:1	55	2.50 $^{b, c}$	10.25 $^{a, b}$	1.70 $^{a, b}$	8.75 ^{a}
Woody media	-	51	10.5 $^{a, b}$	3.20 $^{a, b}$	2.5 ^{a}	11.50 ^{a}

Table 2.6.1. A Comparative response of *G. asiatica* under different media conditions. Comparative responses of shoot proliferation and elongation from secondary axenic explants with multiple shoot buds on WM supplemented with different molar ratios of Kn/IBA and Kn/NAA, after 4 weeks of culture. Values fallowed by same letters are not significantly different ($P \leqslant 0.05$) as per Duchene's multiple range test.

morphogenetic response obtained with different media supplemented with various concentrations and combinations of phytohormones is summarized in Table 2.6.1.

MS medium with different phytoharmonal combinations like kinetin (Kn) in combination with auxins IBA and NAA proved to be least effective and failed to induce microshoots from axillary buds of nodal explants. It also triggered profuse

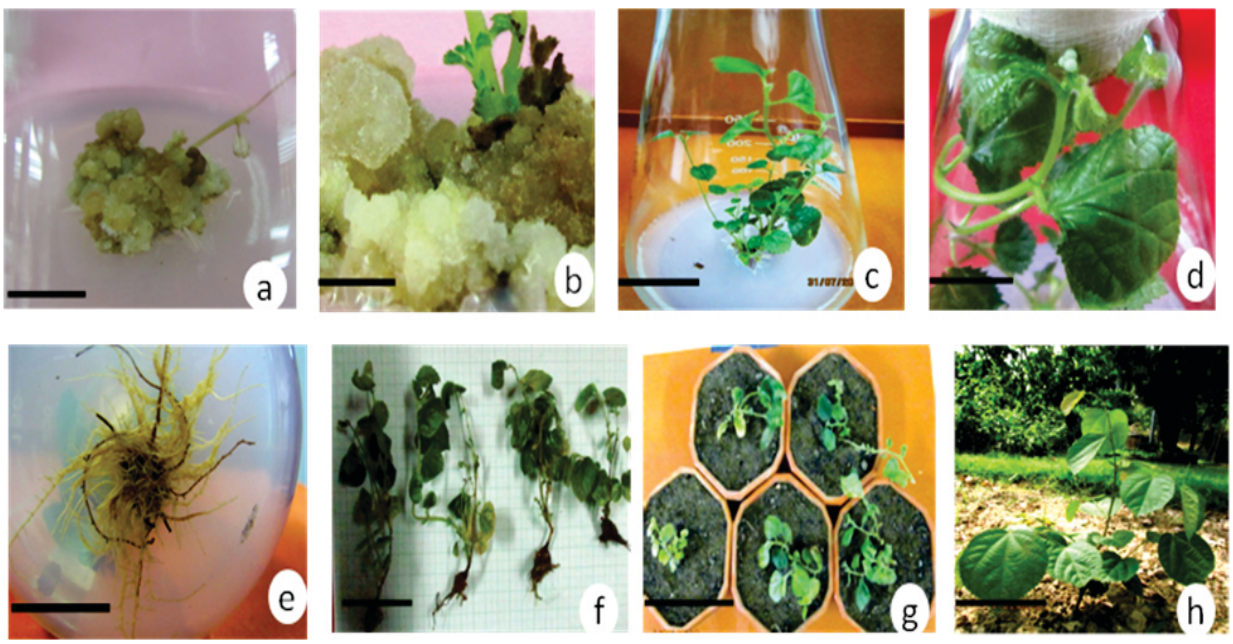


Figure 2.6.1.: Plant regeneration in *Grewia asiatica* **(a-h):** Profuse callusing with sparse shoot regeneration on MS minimal organic medium supplemented with Kn 1×10^{-5} M and IBA 5×10^{-6} M (bar = 8 mm) **(a,b).** Multiple shoot induction and regeneration from nodal explants on WM containing Kn 2×10^{-6}M and IBA 5×10^{-7}M. (bar = 10 mm) **(c).** Healthy regenerated shoots with well differentiated foliage and floral buds after 7 weeks of culture (bar =13 mm) **(d).** Rooted individual shoots with profuse tapering roots (bar =15 mm) **(e).** Healthy regenerated shoots with well-developed roots (bars =25 mm) **(f).** Established plants under hardening (bar =12 mm) **(g).** Field grown hardened plant (bar =31.0 cm) **(h).**

callusing at the cut surface of the explants (Figure 2.6.1.a, b). Healthy regenerated shoots showed prolific rooting of more than 95% on WM supplemented with 4.8×10^{-6} M indole-3-butyric acid (IBA). Following simple hardening procedures, rooted plantlets, were transferred to soil-sand (1:1; v/v) with about 92% success (Figure 2.6.2. c-h).

Successfully established *in vitro* plants under field conditions were explant donor Figure 2.6.2 Genetic fidelity of micro-propagated plants has immense practical utility and commercial implications.

Additionally, *Agrobacterium*-mediated genetic transformation protocol was developed using *A. tumefaciens* strain GV2260 harboring binary vector p35SGUSINT containing hygromycin phosphotransferase gene (*hpt*). Media used for bacterial putative transformants were selected transformation followed by young internodes. Direct shoot organogenesis from the cut edges of leaf petiolar explants was observed at the end of 4–5 week of culture. Leaf petiolar explants were used as the explant source for further transformation studies. *Agrobacterium* strain GV2260 was effective for transformation in *G. asiatica* producing GUS positive explants harboring p35SGUSINT (Figures 2.6.3 a, d). The media used for culture, co-cultivation and

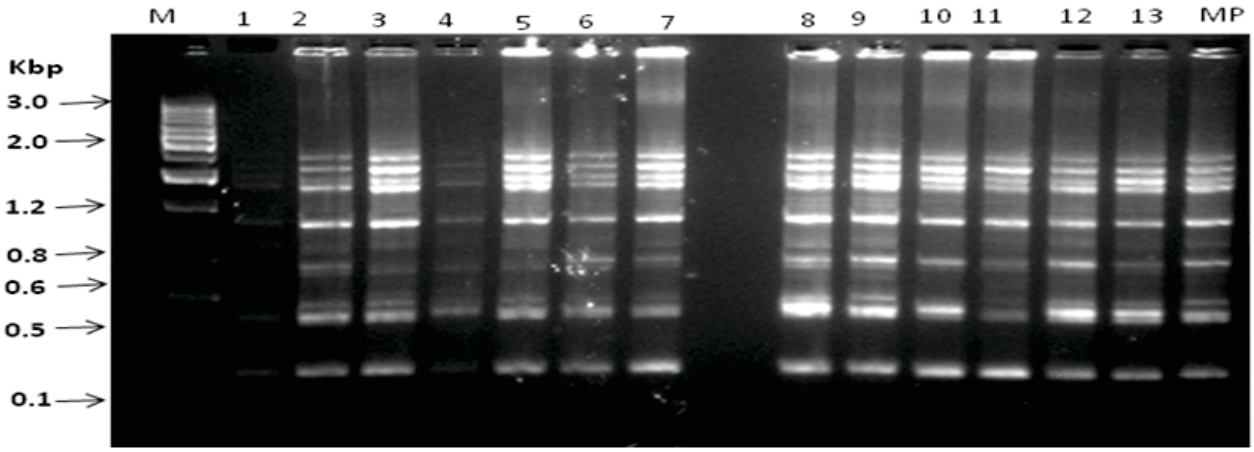


Figure 26.2: DNA amplification obtained with primer OPD-05: Mother plant (MP), micropropagated plants (lanes 1–13) and M, Molecular Weight Markers (3 kb DNA Ladder)

free of any detectable phenotypic variability compared to the donor mother plant. Genetic fidelity was assessed using random amplified polymorphic DNA (RAPD). Five arbitrary decamers displayed same banding profile within all the micropropagated plants and *in vivo* using media containing 15 mg/L hygromycin. Transformation was verified by GUS assay and detection of the hygromycin phosphotransferase (*hpt*) by polymerase chain reaction. In present study shoot apices and petiole of leaf were highly responsive to transformation study of *Grewia asiatica* is given in Table 2.6.2.

Stage	Medium composition	Medium	Duration
Bacterial culture	0.5 g/L K_2HPO_4 + 0.2 g/L $MgSO_4$ +0.1 g/L NaCl+0.4 g/L yeast extract+10 g/L mannitol	YMB	1-2 days
Pre-culture	WM + 4×10^{-6} M Kn+ 2.4×10^{-6} M IBA	RM	3 days
Co-cultivation	WM + 4×10^{-6} M Kn+ 2.4×10^{-6} M IBA+ 200 µM acetosyringone	RM + acetosyringone	3-5 days
Transformant selection	WM +4×10^{-6} M Kn+ 2.4×10^{-6} M IBA+15mg/L hygromycin	SM	8-9 Weeks

Table. 2.6.2. Media used for bacterial culture and transformation study of *Grewia asiatica*.

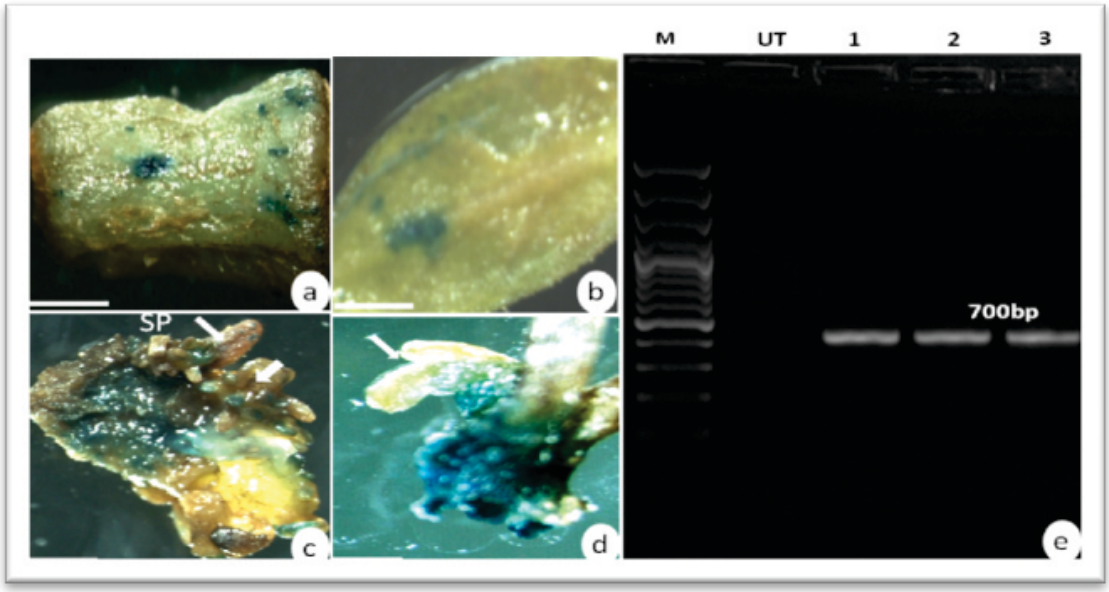


Figure 2.6.3. *Agrobacterium tumifacians*-mediated transformation of *G. asiatica* using aseptic petiole and leaf explants **(a-d)**. β-glucuronidase (GUS) transient expression shown by infected petiole after co-cultivation on WM **(a,c and d)** and leaf explants **(b)** (SP=Shoot primordia) (bar = 2 mm). PCR detection of 700-bp fragment of *hpt*, M molecular weight ladder, UT untransformed control, 1–3 independent putative transgenic shoot buds **(e).**

2.7 Polyketide synthases from Rheum *emodi* Wall ex. Meisn. as major scaffolds for the generation of "unnatural" product libraries

Shahzad A Pandith, Niha Dhar and Surrinder K Lattoo

Rheum emodi (Polygonaceae), endemic to North Western Himalayas is a multipurpose endangered medicinal herb of immense therapeutic importance. The major bioactive phytoconstituents include anthraquinones and stilbenes, and their respective glycoside derivatives that are synthesized *via* polyketide pathway which is yet to be fully elucidated. The polyketides represent a family of highly structurally diverse compounds all produced *via* iterative decarboxylative condensations of starter and extender units. The manipulation of substrate selection in a PKS is an important milestone towards the goal of generating large libraries of unnatural natural products for biological and pharmaceutical application. In an endeavor towards deciphering the role of some of the key genes of the polyketide pathway, we have successfully cloned, expressed and further purified three genes viz, aloesone synthase (*Re*ALS) and two isoforms of chalcone synthase: *Re*CHS-1 and *Re*CHS-2. These three plant-specific type III polyketide synthases share about 60 % amino acid sequence identity. *Re*ALS takes acetyl-CoA as a starter unit and carries out six successive condensations with malonyl-CoA to produce a heptaketide aloesone, whereas *Re*CHS-1 and *Re*CHS-2 catalyze condensation of 4-coumaroyl-CoA with three molecules of

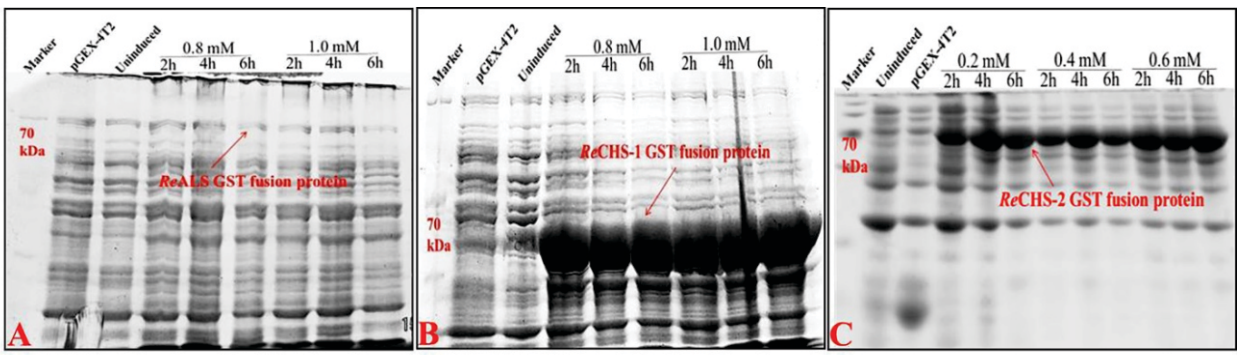


Figure 2.7.1: Time-course expression of *Re*ALS (A), *Re*CHS-1 (B) and *Re* CHS-2 (C) gene in *E. coli* BL21 with different concentrations of IPTG.

Location code	Location	Geographic Co-ordinate
1	Bonera Farm, Pulwama	33° 52' 59" N, 74° 55' 00" E; 1630 m asl
2	Yarikhah Farm, Srinagar	34° 04' 797" N, 74° 26' 448" E; 2119 m asl
3	Pense La Top, Ladakh	33° 51' 08" N, 76° 21' 57" E; 4287 m asl
4	Nyoma Valley, Ladakh	33° 08' 661" N, 78° 34' 742" E; 4415 m asl

Table 2.7.1. Places of collection of different samples of *Rheum emodi*

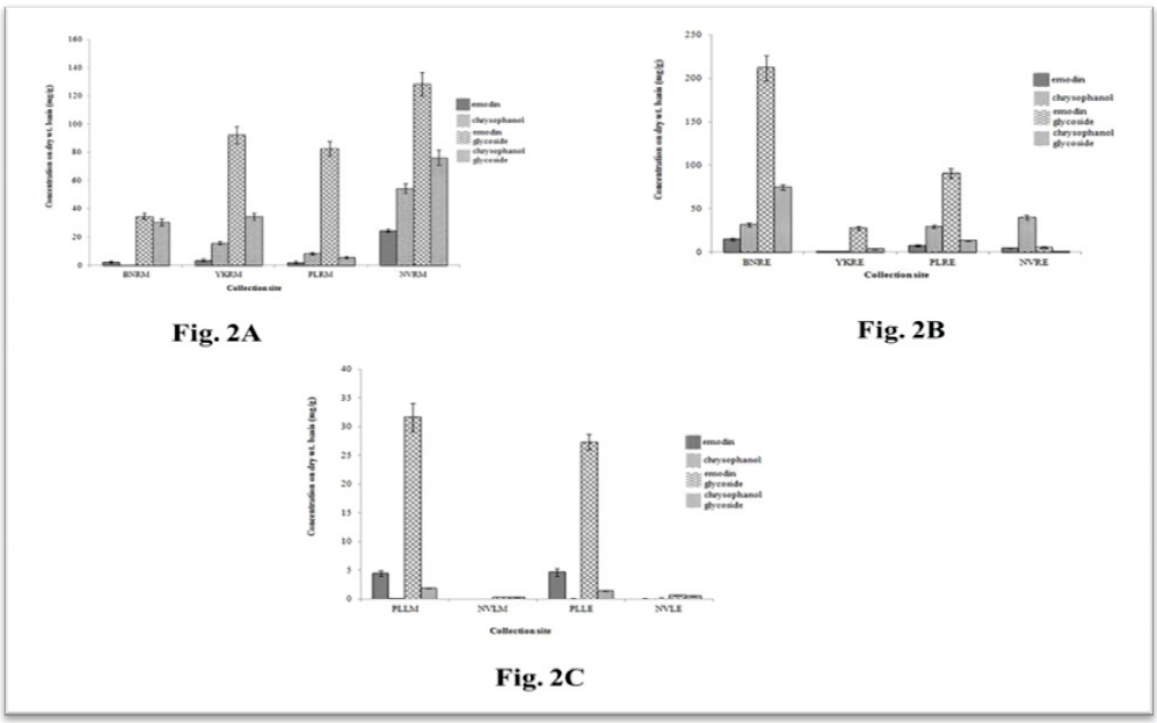


Figure 2.7.1. Anthraquinone concentrations in extracts. *A)* graph depicting concentration of major anthraquinones in methanolic extracts of rhizomes; *B)* in ethyl-acetate extracts of rhizomes; *C)* in methanolic and ethyl-acetate leaf extracts. BNRM, YKRM, PLRM and NVRM are the methanolic rhizome extracts from location 1, 2, 3, and 4 respectively; BNRE, YKRE, PLRE and NVRE are ethyl-acetate rhizome extracts from location 1, 2, 3 and 4 respectively; PLLM, NVLM and PLLE, NVLE are methanolic and ethyl-acetate leaf extracts from location 3 and 4 respectively. All values obtained were means of triplicate with standard error.

malonyl-CoA to generate naringenin chalcone which then isomerizes to chalcone. Using degenerate primers and RACE PCR strategy the full-length cDNAs of *Re*ALS (1176 bp; Acc. KC473812), *Re*CHS-1 (1179 bp; Acc. KF850684) and *Re*CHS-2 (1179 bp; Acc. KC822472) were generated. All the three genes encode a polypeptide of about 43 kDa with theoretical PI of 5.74, 6.03 and 9.14 for *Re*ALS, *Re*CHS-1 and *Re*CHS-2 respectively.

Tissue-specific chemoprofiling revealed preponderance of anthraquinones and their glycosides in rhizomes in comparison to leaves. The methanolic extracts of the rhizomes showed the highest concentration out of the four chemical constituents at the highest altitude in Nyoma Valley, Ladakh (Table 2.7.1). The results showed interesting differences in the content of anthraquinone constituents (Figure 2.7.1). It has a prospect of providing high yielding resources of *R. emodi* for pharmacological and commercial utilization.

2.8 Molecular cloning and characterization of genes related to glycyrrhizin biosynthesis in Glycyrrhiza *glabra*.

Pankaj Pandotra, Saima Khan, Malick Mujafar Manzoor, Prashant Misra, Ajai P Gupta, Ram Vishwakarma & Suphla Gupta

The roots of Glycyrrhiza (*Fabaceae*) species (*glabra* & *uralensis*) are known to produce a variety of phytochemicals including many terpenoids and flavonoids. Their beneficial effects on human health (antiviral, anticancer etc) (Manach et al. 2009) have made the licorice root a valuable trade item (Hayashi and Sudo 2009), with an estimated trade value of US$42 million in 2007. Unfortunately, limited genomic information on many medicinal plants as in *Glycyrrhiza* species, have restricted their research as biosynthetic mechanisms of many important phytochemicals are still poorly understood. Also, the precursors and intermediates involved are produced in distinct sub-cellular locations and are known to accumulate in a tissue- or organ specific manner. The bioengineering of plants (Joshi and Lopez 2005) has emerged as one of the solutions to understand the molecular interplay of the related genes. Discovering the enzymes related to a given biosynthetic pathway is the first crucial step in optimizing bioengineered synthesis (Shan et al. 2001). Also, elucidation and optimization transport and accumulation mechanisms of the molecules become important in understanding the flux of the target pathway. Since many medicinal plants are non-model organisms, mechanisms of phyto-chemical biosynthesis and other related aspects are poorly understood or even completely unknown. Glycyrrhizin (triterpenoid saponin) is synthesized from b-amyrin by at least five oxidative reactions and two glycosylations. The early stages of triterpenoid saponin biosynthesis involve the dimerization of two farnesyl diphosphate molecules to produces 2,3-oxidosqualene, catalyzed by Squalene epoxidase. 2,3-oxidosqualene is an important intermediate precursor for both triterpenes and sterols (Abe et al., 1993). In later stages the biosynthesis of glycyrrhizin involves cyclization of 2,3-oxidosqualene by a specific OSC, b-amyrin synthase (bAS), to for triterpene b-amyrin, which is one of the most commonly occurring triterpenes in plants. The subsequent steps involve a series of oxidative reactions at positions C-11 (two-step oxidation) and C-30 (three-step oxidation), followed by glycosyl transfers to the C-3 hydroxyl group (Figure 1). Genes encoding enzymes involved in the early stages of glycyrrhizin biosynthesis, namely, squalene synthase and bAS, have been functionally isolated from G. glabra (Hayashi et al., 1999, 2001) and several other plants (Shibuya et al., 2009; Qi et al., 2004; Sawai et al., 2006;Suzuki et al., 2002), however, most of the steps in the modification of the b-amyrin skeleton remain uncharacterized at the molecular level in Glycyrrhiza species. Recently two CYP genes (CYP88D6 &CYP72A4) have been cloned from *G. uralensis*. Here we report cloning of seven full length genes (Table 2.8.1; Figure 2.8.1a,b) involved in glycyrrhizin biosynthesis. Further characterization of these genes is in progress.

Name	Sequence Length (bp)	Homolgy (%)	NCBI homology
Squalene synthase	1317	96	HM012846.1
Squalene epoxidase	2134	90	KJ010819.1
Beta amyrin synthase	2671	98	AB0237203.1
Cycloartenol synthase	2889	99	AB0256968.1
Lupeol synthase	2657	98	AB116228.1
CYP88D6	1482		AB433179.1
CYP72A	1592	96	AB558153.1

Table 2.8.1: The seven full length genes cloned in the present study on *Glycyrrhiza glabra*

3. DISCOVERY INFORMATICS

3.1 Development of theoretical models for the screening of Mycobacterium tuberculosis (Mtb) GlmU protein inhibitors

Rukmankesh, Amit Nargotra, Chitra Rani, Inshad Ali Khan

The bacterial GlmU protein, involved in peptidoglycan and lipopolysaccharide, has recently been identified as an important drug target for tuberculosis. The gene glmU has been identified as essential for optimal growth of *M. tuberculosis* and the absence of gene in humans makes GlmU a suitable target for inhibitor design. *In silico* studies have been initiated for identification of potent GlmU inhibitors from the 20,000 compound library of this Institute procured from Chembridge. The dataset of 125 GlmU inhibitors was taken from the Pubchem database for designing the computational studies. GlmU is reported to exist as trimer and hence the trimeric biological assembly of PDB ID 3ST8 was retrieved from PDB. Docking studies of the 125 inhibitors was carried out on this trimer assembly. No significant correlation could be established between the dock scores and the reported activity of the inhibitors. This might be due to the disordered loop in the monomer in the vicinity of the binding site.

Further, ligand based strategies were adopted for the identification of potent inhibitors from the compound repository. From the set of 125 inhibitors, similarity search was carried out for all the molecules having IC_{50} less than 30μM, and 655 unique hits could be identified. Further, the inhibitor compound dataset was divided into three clusters and QSAR models were developed for all the three clusters. Based on the statistical parameters, two robust QSAR models were selected for developing the filtering criteria. For the screening of the compound library using QSAR models, activity of the library compounds was predicted using each QSAR model developed (cluster-A and cluster-B). The cut-off of the predicted activity (pIC50) for the selection of the hits was taken as 4.87 as

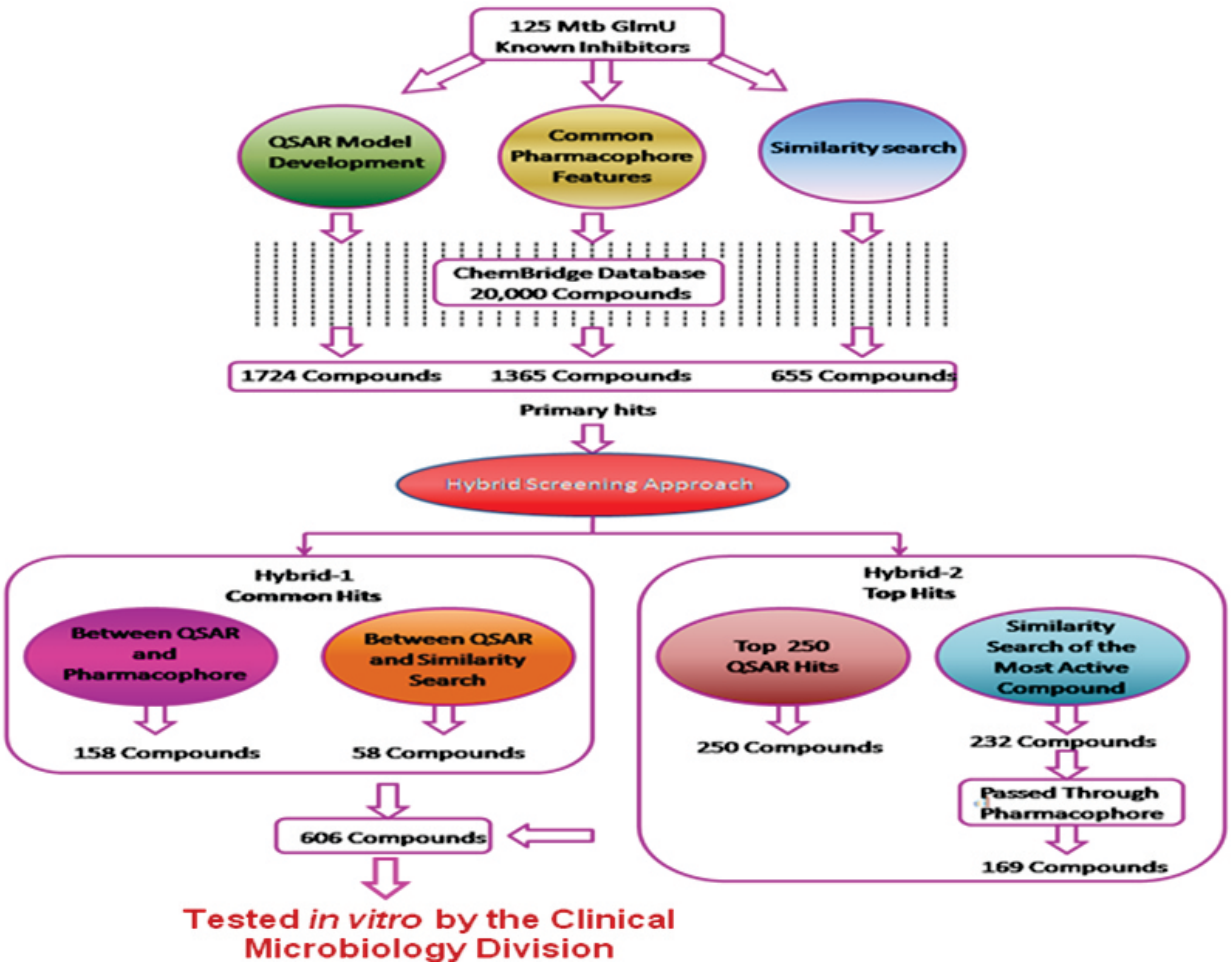


Figure 3.1.1. *In silico* filtering criteria adopted for screening of drug like compound library for the identification of potent Mtb GlmU inhibitors.

this value specified the highest actual activity of the training set compound of both the clusters (cluster-A and cluster-B). The hits above 4.87 predicted pIC50 from both QSAR models resulted in 1724 unique compounds. Two pharmacophore models were also built based on the most active compound and a set of 16 active compounds. Since no good correlation was found based on the docking protocol, all the ligand based filters were applied independently on the entire dataset for the screening of 20,000 compounds from Chembridge database. By applying a hybrid filtering approach (figure 3.1.1), a total of 606 potential inhibitor candidates of Mtb GlmU were identified based on *in silico* screening for *in vitro* evaluation. The *in vitro* screening of the 606 potential inhibitor candidates was carried out by the Clinical Microbiology Division of the institute. From the *in vitro* screening, 93 compounds were found to have more than 20% inhibition of the acetyltransferase activity of GlmU at 100 μM. Out of these, 15 compounds showed more than 40% inhibition. All these compounds could be classified into eight different structural moieties. Thus the *in silico* filtering criteria helped in identification of 8 structural moieties from a diverse set of close to 200 scaffolds, for the identification of novel Mtb GlmU inhibitors. These inhibitors were docked onto the acetyltransferase binding pocket of Mtb GlmU and a robust strategy for the modification of these structures was also proposed for lead optimization studies.

3.2 Development of an in *silico* model for identification of α-Cobratoxin inhibitors from Pinwheel flower

Priya Mahajan, Amit Nargotra, K.S.Krishnan (NCBS), Ram Vishwakarma

α-Cobratoxin (Cbtx), the neurotoxin isolated from the venom of the Thai cobra *Naja kaouthia*, causes paralysis by preventing acetylcholine (ACh) binding to nicotinic acetylcholine receptors (nAChRs). The current study is aimed at development of *in silico* model for identification of inhibitors of Cbtx from pinwheel flower (*Tabernaemontana divaricata*). The idea for the same was conceived by Dr. K.S. Krishnan, NCBS Bangalore. The region of the Cbtx molecule that is directly involved in binding to nAChRs was used as the target for identification of Cbtx inhibitors. Cbtx has 71 amino acid residues with 5 disulfide bridges. It consists of 3 finger-like loops: loops I, II, and III. For carrying out molecular docking studies against Cbtx three crystal structures with pdb Ids ICTX, 2CTX and 1Y15 were considered. These crystal structures were first prepared in protein preparation wizard of Schrodinger suit 2012 and further taken for molecular docking studies on autodock vina software. The active site of Cbtx is very well reported in literature. *Tabernaemontana divaricata*, a common garden plant in tropical countries has been used as a traditional medicine. *Tabernaemontana* is one of the genera that are used in Chinese, Ayurvedic and Thai traditional medicine for the treatment of fever, pain and dysentery. To identify the alkaloids for pinwheel flower (*Tabernaemontana divaricata*), the synonym for this plant was searched for in literature. Search in DNP was carried out for compounds from Pinwheel flower using synonyms viz., *Tabernaemontana divaricate*, *Ervatamia coronariab*, *Ervatamia microphylla*, *Ervatamia divaricate* and *Tabernaemontana coronaria*. In total 49 compounds were found reported, out of which 5 were common and hence 44 compounds were considered for further studies. Besides this, other reported compounds from this plant were also explored for binding to cobratoxin, making the total number to 75. These molecules were sketched on schrodinger 2012 suite and further taken to Autodock vina software for

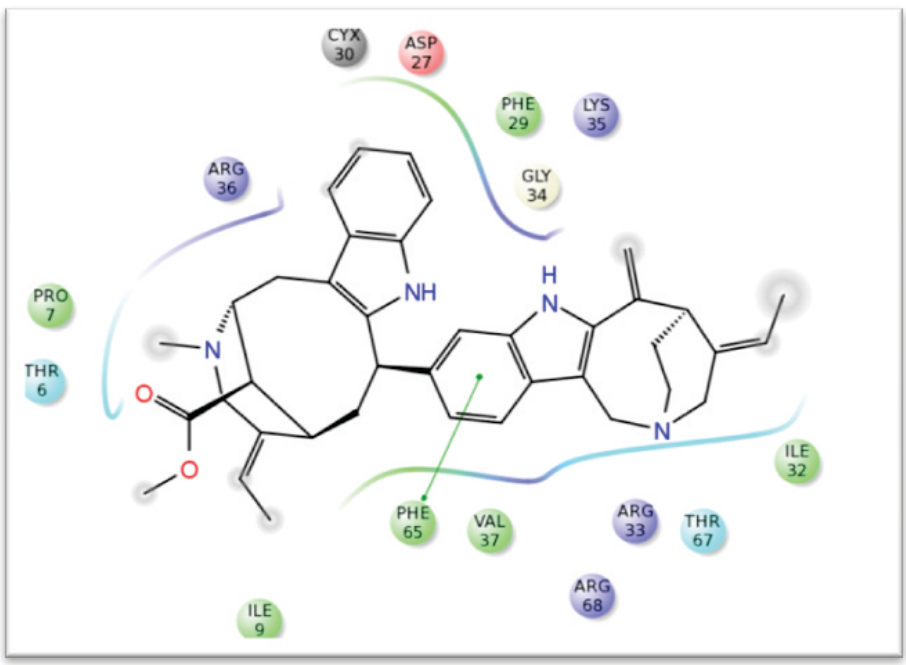


Figure 3.2.1. Interaction of Pseudovobparicine, an alkaloid from the root bark of Tabernaemontana divaricata, within the binding pocket of α-cobratoxin

carring out molecular docking studies. Cross docking of all the 75 co mpounds along with the known inhibitors was carried out on the three downloaded structures of Cbtx and the consensus score was taken into consideration.

Based on the docking analysis, it was observed that Pseudovobparicine (an alkaloid from the root bark of *Tabernaemontana divaricata*) showed the best binding affinity, among all, with Cbtx. The interaction of Pseudovobparicine within the binding pocket of α-cobratoxin is shown in figure 3.2.1 Besides this, two other compounds Dregamine and Stapfinine_11-Hydroxy,5-Ketone also showed comparatively better consensus dock score than others, but Pseudovobparicine.

3.3 Molecular modeling studies on Dot1L protein for identification of novel inhibitors

Priya Mahajan, Amit Nargotra, Syed Sajad Hussain, Ram Vishwakarma

Histone H3-lysine79 (H3K79) methyl transferase DOT1L plays critical roles in normal cell differentiation as well as initiation of acute leukemia. Selective inhibition of protein methyltransferases is a promising new approach to drug discovery. Here, we had applied a strategy for identifying compounds that selectively inhibit the binding of the co-factor, S-adenosylmethionine (SAM), within specific protein methyltransferases. During the reporting period hit identification and lead optimization studies were carried out in order to design better inhibitors for Dot1L. Fragment based design approach was applied using surface volume analysis of active sites of the selected target protein, in order to identify and design novel potent inhibitors of these targets. For the purpose of hit identification from the Institutional compound repository, all the reported inhibitors of the selected target Dot1L were downloaded and used for developing the filtering criteria based on structural similarity and SAR studies. Based on the above mentioned structure based and ligand based inhibitor design strategies, several hits were identified and have been submitted for their biological evaluation. A total of 15 crystal structures of Dot1L reported in Protein Data Bank, having resolution between 2.05 and 2.85 Å, were downloaded. All the co-crystalised structures of these proteins were taken for similarity search on the Institutional compound library. In addition to these the structure of EPZ-5676, an S-adenosyl methionine (SAM) competitive inhibitor of DOT11L, was also taken for carrying out lead optimization studies. A thorough surface volume analysis of the active site of Dot1L protein was carried out as shown in figure 1. Due to the slight conformational change in the binding site of Dot1L based on the kind of ligand binding to it, we selected INW3 protein bound with SAM: S-ADENOSYLMETHIONINE and 4EQZ protein bound with comparatively bigger ligand, and carried out cross docking studies on natural and synthetic in-house library on these targets. Ligand based and structure based *in silico* strategies comprising of molecular docking, pharmacophore and e-pharmacophore studies, fragment based design and similarity and substructural search were applied on the Insitutional compound repository for identification of hits for designing novel Dot1L inhibitors. We could identify a total of 66 compounds from across the different in-house libraries of the Institute. All these 66 compounds were submitted for bio-evaluation studies, and 13 molecules were found to inhibit the protein more than 20% at 10μM concentration. Though these molecules did not show any $IC_{50,}$ but these proved to be a good starting point for lead optimisation studies based on the structural information of the protein, which would be carried out further. In this regard, four molecules were selected based on medicinal chemistry Scientist's inputs for lead optimizations studies and the work is in progress for the same. The structure of these four compounds is shown in figure 3.3.1.

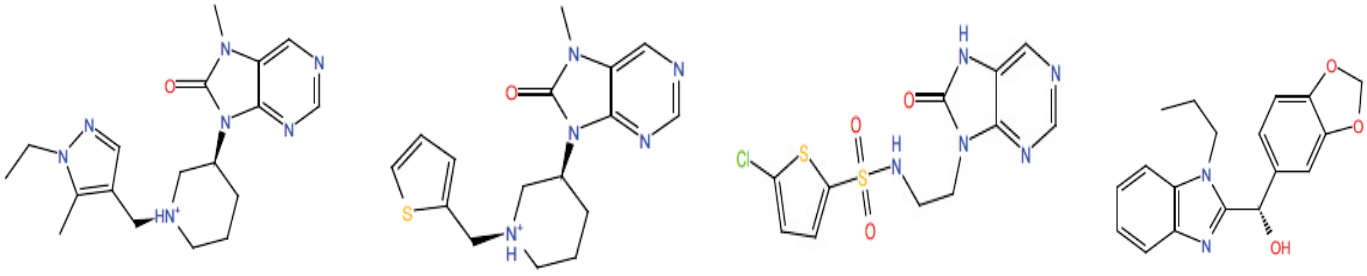


Figure 3.3.1. Molecules selected based on *in silico* output for optimization studies to design selective Dot1L inhibitors.

3.4 Structure prediction of PKUGT1 and PKUGT2 and their docking studies

Rukmankesh, Amit Nargotra, Wajid Bhat, Surrinder Lattoo, Ram Vishwakarma

In order to carry out comparative structural insight and evaluation of substrate recognition of two glycosyltransferases, PKUGT1 and PKUGT2, from *Picrorhiza kurrooa in silico* structure prediction of these enzymes was carried out using PHYRE2 server. The compounds iridotrial, 7-deoxyloganetic acid, 7-deoxyloganetin, apigenin, kaempferol and naringenin were docked on these predicted structures in order to ascertain their binding affinity. The docking studies of this ligand data set with PKUGT1 showed comparatively similar binding affinity except for kaempferol and also naringenin where the binding affinity was comparatively higher. The best among the two, kaempferol, was quite suitably placed within the proposed binding pocket of PKUGT1 (figure 3.4.1) and was proposed to involve in seven H-bond formation with Asp122 (at 1.81Å), Lys193 (2.38Å), Ser286 (at 1.7Å and 2.04Å), Leu287 (at 2.08Å) and Asn365 (at 1.85Å and 1.94Å).

Based on the docking and Prime MMGBSA results, it was found that PKUGT2 has strong binding affinity for iridotrial, 7-deoxyloganetic acid, 7-deoxyloganetin in comparison to apigenin, kaempferol and naringenin which indicates that this protein has specific affinity for iridotrial class of compounds, particularly 7-deoxyloganetin, which has the maximum binding affinity. The compounds apigenin, kaempferol and naringenin showed very poor binding affinity towards the protein's acceptor site both in terms of dock score and binding energy parameters. The interaction of 7-deoxyloganetin within the proposed binding pocket of PKUGT2 is shown in figure 3.4.2.

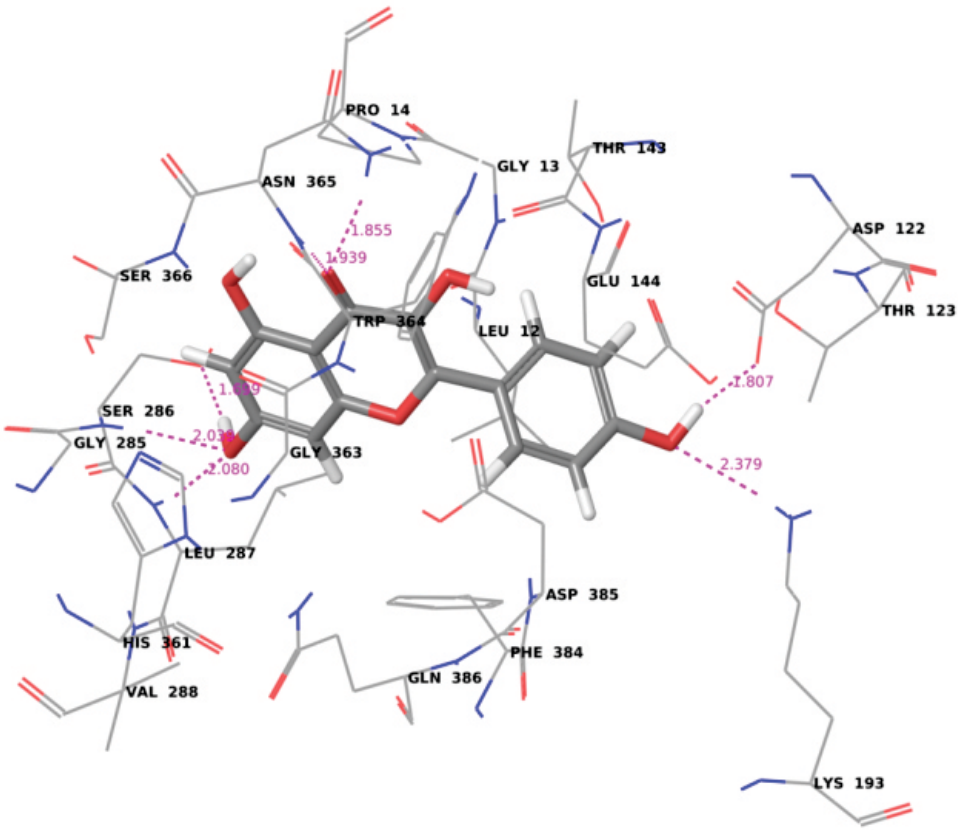


Figure 3.4.2. Interaction of Kaempferol within the binding pocket of PKUGT1

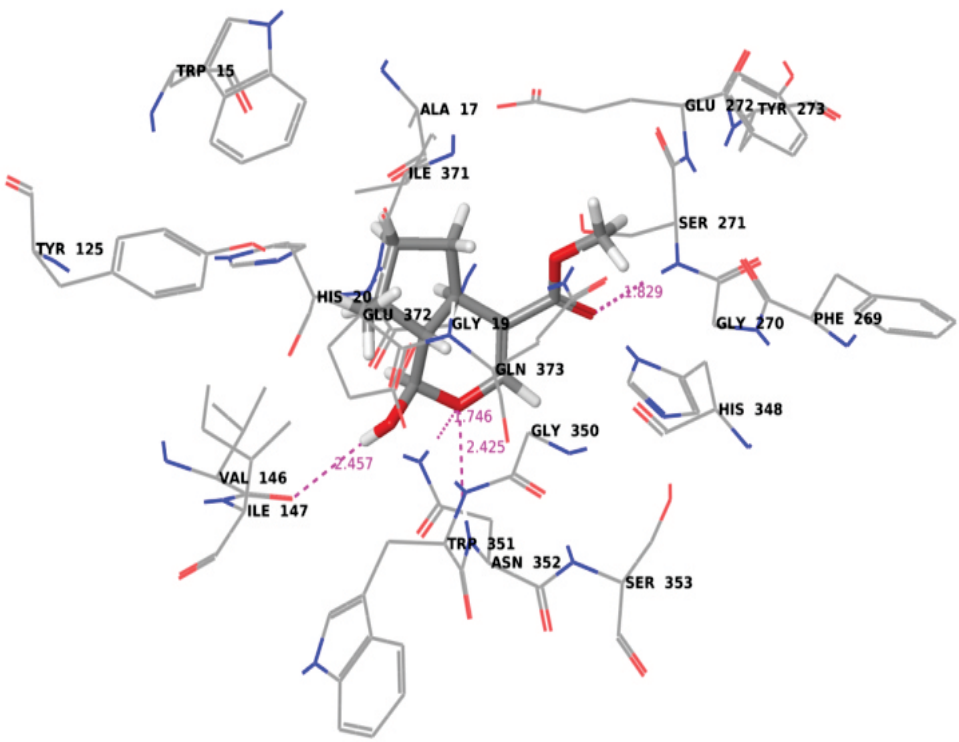


Figure 3.4.2. Interaction of 7-deoxyloganetin within the binding pocket of PKUGT2

3.5 Compilation of the activity data of kinase inhibitors at IIIM

Rukmankesh, Amit Nargotra, Ram Vishwakarma.

In order to take a decision about the scaffolds to be taken forward in various ongoing Medchem projects related to cancer, the activity data of kinase inhibitors developed from the in house experiments were compiled based on the scaffolds. There are a total of 18 scaffolds of kinases inhibitors on which the work is going on at IIIM to develop novel kinase inhibitors. A total of 44 potent inhibitors of different kinases have been identified, so far, from the analogs of ZSTK-474, NVPBEZ-235, PI-103, rohitukine, meriolin, kenpaullone, fascaplycin, OSI-930 and meridianin. This kinase inhibitor database is being updated regularly.

3.6 Compilation of the activity data of Mycobacterium tuberculosis inhibitors

Rukmankesh, Amit Nargotra, Ram Vishwakarma

In order to take a decision about the scaffolds to be taken forward in various ongoing Medchem projects related to tuberculosis, the activity data of inhibitors of *Mycobacterium tuberculosis* reported from the *in house* experiments have been compiled based on the scaffolds. There are a total of 11 scaffolds on which the work is going on at Indian Institute of Integrative Medicine, Jammu to develop novel inhibitors of *Mycobacterium tuberculosis*. A total of 54 potent inhibitors have been identified having MIC $<=0.25$ μg/ml. The data of these inhibitors is being updated regularly.

3.7 Repository database updation and compound flow management

Monika Gupta, Amit Nargotra, Naresh Satti, Ram Vishwakarma

The compound repository is being maintained and a proper mechanism of flow has been established for submission of compounds to the repository and out of repository with a three code system. During the reporting period, 323 compounds were submitted to the repository and the database for the same was created. A total of 1427 compounds were issued after prior approval for various biological activities within and outside the Institute.

3.8 Identification and optimization of E. coli GlmU inhibitors using silico approach

Rukmankesh, Amit Nargotra, Rashmi Sharma, Inshad Ali Khan.

Bacterial infections are causing havoc on the populace. Continuous rising of antibiotic resistance in bacteria causes pressing requirement of new drugs and drug therapies that are effective against these multidrug resistance bacteria. GlmU, which is a bifunctional acetyltransferase/uridyltransferase enzyme, is novel target to treat bacterial infections. An effort has been made to identify and develop novel inhibitors of acetyltransferase activity of *Escherichia coli* (Ec) GlmU protein. *In silico* approach has been applied to screen chemical library of 50,000 drug like compounds procured from ChemBridge (20,000 compounds) and ChemDiv (30,000 compounds). This chemical library was screened by using a combination of ligand guided and structure guided techniques. *In vitro* evaluation of the *in silico* identified hits helped in the discovery of 8 promising inhibitors of acetyltransferase activity of Ec GlmU (figure 3.8.1). Further, the binding site analysis was carried out to

suggest suitable modifications around the identified structural moieties for designing specific inhibitors of acetyltransferase activity of *E. coli* GlmU. Structure guided lead optimization strategy presented the scope of modification around three different structural moieties identified through *in vitro* hits. In addition, molecular dynamics studies revealed the stability of the protein-inhibitor complexes of the two most promising inhibitors identified in this study. Overall, the study emphasize that an appropriate rational *in silico* approach proves to be very effective in current drug discovery programs for designing new and potent inhibitors of therapeutically important targets.

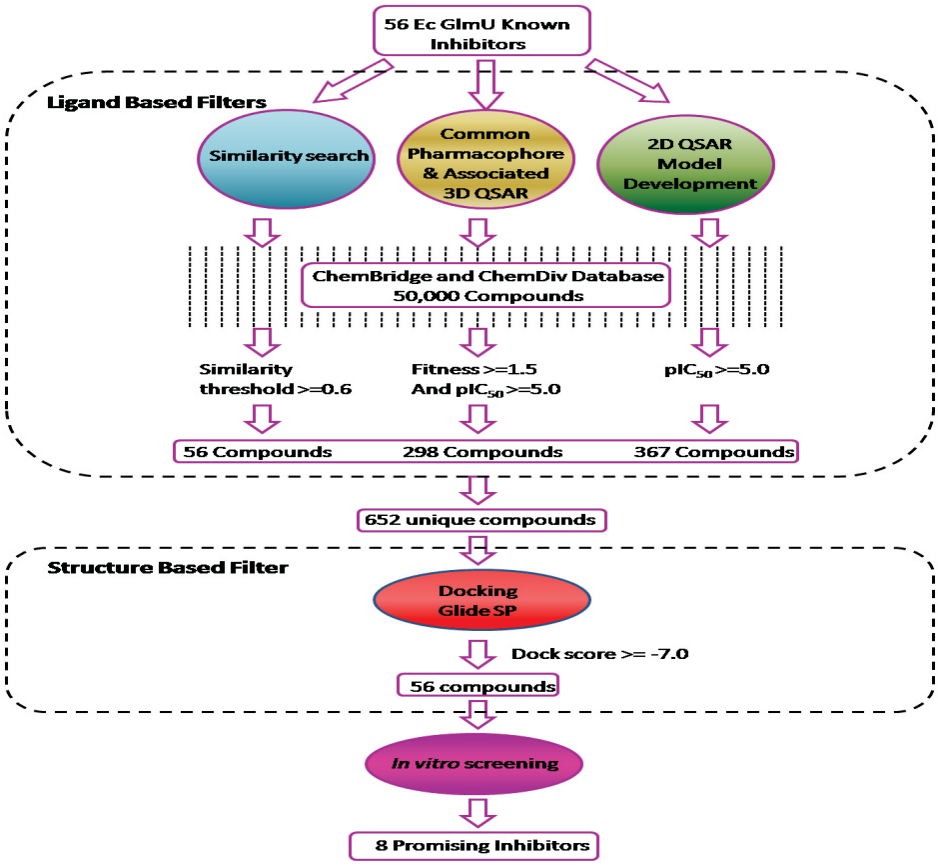


Figure 3.8.1. Screening protocol for the identification of potent Ec GlmU inhibitors from the compound repository.

3.9 Discovery of Novel Small Molecule EGFR inhibitory leads by Structure and Ligand Based Virtual Screening

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

Virtual screening is an attractive and cost effective approach which is widely applied to filter the compound library for the identification of novel inhibitors. Epidermal growth factor receptor tyrosine kinase (EGFR-TK) protein is a well reported anticancer molecular target due to its over expression and mutation in many solid tumours. Reduction of EGFR-TK activity by small or medium sized molecules has proved to be an effective treatment for cancer. To design inhibitors for this target, the crystal structures of EGFR-TKs co-crystallized with its inhibitors provide a gateway to perform receptor based drug designing programme (vHTS, e-pharmacophore modelling) whereas the inhibitors reported in literature provide a ligand based drug designing programme (pharmacophore based 3D QSAR studies, substructure and similarity search). These drug designing programmes have been used to perform virtual screening of a procured drug like library of 50,000 compounds from ChemDiv and ChemBridge databases against EGFR as shown in figure 3.9.1. From virtual screening of these procured compounds, 87 common hits were identified based on

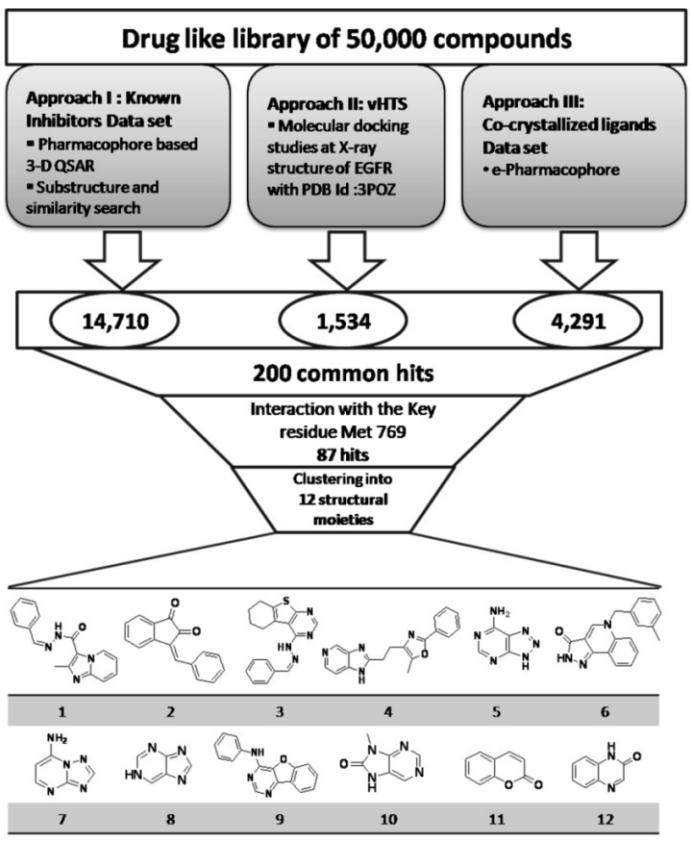


Figure 3.9.1 . In silico filtering criteria for the identification of potent EGFR inhibitors from the institutional compound library of drug like compounds.

the knowledge based screening, which were clustered into 12 different structural moieties. *In vitro* studies of some of these hits were also carried out for validation of the results. Further the lead optimization studies were performed by analyzing the binding poses of these inhibitors in order to ascertain the scope of modifications around the identified structural moieties for designing novel and specific EGFR inhibitors.

3.10 Optimization studies on earlier identified Dot1L inhibitors

Priya Mahajan, Amit Nargotra, Syed Sajad Hussain, Ram Vishwakarma.

As a result of our previous work related to molecular modeling studies on Dot1L protein, we had identified four hits out of thirteen, for their optimization studies. Detailed binding site analysis of Dot1L was done and all the four hits were analysed with respect to the vacant spaces around these structures within the Dot1L binding site (figure 3.10.1). With the knowledge of the vacant spaces and their type, combinatorial chemistry studies were carried out on these molecules by substituting various Schrodinger fragments on these hits. The entire library thus generated was against screened against the target. It was observed that there was improvement in the Glide score in all the four compounds, with maximum variation/ improvement seen in compound id **5655053**, where the Glide score was improved more than double. The results have been submitted to the medicinal chemists, and their synthesis is being explored for further validation studies. The selected compounds for this study, along with the scope of modification and the glide score before and after the structural modification are summarized in table 3.10.1.

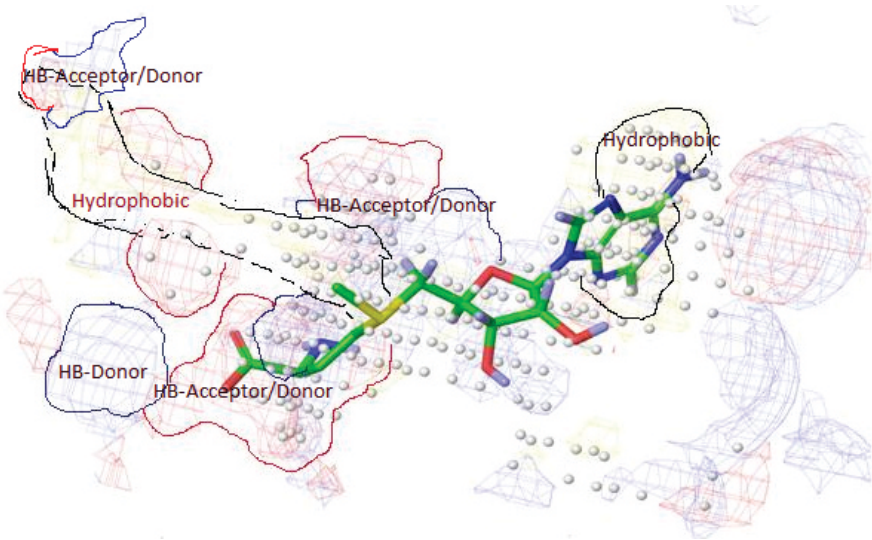
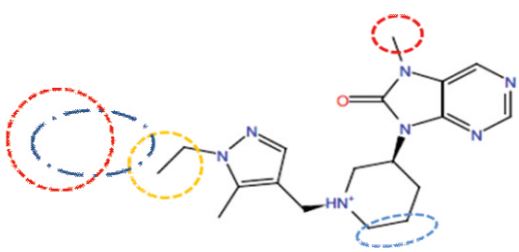
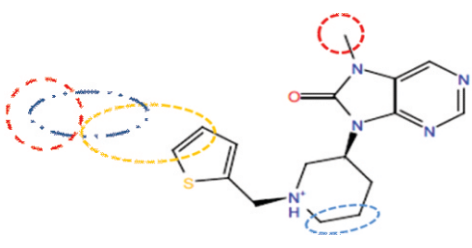
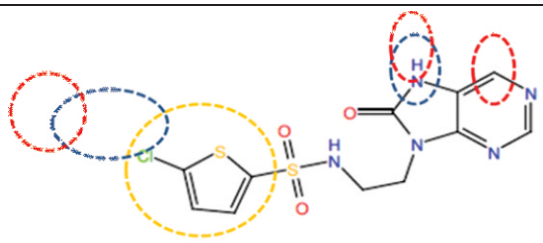
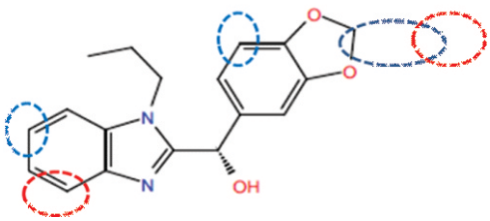


Figure 3.10.1 Binding site analysis of Dot1L showing vacant spaces with respect to the co-crystallized ligand.

Table 3.10.1. Compounds selected for structural optimization for Dot1L inhibition.

S.No	Compound ID	Structure	Initial Glide Score	Final Glide Score (after structural modification)
1	P814-5530		10.395	14.291
2	P814-5532		9.621	13.662

S.No	Compound ID	Structure	Initial Glide Score	Final Glide Score (after structural modification)
3	P814-6413		6.397	10.636
4	5655053		4.697	9.955

3.11 Development and maintenance of Stem cell database (MedchemDB)

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

MedchemDB is the systematic compilation of various pathways, crystal structures and target details related to the stem cell research. Information has been included in the database through various online tools/databases such as PubMed, SciFinder, Integrity etc. and also through authenticated open literature search. The compilation and the overall organization of the data have been done in such a way that the navigation within the database is simpler and user friendly. A snapshot of the home page of MedchemDB is shown in figure 3.11.1. A very important compilation in this database is about the classification of various scaffolds along with their activity data for the selected targets. Apart from other useful information like crystal

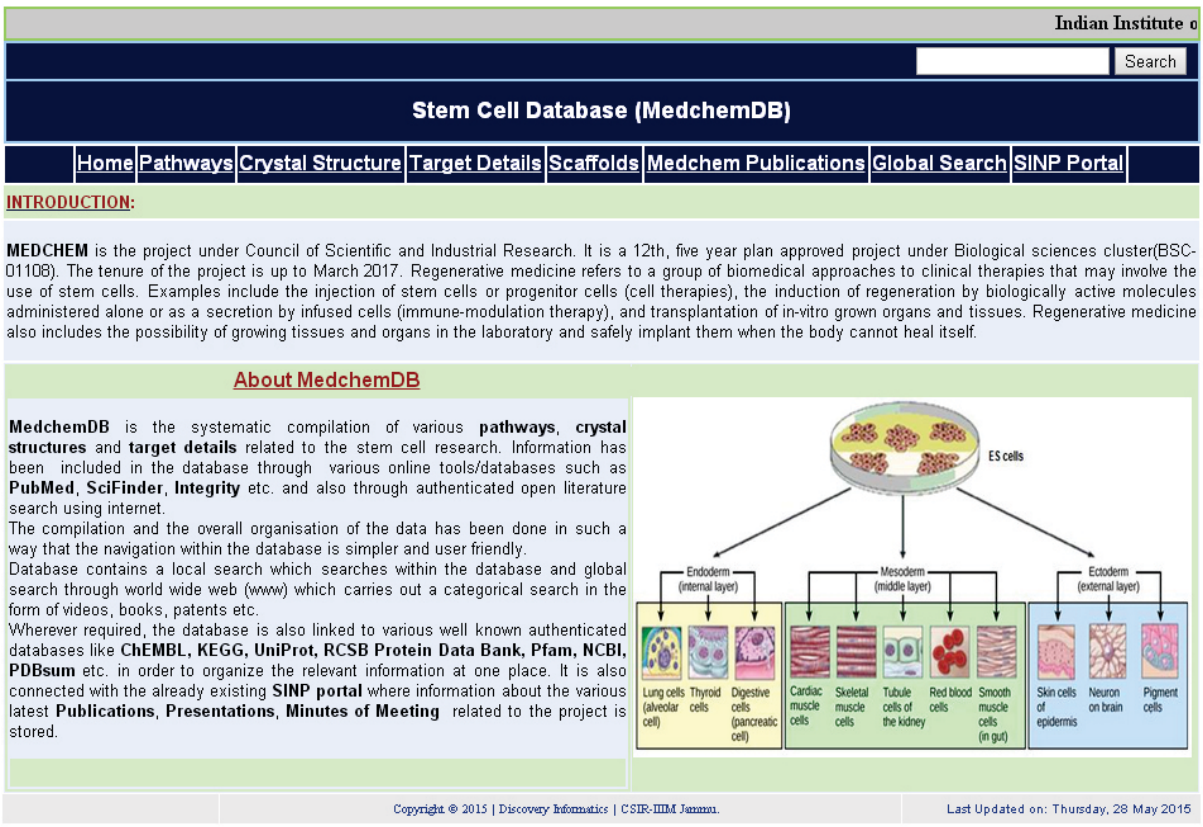


Figure 3.11.1. Home page of MedchemDB

structure details, pathway information, related publications etc., this database also contains a local search which searches within the database and global search through World Wide Web (www) which carries out a categorical search in the form of videos, books, patents etc. Wherever required, the database is also linked to various well known authenticated databases like ChEMBL, KEGG, UniProt, RCSB Protein Data Bank, Pfam, NCBI, PDBsum etc. in order to organize the relevant information at one place. It is also connected with the already existing SINP portal where information about the various latest Publications, Presentations, Minutes of Meeting related to the stem cell project of the Institute is stored.

3.12 Repository database updation and compound flow management

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

The entire compound repository of the Institute is being managed physically as well as electronically based on three code system. The NCE repository is shown in figures 3.12.1 and 3.12.2 respectively.

The Institutional compound repository also hosts the 50,000 through this repository. The repository is being screened for various relevant therapeutic targets even outside the Institute.

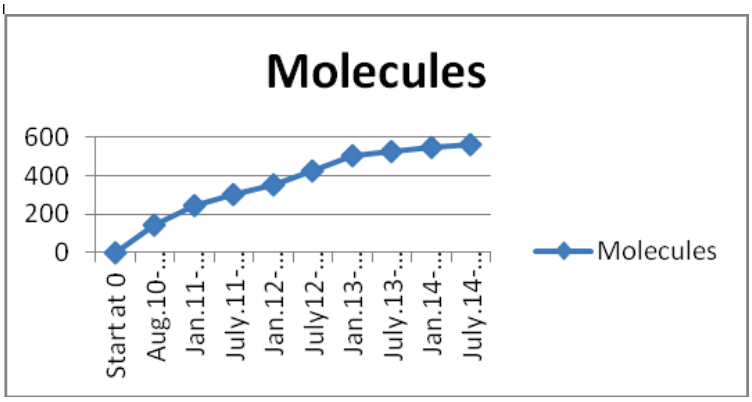


Figure 3.12.1 Progress of the Natural product repository up to Dec 2014

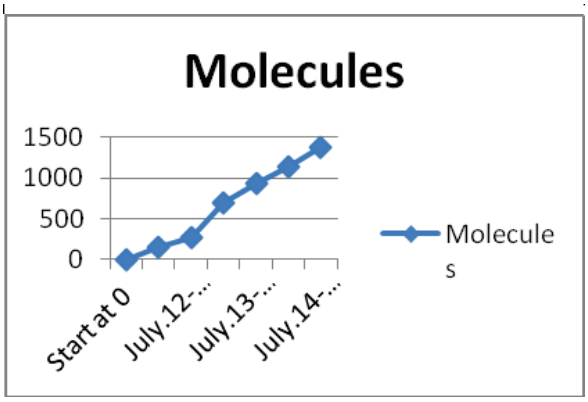


Figure 3.12.2 Submission progress of the New chemical entities of the medhcem projects of Institute up to Dec 2014

submission of compounds by the chemists and the withdrawal of compounds from the repository is properly monitored and recorded. This management system is of utmost importance for any drug discovery Institute. The database is web-enabled with substructure search feature. During the calendar year 2014, 54 pure natural compounds were submitted in the repository, whereas 448 new chemical entities from the medchem projects were submitted to the repository. The overall growth of the natural product repository and the externally procured drug-like compounds. The library is being very effectively used for the med chem projects of the institute and is assisting the drug discovery projects of the Institute. Figure 3.12.3 gives a glimpse of how this repository is helping the various discovery projects of the Institute. In the year 2014, a total of 2894 compounds were issued for biological evaluation

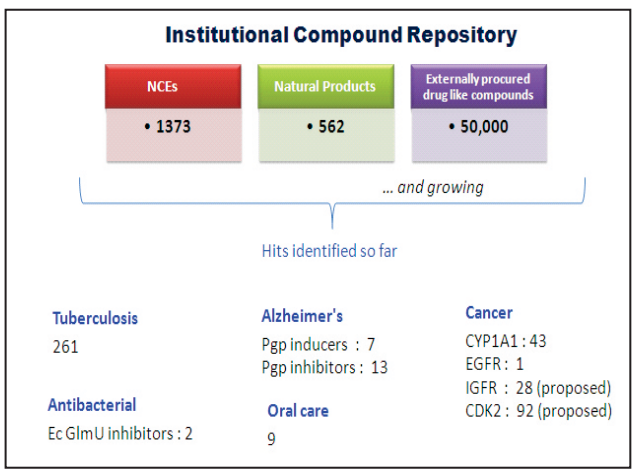


Figure 3.12.3 Screening results of the Institutional compound repository in various discovery projects of the Institute.

4. NATURAL PRODUCT CHEMISTRY

4.1 Extraction and isolation of chemical constituents of RJM/0010

Neha Sharma, N.K.Satti, Prabhu Dutt

The chemical investigation of the stem extract of RJM/0010 has resulted in the isolation of one new compound **1** besides ecdysterone, tinosporaside, TC-1(2,3:15,16-Diepoxy- 4, 6 dihydroxy-13(16),14-clerodadiene-17,12:18,1-diolide), Cordifolioside A (-D Glucopyranoside,4-(3-hydroxy-1-propenyl)- 2,6-dimethoxyphenyl 3-O-D-apio--D-furanosyl), and chemical structures have been established by spectral analysis (Figure 4.1.1).

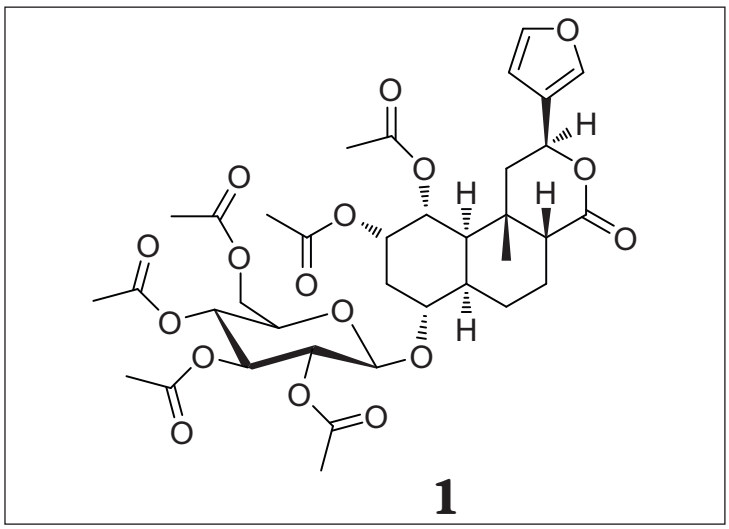
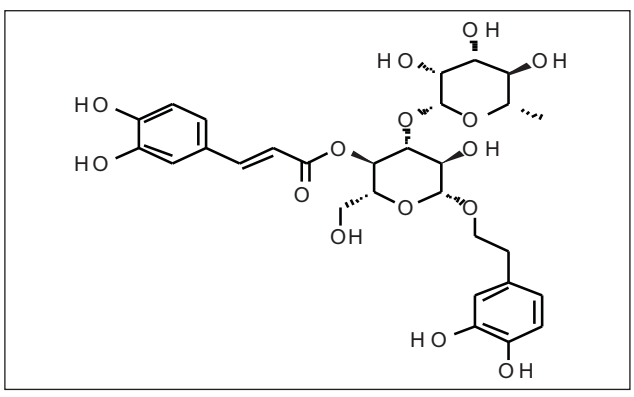


Figure 4.1.1. Stem extract of RJM/0010 has resulted in the isolation of one new compound **1**

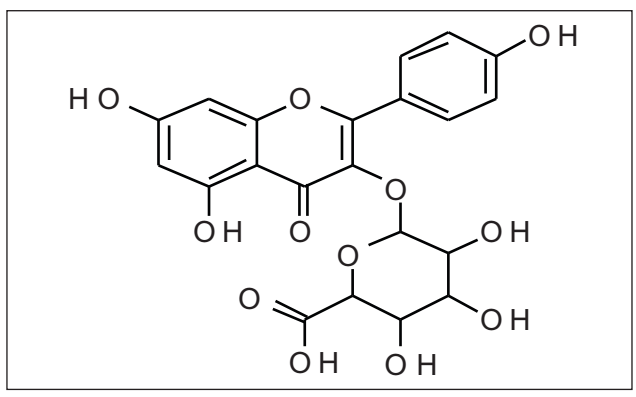
4.2 Extraction and isolation of chemical constituents from *Colebrookea oppositifolia*

Neha Sharma, N.K.Satti, Prabhu Dutt.

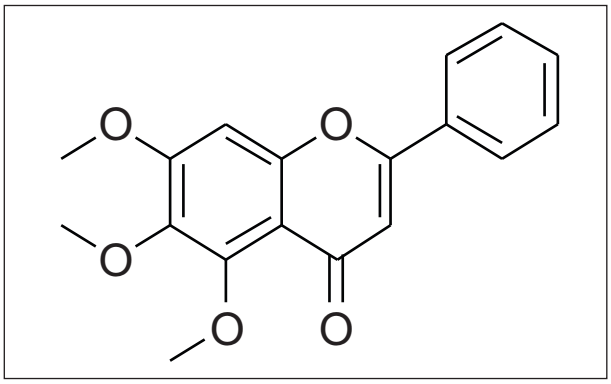
The chemical investigation of the leaves extract of the plant has resulted in the isolation of acteoside, 5,6,7-Trimethoxy flavones (CO-3), 5,6,7,4'-Tetramethoxy flavone (CO-4), 5,7,4'-Trihydroxy flavone -3-O-Glucuronide (CO-1), β-sitosterol glycoside, 5-hydroxy, 6,7,8-Trimethoxy flavones, 5-hydroxy-6,7,8,4'-Tetramethoxy flavones, Hentriacontane in addition to 5 compounds already isolated by column chromatography. Structures of the compounds have been established by spectral analysis.



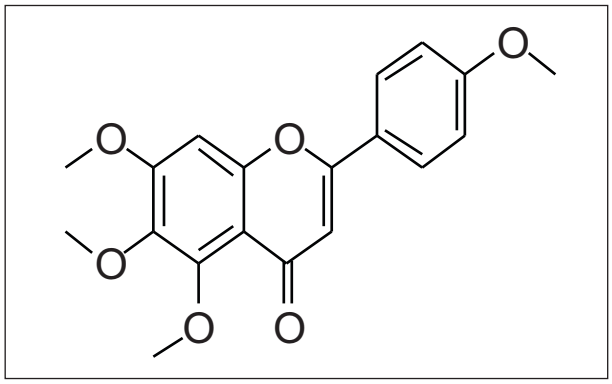
Acteoside (Bioactive marker)



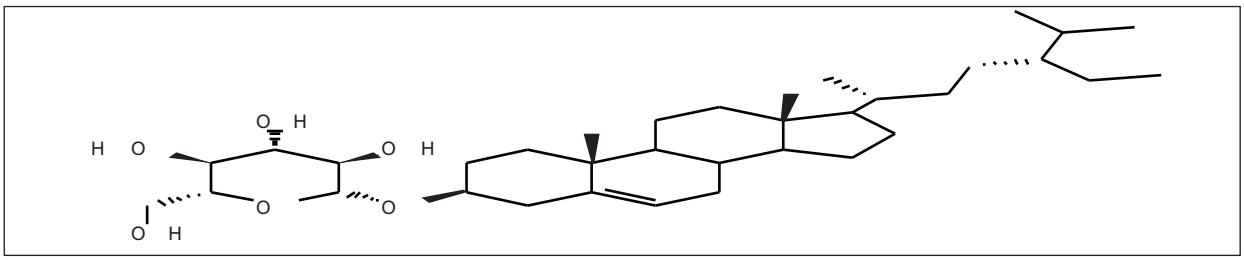
5,7,4'-Trihydroxy flavone -3-O- Glucuronide (CO-1)



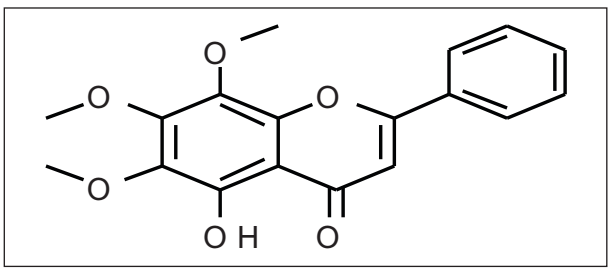
5,6,7-Trimethoxy flavone (**CO-3**)



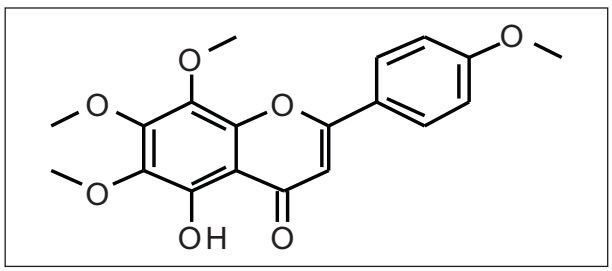
5,6,7,4'-Tetramethoxy flavone (**CO-4**)



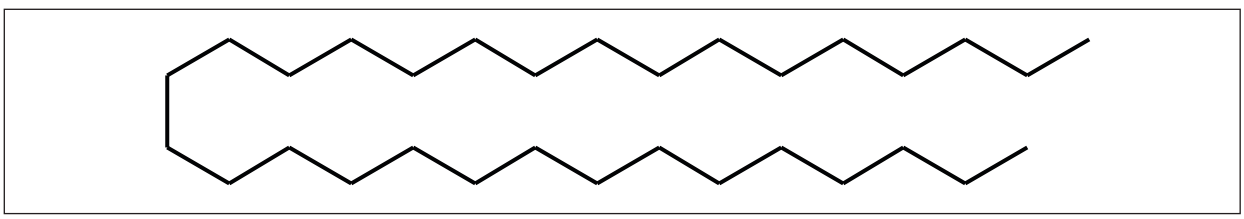
β-Sitosterol glucoside



5-hydroxy, 6,7,8- Trimethoxy flavone



5-hydroxy- 6,7,8,4'-Tetramethoxy flavones



Hentriacontane

Three batches of phenylethanoid glycoside enriched fraction of RJM0862 from plant material were prepared at Pilot plant scale for IND enabling studies and for further work in CGMP plant.

Table:4.2.1. RJM 0862 phenylethanoid glycoside enriched fraction: three batch data

Batch	Dry Plant material taken	RJM 0862 phenylethanoid glycoside enriched fraction obtained	Yield%
Batch 1	6.6 Kg	1.32 Kg	20.0
Batch 2	7.5 Kg	1.36 Kg	18.1
Batch 3	7.2Kg	1.34 Kg	18.6

Table: 4.2.2. Four chemical markers quantification data (By HPLC) of above 3 batches

Chemical markers	RJM0862 (Batch-1)	RJM0862 (Batch-2)	RJM0862 (Batch-3)	% Range of markers as estimated by HPLC on the basis of three experiments
Acteoside content % 1st injection 2nd injection	 33.58 33.65	 24.90 26.34	 29.68 29.68	24.90 - 33.65
CO-1 content % 1st injection 2nd injection	 6.94 6.85	 5.36 5.94	 5.82 5.91	5.36 – 6.94
CO-3 content % 1st injection 2nd injection	 0.194 0.172	 0.423 0.464	 0.10 0.09	0.09 – 0.46
CO-4 content % 1st injection 2nd injection	 0.270 0.246	 0.570 0.617	 0.132 0.119	0.13 – 0.61

Table: 4.2.3 Chemical equivalence of different extracts of RJM 0862 on the basis of acteoside Prepared Three extracts

Extract	% Yield
Ethanolic extract	25
Aqueous extract	22
Hydroethanolic extract	21

General method for the preparation of enriched fraction

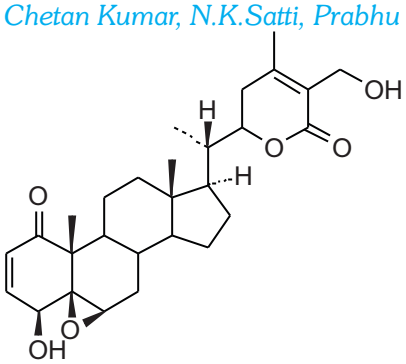
5 gm of above extract was suspended in distilled water 25mL. It was sonicated for 10 minutes and centrifuged. Supernatant was decanted. Residue was extracted once more under similar conditions. Combined water soluble fraction was dried on rotavapour to get residue

Table: 4.2.4. Percentage of chemical marker compounds in the extracts and phenylethanoid glycoside enriched fraction estimated by HPLC

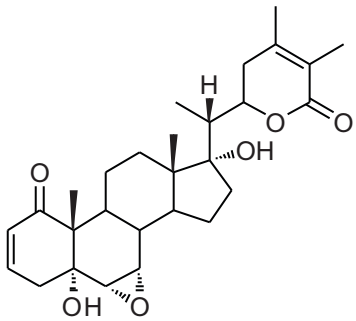
		Acteoside	CO-1	CO-3	CO-4
1	RJM-0862 ethanolic extract	16.75	5.91	0.35	0.142
1a	RJM-0862 enriched fraction from 1	27.19	5.48	0.09	0.143
2	RJM-0862 hydroethanolic extract	1.85	1.74	0.10	0.121
2a	RJM-0862 enriched fraction from 2	2.95	2.23	0.08	0.08
3	RJM-0862 Hot aqueous extract	2.17	2.14	0.06	0.22

4.3 Extraction and isolation of chemical constituents from *Withania somnifera*

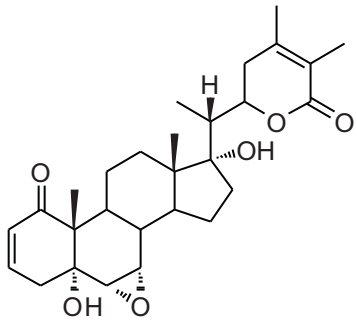
Chetan Kumar, N.K.Satti, Prabhu Dutt



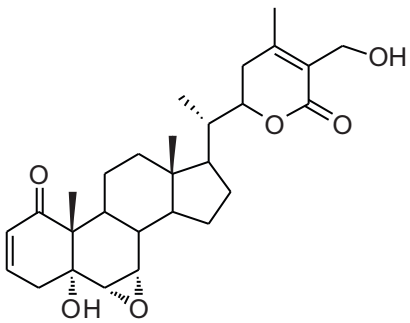
Withaferin A



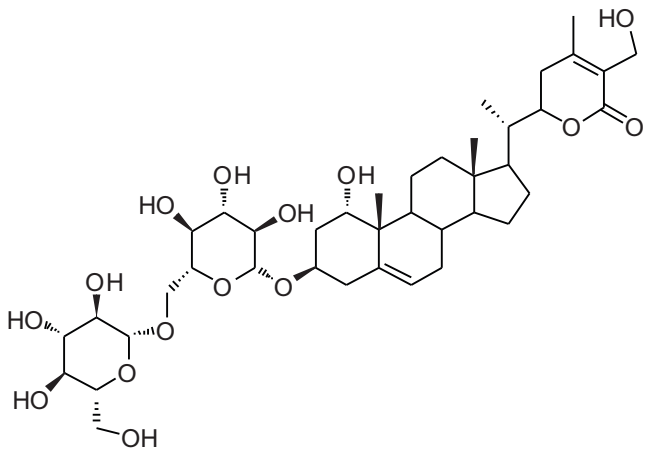
Withanone



Withanolide A



12-Deoxywithastramonolide



Withanoside IV (WSG-3)

The chemical investigation of the roots and leaves extract of the plant has resulted in the isolation of Withaferin A, Withanone, Withanolide A, 12-Deoxywithastramonolide, Withanoside IV (WSG-3) by column chromatography. Structures of the compounds have been established by spectral analysis.

Table: 4.3.1. Extracts and compounds sent for bioevaluation under project BSC 0108 to CCMB, Hyderabad

RJM0862 aqueous extract	25mg
RJM0862 DCM:MeOH::1:1 extract	45mg
IIIM 259(leaves) aqueous extract	25mg
IIIM259(roots) aqueous extract	23mg
IIIM 259(leaves) DCM:MeOH::1:1 extract	42mg
IIIM259(roots) DCM:MeOH::1:1 extract	44mg

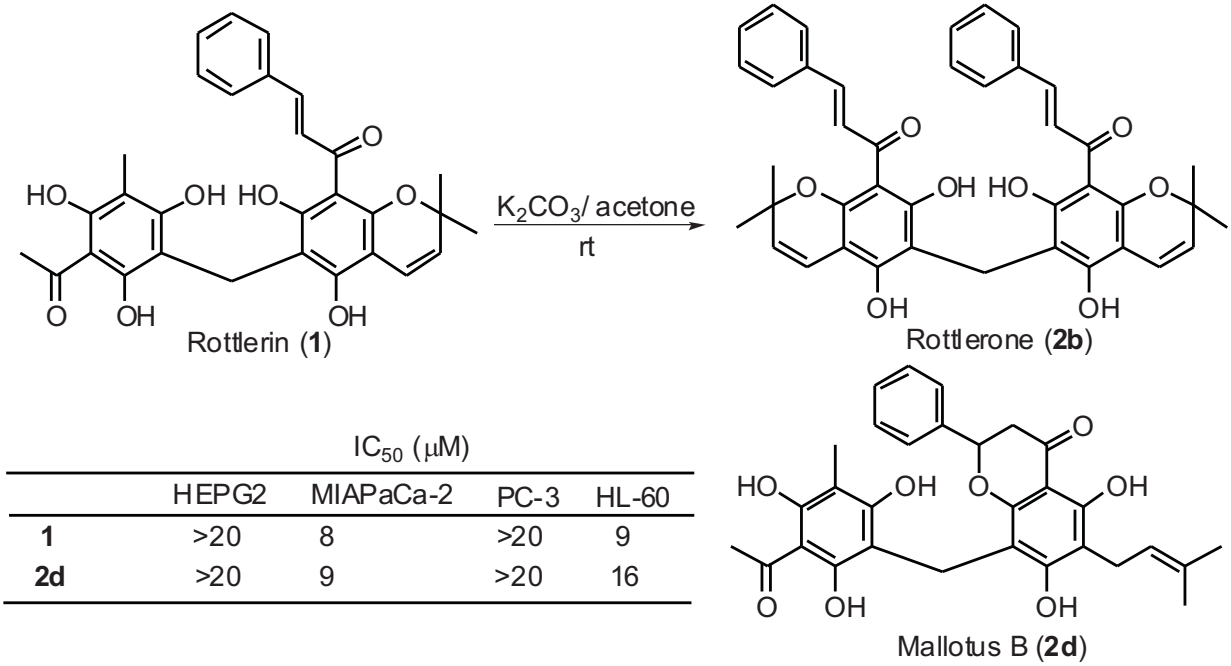
Chemical marker compounds CO-1, CO-3, CO-4, CO-6, acteoside of Plant RJM0862.
Chemical marker compounds withaferin A, withanone, withanolide A, 12-deoxy withastramonolide and withanoside IV of Plant IIIM259.

5. MEDICINAL CHEMISTRY

5.1 Semisynthesis of Mallotus B from Rottlerin: Evaluation of cytotoxicity and apoptosis-inducing activity

Shreyans K. Jain, Anup S. Pathania, Samdarshi Meena, Rajni Sharma, Ashok Sharma, Baljinder Singh, Bishan D. Gupta, Shashi Bhushan, Sandip B. Bharate and Ram A. Vishwakarma

Mallotus B (2d) is a prenylated dimeric phloroglucinol compound isolated from *Mallotus philippensis*. There have been no reports on the synthesis or biological activity of this compound. In the present paper, a semisynthetic preparation of mallotus B is reported via base-mediated intramolecular rearrangement of rottlerin (1), which is one of the major constituent of M. *philippensis*. The homo-dimer "rottlerone" was also formed as one of the products of this base-mediated intramolecular reaction. Rottlerin (1), along with rottlerone (2c) and mallotus B (2d), was evaluated for cytotoxicity against a panel of cancer cell lines including HEPG2, Colo205, MIAPaCa-2, PC-3, and HL-60 cells. Mallotus B (2d) displayed cytotoxicity for MIAPaCa-2 and HL-60 cells with IC_{50} values of 9 and 16 μM, respectively. Microscopic studies in HL-60 cells indicated that mallotus B (2d) induces cell cycle arrest at the G1 phase and causes defective cell division. It also induces apoptosis as evidenced by distinct changes in cell morphology.



IC_{50} (μM)

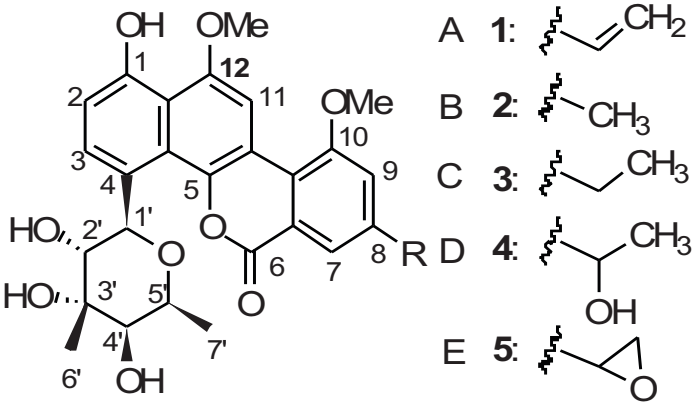
	HEPG2	MIAPaCa-2	PC-3	HL-60
1	>20	8	>20	9
2d	>20	9	>20	16

5.2 Chrysomycins A–C, antileukemic naphthocoumarins from *Streptomyces sporoverrucosus*

Shreyans K. Jain, Anup S. Pathania, Rajinder Parshad, Chandji Raina, Asif Ali, Ajai P. Gupta, Manoj Kushwaha, Subrayashastry Aravinda, Shashi Bhushan, Sandip B. Bharate, Ram A. Vishwakarma

From the antimicrobial strain of *Streptomyces sporoverrucosus* (MTCC11715) isolated from soil samples of Jammu hills, two known naphthocoumarins chrysomycin A (1) and B (2) along with a new naphthocoumarin chrysomycin C (3) were isolated and characterized. The structure of new compound 3 was established by 2D-NMR data. Chrysomycin A (1) and B (2) were identified by a strategic HPLC-

PDA/LCMS and DNP (Dictionary of Natural Products) based fast dereplication. Additionally, two new naphthocoumarins chrysomycin D and E were identified using LCMS, UV and DNP information. Chrysomycins A-C (1-3) were isolated for the first time from *Streptomyces sporoverrucosus* and were screened for cytotoxicity in a panel of cancer cell lines (A549, Colo205, PC-3, MIAPaCa-2, and HL-60), amongst which most potent activity was observed in human leukemia HL-60 cells with IC_{50} values of 0.9, 0.95 and 11 M, respectively. The mechanistic studies indicated that chrysomycin A (1) and B (2) at 1 M concentration distorted cellular and nuclear morphology with significant DNA damage and apoptosis in HL-60 cells.



Chrysomycin	R	HL-60 IC_{50} (μM)
A	$-CH=CH_2$	0.95
B	$-CH_3$	0.90
C	$-CH_2CH_3$	11.0

5.3 Kinase Inhibitors of Marine Origin

Sandip B. Bharate, Sanghapal D. Sawant, Parvinder Pal Singh, and Ram A. Vishwakarma.

More than 20,000 marine natural products (MNPs) have been isolated from ocean life- forms such as sponges, ascidian, aplysia, algae, corals, bryozoa, worm, sea-squirts, sea-hares, sea-cucumbers, fish species and microorganisms. Molecules with potential biomedical applications include alkaloids, terpenoids, steroids, polypeptides, polyethers, macrolides, and polysaccharides. Marine organisms produce secondary metabolites that are structurally distinct from those produced by terrestrial organisms, due to the unique biosynthetic milieu (high salinity, pressure and temperature), and unusual functional groups such as isocyanate, isonitrile, dichloroimine and halogenated functionalities are predominantly found in marine metabolites. MNP research attracted some interest in the late 1950s with the project 'Drugs from the Sea' which was launched in the US, and led to the discovery of two therapeutic drugs; cytarabine (an anticancer drug approved by the FDA in 1969) and vidarabine (an antiviral drug approved by the FDA in 1976). Despite these early success stories, it was not until 2004 that the next generation of MNPs obtained global regulatory approval after successful clinical trials. During the intervening period, there was a general reluctance on the part of mainstream pharmaceutical industries to pursue drug discovery projects to translate potential hits based on marine natural product scaffolds, largely due to (a) the structural complexity of MNPs, which is not amenable to standard medicinal chemistry and lead-optimization; (b) the lack of a consistent and reproducible supply of marine flora and fauna required for scale up to the levels necessary for research; and (c) the legal hurdles imposed by various geological territories and countries. However, natural products chemistry efforts continued unabated in several leading academic institutions worldwide, resulting in the discovery of a large number of structurally unique natural products. The majority of these MNPs were not screened against a battery of clinically validated targets in an industry setting. However, recent approvals of some marine-derived drugs for a number of intractable cancers have demonstrated their untapped potential for the discovery of first-in-class drugs. Considering the current dismal scenario of new drug approvals in global pharmaceutical industries, the focus will shift back to natural products-driven drug discovery sooner rather than later. This interest is likely to be enhanced by recent advances in the technologies used for deep-sea collection, extraction, large-scale aquaculture production, high-throughput isolation, dereplication, chemical synthesis, and biotechnology.

The primary aim of this review is to discuss and critically analyze marine-derived small molecule inhibitors of protein and lipid kinases, with an emphasis on medicinal chemistry, lead optimization, patent literature, preclinical profiling and clinical development. Over the last two decades, several reviews have been published on marine natural products and their potential in drug discovery, but there has not been a comprehensive review of marine natural products as inhibitors and modulators of clinically validated protein and lipid kinases. The present comprehensive review covers the natural product chemistry, synthetic/semisynthetic studies, medicinal chemistry, lead optimization, patent literature, preclinical pharmacology and clinical status of marine-derived kinase inhibitors, including 354 compounds and 717 references. The literature was searched by using The Dictionary of Natural Products (Version 11.2, Chapman & Hall, CRC, 2010), PubMed, SciFinder, ISI Web of knowledge, Datamonitor, several patent databases (Delphion, Micropatent, Qpat, Patbase and Total Patent) and Google Scholar.

5.4 Synthesis of non-hydrolysable mimics of glycosylphosphatidylinositol (GPI) anchors

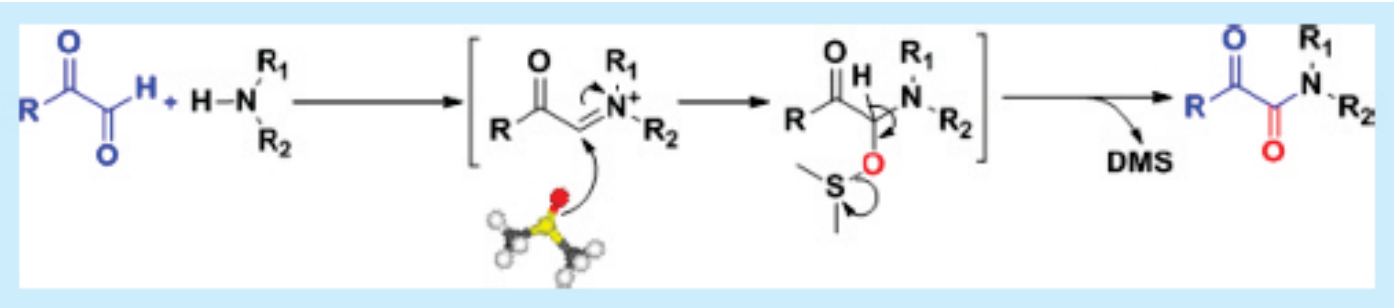
Mahipal Yadav, Riya Raghupathy, Varma Saikam, Saidulu Dara, Parvinder Pal Singh, Sanghapal D. Sawant, Satyajit Mayor and Ram A. Vishwakarma

Synthesis of first generation non-hydrolysable C-phosphonate GPI analogs, viz., 6-O-(2-amino 2-deoxy-α-D-glucopyranosyl)-D-myo-inositol-1-O- (sn-3,4-bis(palmitoyloxy) butyl-1 phosphonate) **23a** and 6-O-(2-amino-2-deoxy-α-D-glucopyranosyl)-D-myo-inositol-1-O-(sn-2,3-bis(palmitoyloxy)propyl-1-phosphonate) **23b**, is reported. The target compounds were synthesized by the coupling of α-pseudodisaccharide 21 with phosphonic acids 18a and 18b respectively in quantitative yield followed by deprotection. These synthetic C-phosphonate GPI-probes were resistant to phosphatidylinositol specific phospholipase C (PI-PLC) and also showed moderate inhibition of the enzyme activity.

5.5 Metal-Free Oxidative Amidation of 2-Oxoaldehydes: A Facile Access to α-Ketoamides

Nagaraju Mupparapu, Shahnawaz Khan, Satyanarayana Battula, Manoj Kushwaha, Ajai Prakash Gupta, Qazi Naveed Ahmed and Ram A. Vishwakarma

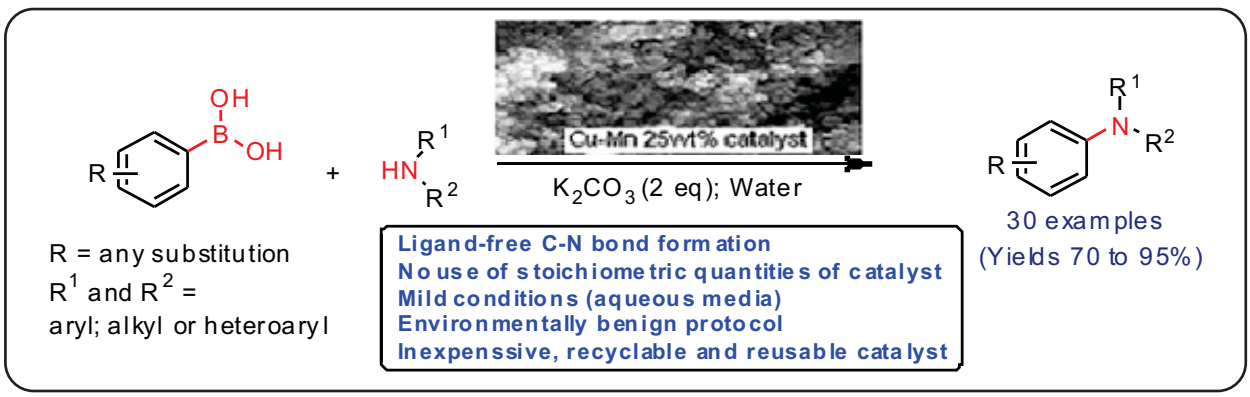
A novel and efficient method for the synthesis of α-ketoamides, employing a dimethyl sulfoxide (DMSO)-promoted oxidative amidation reaction between 2-oxoaldehydes and amines under metal-free conditions is presented. Furthermore, mechanistic studies supported an iminium ionbased intermediate as a central feature of reaction wherein C1-oxygen atom of α-ketoamides is finally derived from DMSO.



5.6 Ligand-free C–N bond formation in aqueous medium using a reusable Cu–Mn bimetallic catalyst

Sawant, S. D., Srinivas, M., Aravinda Kumar, K.A., Reddy, G. L., Singh, P. P., Singh, B., Sharma, A. K., Sharma, P.R., Vishwakarma, R. A.

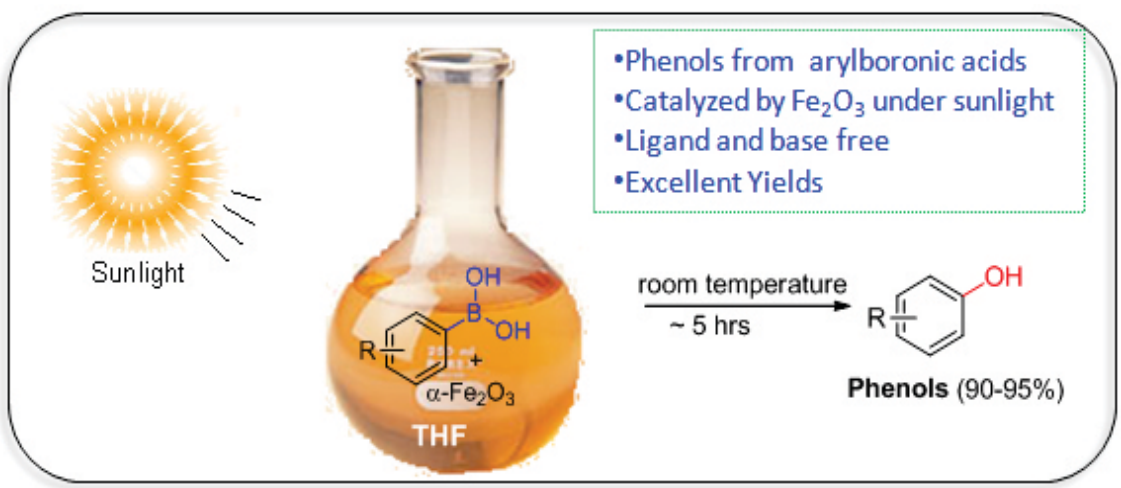
A general ligand-free protocol has been described for the recyclable and reusable Cu–Mn catalyzed C–N bond forming cross coupling reaction of arylboronic acids with various amines to form N-arylated amine products in aqueous medium affording excellent yields under ambient conditions, in 3–4 h.



5.7 Ligand- and base-free synthesis of phenols by rapid oxidation of arylboronic acids using iron(III) oxide

Sawant, S. D.; Hudwekar, A. D.; Kumar,K. A. Aravinda.; Venkateswarlu,V.; Singh, P. P.; Vishwakarma, R. A.

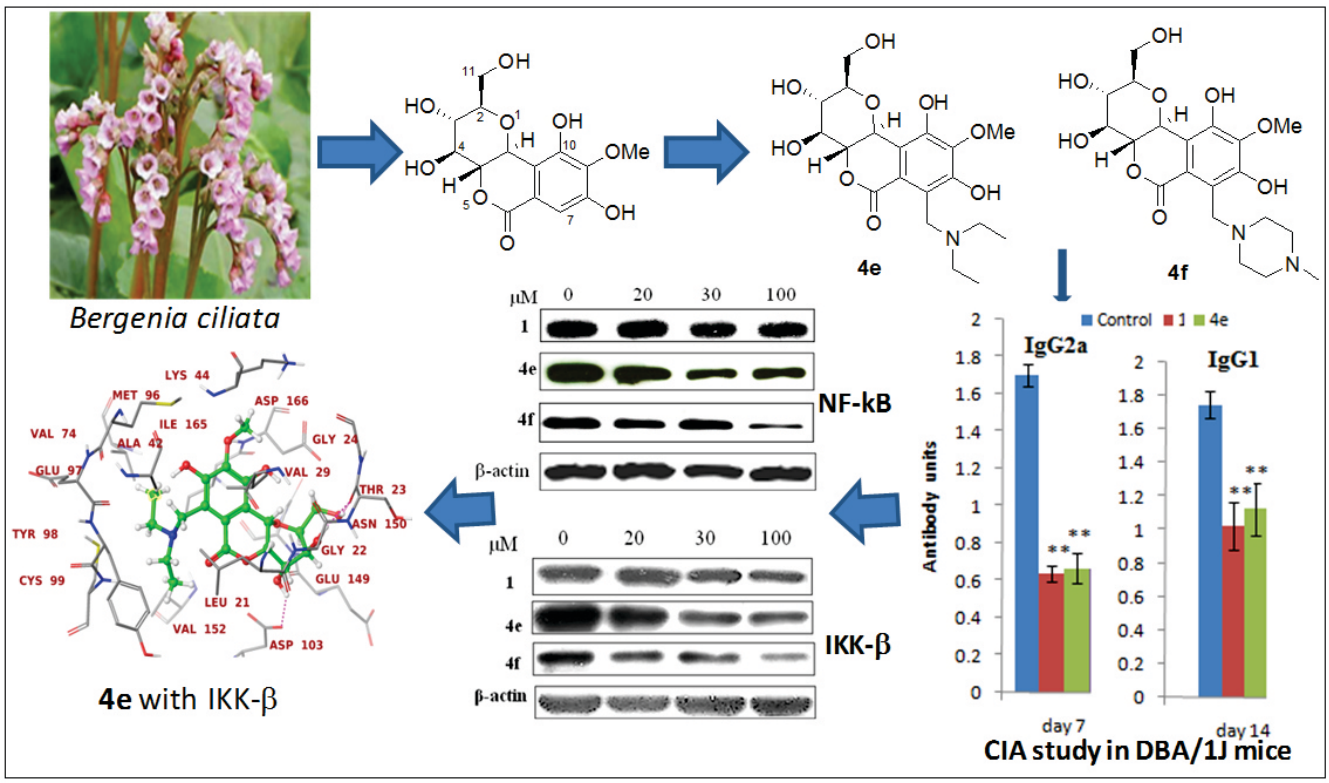
Fe_2O_3 catalyzed rapid oxidation of arylboronic acids to obtain phenols in excellent yields (90 to 95%) in the presence of atmospheric oxygen under solar VIS-light irradiation using α-Fe_2O_3 as a catalyst in ligand- and base-free conditions is presented.



5.8 Pyrano-isochromanones as IL-6 inhibitors: Synthesis, *in-vitro* and *in-vivo* anti-arthritic activity

Shreyans K. Jain, Surjeet Singh, Anamika Khajuria, Santosh K. Guru, Prashant Joshi, Samdarshi Meena, Janhavi R. Nadkarni, Amarinder Singh, Sonali S. Bharate, Shashi Bhushan, Sandip B. Bharate and Ram A. Vishwakarma

Bergenin (1), a unique fused C-glycoside isolated from *Bergenia* species, possesses interesting anti-inflammatory and anti-pain activities. To study SAR of this scaffold, first-generation derivatives were synthesized and evaluated for inhibition of lymphocyte-proliferation and production of pro-inflammatory cytokines. The C-7 substituted derivatives showed inhibition of IL-6 as well as TNF-production. Bergenin and its most potent IL-6 inhibitor derivatives 4e and 4f were then investigated in a panel of *in-vitro* and *in-vivo* inflammation/arthritis models. These compounds significantly decreased the expression of NF-kB and IKK-β in THP-1 cells. In *in-vivo* study in BALB/c mice, a dose-dependent inhibition of SRBC-induced cytokines, reduction in humoral/ cell-mediated immunity and antibody titre was observed. The CIA study in DBA/1J mice indicated that compounds led to reduction in swelling of paws, cytokine levels and anti-collagen IgG1/IgG2a levels. The significant *in-vivo* immunosuppressive efficacy of pyrano-isochromanones demonstrates the promise of this scaffold for development of next-generation anti-arthritic drugs.

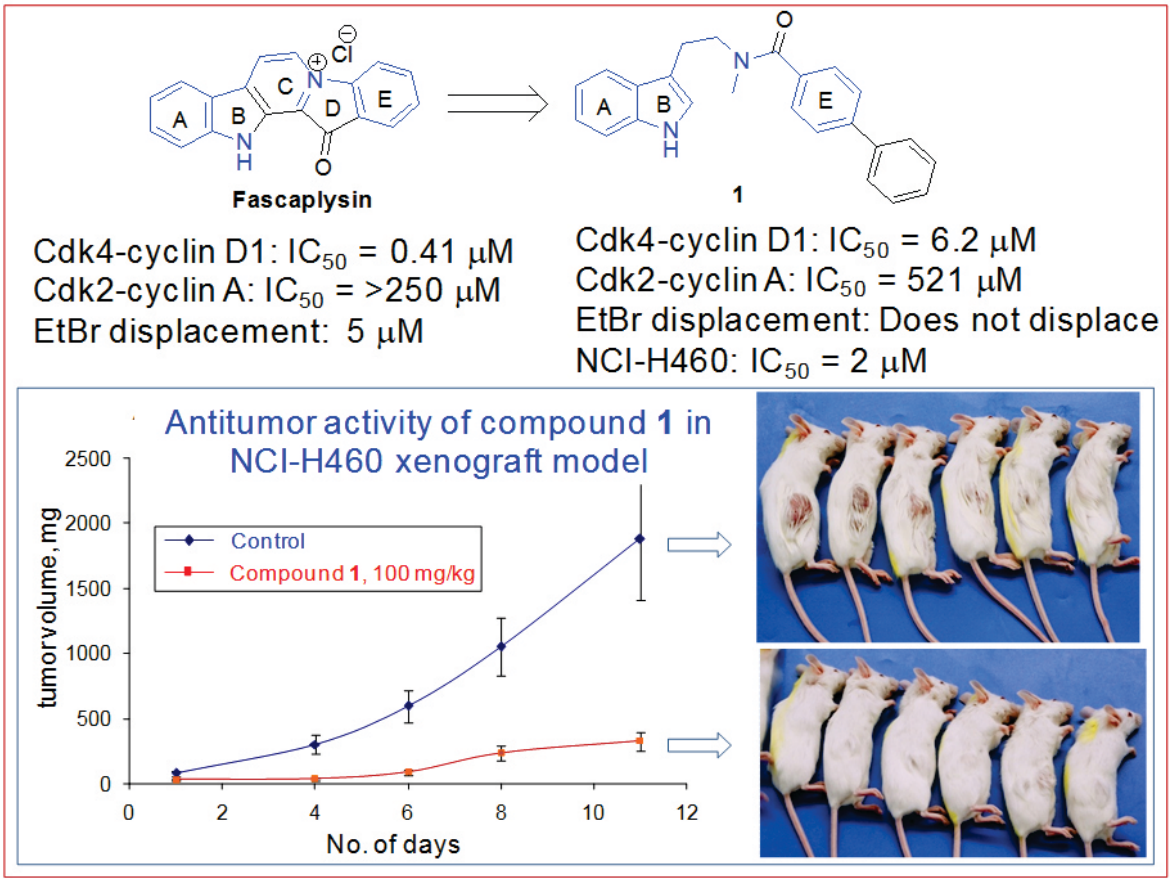


5.9 Biphenyl-4-carboxylic acid [2-(1H-indol-3-yl)-ethyl]-methylamide (CA224), a non-planar analog of fascaplysin inhibits Cdk4 and tubulin polymerization: Evaluation of in vitro and in vivo anticancer activity

Sachin Mahale, Sudhakar Manda, Prashant Joshi, Sonali S. Bharate, Paul R. Jenkins, Sandip B. Bharate, Ram A. Vishwakarma, Bhabatosh Chaudhuri

Biphenyl-4-carboxylic acid-[2-(1H-indol-3-yl)-ethyl]-methylamide 1 (CA224) is a non-planar analog of fascaplysin (2) that specifically inhibits Cdk4-cyclin D1 in-vitro. Compound 1 blocks growth of cancer cells at G_0/G_1 phase of the cell cycle. It also blocks at G_2/M phase which is explained by the fact that it inhibits tubulin polymerization. Besides, it acts as an enhancer of depolymerization for taxol-stabilized tubulin. Western-blot analyses of p53-positive cancer cells treated with compound 1 indicated up-regulation of

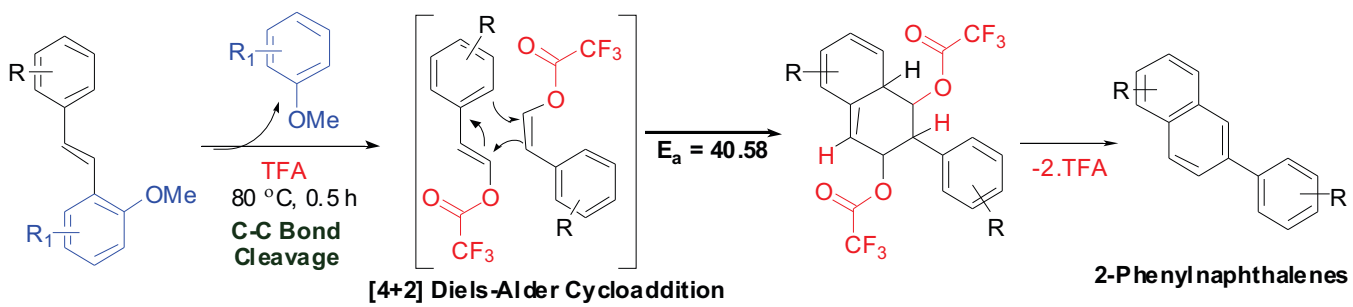
p53, p21 and p27 proteins together with down-regulation of cyclin B1 and Cdk1. Compound 1 selectively induces apoptosis in SV40 large T-antigen transformed cells and significantly reduces colony formation efficiency, in a dose-dependent manner of lung cancer cells. It is efficacious at 1/10th the MTD, against human tumors derived from HCT-116 and NCI-H460 cells in SCID mice models. The promising efficacy of compound 1 in human xenograft models with an excellent therapeutic-window indicates its potential for clinical development.



5.10 Synthesis of 2-phenylnaphthalenes from styryl-2-methoxybenzenes

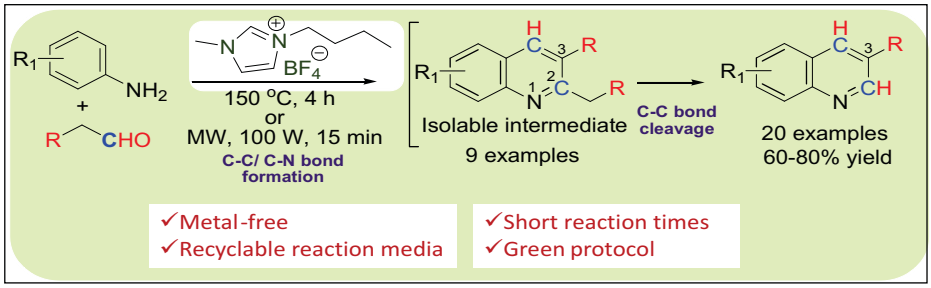
Ramesh Mudududdla, Rohit Sharma, Sheenu Abbat, Prasad V. Bharatam, Ram A. Vishwakarma, Sandip B. Bharate

A new simple and efficient method for the synthesis of 2-phenylnaphthalenes from electron-rich 1-styryl-2-methoxybenzenes has been described. The reaction proceeds via TFA catalyzed C-C bond cleavage followed by intermolecular [4+2]-Diels-Alder cycloaddition of *in situ* formed styrenyl trifluoroacetate intermediate. The quantum chemical calculations identified the transition state for the cycloaddition reaction and helped in tracing reaction mechanism. The method has been efficiently utilized for synthesis of phenanthrene skeleton and a naphthalene-based potent and selective ER-β agonist.



5.11 Metal-free, ionic liquid-mediated synthesis of functionalized quinolines

Jaideep B. Bharate, Sandip B. Bharate and Ram A. Vishwakarma

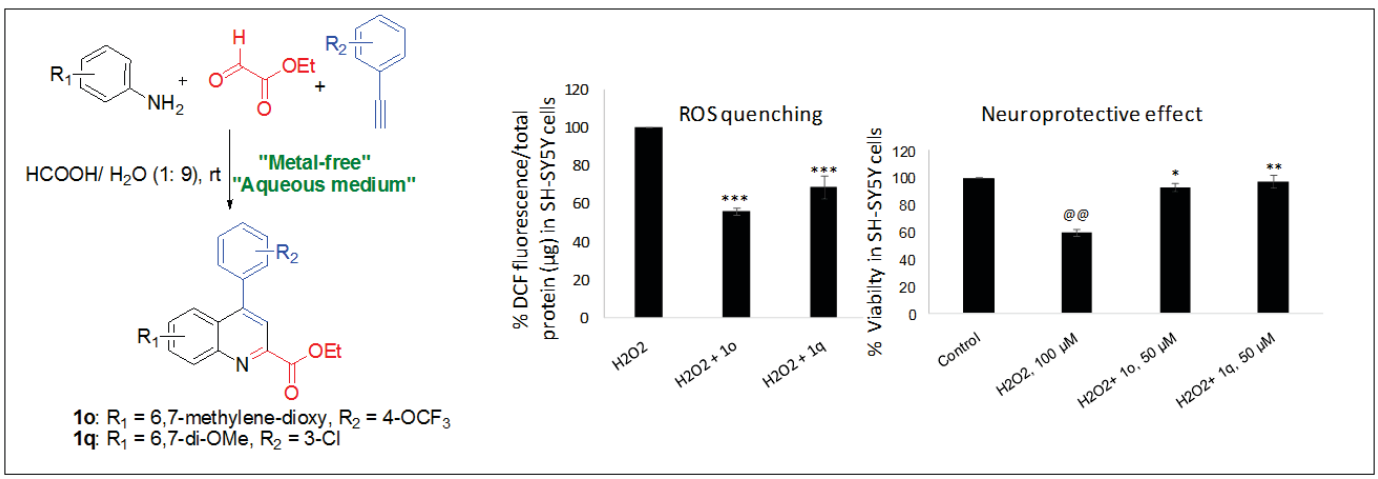


An expedient and metal-free synthetic protocol for construction of substituted quinolines has been developed from anilines and phenylacetaldehydes using imidazolium cation-based ionic liquids as the reaction medium. Mechanistic analysis indicated that the reaction occurs through C-C and C-N bond formation to produce isolable 2,3-disubstituted quinoline intermediates, which undergo C-C bond cleavage to produce 3-substituted quinolines. The reaction proceeds smoothly with a range of functionalities in good to excellent yields. Advantages of this protocol include metal-free, environmentally friendly, recyclable reaction media, higher yields and shorter reaction times, and thus is promising for the efficient combinatorial synthesis of structurally diverse 2,3-disubstituted and 3-substituted quinolines.

5.12 Synthesis, antioxidant, neuroprotective and P-glycoprotein induction activity of 4-arylquinoline-2-carboxylates

Jaideep B. Bharate, Abubakar Wani, Sadhana Sharma, Shahi Imam Reja, Manoj Kumar, Ram A. Vishwakarma, Ajay Kumar and Sandip B. Bharate

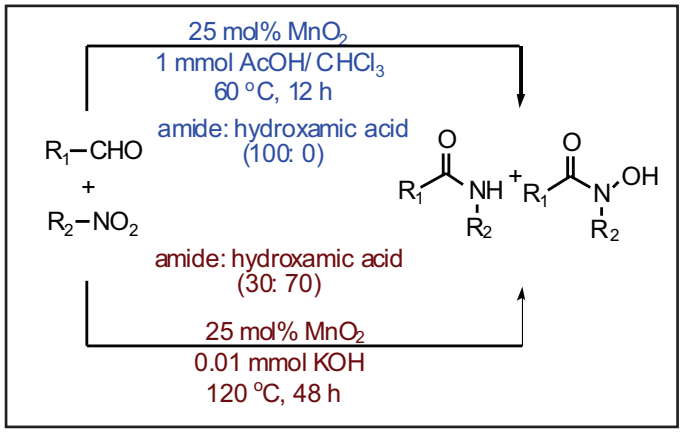
An efficient formic acid catalyzed one-pot synthesis of 4-arylquinoline 2-carboxylates in water via three-component coupling of arylamines, glyoxylates and phenylacetylenes has been described. 4-Arylquinoline 2-carboxylates 1o and 1q displayed significant antioxidant activity as indicated by their Fe-reducing power in ferric reducing ability of plasma (FRAP) assay. The compounds were found to react directly with hydrogen peroxide, which might be one of the mechanism of their antioxidant effect. Compounds 1o and 1q effectively quenched H_2O_2 and amyloid-β-generated reactive oxygen species (ROS) and also displayed significant protection against H_2O_2-induced neurotoxicity in human neuroblastoma SH-SY5Y cells. Additionally, all compounds exhibited promising p-glycoprotein induction activity in human adenocarcinoma LS-180 cells, indicating their potential to enhance amyloid-β clearance from Alzheimer brains. Further, all compounds were relatively non-toxic to SH-SY5Y and LS-180 cells (IC_{50} > 50 μM). The promising antioxidant, ROS quenching, neuroprotective and Pgp-induction activity of these compounds strongly indicate their potential as anti-Alzheimer agents.



5.13 Facile access to amides and hydroxamic acids directly from nitroarenes

Shreyans K. Jain, K.A. Aravinda Kumar, Sandip B. Bharate and Ram A. Vishwakarma

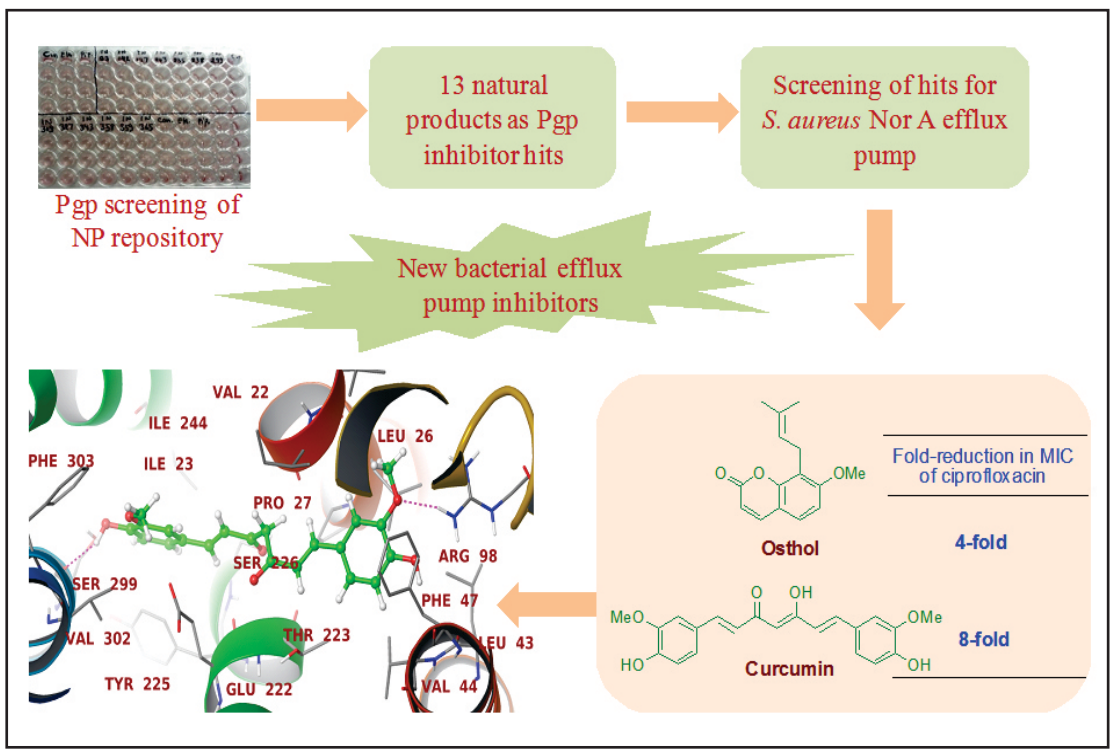
A new method for synthesis of amides and hydroxamic acids from nitroarenes and aldehydes is described. The MnO_2 catalyzed thermal deoxygenation of nitrobenzene resulted in formation of reactive nitroso intermediate which on reaction with aldehydes provided amides and hydroxamic acids. The thermal neat reaction in presence of 0.01 mmol KOH predominantly led to formation of the hydroxamic acid whereas reaction in the presence of 1 mmol acetic acid produced amides as the only product.



5.14 Osthol and curcumin as inhibitors of human Pgp and multidrug efflux pumps of *Staphylococcus aureus*: Reversing the resistance against frontline antibacterial drugs

Prashant Joshi, Samsher Singh, Abubakar Wani, Sadhana Sharma, Shreyans K. Jain, Baljinder Singh, Bishan D. Gupta, Naresh K. Satti, Surrinder Koul, Inshad A. Khan, Ajay Kumar, Sandip B. Bharate and Ram A. Vishwakarma.

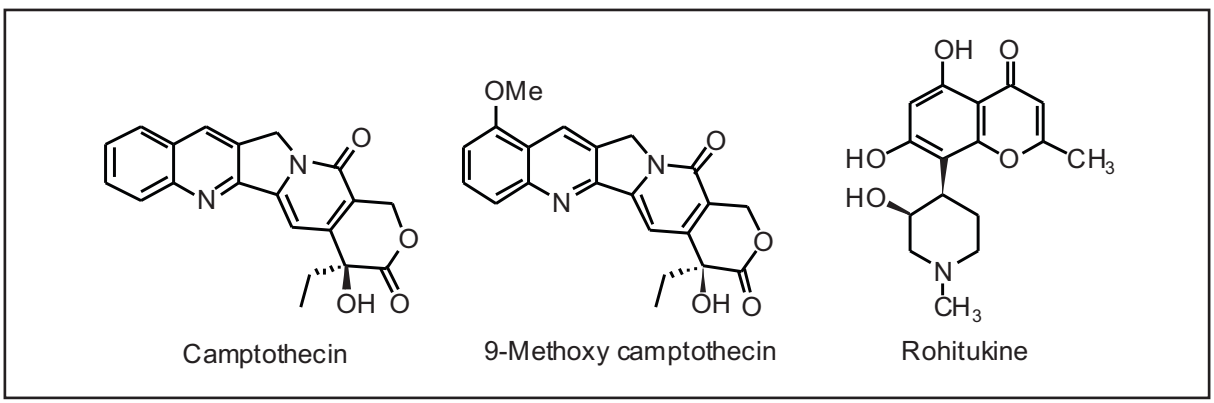
The in-house IIIM natural product repository of 302 small molecules was screened for their ability to inhibit p-glycoprotein (Pgp) in Pgp-overexpressing human adenocarcinoma LS-180 cells. The screening has identified 13 natural products displaying significant Pgp-inhibition activity which include praeruptorin B, curcumin, imperatorin, osthol, 5,7-diacetoxy-8-(3-methyl-2-butenyl)-coumarin, 5,7-dihydroxy-8-(3-methyl-2-butenyl) coumarin, pongamol, phellopterin, tangerettin, 3-(2-methyl but-3-en-2-yl) xanthyletin, 7-demethyl osthol, allorottlerin and tetrahydroangeolide. These natural products were then screened for their effect on bacterial efflux pump inhibition activity against Nor A (*Staphylococcus aureus*), Mde A (*S. aureus* Mup^r-1), Tet K (*S. aureus* SA-K2192), and Msr A (*S. aureus* SA-K2191) efflux pumps. The curcumin and osthol showed significant inhibition of *S. aureus* Nor A efflux pump with 8- and 4-fold reductions in the MIC of ciprofloxacin at 25 μM. The molecular docking studies of curcumin and osthol with the human Pgp and *S. aureus* Nor A efflux pump identified plausible binding mode and binding site for these natural products.



5.15 *Dysoxylum binectariferum* bark as a new source of anticancer drug camptothecin: Bioactivity-guided isolation and LCMS-based quantification

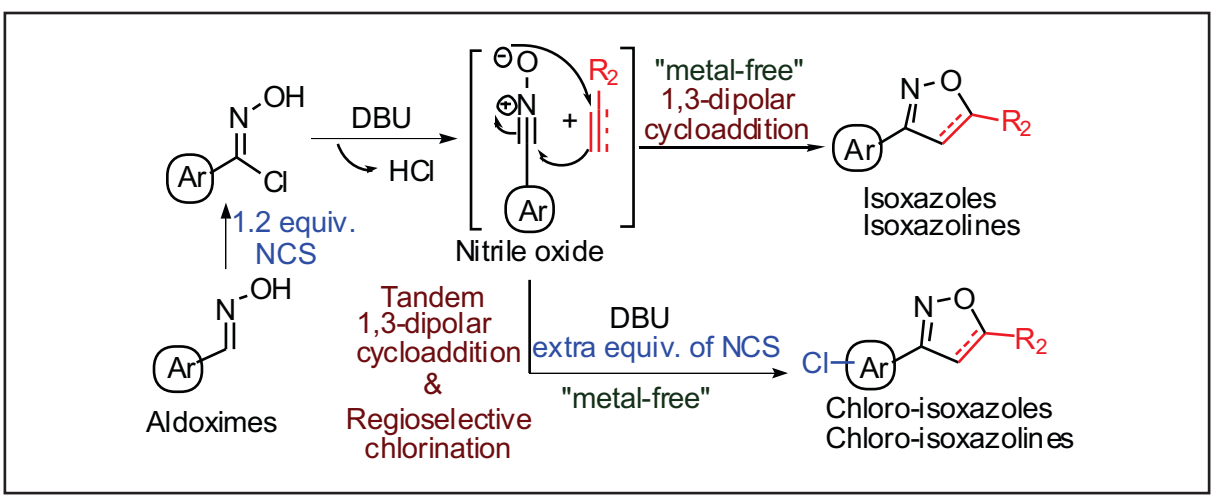
Shreyans K. Jain, Samdarshi Meena, Ajai P. Gupta, Manoj Kushwaha, R. Uma Shaanker, Sundeep Jaglan, Sandip B. Bharate and Ram A. Vishwakarma

Camptothecin (CPT, **1**) is a potent anticancer natural product which led to the discovery of two clinically used anticancer drugs topotecan and irinotecan. These two drugs are semisynthetic analogs of CPT, and thus the commercial production of CPT as a raw material from various plant sources and tissue culture methods is highly demanding. In the present study, the *Dysoxylum binectariferum* bark, was identified as an alternative source of CPT, through bioassay-guided isolation. The barks showed showed presence of CPT (**1**) and its 9-methoxy analog **2**, whereas CPT alkaloids were not present in seeds and leaves. This is the first report on isolation of CPT alkaloids from Meliaceae family. An efficient chromatography-free procotol for enrichment and isolation of CPT from *D. binectariferum* has been established, which was able to enrich CPT up to 21% in the crude extract. The LCMS (MRM)-based quantification method revealed the presence of 0.105% of CPT in dry barks of *D. binectariferum*. The discovery of CPT from *D. binectariferum* bark will certainly create a global interest in cultivation of this plant as a new crop for commercial production of CPT. Isolation of anticancer drug CPT from this plant, indicates that along with rohitukine, CPT and 9-methoxy CPT also contributes significantly to the cytotoxicity of *D. binectariferum*.



5.17 Metal-free DBU promoted regioselective synthesis of isoxazoles and isoxazolines

Shabber Mohammed, Ram A. Vishwakarma, Sandip B. Bharate

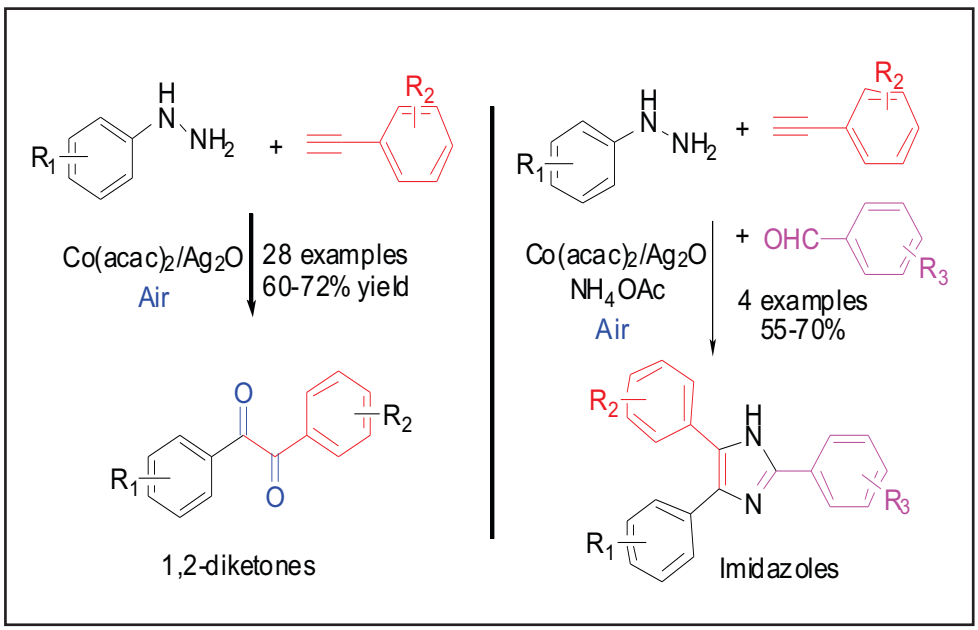


A new simple and efficient metal-free 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) promoted regioselective synthesis of 3,5-disubstituted isoxazoles and isoxazolines from aldoximes has been described. This method allows reaction to proceed efficiently on aldoximes containing unprotected phenolic hydroxyl group. Furthermore, with the use of higher equivalents of N-chlorosuccinimide, chloro-substituted isoxazoles and isoxazolines were obtained as the only products via tandem one-pot 1,3-dipolar cycloaddition followed by regioselective chlorination.

5.18 Cobalt (II) catalyzed C(sp)-H bond functionalization of alkynes with phenyl hydrazines: A facile access to diaryl 1,2-diketones

Jaideep B. Bharate, Sheenu Abbat, Rohit Sharma, P.V. Bharatam, R.A. Vishwakarma and Sandip B. Bharate

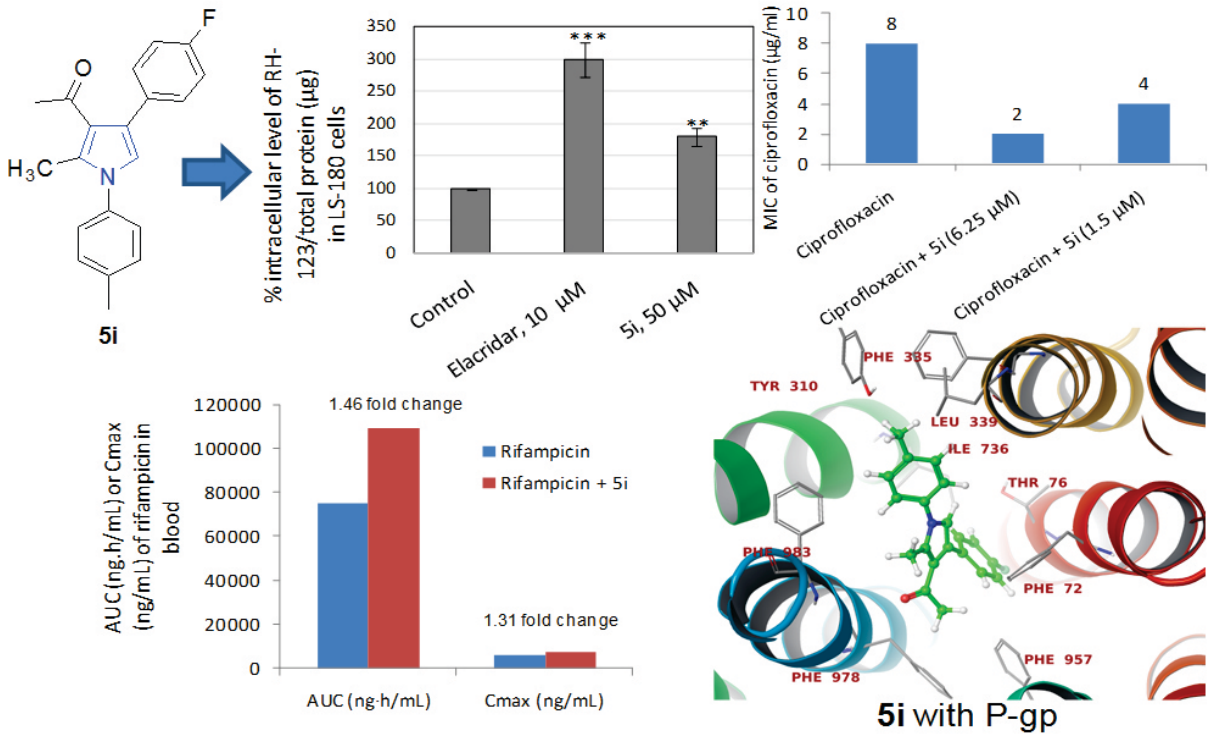
A cobalt acetylacetonate catalyzed oxidative diketonation of alkynes via C(sp)-H bond functionalization has been described. The reaction involves a free-radical mechanism, wherein the phenyl radical formed from phenyl hydrazine couples with Co(II) activated alkyne to produce 1,2-diketones. The reaction proceeds at room temperature in DMF with the use of Ag_2O/air as oxidizing system. The utility of the protocol for synthesis of a series of imidazoles including a potent platelet aggregation inhibitor trifenagrel has been demonstrated.



5.19 Discovery of 4-acetyl-3-(4-fluorophenyl)-1-(p-tolyl)-5-methylpyrrole as a dual inhibitor of human P-glycoprotein and *Staphylococcus aureus* Nor A efflux pump

Jaideep B. Bharate, Samsher Singh, Abubakar Wani, Sadhana Sharma, Prashant Joshi, Inshad A. Khan, Ajay Kumar, R.A. Vishwakarma, Sandip B. Bharate

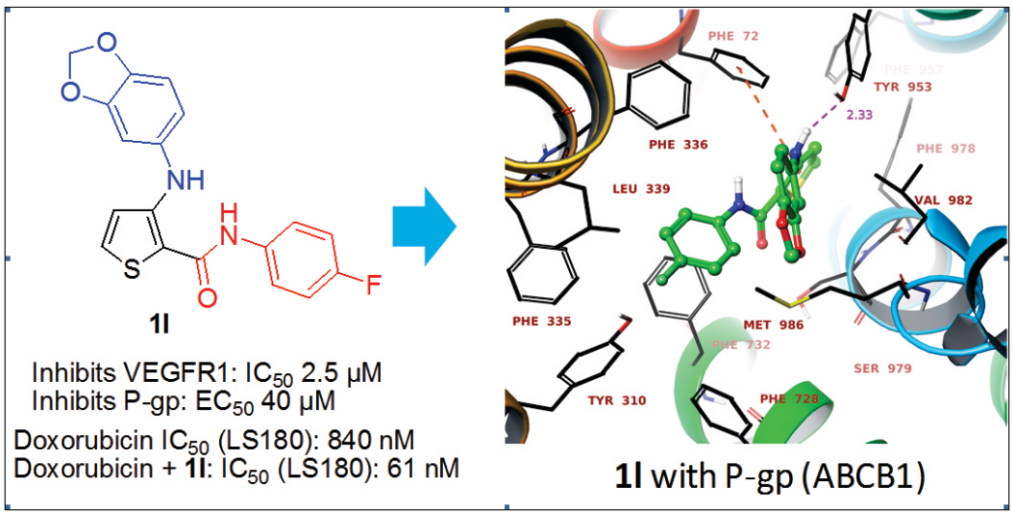
Polysubstituted pyrrole natural products lamellarins are known to overcome multi-drug resistance in cancer via inhibition of p-glycoprotein (P-gp) and breast cancer resistance protein (BCRP) efflux pumps. Herein, a series of simplied polysubstituted pyrroles, prepared via one-pot domino protocol, were screened for P-gp inhibition in P-gp overexpressing human adenocarcinoma LS-180 cells using rhodamine 123 efflux assay. Several compounds showed significant inhibition of P-gp at 50 μM, as indicated by increase in intracellular accumulation of Rh123 in LS-180 cells. Furthermore, pyrrole 5i decreased the efflux of digoxin, a FDA approved P-gp substrate in MDCK-MDR1 cells with IC_{50} of 11.2 μM. In in-vivo studies, following oral administration of a P-gp substrate drug rifampicin along with compound 5i, the C_{max} and AUC_{0-} of rifampicin was enhanced by 31 and 46%. All compounds were then screened for their ability to potentiate ciprofloxacin activity via inhibition of *Staphylococcus aureus* Nor A efflux pump. Pyrrole 5i showed significant inhibition of *S. aureus* Nor A efflux pump with 8- and 4-fold reductions in the MIC of ciprofloxacin at 50 and 6.25 μM, respectively. The molecular docking studies of compound 5i with the human P-gp and *S. aureus* Nor A efflux pump identified its plausible binding site and key interactions. Thus, the results presented herein strongly indicate the potential of this scaffold for use as multi-drug resistance reversal agents or bioavailability enhancers.



5.20 3-(Benzo[d][1,3]dioxol-5-ylamino)-N-(4-fluorophenyl)thiophene-2-carboxamide overcomes cancer chemoresistance via inhibition of angiogenesis and P-glycoprotein efflux pump activity

Ramesh Mudududdla, Santosh K. Guru, Abubakar Wani, Sadhana Sharma, Prashant Joshi, R.A. Vishwakarma, Ajay Kumar, Shashi Bhushan, Sandip B. Bharate

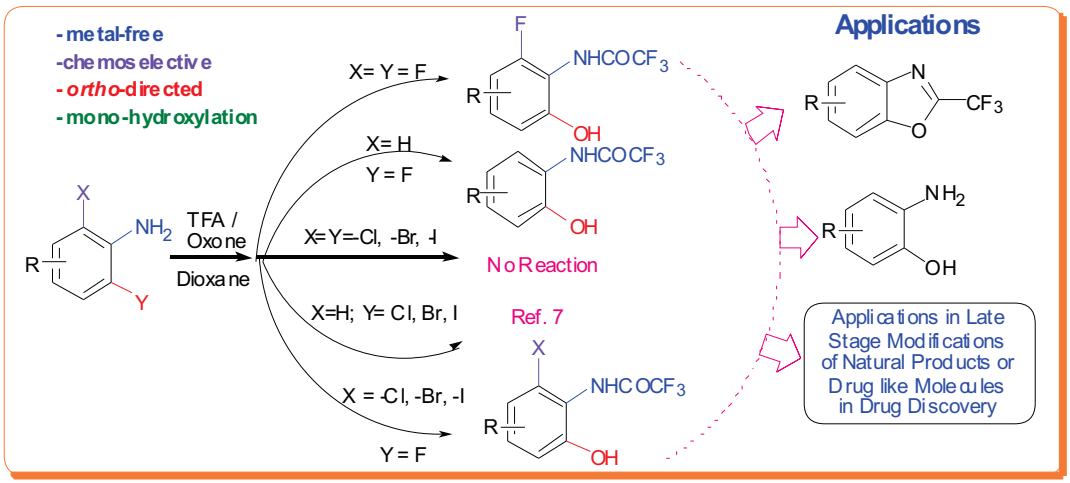
3-((Quinolin-4-yl)methylamino)-N-(4-(trifluoromethoxy) phenyl) thiophene-2-carboxamide (OSI-930, 1) is a potent inhibitor of c-kit and VEGFR2, currently under phase I clinical trials in patients with advanced solid tumors. In order to understand the structure-activity relationship, a series of 3-arylamino N-aryl thiophene 2-carboxamides were synthesized by modifications at both quinoline and amide domain of OSI-930 scaffold. All synthesized compounds were screened for in-vitro cytotoxicity in a panel of cancer cell lines and for VEGFR1 and VEGFR2 inhibition. Thiophene 2-carboxamides substituted with benzo[d][1,3] dioxol-5-yl and 2,3-dihydrobenzo[b] [1,4] dioxin-6-yl groups 1l and 1m displayed inhibition of VEGFR1 with IC_{50} values of 2.5 and 1.9 μM, respectively. Compounds 1l and 1m also inhibited the VEGF-induced HUVEC cell migration, indicating its anti-angiogenic activity. OSI-930 along with compounds 1l and 1m showed inhibition of P-gp efflux pump (MDR1, ABCB1) with EC_{50} values in the range of 35-74 μM. The combination of these compounds with doxorubicin led to significant enhancement of the anticancer activity of doxorubicin in human colorectal carcinoma LS180 cells, which was evident by the improved IC_{50} of doxorubicin, increased activity of caspase-3 and significant reduction in colony formation ability of LS180 cells after treatment with doxorubicin. Compound 1l showed 13.8-fold improvement in the IC_{50} of doxorubicin in LS180 cells. The ability of these compounds to possess dual inhibition of VEGFR and P-gp efflux pump demonstrates the promise of this scaffold for development as multi-drug resistance-reversal agents.



5.21 Metal-free Chemoselective ortho-C(sp2)–F Bond Hydroxylation and N-trifluoroacylation of Fluoroarylamines for Domino Synthesis of N-trifluoroacyl-ortho-aminophenols

V. Venkateswarlu, S. Balgotra, R. A. Vishwakarma, S. D. Sawant.

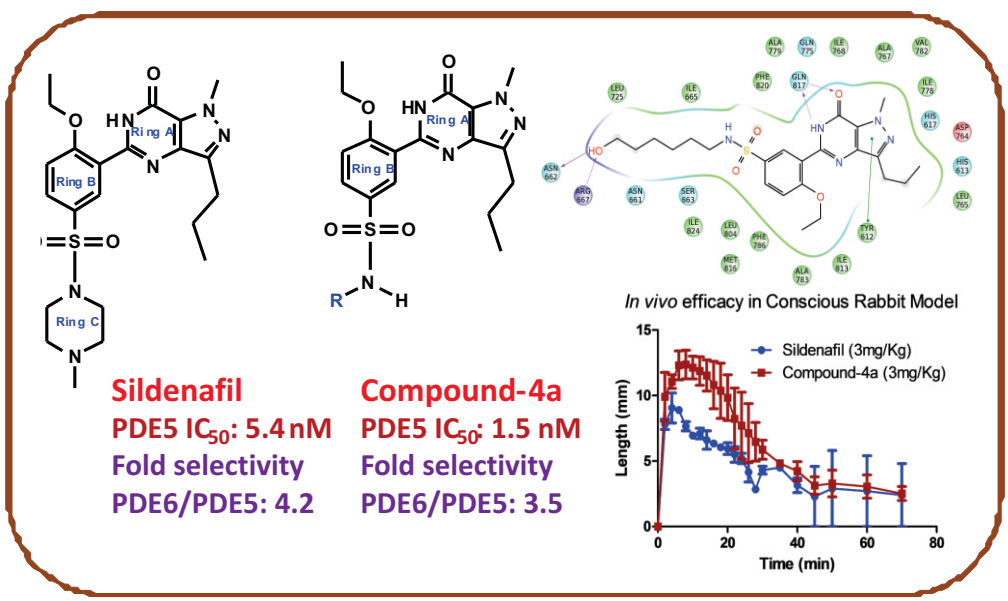
A novel reaction in the context of chemoselectivity for formation of C–O bond by C(sp^2)–F bond cleavage and concomitant *N*-trifluoroacylation of fluoroanilines using TFA/oxone is presented. This domino reaction gives *ortho*-hydroxy-*N*-trifluoroacetanilides in good yields under metal-free conditions in a single step. Selective *ortho*-directed mono-hydroxylation and *N*-trifluoroacylation of 2- and 6-fluoro or 2, 6-difluoro substituted anilines takes place in this transformation.



5.22 Discovery of Novel Pyrazolopyrimidinone Analogs as Potent Inhibitors of Phosphodiesterase Type-5

S. D. Sawant, G.L. Reddy, M. Ishaq Dar, M. Srinivas, G. Gupta, P. K. Sahu, P. Mahajan, S. Singh, S.C. Sharma, M. Tikoo, G. D. Singh, A. Nargotra, R. A. Vishwakarma, Sajad Hussain Syed

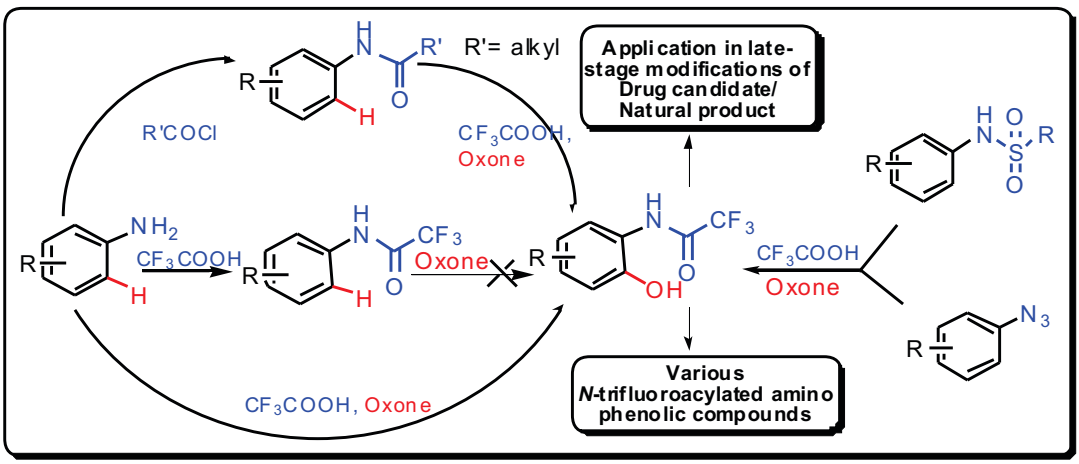
Cyclic guanosine monophosphate (cGMP) specific phosphodiesterase type-5 (PDE5), a clinically proven target to treat erectile dysfunction and diseases associated with lower cGMP levels in humans, is present in corpus cavernosum, heart, lung, platelets, prostate, urethra, bladder, liver, brain, and stomach. Sildenafil, Vardenail,Tadalafil and Avanafil are FDA approved drugs in the market as PDE5 inhibitors for treating erectile dysfunction. In the present study a lead molecule 4-ethoxy-N-(6-hydroxyhexyl)-3-(1-methyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl) benzenesulfonamide *i.e.* Compound-4a, an analog of pyrazolopyrimidinone scaffold has been identified as selective PDE5 inhibitor. A series of compounds was synthesized by replacing *N*-methylpiperazine moiety (ring-C) of sildenafil structure with different *N*-substitutions towards sulfonamide end. Compound-4a showed lower IC_{50} value (1.5 nM) against PDE5 than parent sildenafil (5.6 nM) in *in vitro* enzyme assay. The isoform selectivity of the compound-4a against other PDE isoforms was similar



to that of the Sildenafil. In corroboration with the *in vitro* data, this molecule showed better efficacy in *in vivo* studies using the Conscious Rabbit Model. Also compound-**4a** exhibited good physicochemical properties like solubility, Caco-2 permeability, cLogP along with optimal PK profile having no significant CYP enzyme inhibitory liabilities. Discovery of these novel bioactive compounds may open a new alternative for developing novel preclinical candidates based on this drugable scaffold.

5.23 C-H Oxygenation and N-Trifluoroacylation of Arylamines under Metal-Free Conditions: A Convenient Approach to 2-Aminophenols and N-Trifluoroacyl-ortho-aminophenols

V. Venkateswarlu, K. A. Aravinda Kumar, S. Balgotra, G. L. Reddy, M. Srinivas, R. A. Vishwakarma, S. D. Sawant

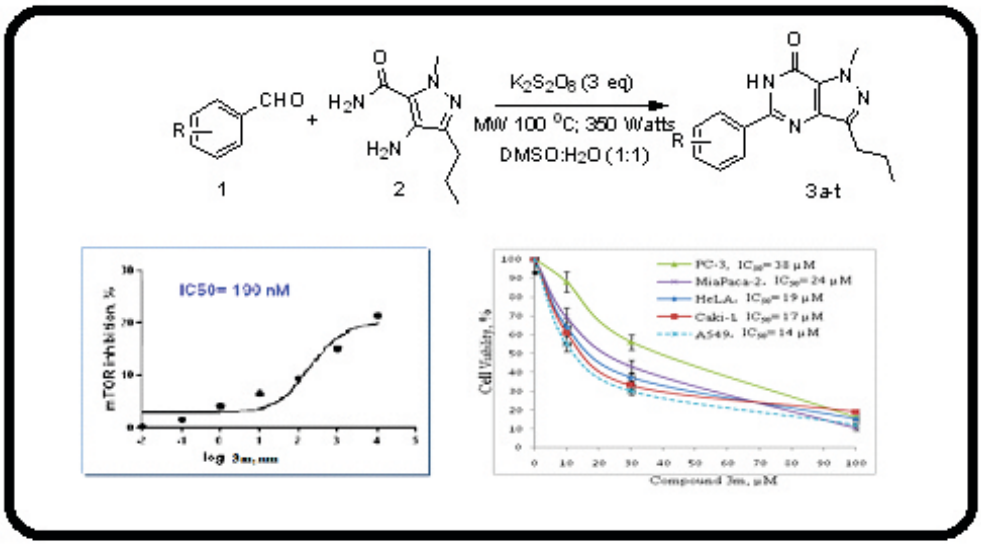


The unique reaction in the context of selective and direct *ortho*-hydroxylation *via* C–H oxygenation and *N*-trifluoroacylation of anilines in a single step under metal-free conditions is presented using oxidative combination of TFA/oxone for the formation of functionalized amino phenolic compounds *i.e.* *ortho*-hydroxy-*N*-trifluoroacetanilides in good yields with wide substrate scope and applications of method.

5.24 Synthesis of 5-substituted-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one analogs and their biological evaluation as anticancer agents: mTOR inhibitors

G. L. Reddy, S. K. Guru, M. Srinivas, A. S. Pathania, P. Mahajan, A. Nargotra, S. Bhushan, R. A. Vishwakarma, S. D. Sawant

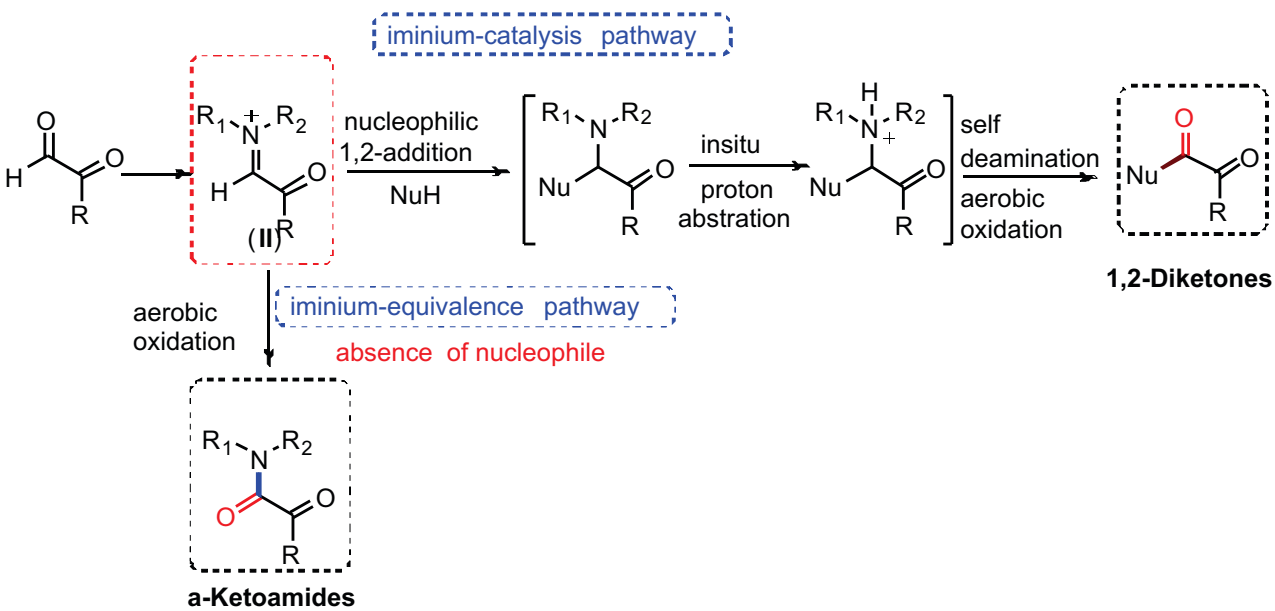
A microwave assisted strategy for synthesis of series of 1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-ones has been developed and their biological evaluation as anticancer agents is described. The synthetic protocol involves simple procedure by oxidative coupling of 4-amino-1-methyl-3-propyl-1*H*-pyrazole-5-carboxamide with different aldehydes in presence of $K_2S_2O_8$ offering 5-substituted-1*H*-pyrazolo[4,3-*d*]pyrimidin-7(6*H*)-one compounds in excellent yields. The *in vitro* anticancer activity screening against human cancer cell lines HeLa, CAKI-I, PC-3, MiaPaca-2, A549 gave good results. The in detailed mechanistic correlation studies of compound **3m** revealed that the compound shows anticancer activity through apoptosis mechanism and also inhibits mTOR with nonomolar potency. The design was based on docking with mTOR protein. The concentration dependent cell cycle analysis, western blotting experiment and nuclear cell morphology studies have been described.



5.25 Aminocatalytic Cross-Coupling Approach via Iminium Ions to Different C_C Bonds.

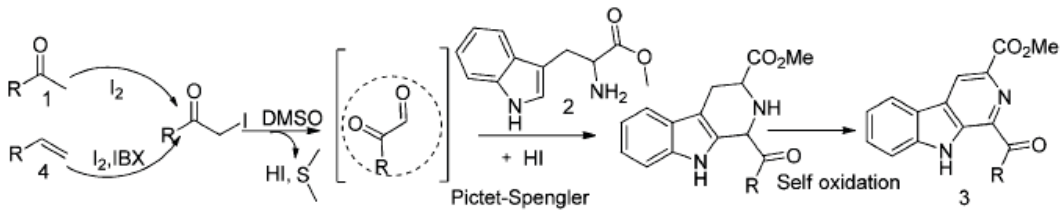
Nagaraju Mupparapu, Narsaiah Battini, Satyanarayana Battula, Shahnawaz Khan, Ram A. Vishwakarma, and Qazi Naveed Ahmed.

Given the attractive ability of iminium ions to functionalize molecules directly at ostensibly unreactive positions, the reactivity of iminium ions, in which an a CH2 group is replaced by C=O was explored. Background studies on the ability of such iminium cations to promote reactions via an iminium-catalyzed or iminium-equivalent pathway are apparently unavailable. Previously, tandem cross-coupling reactions were reported, in which an iminium ion undergoes nucleophilic 1,2-addition to give a putative three-component intermediate that abstracts a proton in situ and undergoes self-deamination followed by unprecedented DMSO/ aerobic oxidation to generate a-ketoamides. However, later it was observed that iminium ions can generate valuable aketoamides through simple aerobic oxidation. In all reactions, iminium ions were generated in situ by reaction of 2-oxoaldehydes with secondary amines.



5.26 Unexplored reactivity of 2-oxoaldehydes towards Pictet–Spengler conditions: concise approach to b-carboline based marine natural products.

Narsaiah Battini Anil K. Padala,Nagaraju Mupparapu,Ram A. Vishwakarma and Qazi Naveed Ahmed

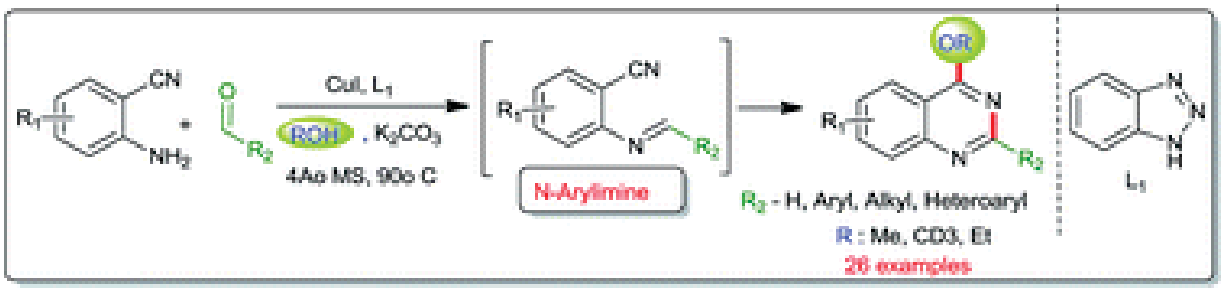


Novel reactions under Pictet–Spengler conditions between tryptophan methyl ester/tryptamine and 2-oxoaldehydes have been developed and successfully utilized for the total synthesis of Merinacarboline (A and B), Eudistomin Y1, Pityriacitrin B, Pityriacitrin, Fascaplysin and analogues.

5.27 Cu–benzotriazole-catalyzed electrophilic cyclization of N-arylimines: a methodical tandem approach to O-protected -4hydroxyquinazolines.

Satyanarayana Battula, Ram A. Vishwakarma and Qazi Naveed Ahmed.

A remarkably efficient approach to O-protected-4-hydroxyquinazolines has been developed via the copper–benzotriazole (Cu–BtH)-catalyzed intramolecular electrophilic cyclization of N-arylimines, achieved through the reaction of 2-aminobenzonitriles and various aldehydes.



5.28 A novel quinazolinone derivative induces cytochrome cinterdependent apoptosis and autophagy in human leukemiaMOLT-4 cells.

Suresh Kumara, Santosh Kumar Gurua Anup Singh Pathaniaa, Nagaraju Mupparapua,Ajay Kumarb, Fayaz Malika, Sandip B. Bharatea Qazi Naveed Ahmeda, Ram A. Vishwakarma, Shashi Bhushana.

Crosstalk between apoptosis and autophagy is budding as one of the novel strate-gies in the cancer therapeutics. The present study tinted toward the interdependenceof autophagy and apoptosis induce by a novel quinazolinone derivative 2,3-dihydro-2-(quinoline-5-yl) quinazolin-4(1H)-one structure [DQQ] in human leukemia MOLT-4 cells.DQQ induces cytochrome c arbitrated apoptosis and autophagy in MOLT-4 cells. Apopto-sis induces by DQQ was confirmed through a battery of assay e.g. cellular and nuclearmicroscopy, annexin-V assay, cell cycle analysis, loss of mitochondrial membrane poten-tial and immune-expression of cytochrome c, caspases and PARP. Furthermore, acridineorange staining, LC3 immunofluorescence and western blotting of key autophagy pro-teins revealed the autophagic potential of DQQ. A universal caspase inhibitor, Z-VAD-FMKand cytochrome c silencing, strongly inhibited the DQQ induce autophagy and apopto-sis. Beclin1 silencing through siRNA partially reversed the cell death, which was not assignificant as by cytochrome c silencing. Although, it partially reversed the PARP cleav-age induced by DQQ, indicating the role of autophagy in the regulation of apoptosis. Thepresent study first time portrays the negative feedback potential of cytochrome c regulatedautophagy and the importance of quinazolinone derivative in discovery of novel anticancer therapeutics.

6. FERMENTATION TECHNOLOGY

6.1 Production of borrelidin from *Streptomyces rochei* (ATCC 10739)

Ankita Magotra, Chand Raina, Asif Ali, AP Gupta, Ram Vishwakarma and Asha Chaubey

Borrelidin, originally discovered as active against Borrelia species, is an 18 member polyketide macrolide with molecular formula $C_{28}H_{43}NO_6$. It is a crystalline white solid having molecular weight of 489.6 Da. Borrelidin is a selective inhibitor of bacterial and eukaryote threonyl-tRNA synthetase. Examples of highly sensitive organisms are *S. aureus*, *E.coli* and *S.cerevisiae*. Borrelidin also inhibits the cyclin-dependent kinase Cdc28/Cln2 in *S.cerevicae*. Apart from this, it has the property of inhibiting ThrRS and hence has a great potential to inhibit angiogenesis. Keeping in view the biological significance of borrelidin, and in order to produce borrelidin indigenously in larger quantities for the synthesis of new analogues, we initiated efforts towards optimization of fermentation conditions to get maximum production of borrelidin. A rapid, precise and sensitive LC-ESI-MS/MS method for detection and quantification of borrelidin produced by *Streptomyces rochei* (ATCC 10739) was developed.

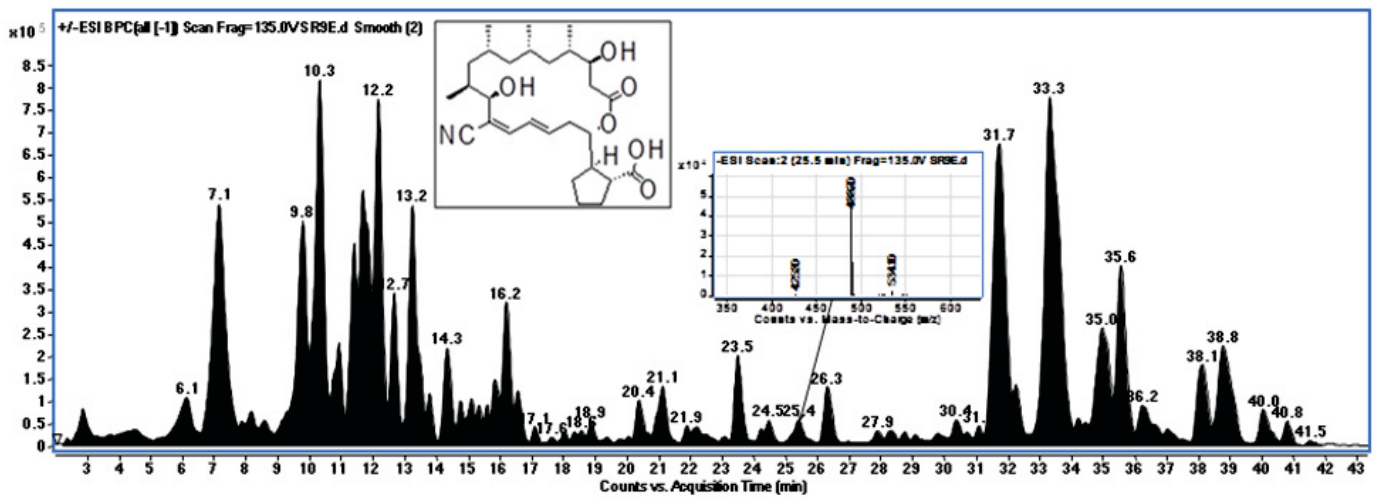


Figure 6.1.1. TIC of crude ethyl acetate extract of Streptomyces rochei (Insight MS spectra of borrelidin in negative mode and structure) for identification

Effect of fermentation conditions, seed and production media on borrelidin production

Present study was aimed to optimize the conditions for borrelidin production from S. rochei and its isolation. We, therefore, used two seed media and based on the results of antimicrobial activity profile and quantity of crude extract, we selected a suitable seed medium for further studies. Similarly, amongst several production media, PM-1 was found to provide better borrelidin production (Figure 6.1.1) as well as anti-microbial activities. To evaluate the effect of pH of the production medium, initial pH of the production medium was set from 5.0 to 9.0 and culture was allowed to grow for two weeks. Ethyl acetate extracts were analysed for borrelidin content followed by evaluation of antimicrobial activities. The experiments revealed that pH 7.0 supported better production as well as antimicrobial activities. Fermentation experiment was carried out in a 50L fermentor (30L working volume) under optimised conditions as described above. The biomass and supernatant were separated by centrifugation, followed by extraction of biomass with methanol and supernatant with ethyl acetate and butanol. With all the optimized conditions, 2.052 mg of borrelidin per gram of crude extract was achieved as shown in figure 6.1.2.

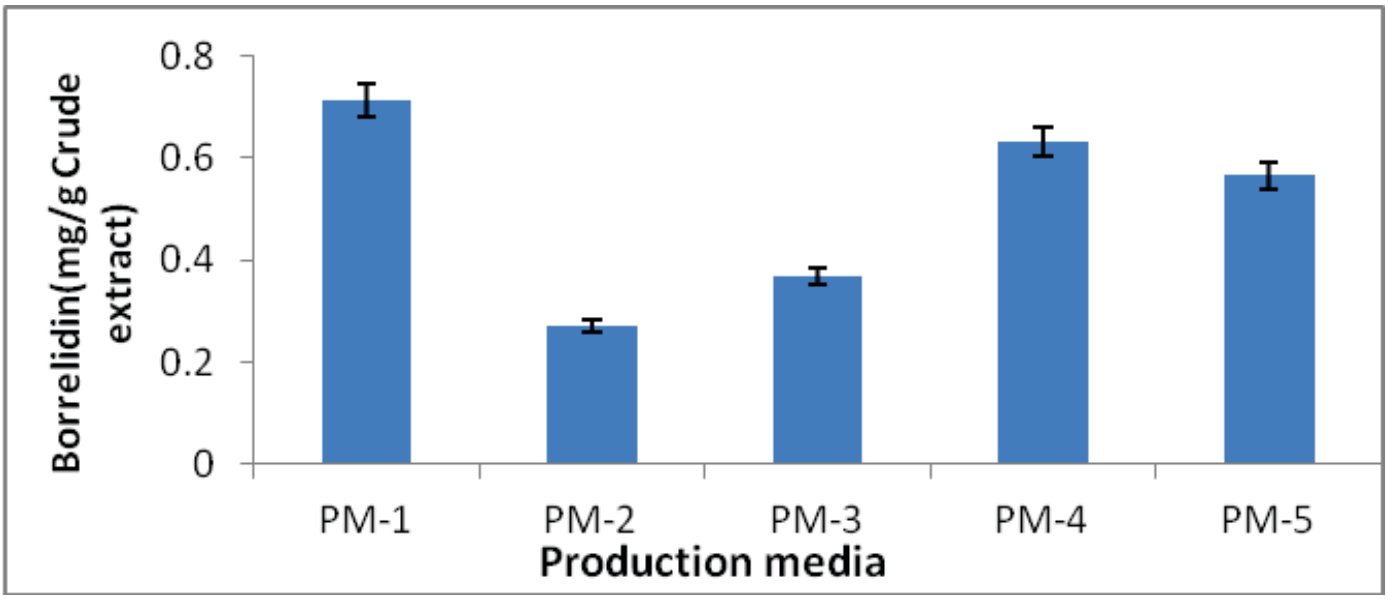


Figure 6.1.2. Effect of production media on antimicrobial activity of ethyl acetate crude extract

6.2 Saccharonol B: a new cytotoxic methylated isocoumarin from *Saccharomonospora azurea*

RK Khajuria, Sandip Bharate, Ram Vishwakarma and Rajinder Parshad

From an actinomycete strain of *Saccharomonospora azurea* (MTCC11714) isolated from high altitude soil of Kargil (J&K, India), a new isocoumarin saccharonol B (2), along with two known compounds viz. saccharonol A (1) and piericidin A3 (3) was isolated and characterized. *Saccharomonospora azurea* (MTCC11714) was grown in 7 L fermenter using CYPS (casein starch medium without agar) keeping the agitation 300 rpm, temperature 28°C and air 1 vvm for 120 h. The fermented broth was extracted following the NCI protocol and passed through Dianion HP-20 resin. Sephadex LH-20. Saccharonol B (2) exhibited mild antimicrobial activity against a standard panel of microorganisms *Staphylococcus aureus* ATCC 29213, *Candida albicans* ATCC 90028, and *Aspergillus fumigatus* MTCC 1811 with MIC values in the range of 128–248 μg/mL. Saccharonol B (2) and piericidin A3 (3) showed selective cytotoxic activity against human pancreatic carcinoma cell line (MIAPaCa-2) with IC50 values of 9 and 8 μM, respectively. Mechanistic studies indicated that saccharonol B (2) arrests S-phase of the cell cycle and causes dose-dependent loss of mitochondrial potential in MIAPaCa-2 cells.

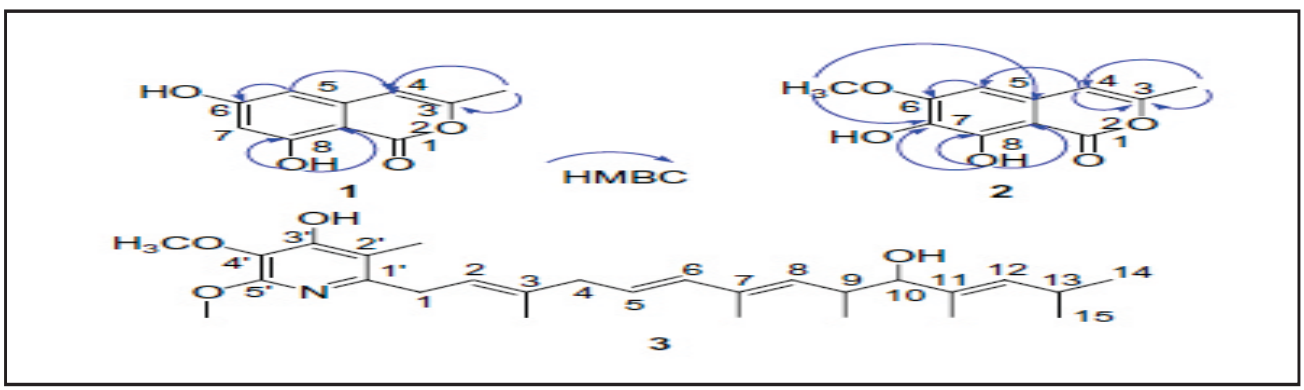


Figure 6.2.1. Compounds isolated from Saccharomonospora azurea (MTCC11714)

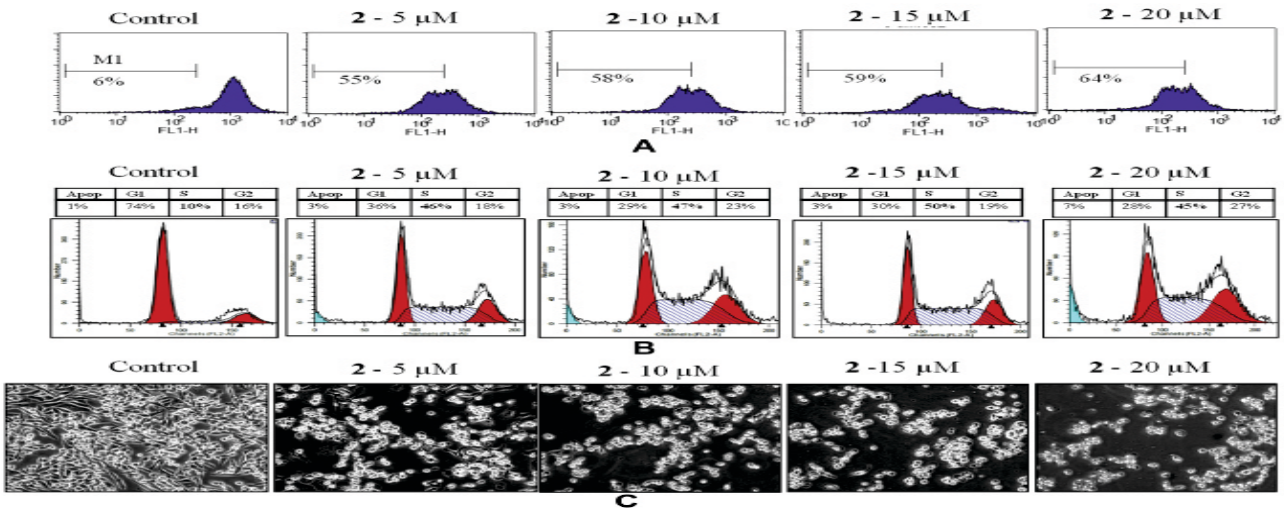


Figure 6.2.2 Compound 2 induced mitochondrial potential loss in pancreatic cancer MIAPaCa-2 cells. Cells were treated with compound 2 at 5, 10, 15, and 20 μm concentration for 48 h. Cells were stained with rhodamine-123 (final conc 10 nM) for 30 min and analyzed in FL-1 versus count channels of flow cytometer. Data are representative of one of three similar experiments at different time periods. (B) Cell cycle analysis of compound 2 in MIAPaCa-2 cells. Pancreatic cancer MIAPaCa-2 cells were treated with compound 2 for 48 h at 5, 10, 15, and 20 μm concentrations. Cells were stained with Propidium iodide, PI (10 μg/ml) to determine DNA fluorescence and cell cycle phase distribution. The fraction of cells from apoptosis, G1, S, and G2 phases analyzed from FL2-A versus cell counts is shown in percentage. Data are representative of one of three similar experiments. (C) Effect of compound 2 on cellular and nuclear morphology of pancreatic cancer MIAPaCa-2 cells. Cells were treated with 5, 10, 15, and 20 μm concentration of compound 2 for 48 h time period. Cells were visualized for cellular morphology using phase contrast microscopy.

6.3 Chrysomycins A–C, antileukemic naphthocoumarins from Streptomyces sporoverrucosus

Chand Raina, Sandip Bharate, Ram Vishwakarma and Rajinder Parshad

Two known naphthocoumarins, chrysomycins A (1) and B (2), along with one new naphthocoumarin chrysomycin C (3) were isolated from the antimicrobial strain of *Streptomyces sporoverrucosus* (MTCC11715) and characterized. chrysomycins D and E were identified using LCMS, UV and DNP information as shown in figure 6.3.1.

Streptomyces sporoverrucosus (MTCC11715) was grown in 7 L fermenter (NBS, USA Model, Biofow110) with a working volume of was centrifuged at 10000 x g for 5 mins. and the supernatant was treated with hydrophobic resin HP 20. The resin was washed with sterilized distilled water and then eluted with methanol. The methanol extract was concentrated to dryness using a speed-vac. The pellet

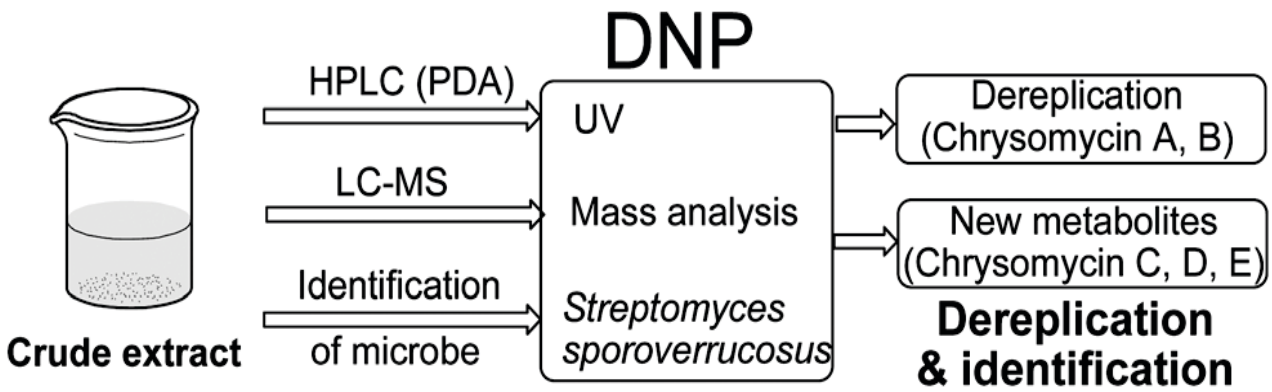


Figure 6.3.1. Dereplication strategy employed in the present study.

Chrysomycins A (1) and B (2) were identified using a strategic HPLC–PDA/LCMS and Dictionary of Natural Products (DNP) based fast dereplication. Additionally, two new naphthocoumarins, 5.0 L using CYP (casein starch without agar) by keeping the agitation at 300 rpm, temperature 28^{0}C and air 1 vvm for 120 h. The fermenter was terminated after 120 h fermentation. the fermented broth was homogenized in methanol and the methanol fraction was concentrated using a rotavapor. Chrysomycins A–C (1–3) were isolated for the first time from *Streptomyces sporoverrucosus*.

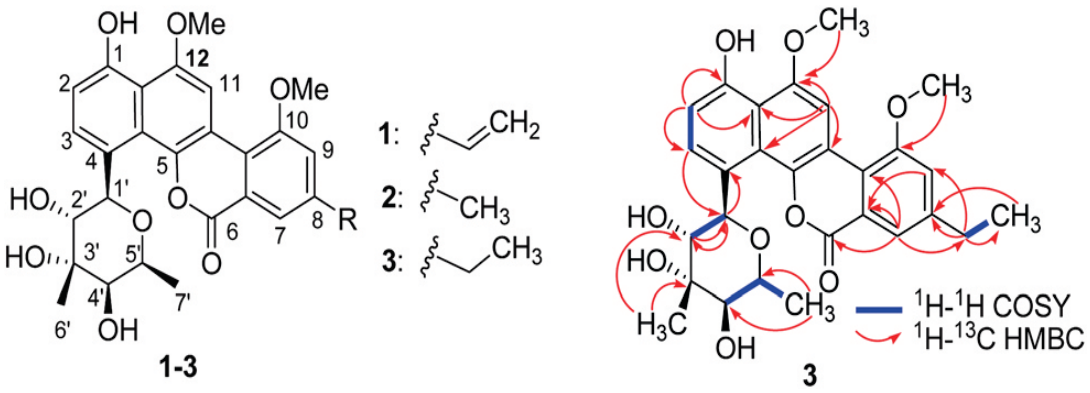


Figure 6.3.2 Chemical structures of chrysomycins A–C (1–3). COSY and HBMC correlations for chrysomycin C (3) are also shown.

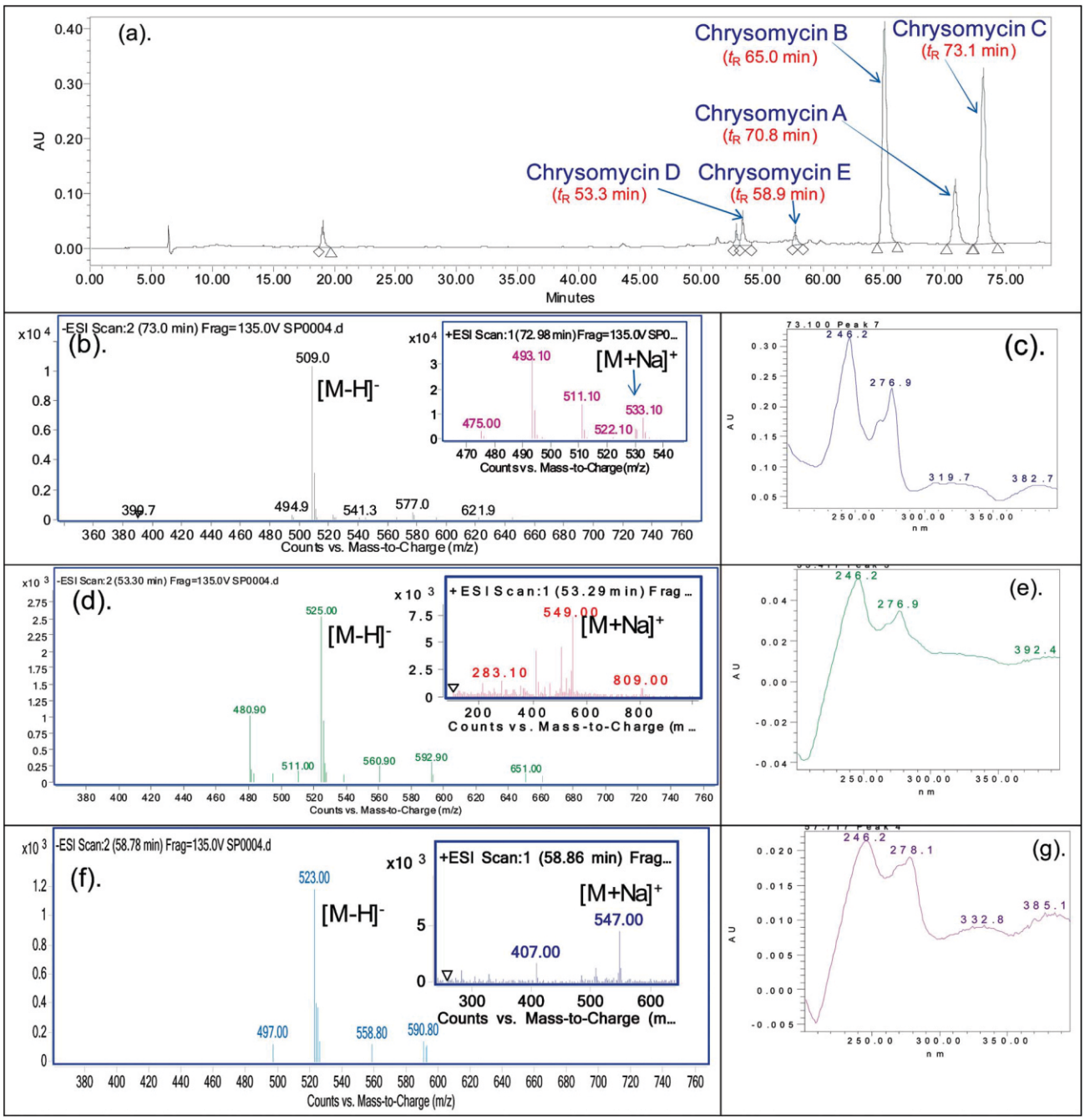


Figure 6.3.3 (a) LC–ESI–MS chromatogram of the crude fraction showing the identification of two known chrysomycins A–B (1–2) and three new chrysomycins C–E (3–5); (b and c) ESI–MS (negative mode) chromatogram and UV spectrum for the peak at tR 73.0 min; (d and e) ESI–MS (negative mode) chromatogram and UV spectrum for the peak at tR 53.3min; (f and g) ESI–MS (negativemode) chromatogram and UV spectrumfor the peak at tR 58.8min; LC conditions: lmax: 244 nm; column: chromolith (150mm_ 4.6mm, RP-18); mobile phase: acetonitrile–water (0.1% formic acid) gradient over 78 min (0 min: 0 : 100, 10 min: 15 : 25, 25 min: 20 : 80, 40 min: 25 : 75, 45 min: 35 : 65, 50 min:35 : 65, 65 min: 40 : 60, 75 min: 45 : 55, 76 min: 100 : 0, 78 min: 100 : 0.) with flow rate: 0.42 ml min_1 (insets in Fig. 4b, d, f: ESI–MS spectra in positive mode).

The compounds were evaluated for their cytotoxicity efficacy against a panel of cancer cell lines (A549, Colo205, PC-3, MIAPaCa-2, and HL-60), amongst which the most potent activity was observed against human leukemia HL-60 cells with IC50 values of 0.9, 0.95 and 11 mM, respectively. The mechanistic studies indicated that chrysomycins A (1) and B (2), at 1 mM concentration, distorted the cellular and nuclear morphology with significant DNA damage and apoptosis in HL-60 cells.

6.4 Cloning, heterologous expression and functional characterization of Nitrilase from *Fusarium proliferatum* AUF-2

Farnaz Yusuf, Irshad Ahmed, Urmila Jamwal, Sumit G. Gandhi and Asha Chaubey

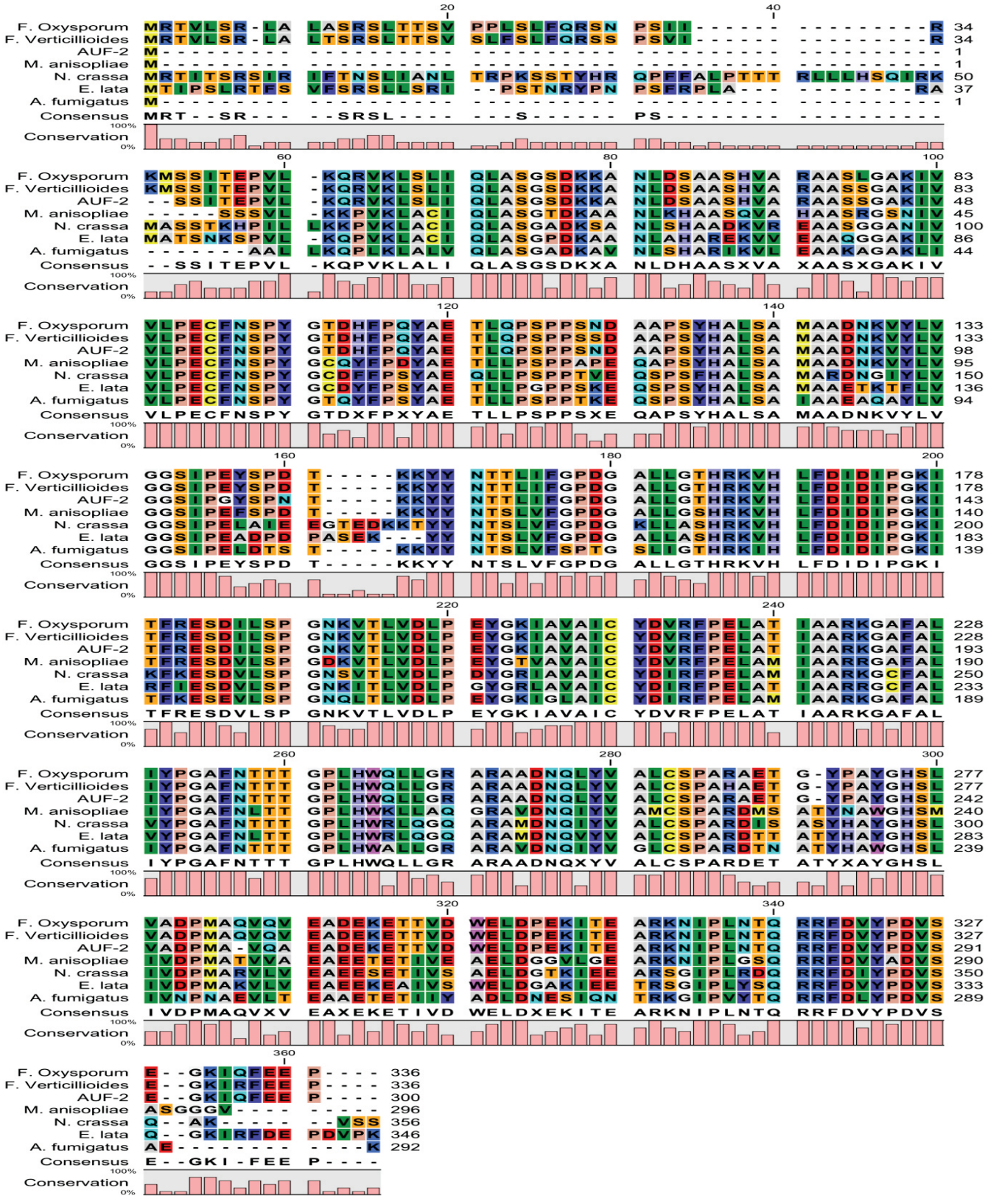


Figure 6.4.1 Amino acid sequence alignment of nitrilases from different origin.

Biocatalysts from the native source have limitations with respect to some enzymatic properties in process development. A recombinant enzyme may provide the possibility to meet the synthetic application requirements with high efficiency. It may also lead to a better understanding and improvement in enzyme function for various biotechnological applications. Several nitrilase genes have been cloned from various organisms and introduced into appropriate host strains. Therefore, studies on *F. proliferatum* nitrilase gene expression needs to be done in order to advance our understanding for nitrile hydrolysis. In our previous work, a fungus *F. proliferatum* strain AUF-2 was shown to be a promising strain for nitrilase production. Present report relates to cloning of its nitrilase gene through reverse transcription-PCR (RT-PCR) and its heterologous expression in *E. coli* for use in possible pharmaceutical applications.

Cloning and of Heterologous expression nitrilase gene from *F. proliferatum* nitrilase

The nitrilase sequences available in NCBI GenBank were used to design degenerate primers, based on the conserved domain deduced from the reported amino acid and nucleotide sequences encoding nitrilase from fungal source. The core amplicon of 573 bp was obtained. Sequence of the core amplicon was used for designing 5' and 3' RACE primers. RACE-PCR was carried out to obtain the 5' and 3' ends of the cDNA, giving an amplicon size of approximately 504 bp and 488 bp respectively. The full length clone of 903 bp was sequenced and submitted to NCBI GenBank (Accession No.KF003025). The sequence analysis demonstrated that the target fragment contained an open reading frame of 903 nucleotides, starting with an ATG codon at position 166 and ending with TAA codon at position 903. The 5' and 3' UTR are 165 bp and 122 bp including polyA tail respectively.

To express the gene encoding nitrilase, primers Pnitf and Pnitr were designed according to the sequencing result of pTZ57R/T-NIT, with NcoI and HindIII sites, respectively. PCR amplification was conducted by adopting the recombined plasmid pTZ57R/T-NIT obtained above as the template, and the DNA fragment encoding the nitrilase gene was subcloned into an expression vector pET28a(+) to construct the recombinant plasmid pET28a(+)NIT. Subsequently, the recombinant plasmids were then transformed into chemically competent cells of *E. coli* BL21 (DE3). The positive transformant containing recombinant pET28a(+)-NIT was identified by colony PCR and double enzymatic digestion. The molecular mass of the recombinant nitrilase was approximately 37kDa. These data are in agreement with those derived from DNA sequencing.

Effects of the environmental factors on the nitrilase activity

The highest nitrilase activity was found in the temperature range of 35°C to 40°C. The nitrilase activity gradually increased from 20°C to 40°C and decreased drastically above 45°C. The nitrilase showed optimum activity at pH 8.0. This enzyme exhibited activity in a broad pH range i.e. pH 6.0 to10.0. The enzyme activity was strongly inhibited by Ag^{+}. The metal ions like $Ni^{2+,}$ Co^{2+}, Cu^{2+} caused decrease in enzymatic activity, while Zn^{2+}, Ca^{2+}, Mg^{2+}, Mn^{2+},Fe^{2+}, Fe^{3+} and EDTA improved the nitrilase activity. It was observed that the enzyme was relatively active in methanol followed by ethanol. The activity decreased drastically in other solvents like propanol, hexane, toluene and dichloromethane.

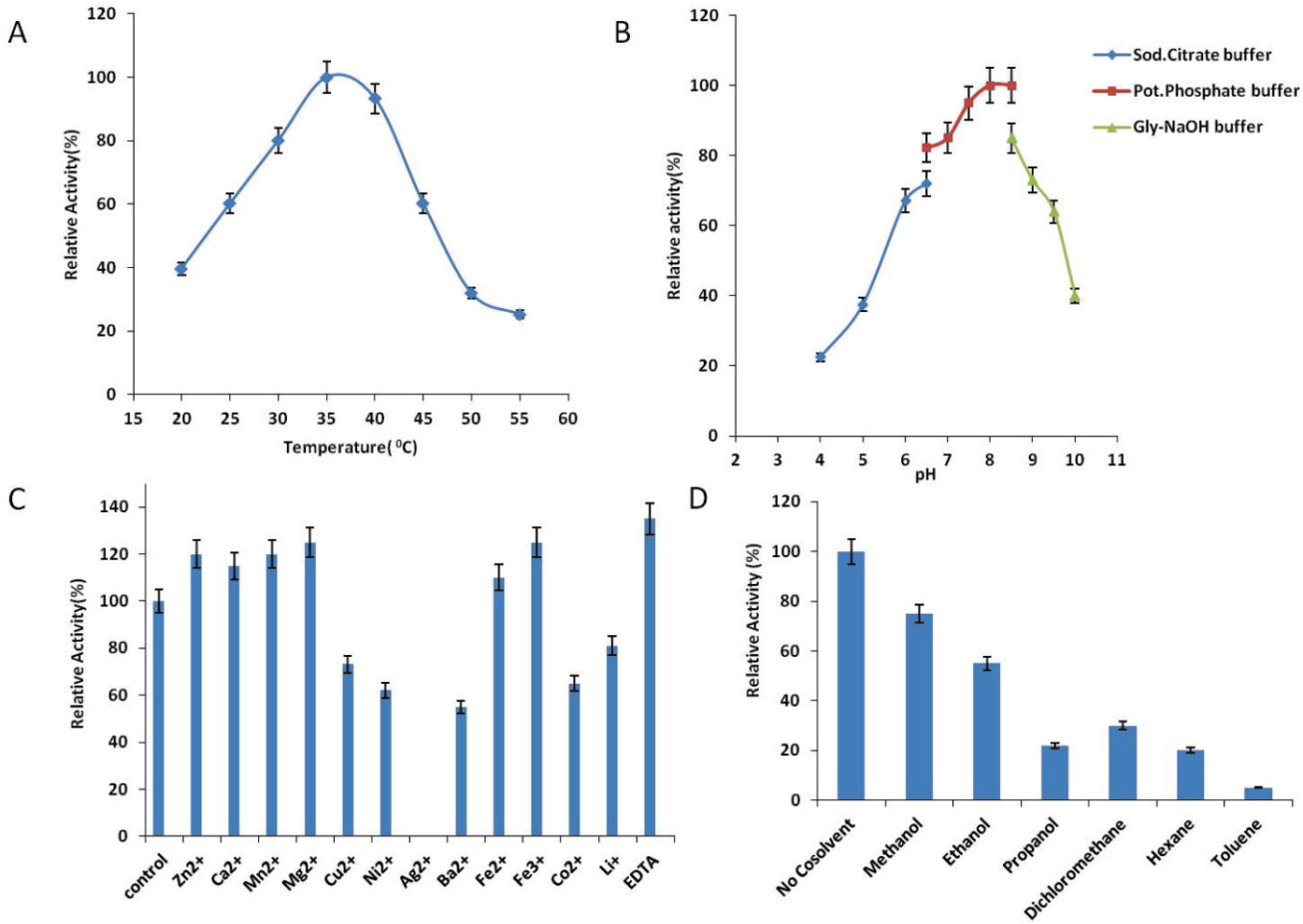


Figure 6.4.2. Effects of environmental factors on the activity of nitrilase for benzonitrile substrate.

7. CANCER PHARMACOLOGY

7.1 Anticancer potential of *Ipomoea asarifolia*, a Nigerian Medicinal Plant

Z. A. Wani, Akanksha Behl, Mubashir Javed Mintoo, Girish Mahajan, Abidemi J. Akindele, Dilip M. Mondhe

Cancer is a disease of multicellular organisms characterized by uncontrolled multiplication of subtly modified normal human cells (Denny and Wansbrough, 2010). The burden of cancer is increasing in economically developing countries as a result of population aging and growth as well as increasingly, an adaptation of cancer- associated lifestyle choices including smoking, physical inactivity, and "westernized diets" (Jemal *et al*.,2011). Normal diploid human cells multiply for a finite number of generations and then enter a state of replicative senescence but cancer cells can proliferate indefinitely (Rao *et al.,* 2007). The most commonly occurring cancers are prostrate, lung, bladder, breast, colorectal, cutaneous melanoma and non-Hodgkin lymphoma. Over the years, different approaches have been employed and are still in use, individually or in combination, in the treatment of cancer. In the past, herbal drugs were used as tinctures, poultices, powders and teas but in recent times formulations and pure compounds are additional derivatives, and medicinal plant drug discovery continues to provide new and important leads against various pharmacological targets for cancer, malaria etc. According to Park (2012), a good number of the current day commercially approved anticancer drugs as well as the natural product-derived compounds in various stages of clinical development as anticancer agents have originated from plants.

Ipomoea asarifolia is a long trailing herbaceous perennial plant of sandy area and waste places throughout west tropical Africa, Cape Verde Islands, tropical Asia and America. Approximately 600-700 species of *Ipomoea* (Convolvulaceae family) are found throughout tropical and subtropical regions of the world. These species are used in different parts of the world for the treatment of several diseases, such as, diabetes, hypertension, dysentery, constipation, fatigue, arthritis, rheumatism, hydrocephaly, meningitis, kidney ailments and inflammations. Some of these species showed antimicrobial, analgesic, spasmolytic, spasmogenic, hypoglycemic, hypotensive, anticoagulant, anti-inflammatory, psychotomimetic and anticancer activities. Alkaloids, glycolipids and phenolic compounds are the most common biologically active constituents from these plants.

In-Vitro Evluation of Extracts:

Sulphorhodamine B (SRB)assay was used to test the cytotoxic potential of extracts of *Ipomoea asarifolia*. Human cancer cell lines viz., A549, HCT-116, PC3, A4531, HeLa and THP-1 were allowed to grow in the tissue culture plates in the presence of different extracts of *Ipomoea asarifolia*. The cell growth in the presence and absence of test materials was measured on ELISA reader after staining with Sulphorhodamine B (SRB) dye (100μl in each well) which binds to basic amino acid residues in trichloroacetic

Figure 7.1.1. *Ipomoeaasarifolia*

acid (100μl) fixed cells.

***In-Vivo* Evaluation:** The *in vivo* experiments were conducted on BALB/c females weighing 18-23g. On day 0, 10^7 Sarcoma-180 cells were transplanted intra-peritoneally in animals selected for the experiment that were taken from the animals bearing 8-12 days old ascitic tumor. The test materials were administered to experimental animals intra- peritoneally for the next 9 days consecutively. On day 12, all animals were sacrificed and the cells present in the peritoneal fluid of all animals were counted. The extracts IA-A001, IA-A003 and IA-A004 were evaluated at a dose of 100mg/kg and IA-A002 at a dose of 80mg/kg. 5-fluorouracil was used as positive control at a dose of 20 mg/kg and normal saline (0.85% w/v) was administered to normal control animals.

***In vitro* cytotoxic activity:** Results on the cytotoxic effect of IA-A001, IA-A002, IA-A003 and IA-A004 against human cancer cell lines in the SRB assay are presented in figures (7.1.1-7.1.4). None of IA Extracts elicited significant cytotoxic activity against human cancer cell lines used in this study and showed IC_{50} values generally >100 μg/ml except in the case of IA-A003 and IA-A004 which showed IC_{50} values of 89 and 70 μg/ml against PC3 and THP-1 human cancer cell lines, respectively.

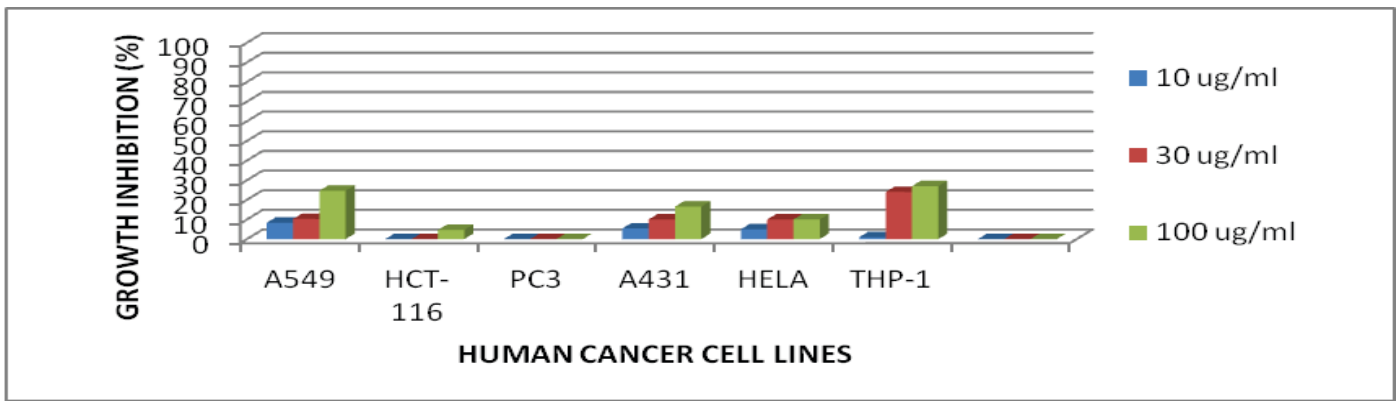


Figure 7.1.2. *In vitro* cytotoxic activity of IA-A001 against various human cancer cells lines in the SRB assay.

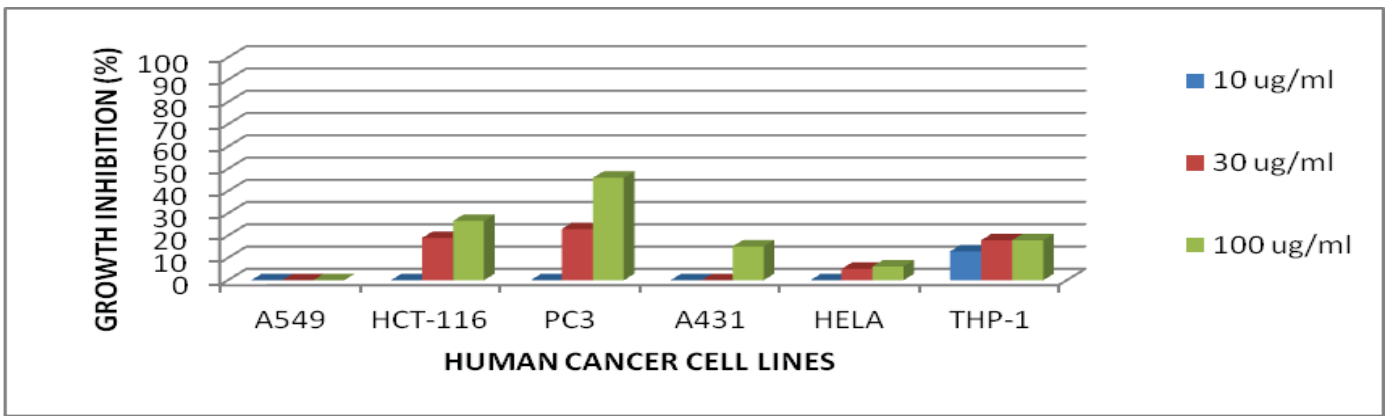


Figure 7.1.2. *In vitro* cytotoxic activity of IA-A002 against various human cancer cells lines in the SRB assay.

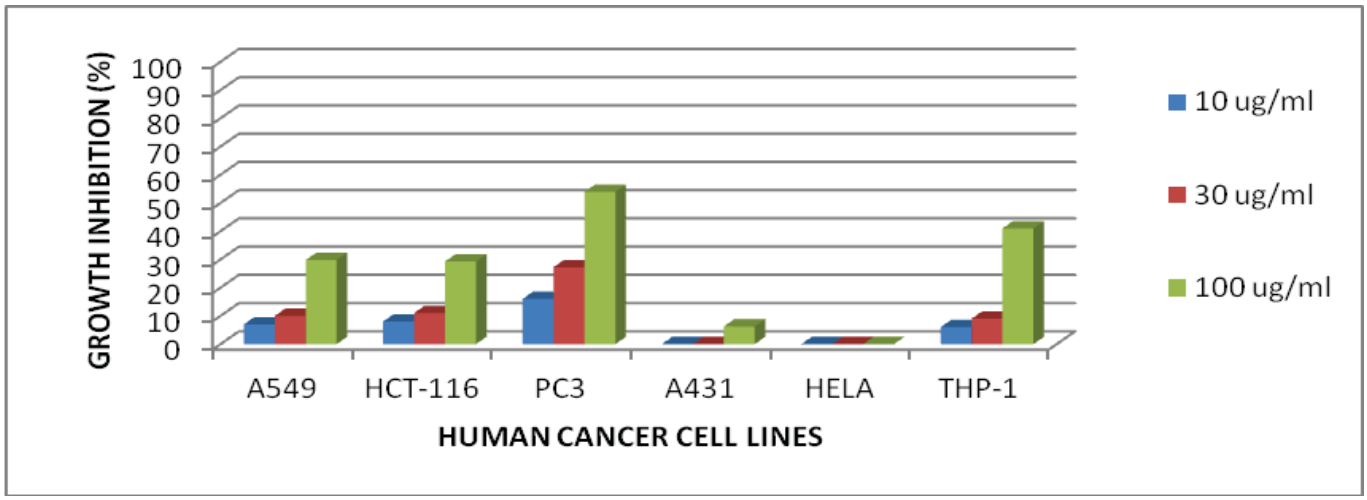


Figure. 7.1.3. *In vitro* cytotoxic activity of IA-A003 against various human cancer cells lines in the SRB assay

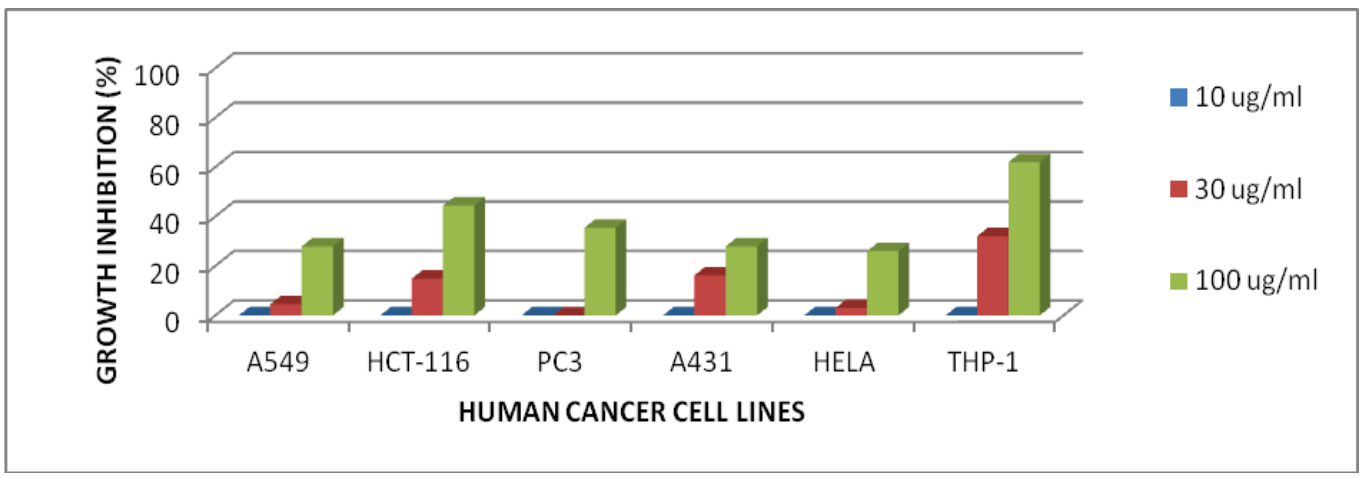


Figure. 7.1.4. *In vitro* cytotoxic activity of IA-A004 against various human cancer cells lines in the SRB assay.

The results of initial screening of IA Extracts against murine Sarcoma-180 (ascites) are presented in figures 5 and 6. IA-A001 did not produce any inhibitory effect on the growth of tumor cells in the peritoneal cavity of experimental mice at 100mg/kg dose level. IA-A002 (100mg/kg), IA-A003 (100mg/kg) and IA-A004 (100mg/kg) however showed tumor growth inhibition of 60.09, 58.75 and 43.45 per cent, respectively. The inhibitory effect of IA-A002 and IA-A003 has been statistically highly significant.

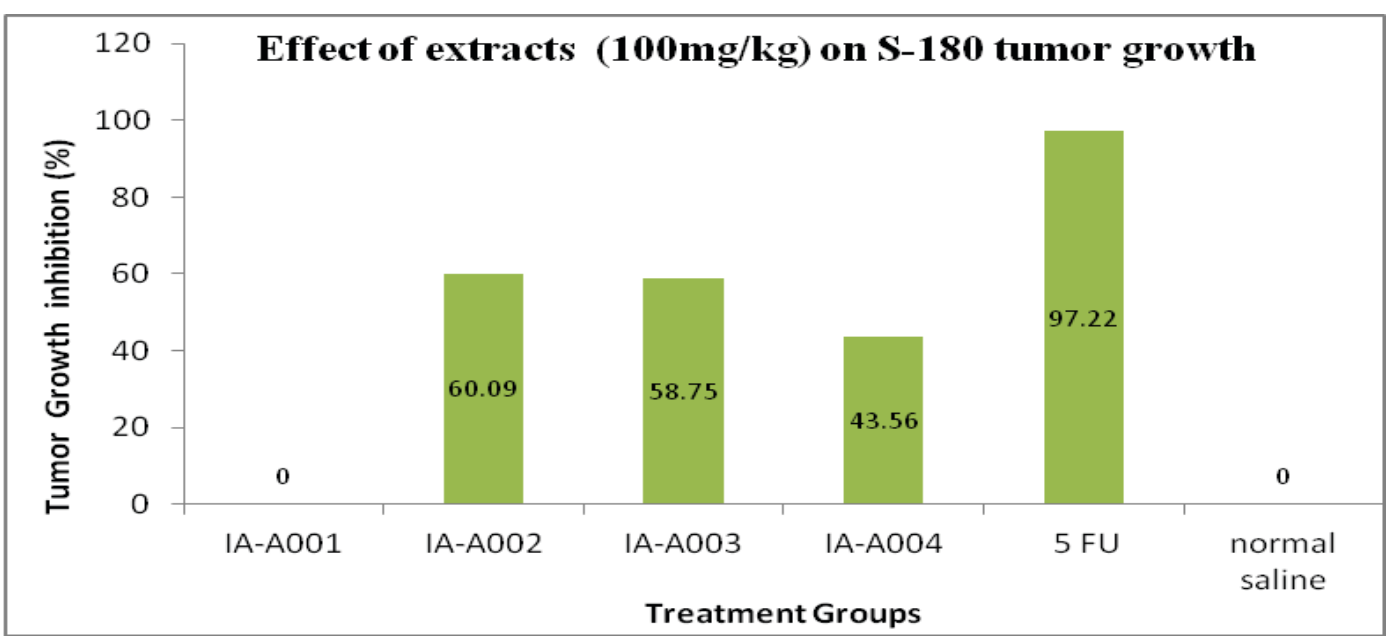


Figure 7.1.5. *In vivo* anti cancer activity of IA-A002, IA-A003 and IA-A004 against murine Sarcoma-180 (ascites).

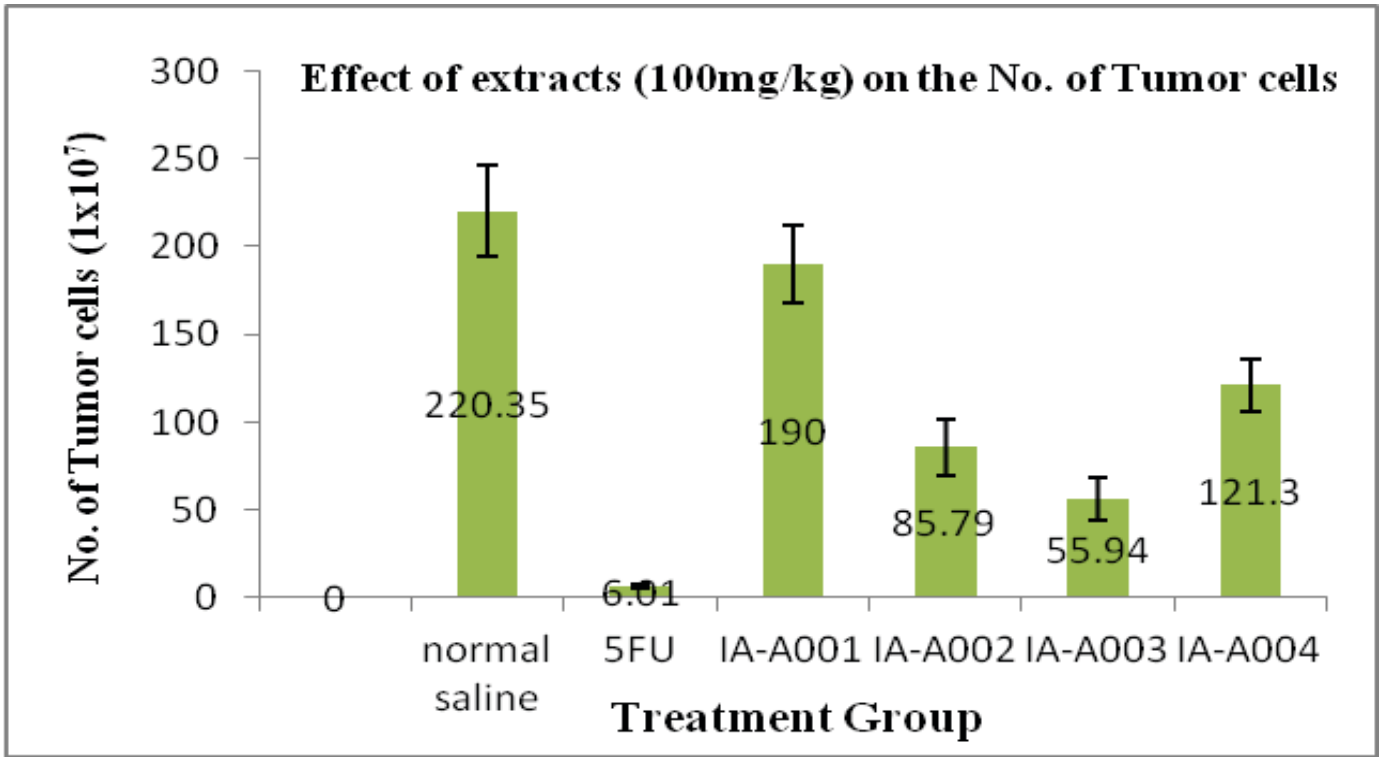


Figure 7.1.6. Effect of IA-A001, IA-A002, IA-A003 and IA-A004 (100mg/kg) each on the number of Tumor cells. IA-A002 and IA-A003 showed a significant decrease in No. of Tumor cells.

7.2 The anti-angiogenic and cytotoxic effects of the boswellic acid analog BA145 are potentiated by autophagy inhibitors

Anup S Pathania, Zahoor A Wani, Santosh K Guru, Suresh Kumar, Shashi Bhushan, Hasan Korkaya, Darren F Seals, Ajay Kumar, Dilip M Mondhe, Zabeer Ahmed, Bal K Chandan, Fayaz Malik

While angiogenesis inhibitors represent a viable cancer therapy, there is preclinical and clinical data to suggest that many tumors develop resistance to such treatments. Moreover, previous studies have revealed a complex association between autophagy and angiogenesis, and their collective influence on tumorigenesis. Autophagy has been implicated in cytoprotection and tumor promotion, and as such may represent an alternative way of targeting apoptosis-resistant cancer cells. This study explored the anti-cancer agent and boswellic acid analog BA145 as an inducer of autophagy and angiogenesis-mediated cytoprotection of tumor cells. Flow cytometry, western blotting, and confocal microscopy were used to investigate the role of BA145 mediated autophagy. ELISA, microvessel sprouting, capillary structure formation, aortic ring and wound healing assays were performed to determine the relationship between BA145 triggered autophagy and angiogenesis. Flow cytometery, western blotting, and microscopy were employed to examine the mechanism of BA145 induced cell death and apoptosis. Live imaging and tumor volume analysis were carried out to evaluate the effect of BA145 triggered autophagy on mouse tumor xenografts. BA145 induced autophagy in PC-3 cancer cells and HUVECs significantly impeded its negative regulation on cell proliferation, migration, invasion and tube formation. These effects of BA145 induced autophagy were observed under both normoxic and hypoxic conditions. However, inhibition of autophagy using either pharmacological inhibitors or RNA interference enhanced the BA145 mediated death of these cells. Similar observations were noticed with sunitinib, the anti-angiogenic properties of which were significantly enhanced during combination treatments with autophagy inhibitors. In mouse tumor xenografts, co-treatment with chloroquinone and BA145 led to a considerable reduction in tumor burden and angiogenesis compared to BA145 alone. These studies reveal the essential role of BA145 triggered autophagy in the regulation of angiogenesis and cytoprotection. It also suggests that the combination of the autophagy inhibitors with chemotherapy or anti-angiogenic agents may be an effective therapeutic approach against cancer.

7.3 Quinazoline based small molecule exerts potent tumor suppressive properties by inhibiting PI3K/Akt/FoxO3a signalling in experimental colon cancer

Mushtaq Ahmad Aga, Akanksha Behl, Shakir Ali, Shashank Kumar Singh, Asif Khurshid Qazi, Aashiq Hussain, Saima Khan, Subhash Chandra Taneja, Bhahwal Ali Shah, Ajit Kumar Saxena, Dilip Manikrao Mondhe, Abid Hamid

	PI				Rh-123	PI/ Annexin V-FITC		
	Sub-GI	G 1	S	M	MMP Loss	Early Apoptosis	Late Apoptosis	Necrosis
Conc (μM)	% Cell population							
BEZ 235 (10nM)	15.1	31.6	7.9	13.5	8.4	7.6	9.3	0.2
0	11.3	35.1	8.7	12.7	4.8	0.4	8.7	0.8
10	16.4	30.7	7.9	12.2	7.4	3.2	6.7	0.4
30	29.7	35.8	7.4	10.4	33.55	8.3	16.5	2.2

Table 7.3.1. HCT-116 cells were treated with indicated concentration of RLX for 48h and labelled with PI, Rh 123 and Annexin V-FITC/PI in different experiments depicting cell cycle arrest, mitochondrial memberane potential loss and apoptosis using a Flow cytometery. PI; Propidium Iodide, Rh-123; Rhodamine 123, Annexin V-FITC; Annexin V labelled with fluorescein isothiocyanate

Phosphatidylinositol-3-kinase (PI3K) as a lipid kinase generates second messengers which have been involved in regulation of a wide spectrum of cellular functions including proliferation, survival, cell cycle progression and invasion. More importantly, the PI3K/Akt signaling pathway is frequently activated in many types of human cancers including colorectal carcinoma and has been linked to cancer development. Phosphoinositide 3-kinase (PI3K) signaling pathway components are crucial to many aspects of cell growth and survival in colorectal carcinoma (CRC) via its regulation in diverse physiologic processes that include cell proliferation, cell cycle progression, invasion and apoptosis.This pathway controls several growth regulatory transcription factors. One of the prominent examples is Forkhead box O (FoxO) transcription factor, the mammalian orthologs of *Caenorhabditis elegans* DAF-16, which are emerging as an important family of proteins implicated with modulation of gene expression in apoptosis, cell cycle arrest, metastasis, DNA damage repair, oxidative stress, cell differentiation, glucose metabolism and other cellular functions. Moreover, the FoxO family of transcription factors (FOXO1, FOXO3 and FOXO4) functions as tumor suppressors and is directly inactivated by oncogenic signaling through the PI3K signaling pathway. Thus, FoxO transcription factors appear to be involved in various signaling pathways and controls diverse biochemical processes. Furthermore, FoxO regulates cell cycle and apoptotic genes such as cyclin D , Bim and Bcl_2 . Consequently, activation of PI3K/Akt pathway serves to repress FoxO mediated growth arrest and apoptosis. An emerging understanding of the molecular pathways that characterize cell growth, cell cycle, apoptosis, angiogenesis and invasion has provided novel cancer therapy approaches. RLX, a vasicinone analogue is believed to possess potent bronchodilator, anti- asthmatic and anti-inflammatory properties, and has 6 to 10 times strong bronchodilator and anti-asthmatic properties than aminophylline. These constellation of features of RLX has provided the basis and extended the opportunity to evaluate its target based anti-cancer property via targeting PI3K/Akt/FoxO3a signaling against colon cancer HCT-116 cells line having PI3K (PI3KCA) amplification and tumor regression *in vivo*. The present studies evaluated the mechanistic basis of RLX (a quinazoline representative) action and this can form the basis of understanding the Cal-101 clinical action belonging to the similar scaffold. The effects of compound on cytotoxicity were evaluated by MTT

assay. After 48h of exposure to different concentrations of compound, 20μl of MTT was added to each well and incubated for further 4 hours. After the removal of medium, 150μl DMSO was added to each well. The absorbance was recorded at the wavelength of 570 nm in the micro-plate reader and cytotoxicity was calculated.Cell proliferation was evaluated by clonogenic assay preceded by seeding of cells (HCT-116) in six-well plate at a density of 200 cells per ml/well. After 4 h, the cells were treated with different concentrations of RLX. Following treatment for 48h, medium was changed to stop the treatment and fresh medium was added alternatively up to 12 days. To explore the stages of apoptosis, treated HCT-116 cells were stained with Annexin V–FITC (fluorescein isothiocyanate) and analysed by performing flow cytometery. RLX treatment, we observed increased apoptotic cells in a dose dependent manner i.e. 3.2% and 8.3% at 10μM and 30μM of RLX respectively. However, on the contrary, 0.4% of early apoptosis was shown by untreated control. Additionally, late apoptotic population was of the order of 6.7% and 16.5% at 10μM and 30μM of RLX (Table 1).

Treatment with 50 mg/kg body weight and 100 mg/kg body weight of RLX decreased the tumour by 46.39% and 63.49% respectively (Table 7.3.2A). In continuation to our *in vitro* data, we observed maximum tumour growth inhibition upto 29.60% and 35.59%. On the basis of average tumour weight as compared to control group at doses of 50 mg/kg body weight and 100 mg/kg body weight there was significant decrease in body weight and average tumour weight (Table 7.3.2B).

Sample	Tumor Model	Dose	Av. Body Weight (gm)				Av.Vol. of ascetic fluid(ml)	Av. Wt. of ascetic Fluid(gm)	Av. No. Of tumor cells($x10^7$)	Mortality	TGI (%)
			Day 1	Day 5	Day 9	Day 12					
RLX	Ehrlich Ascitic Carcinoma	50mg/kg	21.7	23.57	25.2	28.33	9±2.8	8.67±2.54	150.24±64.56	1/7	46.39
		100mg/kg	22	22.42	23.5	25.5	4.64±2.32	4.52±2.26	114.62±57.31	3/7	63.49
5-FU	Ehrlich Ascitic Carcinoma	20mg/kg	22.57	22.71	21.57	20.71	0.91±0.34	0.61±0.23	16.94±6.4	0/7	96.07
NS	Ehrlich Ascitic Carcinoma	0.2ml	23.4	26.1	27.7	29.7	10.25±3.09	10.37±3.12	280.27±84.52	0/10	-

Table 7.3.2.A

Table 7.3.2.(A) Ehlich Ascitic Carcinoma bearing animals were treated with RLX at 50mg/kg/i.p and 100mg/kg/i.p each for 9 consecutive days and body weight (g) were recorded on day1, 5, 9 and 12 and percent tumor growth inhibition was calculated. 5-Flurouracil (5-FU) at 20mg/kg/i.p was used as positive control. Comparisions were made between control and treated groups using student's t-test.

Sample	Tumor Model	Dose	Av. Body Weight (g)			Day 13		% Tumor Growth Inhibition	Mortality
			Day 1	Day 5	Day 9	Av.Body weight (g)	Av.Tumor weights(mg)		
RLX	Ehrlich Tumor(Solid)	50mg/kg	20.14±0.73	21.85±0.93	21.57±0.94	21.71±0.94	1041.0±34.34	29.60	0/7
		100mg/kg	20.42±0.65	21.71±0.83	22.14±0.73	22.42±0.92	952.51±108.83	35.59	0/7
5-FU	Ehrlich Tumor(Solid)	22mg/kg	20.54±0.75	21.28±0.77	20.0±0.84	19.85±1.01	613.71±61.72	58.50	0/7
N S	Ehrlich Tumor(Solid)	0.2ml	21.8±0.78	23.1±0.76	23.1±0.64	23.1±0.71	1478.9±119.52	-	0/10

Table 7.3.2B

Table 7.3.2(B) Ehlich Ascitic tumor bearing animals were treated with RLX at 50mg/kg/i.p and 100mg/kg/i.p each for 9 consecutive days and body weight (g) were recorded on day 1, 5, 9 and 13 and percent tumor growth inhibition was calculated. 5-Flurouracil (5-FU) at 22mg/kg/i.p was used as positive control. Comparisons were made between control and treated groups using student's t-test. Data are expressed as mean±SD (n=7) of three similar experiments carried out in triplicate. $p \leqslant 0.001$, $p \leqslant 0.01$ for each analysis *versus* control.

8. ANIMAL HOUSE

8.1 Establishment of Mutagen Testing Facility for the Assessment of Mutagenic Potential of the Lead Compounds from Drug Discovery Programme: A Carcinogenicity Risk Assessment

Govind Yadav, Rakesh Nagar,Amit kumar Choudhary, Parvinder Pal Singh

Our efforts to setting up facility in IIIM to fill the gaps in pre-existing capabilities to meet the regulatory requirement for the submission compound/drug/biocides to regulatory agencies (OECD,ICH,FDA) for registration acceptance of compounds from drug discovery programme of CSIR-IIIM. The identification of substances capable of inducing mutations has become an important procedure in cancer Risk assessment. Chemicals that can induce mutations can potentially damage the germ line leading to fertility problems and to mutations in future generations. Mutagenic chemicals are also capable of inducing cancer, and this concern has driven most of the mutagenicity testing programs. Mutations can occur as gene (point) mutations, where only a single base is modified, or one or a relatively few bases are inserted or deleted, as large deletions or rearrangements of DNA, as chromosome breaks or rearrangements, or as gain or loss of whole chromosomes. Gene mutations are readily measured in bacteria and other cell systems when they cause a change in the growth requirements of the cell, whereas chromosome damage in mammalian cells is typically measured by observing the cell's chromosomes under magnification for breaks or rearrangements.

Testing of lead compounds in Bacterial Reverse mutation Assay

The Salmonella typhimurium/microsome assay (Salmonella test; Ames test) is a widely accepted short-term bacterial assay for identifying substances that can produce genetic damage that leads to gene mutations. The test uses a number of Salmonella strains with preexisting muta-tions that leave the bacteria unable to synthesize the required amino acid, histidine, and therefore unable to grow and form colonies in its absence. New mutations at the site of these preexisting mutations, or nearby in the genes, can restore the gene's function and allow the cells to synthesize histidine. These newly mutated cells

Strategy for mutagenicity testing as per WHO/IPCS harmonized scheme is mentioned bellow:-

Invitro tests

- ***Bacterial gene mutation(Bacterial reverse gene mutation)***
- ***Mammalian cell gene mutation(MLA,HPRT gene mutations,***
- ***Detection of chromosomal mutations***

↓

In vivo test (as per MOA of compound/drug)

- ***cytogenetic or gene mutation assay, Depending upon class of compound, reactivity, bioavailability, metabolism, etc.***
- ***Additional tests eg. Comet ,transgenic mutation test etc***

↓

Invivo somatic cell mutagen

↓

Germ cell testing

can grow in the absence of histidine and form colonies. For this reason, the test is often referred to as a "reversion assay." The Salmonella strains used in the test have different mutations in various genes in the histidine operon; each of these mutations is designed to be responsive to mutagens that act via different mechanisms. Additional mutations were engineered into these strains to make them more sensitive to a wide variety of substances. The Salmonella mutagenicity test was specifically designed to detect chemically induced mutagenesis. Over the years its value as such has been recognized by the scientific community, and by government agencies and corporations. The test is used world-wide as an initial screen to determine the mutagenic potential of new chemicals and drugs because there is a high predictive value for rodent carcinogenicity when a mutagenic response is obtained. International guidelines have also been developed (e.g., Organisation for Economic Co-operation and Development (OECD); International Commission on Harmonization (ICH)) for use by corporations and testing laboratories to ensure uniformity of testing procedures prior to submission of data to regulatory agencies for registration or acceptance of many chemicals, including drugs and biocides.

Table-8.1.1. Details of the available standard salmonella and E.coli strains and their Genotype

Bacterial strain	Hot spot in histidine/trypt gene	Genotype	Reversion events
1. S. typhimurium			
TA100	hisG46	Dgal chlD bio *uvr*B rfa (pKM101)	Primarily detects G/C base pair substitution
TA1535	hisG46	Dgal chlD bio *uvr*B rfa	Detects G/C base pair substitution
TA98	hisD3052	rfa Dgal chlD bio *uvr*B (pKM101)	Frame shift mutation
TA1537	Hisc3076	rfa Dgal chlD bio *uvr*B	Frame shift mutation
TA102	his G428	his D (G) $_{8476}$rfa gale (pAQ1) (pKM101)	Transitions /transversions, A/T Base pair , small deletions
2. E.coli			
WP2uvrA	Trp E	uvr A	Transitions / transversions , A/T Base pair,small deletions
WP2uvrA(pKM101)	Trp E	uvr A (pKM101)	

Table- 8.1.2. Details of the positive mutagens

***Sallmonella typhimurium, Ecoli* strains**	**Positive controls Without-S9**	**With + S9**
TA 98	**2-Nitroflurene(7.5µg)**	**2-AA (2.5µg)**
TA100	**Sodium Azide (5µg)**	**2-AA (5µg)**
TA 1535	**Sodium Azide(0.5µg)**	**2-AA (2.5µg)**
TA1537	**9-Aminoacridine(75µg)**	**2-AA(2.5µg)**
TA 102	**Mitomycin-c(0.5µg)**	**2-AA(5µg)**
E.Coli WP2uvrA	**MMS (2.5µl/plate)**	**2-AA (2.5µg)**

Table 8.1.3. Following compounds were evaluated for mutagenicity

S.no	Name of compound	Strain used *Salmonella typhimurium /E.coli strains*	Results (Mutagenic/ Non-Mutagenic)
1	IIIM TB-200	*TA98,TA100,TA1535,TA1537,TA102 E.Coli*	Non-Mutagenic
2	MCD TB 53	*TA98, E.Coli ,TA1537,E.coliwp2uvrA*	Non-Mutagenic
		TA100, TA1535,TA102	Mutagenic
3	PPS-SIM-002	*TA98,TA1535, E.Coli*	Mutagenic
4	PPS-SIM-003	*TA98,TA1535, E.Coli*	Mutagenic
5	PPS-SIM-005	*TA98, E.Coli*	Mutagenic
6	PPS-US-176	*TA98, E.Coli*	Non-Mutagenic
7	IIIM-K5a	*TA98,TA100,TA1535,TA1537, E.Coli*	Non Mutagenic

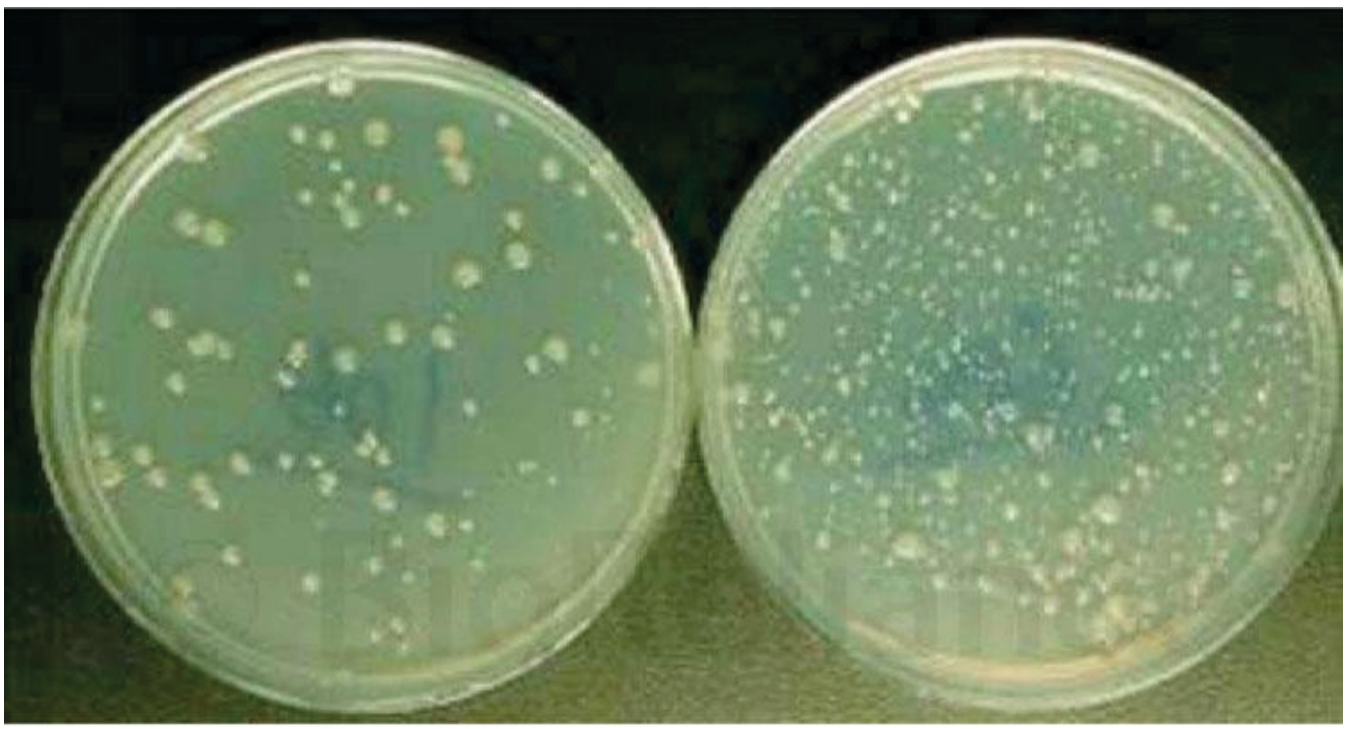


Figure. 8.1.1. Examples of a solvent control plate and a Positive mutagen (S.azide)

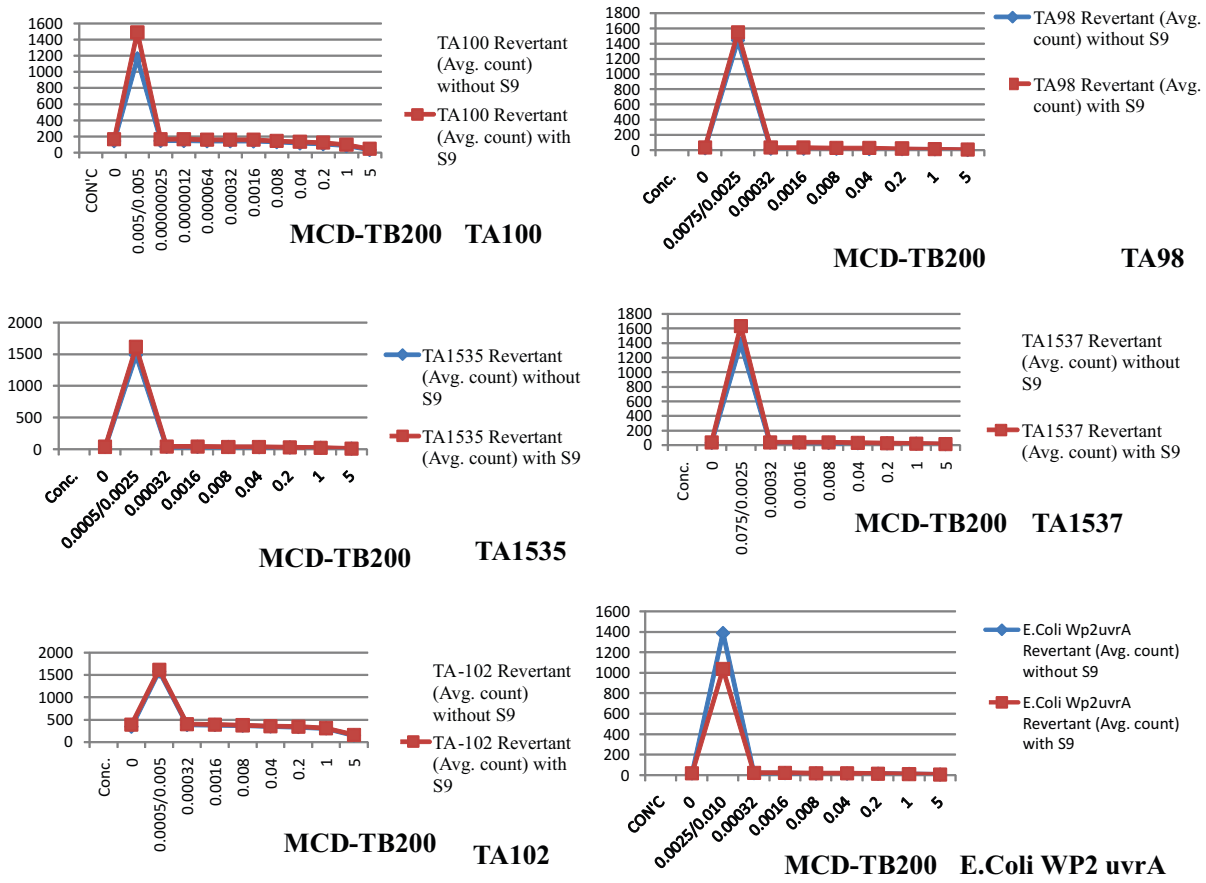


Figure 8.1.2. Evaluation of MCD-TB200 in Salmonella typhimurium and E.Coli wp2 uvrA for mutagenesis with and without S9 metabolic activation (Average number of revertants).

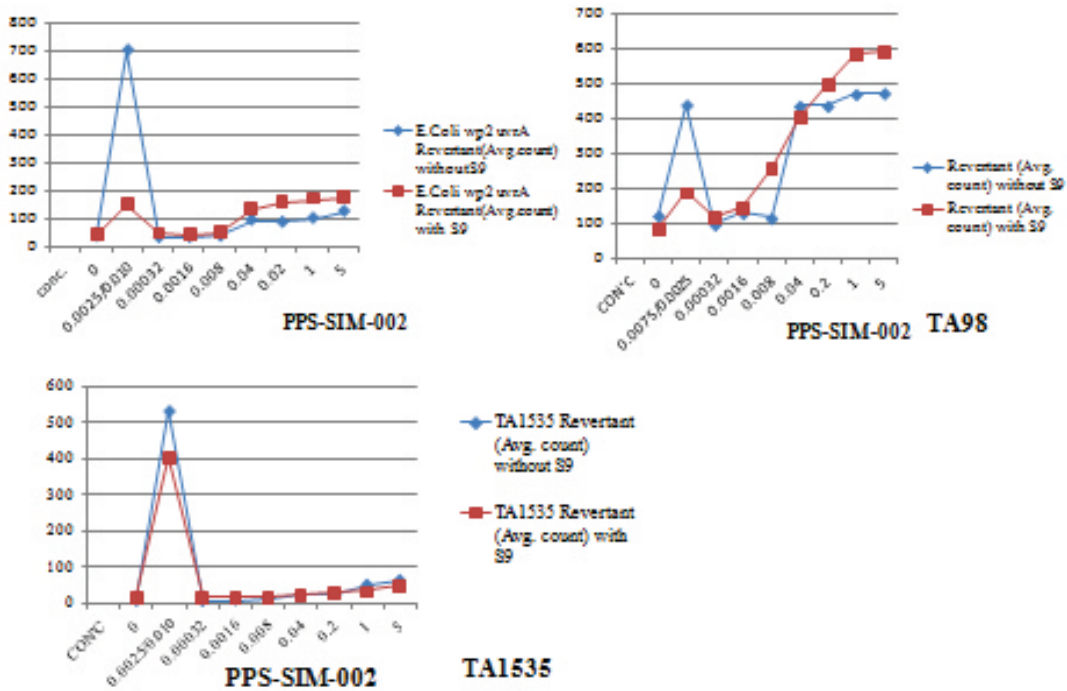


Figure 8.1.3. Table: Evaluation of PPS-SIM-002 in Salmonella typhimurium and E.Coli wp2 uvrA for mutagenesis with and without S9 metabolic activation (Average number of revertants)

LIST OF PUBLICATIONS
(Calender Year: 2013)

1. Kitchlu, S.; Bhadauria, Rekha; Ram, Gandhi; Bindu, Kushal; Khajuria, Ravi K.; Ahuja, Ashok. Chemo-divergence in essential oil composition among thirty one core collections of Ocimum sanctum L. grown under sub-tropical region of Jammu, India By Kitchlu, S.; Bhadauria, Rekha; R. *American Journal of Plant Sciences* **(2013)**, 4(2), 302-308. DOI:10.4236/ajps. 2013.42040

2. Gupta, D. K.; Verma, M. K.; Anand, R.; Khajuria, R. K. Development of a validated UPLC-qTOF-MS/MS method for determination of bioactive constituent from glycyrrhiza glabra. *Journal of Pharmaceutical Analysis* **(2013)**, 3(3), 205-210. DOI:10.1016/j.jpha.2013.01.0 01

3. Khajuria, Ravi K.; Sharma, Neha; Koul, Jawahar L.; Verma, Mahendra K. Concentration dependent electrospray ionisation mass spectrometry and tandem mass spectrometry (MS/MS) studies on (E,E)-1-[5-(1,3-benzodioxol-5yl)-1-oxo-2,4-pentadienyl]-piperidine (piperine) and its analogues. *SpringerPlus* **(2013)**, 2(1), 427/1-427/8, 8 pp. DOI:10.1186/2193-1801- 2-427

4. Yusuf, Farnaz; Chaubey, Asha; Raina, Arvind; Jamwal, Urmila; Parshad, Rajinder. Enhancing nitrilase production from Fusarium proliferatum using response surface methodology. *SpringerPlus* **(2013)**, 2(1), 290/1-290/7, 7 pp. DOI:10.1186/2193-1801-2-290

5. Syed, Saima; Qadri, Masroor; Riyaz-Ul-Hassan, Syed; Johri, Sarojini. A novel exocellulase from an endophytic fungal strain DEF1. *International Journal of Research in Pharmaceutical and Biomedical Sciences* **(2013)**, 4(2), 573-577.

6. Rather, Rayees A.; Shakeel-u-Rehman; Naseer, Syed; Lone, Shabir H.; Bhat, Khursheed A.; Chouhan, Anuja. Flash chromatography guided fractionation and antibacterial activity studies of Angelica archangelica root extracts. IOSR *Journal of Applied Chemistry* **(2013)**, 4(3), 34-38, 5 pp. DOI:10.9790/5736-0433438

7. Dar, Refaz Ahmad; Saba, Iram; Shahnawaz, Mohd.; Sangale, Manisha Kashinath; Ade, Avinash Bapurao; Rather, Shabir Ahmad; Qazi, Parvaiz Hassan. Isolation, purification and characterization of Carboxymethyl cellulase (CMCase) from endophytic Fusarium oxysporum producing podophyllotoxin. *Advances in Enzyme Research* **(2013)**, 1(4), 91-96, 6 pp.. DOI:10.4236/aer.2013.14010

8. Syed, Saima; Riyaz-Ul-Hassan, Syed; Johri, Sarojini. A novel cellulase from an endophyte, Penicillium sp. NFCCI 2862. *American Journal of Microbiological Research* **(2013)**, 1(4), 84-91, 8 pp. DOI:10.12691/ajmr -1 - 4-4

9. Kaur, Tarandeep; Bhat, Hilal A.; Raina, Anuj; Koul, Sushma; Vyas, Dhiraj. Glutathione regulates enzymatic antioxidant defence with differential thiol content in perennial pepperweed and helps adapting to extreme environment. *Acta Physiologiae Plantarum* **(2013)**, 35(8), 2501-2511. DOI:10.1007/s11738-013-1286-x

10. Singh, Baljinder; Guru, Santosh K.; Kour, Smit; Jain, Shreyans K.; Sharma, Rajni; Sharma, Parduman R.; Singh, Shashank K.; Bhushan, Shashi; Bharate, Sandip B.; Vishwakarma, Ram A. Synthesis, antiproliferative and apoptosis-inducing activity of thiazolo[5,4-d]pyrimidines. *European Journal of Medicinal Chemistry* **(2013)**, 70, 864-874. DOI:10.1016/j.ejmech.2013.1 0.039

11. Qazi, Asif Khurshid; Hussain, Aashiq; Hamid, Abid; Qurishi, Yasrib; Majeed, Rabiya; Ahmad, Mudassier; Najar, Rauf Ahmad; Bhat, Javeed Ahmad; Singh, Shashank Kumar; Zargar, Mohmmad Afzal; et al. Recent Development in Targeting PI3K-Akt-mTOR Signaling for Anticancer Therapeutic Strategies. *Anti-Cancer Agents in Medicinal Chemistry*

(2013), 13(10), 1552-1564. DOI:10.2174/18715206136 66131125123241

12. Bharate, Jaideep Bibishan; Vishwakarma, Ram Asrey; Bharate, Sandip Bibishan; Thite, Tukaram Baburao; Kushwaha, Manoj; Gupta, Ajai Prakash. Quantification and validation of two isomeric anticancer compounds, garcinol and isogarcinol, in ultrasound-assisted extracts of Garcinia indica fruits using high-performance thin-layer chromatography. *Journal of Planar Chromatography--Modern TLC* **(2013)**, 26(6), 480-485. DOI:10.1556/JPC.26. 2013.6.4

13. Yousuf, Syed Khalid; Mukherjee, Debaraj; Singh, Baldev; Maity, Sudip; Taneja, Subhash Chandra. Cu-Mn bimetallic catalyst for Huisgen [3+2]-cycloaddition [Erratum to document cited in CA153:480545]. *Green Chemistry* **(2013)**, 15(12), 3487.

14. Chib, Renu; Shah, Bhahwal Ali; Andotra, Samar Singh; Bharadwaj, Vikram; Gupta, Rajinder Kumar; Taneja, Subhash Chandra; Khajuria, Ravi Kant. Quantification of Sesquiterpene Lactones in Parthenium hyterophorous by Normal-Phase HPLC. *Journal of Chromatographic Science* **(2013)**, 51(10), 950-953. DOI:10.1093/chromsci/ bms195

15. Kumar, S.; Guru, S. K.; Pathania, A. S.; Kumar, A.; Bhushan, S.; Malik, F. Autophagy triggered by magnolol derivative negatively regulates angiogenesis. *Cell Death & Disease* **(2013)**, 4 (Oct.), e889. DOI:10.1038/cddis. 2013.399

16. Jain, Shreyans K.; Meena, Samdarshi; Qazi, Asif K.; Hussain, Aashiq; Bhola, Sunil K.; Kshirsagar, Rajendra; Pari, Koteppa; Khajuria, Anamika; Hamid, Abid; Shaanker, R. Uma; et al. Isolation and biological evaluation of chromone alkaloid dysoline, a new regioisomer of rohitukine from Dysoxylum binectariferum. *Tetrahedron Letters* **(2013)**, 54(52), 7140-7143. DOI:10.1016/j.tetlet.2013. 10.096

17. Dhar, Niha; Rana, Satiander; Bhat, Wajid Waheed; Razdan, Sumeer; Pandith, Shahzad A.; Khan, Shabnam; Dutt, Prabhu; Dhar, Rekha S.; Vaishnavi, Samantha; Vishwakarma, Ram; et al. Dynamics of withanolide biosynthesis in relation to temporal expression pattern of metabolic genes in Withania somnifera (L.) Dunal: a comparative study in two morpho-chemovariants. *Molecular Biology Reports* **(2013)**, 40(12), 7007-7016. DOI:10.1007/s11033-013-2820-z

18. y Singh, Parvinder Pal; Bhunia, Debabrata; Verma, Yogesh Kumar; Sidiq, Tabasum; Khajuria, Anamika; Guptha, Amit; Pallavi, M. Preethi; Vamshi, S. Surya; Qazi, Gulam N.; Kumar, Halmuthur M. Sampath. Synthesis of novel lipidated iridoid glycosides as vaccine adjuvants: 6-O-Palmitoyl Agnuside elicit strong Th1 and Th2 response to ovalbumin in mice. *International Immunopharmacology* **(2013)**, 17(3), 593-600DOI:10.1016/j.intimp. 2013.07.018

19. Kannaboina, Prakash; Anilkumar, K.; Aravinda, S.; Vishwakarma, Ram A.; Das, Parthasarathi. Direct C-2 Arylation of 7-Azaindoles: Chemoselective Access to Multiarylated Derivatives. *Organic Letters* **(2013)**, 15(22), 5718-5721. DOI:10.1021/ol4027478

20. Katoch, Meenu; Hussain, M. A.; Ahuja, A. Comparison of SSR and cytochrome P-450 markers for estimating genetic diversity in Picrorhiza kurrooa L. *Plant Systematics and Evolution* **(2013)**, 299(9), 1637-1643. DOI:10.1007/s00606-013-0820-z

21. Lone, Shabir H.; Bhat, Khursheed A.; Naseer, Syed; Rather, Rafiq A.; Khuroo, Mohd A.; Tasduq, Sheikh A. Isolation, cytotoxicity evaluation and HPLC-quantification of the chemical constituents from Artemisia amygdalina Decne. *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences* **(2013)**, 940, 135- 141. DOI:10.1016/j.jchromb.2013. 09.027

22. Singh, Baljinder; Parshad, Rajinder; Khajuria, R. K.; Guru, Santosh K.; Pathania, Anup S.; Sharma, Rashmi; Chib, Reena; Aravinda, Subrayashastry; Gupta, Vivek K.; Khan, Inshad A.; et al. Saccharonol B, a new cytotoxic methylated isocoumarin from Saccharomonospora azurea. *Tetrahedron Letters* **(2013)**, 54(49), 6695-6699. DOI:10.1016/j.tetlet.2013. 09.060

23. Bharate, Jaideep B.; Sharma, Rajni; Aravinda, Subrayashastry; Gupta, Vivek K.; Singh, Baldev; Bharate, Sandip B.; Vishwakarma, Ram A. Montmorillonite clay catalyzed synthesis of functionalized pyrroles through domino four-component coupling of amines, aldehydes, 1,3-dicarbonyl compounds and nitroalkanes. *RSC Advances* **(2013)**, 3(44), 21736-21742. Language: English, Database: CAPLUS, DOI:10.1039/c3ra43324b

24. Jain, Shreyans K.; Pathania, Anup S.; Parshad, Rajinder; Raina, Chandji; Ali, Asif; Gupta, Ajai P.; Kushwaha, Manoj; Aravinda, Subrayashastry; Bhushan, Shashi; Bharate, Sandip B.; et al. Chrysomycins A-C, antileukemic naphthocoumarins from Streptomyces sporoverrucosus. *RSC Advances* **(2013)**, 3(43), 21046-21053. DOI:10.1039/c3ra42884b

25. Bharate, Jaideep B.; Guru, Santosh K.; Jain, Shreyans K.; Meena, Samdarshi; Singh, Parvinder Pal; Bhushan, Shashi; Singh, Baldev; Bharate, Sandip B.; Vishwakarma, Ram A. Cu-Mn spinel oxide catalyzed synthesis of imidazo[1,2-a]pyridines through domino three-component coupling and 5- exo-dig cyclization in water. *RSC Advances* **(2013)**, 3(43), 20869-20876. DOI:10.1039/c3ra42046a

26. Rouf, Abdul; Aga, Mushtaq A.; Kumar, Brijesh; Taneja, Subhash Chandra. A facile approach to chiral 1,4-benzodioxane toward the syntheses of doxazosin, prosympal, piperoxan, and dibozane. *Tetrahedron Letters* **(2013)**, 54(48), 6420-6422. DOI:10.1016/j.tetlet.2013.09.040

27. Dar, Bashir A.; Wani, Abubakar; Rather, Shabir A.; Singh, Baldev. Isothermal Studies of Sorption of Acetic Acid from Waste Water Using Shed Needles from Pine Trees. *Arabian Journal for Science and Engineering* **(2013)**, 38(10), 2595-2599. DOI:10.1007/s13369-012-0492-y

28. Rehman, Shakeel-u-; Latief, Romaisa; Bhat, Khursheed A.; Khuroo, Mohammad A.; Shawl, Abdul S.; Chandra, Suresh. Comparative analysis of the aroma chemicals of Melissa officinalis using hydrodistillation and HS-SPME techniques. Arabian Journal of Chemistry (2013), Ahead of Print. Language: English, Database: CAPLUS, DOI:10.1016/j.arabjc.2013.09.015

29. Gupta, Ajai Prakash; Pandotra, Pankaj; Sharma, Rajni; Kushwaha, Manoj; Gupta, Suphla. Marine resource: a promising future for anticancer drugs. *Studies in Natural Products Chemistry* **(2013)**, 40, 229-235. DOI:10.1016/B978-0-444-59603-1.00008-4

30. Wani, Naiem Ahmad; Gupta, Vivek Kumar; Kant, Rajni; Aravinda, Subrayashastry; Rai, Rajkishor. C5 and C7 intramolecular hydrogen bonds stabilize the structure of N-pyrazinoyl-gabapentin (Pyr-Gpn-OH). *Acta Crystallographica, Section C: Crystal Structure Communications* **(2013)**, 69(10), 1170-1172. DOI:10.1107/S0108270113021781

31. Singh, Baljinder; Vishwakarma, Ram A.; Bharate, Sandip B. QSAR and Pharmacophore Modeling of Natural and Synthetic Antimalarial Prodiginines. *Current Computer-Aided Drug Design* **(2013)**, 9(3), 350-359. DOI:10.2174/15734099113099990020

32. Bhat, Wajid Waheed; Dhar, Niha; Razdan, Sumeer; Rana, Satiander; Mehra, Rukmankesh; Nargotra, Amit; Dhar, Rekha S.; Ashraf, Nasheeman; Vishwakarma, Ram; Lattoo, Surrinder K. Molecular characterization of UGT94F2 and UGT86C4, two glycosyltransferases from Picrorhiza kurrooa: comparative structural insight and evaluation of substrate recognition. *PLoS One* **(2013)**, 8(9), e73804. DOI:10.1371/journal.pone.0073804

33. Jain, Shreyans K.; Pathania, Anup S.; Meena, Samdarshi; Sharma, Rajni; Sharma, Ashok; Singh, Baljinder; Gupta, Bishan D.; Bhushan, Shashi; Bharate, Sandip B.; Vishwakarma, Ram A. Semisynthesis of Mallotus B from Rottlerin: Evaluation of Cytotoxicity and Apoptosis-Inducing Activity. *Journal of Natural Products* **(2013)**, 76(9), 1724-1730. DOI:10.1021/np400433g

34. Lone, Ali Mohd; Bhat, Bilal Ahmad; Mehta, Goverdhan. A general, flexible, ring closing metathesis (RCM) based strategy for accessing the fused furo[3,2-b]furanone moiety present in diverse bioactive natural products. *Tetrahedron*

Letters **(2013)**, 54(41), 5619-5623. DOI:10.1016/j.tetlet.2013.08.021

35. Verma, M. K.; Chandra, Suresh. Monarda citriodora Cerv. ex Lag.: an alternate rich source of thymol. *Indian Perfumer* **(2013)**, 57(2), 43-48.

36. Dar, Bashir Ahmad; Bhatti, Prince; Singh, A. P.; Lazar, Anish; Sharma, Parduman R.; Sharma, Meena; Singh, Baldev. Clay entrapped Cu(OH)x as an efficient heterogeneous catalyst for ipso-hydroxylation of arylboronic acids. *Applied Catalysis, A: General* **(2013)**, 466, 60-67. DOI:10.1016/j.apcata.2013.06.051

37. Bharate, Sonali S.; Vishwakarma, Ram A. Impact of preformulation on drug development. *Expert Opinion on Drug Delivery* **(2013)**, 10(9), 1239-1257. DOI:10.1517/17425247.2013.783563

38. Dar, Abdul Rouf; Aga, Mushtaq A.; Kumar, Brijesh; Yousuf, Syed Khalid; Taneja, Subhash Chandra. Regioselective monochloro-substitution in carbohydrates and non-sugar alcohols via Mitsunobu reaction: applications in the synthesis of reboxetine. *Organic & Biomolecular Chemistry* (2013), 11(36), 6195-6207. DOI:10.1039/c3ob40853a

39. Kaur, Tarandeep; Hussain, Khadim; Koul, Sushma; Vishwakarma, Ram; Vyas, Dhiraj. Evaluation of nutritional and antioxidant status of Lepidium latifolium Linn.: a novel phytofood from Ladakh. *PLoS One* **(2013)**, 8(8), e69112. DOI:10.1371/journal.pone.0069112

40. Shakeel-u-Rehman; Sofi, Shahnawaz Nabi; Khuroo, Mohammad Akbar; Taneja, Subhash Chandra; Bhat, Khursheed Ahmad; Vishwakarma, Ram. New natural compounds from Rhododendron lepidotum. *Natural Product Research* **(2013)**, 27(21), 2033-2038. DOI:10.1080/14786419.2013.824439

41. Sawant, Sanghapal D.; Srinivas, Mahesuni; Aravinda Kumar, K. A.; Lakshma Reddy, G.; Singh, Parvinder Pal; Singh, Baldev; Sharma, Amit Kumar; Sharma, P. R.; Vishwakarma, Ram A. Ligand-free C-N bond formation in aqueous medium using a reusable Cu-Mn bimetallic catalyst. *Tetrahedron Letters* **(2013)**, 54(39), 5351-5354. DOI:10.1016/j.tetlet.2013.07.095

42. Kumar, Sunil; Pathania, Anup Singh; Saxena, A. K.; Vishwakarma, R. A.; Ali, Asif; Bhushan, Shashi. The anticancer potential of flavonoids isolated from the stem bark of Erythrina suberosa through induction of apoptosis and inhibition of STAT signaling pathway in human leukemia HL-60 cells. *Chemico-Biological Interactions* **(2013)**, 205(2), 128-137. DOI:10.1016/j.cbi.2013.06.020

43. Yusuf, Farnaz; Chaubey, Asha; Jamwal, Urmila; Parshad, Rajinder. A new isolate from Fusarium proliferatum (AUF-2) for efficient nitrilase production. *Applied Biochemistry and Biotechnology* **(2013)**, 171(4), 1022-1031. DOI:10.1007/s12010-013-0416-7

44. Khan, Imran; Sangwan, Payare L.; Dar, Alamgir A.; Rafiq, Rather A.; Farrukh, Mufti R.; Dhar, Jagdish K.; Tasduq, Sheikh A.; Koul, Surrinder. A validated high-performance thin-layer chromatography method for the identification and simultaneous quantification of six markers from Platanus orientalis and their cytotoxic profiles against skin cancer cell lines. *Journal of Separation Science* **(2013)**, 36(16), 2602-2610. DOI:10.1002/jssc.201300380

45. Dar, B. A.; Wani, A.; Rather, Sh. A.; Singh, B. Isothermal studies of sorption of acetic acid from wastewater using shed needles of pine trees. *Journal of Environmental Protection and Ecology* **(2013)**, 14(2), 559-565.

46. Rashid, Showkat; Dar, Bilal Ahmad; Majeed, Rabiya; Hamid, Abid; Bhat, Bilal Ahmad. Synthesis and biological evaluation of ursolic acid-triazolyl derivatives as potential anti-cancer agents. *European Journal of Medicinal Chemistry* **(2013)**, 66, 238-245. Language: English, Database: CAPLUS, DOI:10.1016/j.ejmech.2013.05.029

47. Dar, Bashir Ahmad; Bhowmik, Amrita; Sharma, Amit; Sharma, Parduman R.; Lazar, Anish; Singh, A. P.; Sharma, Meena; Singh, Baldev. Ultrasound promoted efficient and green protocol for the expeditious synthesis of 1, 4 disubstituted 1, 2, 3-triazoles

using Cu(II) doped clay as catalyst. *Applied Clay Science* **(2013)**, 80-81, 351-357. DOI:10.1016/j.clay.2013.06.030

48. Lone, Shabir H.; Bhat, Khursheed A.; Shakeel-u-Rehman; Majeed, Rabiya; Hamid, Abid; Khuroo, Mohd A. Synthesis and biological evaluation of amino analogs of Ludartin: Potent and selective cytotoxic agents. *Bioorganic & Medicinal Chemistry Letters* **(2013)**, 23(17), 4931-4934. DOI:10.1016/j.bmcl.2013.06.068

49. Dar, Bashir Ahmad; Ahmad, Syed Naseer; Wagay, Mohammad Arif; Hussain, Altaf; Ahmad, Nisar; Bhat, Khursheed Ahmad; Khuroo, Mohammad Akbar; Sharma, Meena; Singh, Baldev. Ultrasound promoted expeditious, catalyst-free and solvent-free approach for the synthesis of N,N'-diaryl-substituted formamidines at room temperature. *Tetrahedron Letters* **(2013)**, 54(36), 4880-4884. DOI:10.1016/j.tetlet.2013.06.131

50. Zilla, Mahesh K.; Qadri, Masroor; Pathania, Anup S.; Strobel, Gary A.; Nalli, Yedukondalu; Kumar, Sunil; Guru, Santosh K.; Bhushan, Shashi; Singh, Sanjay K.; Vishwakarma, Ram A.; et al. Bioactive metabolites from an endophytic Cryptosporiopsis sp. inhabiting Clidemia hirta. *Phytochemistry* (Elsevier) **(2013)**, 95, 291-297. DOI:10.1016/j.phytochem.2013.06.021

51. Sharma, Rajni. Chloroacetonitrile. *Synlett* **(2013)**, 24(9), 1160-1161.

52. Reddy, Aleti R.; Sangwan, Payare L.; Chinthakindi, Praveen K.; Farooq, Saleem; Siddaiah, Vidavalur; Koul, Surrinder. N-Iodosuccinimide: A Highly Effective Regioselective Reagent for Iodoesterification of Alkenes. *Helvetica Chimica Acta* **(2013)**, 96(7), 1313-1324. DOI:10.1002/hlca.201200383

53. Singh, Inderpal; Amin, Hina; Rah, Bilal; Goswami, Anindya. Targeting EGFR and IGF 1R: a promising combination therapy for metastatic cancer. *Frontiers in Bioscience*, Scholar Edition **(2013)**, S5(1), 231-246.

54. Dar, Bashir A.; Patidar, Praveen; Kumar, Sunil; Wagay, Mohammad Arif; Sahoo, Akshay K.; Sharma, Parduman R.; Pandey, Sanjay; Sharma, Meena; Singh, Baldev. Fe-Al/clay as an efficient heterogeneous catalyst for solvent-free synthesis of 3, 4-dihydropyrimidones. *Journal of Chemical Sciences* (Bangalore, India) **(2013)**, 125(3), 545-553. DOI:10.1007/s12039-013-0413-y

55. Rao, D. Nageswar; Rasheed, Sk.; Aravinda, S.; Vishwakarma, Ram A.; Das, Parthasarathi. Base and ligand free copper-catalyzed N-arylation of 2-amino-N-heterocycles with boronic acids in air. *RSC Advances* **(2013)**, 3(29), 11472-11475. Language: English, Database: CAPLUS, DOI:10.1039/c3ra40735g

56. Qurishi, Yasrib; Hamid, Abid; Sharma, Parduman R.; Wani, Zahoor A.; Mondhe, Dilip M.; Singh, Shashank K.; Zargar, Mohmmad A.; Andotra, Samar S.; Shah, Bhahwal A.; Taneja, Subhash C.; et al. NF-[redacted]B down-regulation and PARP cleavage by novel 3-[redacted]butyryloxy-[redacted] boswellic acid results in cancer cell specific apoptosis and in vivo tumor regression. *Anti-Cancer Agents in Medicinal Chemistry* **(2013)**, 13(5), 777-790. DOI:10.2174/1871520611313050012

57. Singh, Baljinder; Sidiq, Tabasum; Joshi, Prashant; Jain, Shreyans K.; Lawaniya, Yogesh; Kichlu, Surinder; Khajuria, Anamika; Vishwakarma, Ram A.; Bharate, Sandip B. Anti-inflammatory and immunomodulatory flavones from Actinocarya tibetica Benth. *Natural Product Research* **(2013)**, 27(23), 2227-2230. DOI:10.1080/14786419.2013.805334

58. Yousuf, Syed Khalid; Mukherjee, Debaraj; Mallikharjunrao, L.; Taneja, Subhash C. Highly Regio- and Stereoselective One-Pot Synthesis of Carbohydrate-Based Butyrolactones [Erratum to document cited in CA154:234946]. *Organic Letters* **(2013)**, 15(12), 3178-3179. DOI:10.1021/ol400407z

59. Mukherjee, Debaraj; Yousuf, Syed Khalid; Taneja, Subhash Chandra. Domino Transformation of D-Glucal to Racemic [redacted]Substituted [redacted] Hydroxymethyl Furfuryl Derivatives [Erratum to document cited in CA149:513638]. *Organic Letters* **(2013)**, 15(12), 3180. DOI:10.1021/ol400406v

60. Majeed, Rabiya; Sangwan, Payare L.; Chinthakindi, Praveen K.; Khan, Imran; Dangroo, Nisar A.; Thota, Niranjan; Hamid, Abid; Sharma, Parduman R.; Saxena, Ajit K.; Koul, Surrinder. Synthesis of 3-O-propargylated betulinic acid and its 1,2,3-triazoles as potential apoptotic agents. *European Journal of Medicinal Chemistry* **(2013)**, 63, 782-792. DOI:10.1016/j.ejmech.2013.03.028

61. Khazir, Jabeena; Singh, Parvinder Pal; Reddy, D. Mahendhar; Hyder, Irfan; Shafi, Syed; Sawant, S. D.; Chashoo, Gousia; Mahajan, Ajay; Alam, M. S.; Saxena, A. K.; et al. Synthesis and anticancer activity of novel spiro-isoxazoline and spiro-isoxazolidine derivatives of [redacted] santonin. *European Journal of Medicinal Chemistry* **(2013)**, 63, 279-289. DOI:10.1016/j.ejmech.2013.01.003

62. Bharate, Sandip B.; Bharate, Jaideep B.; Khan, Shabana I.; Tekwani, Babu L.; Jacob, Melissa R.; Mudududdla, Ramesh; Yadav, Rammohan R.; Singh, Baljinder; Sharma, P. R.; Maity, Sudip; et al. Discovery of 3,3'-diindolylmethanes as potent antileishmanial agents. *European Journal of Medicinal Chemistry* **(2013)**, 63, 435-443. DOI:10.1016/j.ejmech.2013.02.024

63. Ahmad Wani, Naiem; Gupta, Vivek K.; Kant, Rajni; Aravinda, Subrayashastry; Rai, Rajkishor. 2-(1-Amino-4-tert-butylcyclohexyl)acetic acid (tBu-[redacted],3-Ac6c) hemihydrates. *Acta Crystallographica, Section E: Structure Reports Online* **(2013)**, 69(6), o888. Language: English, Database: CAPLUS, DOI:10.1107/S1600536813012725

64. Bharate, Sandip B.; Yadav, Rammohan R.; Khan, Shabana I.; Tekwani, Babu L.; Jacob, Melissa R.; Khan, Ikhlas A.; Vishwakarma, Ram A. Meridianin G and its analogs as antimalarial agents. *MedChemComm* **(2013)**, 4(6), 1042-1048. DOI:10.1039/c3md00097d.

65. Bharate, Sandip B.; Padala, Anil K.; Dar, Bashir A.; Yadav, Rammohan R.; Singh, Baldev; Vishwakarma, Ram A. Montmorillonite clay Cu(II) catalyzed domino one-pot multicomponent synthesis of 3,5-disubstituted isoxazoles. *Tetrahedron Letters* **(2013)**, 54(27), 3558-3561. DOI:10.1016/j.tetlet.2013.04.102

66. Khazir, Jabeena; Mir, Bilal Ahmad; Mir, Shabir Ahmad; Cowan, Don. Natural products as lead compounds in drug discovery. *Journal of Asian Natural Products Research* **(2013),** 15(7), 764-788. DOI:10.1080/10286020.2013.798314

67. Gupta, P. N.; Singh, G. D.; Sharma, S. C.; Singh, S.; Tikoo, M. K.; Gupta, N.; Johri, R. K. Nanoparticles as adjuvant(S) for mucosal vaccine delivery. *Advances in Nanoscience and Nanotechnology* **(2013)**, 1(Nanomedicine and Drug Delivery), 65-85

68. Aga, Mushtaq A.; Kumar, Brijesh; Rouf, Abdul; Shah, Bhahwal A.; Andotra, Samar S.; Taneja, Subhash C. Natural (-)-Vasicine as a Novel Source of Optically Pure 1-Benzylpyrrolidin-3-ol. *Helvetica Chimica Acta* **(2013)**, 96(5), 969-977. DOI:10.1002/hlca.201200307

69. Bharate, Sandip B.; Sawant, Sanghapal D.; Singh, Parvinder Pal; Vishwakarma, Ram A. Kinase Inhibitors of Marine Origin. *Chemical Reviews* (Washington, DC, United States) **(2013)**, 113(8), 6761-6815. DOI:10.1021/cr300410v

70. Hussain, Altaf; Yousuf, Syed Khalid; Sharma, Deepak K.; Mallikharjuna Rao, L.; Singh, Baldev; Mukherjee, Debaraj. Design and synthesis of carbohydrate based medium sized sulfur containing benzannulated macrocycles: applications of Sonogashira and Heck coupling. *Tetrahedron* **(2013)**, 69(26), 5517-5524. Language: English, Database: CAPLUS, DOI:10.1016/j.tet.2013.04.090

71. Bharate, Sandip B.; Mudududdla, Ramesh; Sharma, Rohit; Vishwakarma, Ram A. The first method for C-devinylation of aromatic systems. *Tetrahedron Letters* **(2013)**, 54(23), 2913-2915. DOI:10.1016/j.tetlet.2013.03.064

72. Sidiq, Tabasum; Khajuria, Anamika; Shafi, Syed; Ismail, Tabasum; Sampath Kumar, Halmathur; Kannappa Srinivas, Vellimedu; Krishna, Ella; Kamal Johri, Rakesh. Efficacy evaluation of two synthetic lysine lipidated

tripeptides as vaccine adjuvants against HBsAg. *European Journal of Pharmacology* **(2013)**, 705(1-3), 68-78. DOI:10.1016/j.ejphar.2013.01.064

73. Nissar, Ashraf U.; Farrukh, Mufti R.; Kaiser, Peerzada J.; Rafiq, Rather A.; Afnan, Quadri; Bhushan, Shashi; Adil, Hassan S.; Subhash, Bhardjwaj C.; Tasduq, Sheikh A. Effect of N-acetyl cysteine (NAC), an organosulfur compound from Allium plants, on experimentally induced hepatic prefibrogenic events in wistar rat. *Phytomedicine* **(2013)**, 20(10), 828-833. DOI:10.1016/j.phymed.2013.03.009

74. Kumar, Suresh; Kumar, Ajay; Pathania, Anup Singh; Guru, Santosh Kumar; Jada, Srinivas; Sharma, Parduman Raj; Bhushan, Shashi; Saxena, Ajit Kumar; Kumar, H. M. Sampath; Malik, Fayaz. Tiron and trolox potentiate the autophagic cell death induced by magnolol analog Ery5 by activation of Bax in HL-60 cells. *Apoptosis* **(2013)**, 18(5), 605-617. DOI:10.1007/s10495-013-0805-y

75. Chaubey, Asha; Raina, Chand; Parshad, Rajinder; Rouf, Abdul; Gupta, Pankaj; Taneja, Subhash C. Bioconversion of sucralose-6-acetate to sucralose using immobilized microbial cells. *Journal of Molecular Catalysis B: Enzymatic* **(2013)**, 91, 81-86. DOI:10.1016/j.molcatb.2013.02.007

76. Verma, Mahendra K.; Najar, Ishtiyaq A.; Tikoo, Manoj K.; Singh, Gurdarshan; Gupta, Devinder K.; Anand, Rajneesh; Khajuria, Ravi K.; Sharma, Subhash C.; Johri, Rakesh K. Development of a validated UPLC-qTOF-MS method for the determination of curcuminoids and their pharmacokinetic study in mice. Daru, *Journal of Pharmaceutical Sciences* **(2013)**, 21, 11. DOI:10.1186/2008- 2231-21-11

77. Tantry, M. A.; Shawl, A. S.; Khuroo, M. A.; Ali, N. Erratum to the article "Homoisoflavanones from Lespedeza juncea. *Chemistry of Natural Compounds* **(2013)**, 49(1), 198. DOI:10.1007/s10600-013-0559-3

78. Tantry, M. A.; Shawl, A. S.; Arora, B. S.; Purinima, B.; Ahmad, K.; Khuroo, M. A. Erratum to: Glutinane triterpenes from the stem bark of Euonymus hamiltonianus. *Chemistry of Natural Compounds* **(2013)**, 49(1), 200. DOI:10.1007/s10600-013-0561-9

79. Tantry, M. A.; Khan, R.; Shawl, A. S.; Khuroo, M. A. Erratum to the article "Phenolic glycosides from Lespedeza juncea. *Chemistry of Natural Compounds* **(2013)**, 49(1), 199. DOI:10.1007/s10600-013-0560-x

80. Shairgojray, Bashir Ahmad; Dar, Aijaz Ahmad; Bhat, Bilal Ahmad. Micellar promiscuity: an expeditious approach to Morita-Baylis-Hillman reaction. *Tetrahedron Letters* **(2013)**, 54(19), 2391-2394. DOI:10.1016/j.tetlet.2013.02.097

81. Pandotra, Pankaj; Gupta, Ajai P.; Husain, Mohd. K.; Gandhiram; Gupta, Suphla. Evaluation of genetic diversity and chemical profile of ginger cultivars in north-western Himalayas. *Biochemical Systematics and Ecology* **(2013)**, 48, 281-287. DOI:10.1016/j.bse.2013.01.004

82. Bharate, Sandip B.; Yadav, Rammohan R.; Vishwakarma, Ram A. QSAR and pharmacophore study of Dyrk1A inhibitory meridianin analogs as potential agents for treatment of neurodegenerative diseases. *Medicinal Chemistry* **(2013)**, 9(1), 152-161.

83. Riyaz-Ul-Hassan, S.; Verma, V.; Qazi, G. N. Real-time PCR-based rapid and culture-independent detection of Salmonella in dairy milk - addressing some core issues. *Letters in Applied Microbiology* **(2013)**, 56(4), 275-282. DOI:10.1111/lam.12046

84. Ali, Asif; Khajuria, Anamika; Sidiq, Tabasum; Kumar, Ashok; Thakur, Narsinh L.; Naik, Deepak; Vishwakarma, Ram A. Modulation of LPS induced inflammatory response by Lawsonyl monocyclic terpene from the marine derived Streptomyces sp. *Immunology Letters* **(2013)**, 150(1-2), 79-86. DOI:10.1016/j.imlet.2012.09.001

85. Rana, Satiander; Lattoo, Surrinder K.; Dhar, Niha; Razdan, Sumeer; Bhat, Wajid Waheed; Dhar, Rekha S.; Vishwakarma, Ram. NADPH-cytochrome P450 reductase: molecular cloning and

functional characterization of two paralogs from Withania somnifera (L.) Dunal. *PLoS One* **(2013)**, 8(2), e57068. DOI:10.1371/journal.pone.0057068

86. Bhat, Archana; Riyaz-Ul-Hassan, Syed; Ahmad, Nasier; Srivastava, Nidhi; Johri, Sarojini. Isolation of cold-active, acidic endocellulase from Ladakh soil by functional metagenomics. *Extremophiles* **(2013)**, 17(2), 229-239. Language. DOI:10.1007/s00792-012-0510-8

87. Dar, Bashir Ahmad; Chakraborty, Arup; Sharma, Parduman R.; Shrivastava, Varsha; Bhowmik, Amrita; Vyas, Dushyant; Bhatti, Prince; Sharma, Meena; Singh, Baldev. Grinding-induced rapid, convenient and solvent free approach for the one pot synthesis of -aminophosphonates using aluminium pillared interlayered clay catalyst. *Journal of Industrial and Engineering Chemistry* (Amsterdam, Netherlands) **(2013)**, 19(3), 732-738. DOI:10.1016/j.jiec.2012.10.018

88. Riyaz-Ul-Hassan, Syed; Strobel, Gary; Geary, Brad; Sears, Joe. An endophytic Nodulisporium sp. from Central America producing volatile organic compounds with both biological and fuel potential. *Journal of Microbiology and Biotechnology* **(2013)**, 23(1), 29-35. DOI:10.4014/jmb.1208.04062

89. Chinthakindi, Praveen K.; Sangwan, Payare L.; Farooq, Saleem; Aleti, Rajeshwar R.; Kaul, Anupurna; Saxena, Ajit K.; Murthy, Y. L. N.; Vishwakarma, Ram A.; Koul, Surrinder. Diminutive effect on T and B-cell proliferation of non-cytotoxic [redacted]santonin derived 1,2,3-triazoles: A report. *European Journal of Medicinal Chemistry* **(2013)**, 60, 365-375. DOI:10.1016/j.ejmech.2012.12.018

90. Singh, Parvinder Pal; Aithagani, Sravan Kumar; Yadav, Mahipal; Singh, Varun Pratap; Vishwakarma, Ram A. Iron-catalyzed Cross-Coupling of Electron-Deficient Heterocycles and Quinone with Organoboron Species via Innate C-H Functionalization: Application in Total Synthesis of Pyrazine Alkaloid Botryllazine A. *Journal of Organic Chemistry* **(2013)**, 78(6), 2639-2648. DOI:10.1021/jo302797r

91. Kumar, Manjeet; Qadri, Masroor; Sharma, Parduman Raj; Kumar, Arvind; Andotra, Samar S.; Kaur, Tandeep; Kapoor, Kamini; Gupta, Vivek K.; Kant, Rajni; Hamid, Abid; et al. Tubulin Inhibitors from an Endophytic Fungus Isolated from Cedrus deodara. *Journal of Natural Products* **(2013)**, 76(2), 194-199. DOI:10.1021/np3006666

92. Sharma, Deepak K.; Hussain, Altaf; Lambu, Mallikharjuna Rao; Yousuf, Syed Khalid; Maiety, Sudip; Singh, Baldev; Mukherjee, Debaraj. Fe/Al pillared clay catalyzed solvent-free synthesis of bisindolylmethanes using diversely substituted indoles and carbonyl compounds. *RSC Advances* **(2013)**, 3(7), 2211-2215. DOI:10.1039/c2ra22258b

93. Sharma, Punita; Kumar, Suresh; Ali, Furqan; Anthal, Sumati; Gupta, Vivek K.; Khan, Inshad A.; Singh, Surjeet; Sangwan, Payare L.; Suri, Krishan A.; Gupta, Bishan D.; et al. Synthesis and biologic activities of some novel heterocyclic chalcone derivatives [Erratum to document cited in CA159:042483]. *Medicinal Chemistry Research* **(2013)**, 22(9), 4547. Language: English, Database: CAPLUS, DOI:10.1007/s00044-012-0444-9

94. Razdan, Sumeer; Bhat, Wajid Waheed; Rana, Satiander; Dhar, Niha; Lattoo, Surrinder K.; Dhar, Rekha S.; Vishwakarma, Ram A. Molecular characterization and promoter analysis of squalene epoxidase gene from Withania somnifera (L.) Dunal. *Molecular Biology Reports* **(2013)**, 40(2), 905-916. DOI:10.1007/s11033-012-2131-9

95. Dar, Bashir A.; Dadhwal, Sumit; Singh, Gurkirpal; Garg, Pankaj; Sharma, Pushpa; Singh, Baldev. Vapour Phase Conversion of Glycerol to Acrolein over Supported Copper. *Arabian Journal for Science and Engineering* **(2013)**, 38(1), 37-40. DOI:10.1007/s13369-012-0395-y

96. Rashid, Showkat; Rather, Manzoor Ahmad; Shah, Wajaht Amin; Bhat, Bilal Ahmad. Chemical composition, antimicrobial, cytotoxic and antioxidant activities of the essential oil of Artemisia indica Willd. *Food Chemistry* **(2013)**, 138(1), 693-700. DOI:10.1016/j.foodchem.2012.10.102

97. Dar, Bashir A.; Sahu, Akshya K.; Patidar, Praveen; Sharma, Parduman R.; Mupparapu, Nagaraju; Vyas, Dushyant; Maity, Sudip; Sharma, Meena; Singh, Baldev. Heteropolyacid-clay nano-composite as a novel heterogeneous catalyst for the synthesis of 2,3-dihydroquinazolinones. *Journal of Industrial and Engineering Chemistry* (Amsterdam, Netherlands) **(2013)**, 19(2), 407-412. DOI:10.1016/j.jiec.2012.08.027

98. Sharma, Punita; Kumar, Suresh; Ali, Furqan; Anthal, Sumati; Gupta, Vivek K.; Khan, Inshad A.; Singh, Surjeet; Sangwan, Payare L.; Suri, Krishan A.; Gupta, Bishan D.; et al. Synthesis and biologic activities of some novel heterocyclic chalcone derivatives. *Medicinal Chemistry Research* **(2013)**, 22(8), 3969-3983. DOI:10.1007/s00044-012-0401-7

99. Bhushan, Shashi; Kakkar, Vandita; Pal, Harish Chandra; Guru, Santosh Kumar; Kumar, Ajay; Mondhe, D. M.; Sharma, P. R.; Taneja, Subhash Chandra; Kaur, Indu Pal; Singh, Jaswant; et al. Enhanced Anticancer Potential of Encapsulated Solid Lipid Nanoparticles of TPD: A Novel Triterpenediol from Boswellia serrata. *Molecular Pharmaceutics* **(2013)**, 10(1), 225-235. DOI:10.1021/mp300385m

100. Rayees, Sheikh; Sharma, Rohit; Singh, Gurdarshan; Najar, Ishtiyaq Ahmad; Singh, Amarinder; Ahamad, Dastagir Basheer; Sharma, Subash Chander; Tikoo, Manoj Kumar; Gupta, Vijay Kumar; Sangwan, Payare Lal; et al. Acute, sub-acute and general pharmacological evaluation of 5-(3,4 methylenedioxyphenyl)-4-ethyl-2E,4Epentadienoic acid piperidide (SK-20): A novel drug bioavailability enhancer. *Environmental Toxicology and Pharmacology* **(2013)**, 35(2), 347-359. DOI:10.1016/j.etap.2012.08.007

101. Gupta, Pankaj; Rouf, Abdul; Shah, Bhahwal A.; Mukherjee, Debaraj; Taneja, Subhash C. Efficient Preparation of Biologically Important 1,2-Amino Alcohols. *Synthetic Communications* **(2013)**, 43(4), 505-519. DOI:10.1080/00397911.2011.603876

102. Mehra, Rukmankesh; Nargotra, Amit; Shah, Bhahwal A.; Taneja, Subhash C.; Vishwakarma, Ram A.; Koul, Surrinder. Pro-apoptotic properties of parthenin analogs: a quantitative structure-activity relationship study. *Medicinal Chemistry Research* **(2013)**, 22(5), 2303-2311. DOI:10.1007/s00044-012-0225-5

103. Bharate, Sandip B.; Singh, Baljinder; Bharate, Jaideep B.; Jain, Shreyans K.; Meena, Samdarshi; Vishwakarma, Ram A. QSAR and pharmacophore modeling of N-acetyl-2-aminobenzothiazole class of phosphoinositide-3-kinase-inhibitors. *Medicinal Chemistry Research* **(2013)**, 22(2), 890-899. DOI:10.1007/s00044-012-0081-3

104. Qadri Masroor; Johri Sarojini; Shah Bhahwal A; Khajuria Anamika; Sidiq Tabasum; Lattoo Surrinder K; Abdin Malik Z; Riyaz-Ul-Hassan Syed. Identification and bioactive potential of endophytic fungi isolated from selected plants of the Western Himalayas. *SpringerPlus* **(2013)**, 2(1), 8.

105. Bhatti Rajbir; Singh J; Saxena A K; Suri Nitasha; Ishar M P S. Pharmacognostic standardisation and antiproliferative activity of Aegle marmelos (L.) Correa leaves in various human cancer cell lines. *Indian journal of pharmaceutical sciences* **(2013)**, 75(6), 628-34.

106. Bhanot Abhishek; Sharma Rohini; Singh Satnam; Noolvi Malleshappa N; Singh Shashank. In vitro anti cancer activity of ethanol extract fractions of Aerva lanata L. *Pakistan journal of biological sciences*: PJBS **(2013)**, 16(22), 1612-7.

107. Gairola Sumeet; Sharma Jyotsana; Gaur R D; Painuli R M; Siddiqi T O. Plants used for treatment of dysentery and diarrhoea by the Bhoxa community of district Dehradun, Uttarakhand, India. *Journal of ethnopharmacology* **(2013)**.

108. Kumar Shashank; Pandey Abhay K; Chashoo Gousia; Saxena Ajit K. Parthenium hysterophorus: a probable source of anticancer, antioxidant and anti-HIV agents. *BioMed research international* **(2013)**, 2013810734.

109. Wani Naiem Ahmad; Gupta Vivek Kumar; Kant Rajni; Aravinda Subrayashastry; Rai

Rajkishor. C5 and C7 intramolecular hydrogen bonds stabilize the structure of N-pyrazinoyl-gabapentin (Pyr-Gpn-OH). *Acta crystallographica. Section C, Crystal structure communications* **(2013)**, 69(Pt 10), 1170-2.

110. Rather Manzoor A; Bhat Bilal A; Qurishi Mushtaq A. Multicomponent phytotherapeutic approach gaining momentum: Is the "one drug to fit all" model breaking down? *Phytomedicine* : international journal of phytotherapy and phytopharmacology **(2013)**, 21(1), 1-14.

111. Pathania Anup Singh; Guru Santosh Kumar; Verma M K; Sharma Chetna; Abdullah Sheikh Tasduq; Malik Fayaz; Chandra Suresh; Katoch Meenu; Bhushan Shashi. Disruption of the PI3K/AKT/mTOR signaling cascade and induction of apoptosis in HL-60 cells by an essential oil from Monarda citriodora. *Food and chemical toxicology* : an international journal published for the British Industrial Biological Research Association **(2013)**, 62246-54.

112. Constant Anatole Pieme; Guru Santoh Kumar; Bathelemy Ngamegni; Jeanne Ngogang; Bhushan Shashi; Murayama Tetsuya; Saxena Ajit Kumar. Ethyl acetate fraction of Garcina epunctata induces apoptosis in human promyelocytic cells (HL-60) through the ROS generation and G0/G1 cell cycle arrest: a bioassay-guided approach. *Environmental toxicology and pharmacology* **(2013)**, 36(3), 865-74.

113. Ahmad Wani Naiem; Gupta Vivek K; Kant Rajni; Aravinda Subrayashastry; Rai Rajkishor. 2-(1-Amino-4-tert-butyl-cyclo-hex-yl)acetic acid (tBu-[redacted](3,3)-Ac6c) hemihydrates. *Acta crystallographica. Section E, Structure reports online* **(2013)**, 69(Pt 6), o888.

114. Rayees Sheikh; Kumar Ajay; Rasool Shafaq; Kaiser Peerzada; Satti Naresh Kumar; Sangwan Payare Lal; Singh Surjeet; Johri Rakesh Kamal; Singh Gurdarshan. *Immunological investigations* **(2013)**, 42(6), 470-80.

115. Khazir Jabeena; Singh Parvinder Pal; Reddy D Mahendhar; Hyder Irfan; Shafi Syed; Sawant S D; Chashoo Gousia; Mahajan Ajay; Alam M S; Saxena A K; et al. Synthesis and anticancer activity of novel spiro-isoxazoline and spiro-isoxazolidine derivatives of [redacted] santonin. *European journal of medicinal chemistry* **(2013)**, 63279-89.

116. Chinthakindi Praveen K; Sangwan Payare L; Farooq Saleem; Aleti Rajeshwar R; Kaul Anupurna; Saxena Ajit K; Murthy Y L N; Vishwakarma Ram A; Koul Surrinder. Diminutive effect on T and B-cell proliferation of non-cytotoxic [redacted]santonin derived 1,2,3-triazoles: a report. *European journal of medicinal chemistry* **(2013)**, 60365-75.

LIST OF PUBLICATIONS
(Calender Year: 2014)

1. Nargotra, Amit; Rukmankesh; Ali, Shakir; Koul, Surrinder. Structural Characterization of Bacillus subtilis Membrane Protein Bmr: An In Silico Approach. *Current Computer-Aided Drug Design* **(2014)**, 10(3), 226-236. DOI:10.2174/157340991003150302230455

2. Dar, Bashir A.; Ahmad, Nisar; Patial, Jyoti; Sharma, Parveen; Bindu, Kushal; Maity, Sudip; Singh, Baldev. Sulfated zirconia as an efficient heterogeneous and reusable catalyst for one pot synthesis of flavanones. *Journal of Saudi Chemical Society* **(2014)**, 18(5), 464-468. DOI:10.1016/j.jscs.2011.09.015

3. Rana, Satiander; Bhat, Wajid Waheed; Dhar, Niha; Pandith, Shahzad A.; Razdan, Sumeer; Vishwakarma, Ram; Lattoo, Surrinder K. Molecular characterization of two A-type P450s, WsCYP98A and WsCYP76A from Withania somnifera (L.) Dunal: expression analysis and withanolide accumulation in response to exogenous elicitations. *BMC Biotechnology* **(2014)**, 14, 89/1-89/17. DOI:10.1186/s12896-014-0089-5

4. Pandotra, Pankaj; Husain, Mohd Kashif; Ram, Gandhi; Gupta, Suphla; Gupta, Ajai Prakash. Retrotransposon based genetic status of North-West Himalayan Zingiber officinale revealed high heterogeneity. *Journal of Plant Biochemistry and Biotechnology* **(2014)**, 23(2), 211-216. DOI:10.1007/s13562-013-0196-8

5. Meenu, Katoch; Singh, Gurpreet; Vishwakarma, R. A. Molecular mechanism of cellulase production systems in Trichoderma. *Biotechnology and Biology of Trichoderma* **(2014)**, 319-324. DOI:10.1016/B978-0-444-59576-8.00022-9

6. Qazi, Asif Khurshid; Hussain, Aashiq; Aga, Mushtaq A.; Ali, Shakir; Taneja, Subhash Chandra; Sharma, Parduman Raj; Saxena, Ajit Kumar; Mondhe, Dilip M.; Hamid, Abid. Cell specific apoptosis by RLX is mediated by NFκB in human colon carcinoma HCT-116 cells. *BMC Cell Biology* **(2014)**, 15, 36/1-36/9. DOI:10.1186/1471-2121-15-36

7. Nehate, Chetan; Jain, Sharad; Saneja, Ankit; Khare, Vaibhav; Alam, Noor; Dubey, Ravindra Dhar; Gupta, Prem N. Paclitaxel Formulations: Challenges and Novel Delivery Options. *Current Drug Delivery* **(2014)**, 11(6), 666-686. DOI:10.2174/1567201811666140609154949

8. Katoch, Meenu; Salgotra, Aseem; Singh, Gurpreet. Endophytic fungi found in association with Bacopa monnieri as potential producers of industrial enzymes and antimicrobial bioactive compounds. *Brazilian Archives of Biology and Technology* **(2014)**, 57(5), 714-722. DOI:10.1590/S1516-8913201402502y

9. Devari, Shekaraiah; Kumar, Manjeet; Deshidi, Ramesh; Rizvi, Masood; Shah, Bhahwal Ali. A general metal-free approach for the stereoselective synthesis of C-glycals from unactivated alkynes. *Beilstein Journal of Organic Chemistry* **(2014)**, 10, 2649-2653, 5 pp.. DOI:10.3762/bjoc.10.277

10. Ahmad, Muzamil; Dar, Nawab J.; Bhat, Zubair S.; Hussain, Aehtesham; Shah, Ayatullah; Liu, Hao; Graham, Steven H. Inflammation in Ischemic Stroke: Mechanisms, Consequences and Possible Drug Targets. *CNS & Neurological Disorders: Drug Targets* **(2014)**, 13(8), 1378-1396. DOI:10.2174/1871527313666141023094720

11. Pathania, Anup S.; Kumar, Suresh; Guru, Santosh K.; Bhushan, Shashi; Sharma, Parduman R.; Aithagani, Sravan K.; Singh, Parvinder P.; Vishwakarma, Ram A.; Kumar, Ajay; Malik, Fayaz. The synthetic tryptanthrin analogue suppresses STAT3 signaling and induces caspase dependent apoptosis via ERK up regulation in human leukemia HL-60 cells. *PLoS One* **(2014)**, 9(11), e110411/1-e110411/7, 7 pp. DOI:10.1371/journal.pone.0110411

12. Sahu, Promod Kumar; Sharma, Anjna; Rayees, Sheikh; Kour, Gurieen; Singhi, Amarinder; Khullar, Mowkshi; Magotra, Asmita; Paswan, Shravan Kumar; Gupta, Mehak; Ahmed, Ishtiyaq; et al. Pharmacokinetic study of Piperine in wistar rats after oral and intravenous administration. *International Journal of Drug Delivery* **(2014)**, 6(1), 82-87.

13. Khare, Vaibhav; Alam, Noor; Saneja, Ankit; Dubey, Ravindra Dhar; Gupta, Prem N. Targeted drug delivery systems for pancreatic cancer. *Journal of Biomedical Nanotechnology* **(2014)**, 10(12), 3462-3482. DOI:10.1166/jbn.2014.2036

14. Magotra, Ankita; Nalli, Yedukondalu; Kushwaha, Manoj; Raina, Chand; Gupta, Ajai Prakash; Ali, Asif; Vishwakarma, Ram A.; Chaubey, Asha. An efficient liquid chromatography-tandem mass spectrometry method for the quantification of borrelidin from Streptomyces rochei (ATCC 10739). *Journal of Chemical Technology and Biotechnology* **(2014)**, Ahead of Print. DOI:10.1002/jctb.4562

15. Ahmad Wani, Naiem; Gupta, Vivek K.; Kant, Rajni; Aravinda, Subrayashastry; Rai, Rajkishor. . Conformation and crystal structures of 1-aminocyclohexaneacetic acid (β3,3Ac6c) in N-protected derivatives. *Acta Crystallographica, Section E: Structure Reports Online* **(2014)**, 70(11), 272-277. DOI:10.1107/S1600536814020777

16. Farooq, Saleem; Shakeel-u-Rehman; Dangroo, Nisar Ahmad; Priya, Dev; Banday, Javid Ahmad; Sangwan, Pyare Lal; Qurishi, Mushtaq Ahmad; Koul, Surrinder; Saxena, Ajit Kumar. Isolation, cytotoxicity evaluation and HPLC-quantification of the chemical constituents from Prangos pabularia. *PLoS One* **(2014)**, 9(10), e108713/1-e108713/9, 9 pp.. DOI:10.1371/journal.pone.0108713

17. Bhat, Haroon Mohi-ud-din; Bhat, Khursheed Ahmad; Prabha, Shashi; Hamid, Abid. Antioxidant and cytotoxic activities of Achillea millefolium from Kashmir. *Journal of Academia and Industrial Research* **(2014)**, 2(8), 487-491.

18. Dangroo, Nisar A.; Dar, Alamgir A.; Dar, Bashir Ahmad. An efficient protocol for domino one pot synthesis of 1,2,3-triazoles from natural organic acids and phenols. *Tetrahedron Letters* **(2014)**, 55(49), 6729-6733. DOI:10.1016/j.tetlet.2014.09.123

19. Majeed, R.; Hamid, A.; Sangwan, P. L.; Chinthakindi, P. K.; Koul, S.; Rayees, S.; Singh, G.; Mondhe, D. M.; Mintoo, M. J.; Singh, S. K.; et al. Inhibition of phosphotidylinositol-3 kinase pathway by a novel naphthol derivative of betulinic acid induces cell cycle arrest and apoptosis in cancer cells of different origin. *Cell Death & Disease* **(2014)**, 5(10), e1459. Language: English, Database: CAPLUS, DOI:10.1038/cddis.2014.387

20. Bharate, Jaideep B.; Bharate, Sandip B.; Vishwakarma, Ram A. Metal-Free, Ionic Liquid-Mediated Synthesis of Functionalized Quinolines. *ACS Combinatorial Science* **(2014)**, 16(11), 624-630. DOI:10.1021/co500047w

21. Bharate, Jaideep Bibishan; Vishwakarma, Ram Ashrey; Bharate, Sandip Bibishan; Kushwaha, Manoj; Gupta, Ajai Prakash. Quantification of the polyisoprenylated benzophenones garcinol and isogarcinol using multiple reaction monitoring LC/electrospray ionization-MS/MS analysis of ultrasound-assisted extracts of Garcinia indica fruits. *Journal of AOAC International* **(2014)**, 97(5), 1317-1322. Language: English, Database: CAPLUS, DOI:10.5740/jaoacint.13-137

22. Aithagani, Sravan Kumar; Yempalla, Kushalava Reddy; Munagala, Gurunadham; Vishwakarma, Ram A.; Singh, Parvinder Pal. Metal-free, high yielding synthesis of unsymmetrical biaryl, bi(heteroaryl), aryl vinyl, aryl alkyl sulfones via coupling of aryne with sulfinic acid salts. *RSC Advances* **(2014)**, 4(91), 50208-50211. DOI:10.1039/C4RA07370C

23. Sharma, Deepak K.; Singh, Baldev; Mukherjee, Debaraj. Aldol reaction of kojic acid using alumina supported base catalyst and enzymatic resolution of the aldol adduct by CALB. *Tetrahedron Letters* **(2014)**, 55(42), 5846-5850. DOI:10.1016/j.tetlet.2014.08.113

24. Singh, Baljinder; Guru, Santosh K.; Sharma, Rashmi;

Bharate, Sonali S.; Khan, Inshad Ali; Bhushan, Shashi; Bharate, Sandip B.; Vishwakarma, Ram A. Synthesis and antiproliferative activities of new derivatives of embelin. *Bioorganic & Medicinal Chemistry Letters* **(2014)**, 24(20), 4865-4870. DOI:10.1016/j.bmcl.2014.08.052

25. Bhat, Bilal A.; Maki, Samantha L.; St. Germain, Elijah J.; Maity, Pradip; Lepore, Salvatore D. Annulation Reactions of Allenyl Esters: An Approach to Bicyclic Diones and Medium-Sized Rings. *Journal of Organic Chemistry* **(2014)**, 79(19), 9402-9407. DOI:10.1021/jo501700c

26. Dar, Bilal Ahmad; Bhat, Bilal Ahmad; Qurishi, Mushtaq Ahmad. Synthesis and comparative bioevalvation of aliphatic and aromatic triazolyl derivatives of ursolic acid as anticancer agents. *Journal of Applicable Chemistry* (Lumami, India) **(2014)**, 3(2), 541-550, 10 pp

27. Lone, Ali Mohd; Shah, Wajaht A.; Bhat, Bilal Ahmad. Synthesis and biological evaluation of new triazolyl analogues derived from 1-oxaspiro[4.4]nona-3,6-dien-6-ylmethanol. *Journal of Applicable Chemistry* (Lumami, India) **(2014)**, 3(2), 513-520, 8.

28. Mudududdla, Ramesh; Sharma, Rohit; Abbat, Sheenu; Bharatam, Prasad V.; Vishwakarma, Ram A.; Bharate, Sandip B. Synthesis of 2-phenylnaphthalenes from styryl-2-methoxybenzenes. *Chemical Communications* (Cambridge, United Kingdom) (2014), 50(81), 12076-12079. DOI:10.1039/C4CC05151C

29. Sharma, Simmi; Bhat, Javeed Ahmad; Ahmad, Mudassier; Kumar, Arvind; Kumar, Manjeet; Zargar, Mohmmad Afzal; Hamid, Abid; Shah, Bhahwal Ali. Design, synthesis and biological evaluation of β-boswellic acid based HDAC inhibitors as inducers of cancer cell death. *Bioorganic & Medicinal Chemistry Letters* **(2014)**, 24(19), 4729-4734. DOI:10.1016/j.bmcl.2014.08.007

30. Dar, Alamgir A.; Sangwan, Payare L.; Khan, Imran; Gupta, Nidhi; Qaudri, Afnan; Tasduq, Sheikh A.; Kitchlu, Surinder; Kumar, Anil; Koul, Surrinder. Simultaneous quantification of eight bioactive secondary metabolites from Codonopsis ovata by validated high performance thin layer chromatography and their antioxidant profile. *Journal of Pharmaceutical and Biomedical Analysis* **(2014)**, 100, 300-308. DOI:10.1016/j.jpba.2014.07.034

31. Pandith, Shahzad A.; Hussain, Aashiq; Bhat, Wajid Waheed; Dhar, Niha; Qazi, Asif Khurshid; Rana, Satiander; Razdan, Sumeer; Wani, Tareq A.; Shah, Manzoor A.; Bedi, Y. S.; et al. Evaluation of anthraquinones from Himalayan rhubarb (Rheum emodi Wall. ex Meissn.) as antiproliferative agents. *South African Journal of Botany* **(2014)**, 95, 1-8. DOI:10.1016/j.sajb.2014.07.012

32. Jain, Shreyans K.; Singh, Surjeet; Khajuria, Anamika; Guru, Santosh K.; Joshi, Prashant; Meena, Samdarshi; Nadkarni, Janhavi R.; Singh, Amarinder; Bharate, Sonali S.; Bhushan, Shashi; et al. Pyrano-isochromanones as IL-6 Inhibitors: Synthesis, in Vitro and in Vivo Antiarthritic Activity. *Journal of Medicinal Chemistry* **(2014)**, 57(16), 7085-7097. DOI:10.1021/jm500901e

33. Bhat, Bilal A. Strategies towards furo[3, 2-b]furanones present in bioactive natural products. Abstracts of Papers, *248th ACS National Meeting & Exposition, San Francisco, CA, United States*, August 10-14, 2014 **(2014)**, ORGN-58.

34. Lambu, Mallikharjuna Rao; Mukherjee, Debaraj. Diastereoselective synthesis of highly functionalized cis-1-oxadecalines via 6-endo-tet-cyclizations of 2-C-branched sugars. *RSC Advances* **(2014)**, 4(71), 37908-37913. DOI:10.1039/C4RA06554A

35. Battula, Satyanarayana; Vishwakarma, Ram A.; Ahmed, Qazi Naveed. Cu-benzotriazole-catalyzed electrophilic cyclization of N-arylimines: a methodical tandem approach to O-protected-4hydroxyquinazolines. *RSC Advances* **(2014)**, 4(72), 38375-38378. DOI:10.1039/C4RA07377K

36. Wani, Naiem Ahmad; Gupta, Vivek Kumar; Kant, Rajni; Aravinda, Subrayashastry; Rai, Rajkishor. An unusual conformation of gabapentin (Gpn) in Pyr-Gpn-NH-NH-Pyr stabilized by weak interactions. *Acta Crystallographica, Section C: Structural Chemistry* **(2014)**, 70(8), 776-779. DOI:10.1107/S2053229614015587

37. Shakeel-u-Rehman; Masood-ur-Rahman; Tripathi, Vijay K.; Singh, Jasvinder; Ara, Tabassum; Koul, Surrinder; Farooq, Saleem; Kaul, Anupurna. Synthesis and biological evaluation of novel isoxazoles and triazoles linked 6-hydroxycoumarin as potent cytotoxic agents. *Bioorganic & Medicinal Chemistry Letters* **(2014)**, 24(17), 4243-4246. DOI:10.1016/j.bmcl.2014.07.031

38. Farooq, Saleem; Shakeel-u-Rehman; Hussain, Aashiq; Hamid, Abid; Qurishi, Mushtaq A.; Koul, Surrinder. Click chemistry inspired synthesis and bioevaluation of novel triazolyl derivatives of osthol as potent cytotoxic agents. *European Journal of Medicinal Chemistry* **(2014)**, 84, 545-554. DOI:10.1016/j.ejmech.2014.07.069

39. Bhat, Gulzar; Ganai, Bashir A.; Shawl, Abdul S. New phenolics from the root of Scutellaria prostrata JACQ. ex BENTH. *Natural Product Research* **(2014)**, 28(20), 1685-1690. DOI:10.1080/14786419.2014.939082

40. Joshi, Prashant; Singh, Samsher; Wani, Abubakar; Sharma, Sadhana; Jain, Shreyans K.; Singh, Baljinder; Gupta, Bishan D.; Satti, Naresh K.; Koul, Surrinder; Khan, Inshad A.; et al. Osthol and curcumin as inhibitors of human Pgp and multidrug efflux pumps of Staphylococcus aureus: reversing the resistance against frontline antibacterial drugs. *MedChemComm* **(2014)**, 5(10), 1540-1547. DOI:10.1039/C4MD00196F

41. Gupta, Prem N.; Jain, Sharad; Nehate, Chetan; Alam, Noor; Khare, Vaibhav; Dubey, Ravindra Dhar; Saneja, Ankit; Kour, Smit; Singh, Shashank K. Development and evaluation of paclitaxel loaded PLGA:poloxamer blend nanoparticles for cancer chemotherapy. *International Journal of Biological Macromolecules* **(2014)**, 69, 393-399. DOI:10.1016/j.ijbiomac.2014.05.067

42. Saneja, Ankit; Dubey, Ravindra Dhar; Alam, Noor; Khare, Vaibhav; Gupta, Prem N. Co-formulation of P-glycoprotein Substrate and Inhibitor in Nanocarriers: An Emerging Strategy for Cancer Chemotherapy. *Current Cancer Drug Targets* **(2014)**, 14(5), 419-433. DOI:10.2174/1568009614666140407112034

43. Kumar, Manjeet; Kumar, Arvind; Rizvi, Masood; Mane, Manoj; Vanka, Kumar; Taneja, Subhash C.; Shah, Bhahwal Ali. Synthesis of α,β-Unsaturated δ-Lactones by Vinyl Acetate Mediated Asymmetric Cross-Aldol Reaction of Acetaldehyde: Mechanistic Insights. *European Journal of Organic Chemistry* **(2014)**, 2014(24), 5247-5255. DOI:10.1002/ejoc.201402551

44. Deshidi, Ramesh; Kumar, Manjeet; Devari, Shekaraiah; Shah, Bhahwal Ali. A general metal free approach to α-ketoamides via oxidative amidation-diketonization of terminal alkynes. *Chemical Communications* (Cambridge, United Kingdom) **(2014)**, 50(67), 9533-9535. DOI:10.1039/C4CC03783A

45. Mir, Bilal Ahmad; Khazir, Jabeena; Hakeem, Khalid R.; Kumar, Arun; Koul, Sushma. Withanolides array of Withania ashwagandha sp. novo populations from India. *Industrial Crops and Products* **(2014)**, 59, 9-13. DOI:10.1016/j.indcrop.2014.04.024

46. Bhat, Wajid Waheed; Razdan, Sumeer; Rana, Satiander; Dhar, Niha; Wani, Tariq Ahmad; Qazi, Parvaiz; Vishwakarma, Ram; Lattoo, Surrinder K. A phenylalanine ammonia-lyase ortholog (PkPAL1) from Picrorhiza kurrooa Royle ex. Benth: Molecular cloning, promoter analysis and response to biotic and abiotic elicitors. *Gene* **(2014)**, 547(2), 245-256. DOI:10.1016/j.gene.2014.06.046

47. Jain, Shreyans K.; Aravinda Kumar, K. A.; Bharate, Sandip B.; Vishwakarma, Ram A. Facile access to amides and hydroxamic acids directly from nitroarenes. *Organic & Biomolecular Chemistry* **(2014)**, 12(33), 6465-6469. DOI:10.1039/C4OB01155D

48. Manda, Sudhakar; Khan, Shabana I.; Jain, Surendra K.; Mohammed, Shabber; Tekwani, Babu L.; Khan, Ikhlas A.; Vishwakarma, Ram A.; Bharate, Sandip B. Synthesis, antileishmanial and antitrypanosomal activities of N-substituted tetrahydro-β-carbolines. m *Bioorganic & Medicinal Chemistry Letters* **(2014)**, 24(15), 3247-3250. DOI:10.1016/j.bmcl.2014.06.030

49. Bharate, Jaideep B.; Wani, Abubakar; Sharma, Sadhana; Reja, Shahi Imam; Kumar, Manoj; Vishwakarma, Ram

A.; Kumar, Ajay; Bharate, Sandip B. Synthesis, and the antioxidant, neuroprotective and P-glycoprotein induction activity of 4-arylquinoline-2-carboxylates. *Organic & Biomolecular Chemistry* **(2014)**, 12(32), 6267-6277. DOI:10.1039/C4OB00488D

50. Khazir, Jabeena; Hyder, Irfan; Gayatri, J. Laxmi; Prasad Yandrati, Leela; Nalla, Naresh; Chasoo, Gousia; Mahajan, Ajay; Saxena, A. K.; Alam, M. S.; Qazi, G. N.; et al. Design and synthesis of novel 1,2,3-triazole derivatives of coronopilin as anti-cancer compounds. *European Journal of Medicinal Chemistry* **(2014)**, 82, 255-262. DOI:10.1016/j.ejmech.2014.05.053

51. Mir, Bilal Ahmad; Mir, Shabir Ahmad; Koul, Sushma. In vitro propagation and withaferin A production in Withania ashwagandha, a rare medicinal plant of India. *Physiology and Molecular Biology of Plants* **(2014)**, 20(3), 357-364. DOI:10.1007/s12298-014-0243-5

52. Khare, Vaibhav; Kour, Smit; Alam, Noor; Dubey, Ravindra Dharr; Saneja, Ankit; Koul, Mytre; Gupta, Ajai Prakash; Singh, Deepika; Singh, Shashank K.; Saxena, Ajit K.; et al. Synthesis, characterization and mechanistic-insight into the anti-proliferative potential of PLGA-gemcitabine conjugate. *International Journal of Pharmaceutics* (Amsterdam, Netherlands) **(2014)**, 470(1-2), 51-62. DOI:10.1016/j.ijpharm.2014.05.005

53. Dhar, Niha; Rana, Satiander; Razdan, Sumeer; Bhat, Wajid Waheed; Hussain, Aashiq; Dhar, Rekha S.; Vaishnavi, Samantha; Hamid, Abid; Vishwakarma, Ram; Lattoo, Surrinder K. Cloning and Functional Characterization of Three Branch Point Oxidosqualene Cyclases from Withania somnifera (L.) Dunal. *Journal of Biological Chemistry* **(2014)**, 289(24), 17249-17267. DOI:10.1074/jbc.M114.571919

54. Akther, Nayeema; Andrabi, Khursheed; Nissar, Albeena; Ganaie, Showkat; Chandan, B. K.; Gupta, A. P.; Khuswant, Manoj; Sultana, Sarwat; Shawl, Abdul S. Hepatoprotective activity of LC-ESI-MS standardized Iris spuria rhizome extract on its main bioactive constituents. *Phytomedicine* **(2014)**, 21(10), 1202-1207. DOI:10.1016/j.phymed.2014.04.007

55. Sharma, Sandeep; Kalia, Nitin Pal; Suden, Pankaj; Chauhan, Prashant Singh; Kumar, Manoj; Ram, Anshu Beulah; Khajuria, Anamika; Bani, Sarang; Khan, Inshad Ali. Protective efficacy of piperine against Mycobacterium tuberculosis. *Tuberculosis* (Oxford, United Kingdom) **(2014)**, 94(4), 389-396. DOI:10.1016/j.tube.2014.04.007

56. Reddy, G. Lakshma; Guru, Santosh Kumar; Srinivas, M.; Pathania, Anup Singh; Mahajan, Priya; Nargotra, Amit; Bhushan, Shashi; Vishwakarma, Ram A.; Sawant, Sanghapal D. Synthesis of 5-substituted-1H-pyrazolo[4,3-d]pyrimidin-7(6H)-one analogs and their biological evaluation as anticancer agents: mTOR inhibitors. *European Journal of Medicinal Chemistry* **(2014)**, 80, 201-208. DOI:10.1016/j.ejmech.2014.04.051

57. Jain, Shreyans K.; Meena, Samdarshi; Gupta, Ajai P.; Kushwaha, Manoj; Uma Shaanker, R.; Jaglan, Sundeep; Bharate, Sandip B.; Vishwakarma, Ram A. Dysoxylum binectariferum bark as a new source of anticancer drug camptothecin: Bioactivity-guided isolation and LCMS-based quantification. *Bioorganic & Medicinal Chemistry Letters* **(2014)**, 24(14), 3146-3149. DOI:10.1016/j.bmcl.2014.05.001

58. Lone, Ali Mohd; Bhat, Bilal Ahmad; Shah, Wajaht Amin; Mehta, Goverdhan. A concise synthesis of Hagen's gland lactones. *Tetrahedron Letters* **(2014)**, 55(26), 3610-3612. DOI:10.1016/j.tetlet.2014.04.119

59. Kumar, Brijesh; Aga, Mushtaq A.; Rouf, Abdul; Shah, Bhahwal A.; Taneja, Subhash C. Tetrahydropyranyl ether (THPE) formation in hydroxyl group protection and conversion to other useful functionalities. *RSC Advances* **(2014)**, 4(40), 21121-21130. DOI:10.1039/c4ra02093f

60. Dara, Saidulu; Saikam, Varma; Yadav, Mahipal; Singh, Parvinder Pal; Vishwakarma, Ram A. HClO4-silica-catalysed regioselective opening of benzylidene acetals and its application towards regioselective HO-4 glycosylation of benzylidene acetals in one-pot.

Carbohydrate Research **(2014)**, 391, 93-96. DOI:10.1016/j.carres.2014.01.011

61. Farrukh, Mufti R.; Nissar, Ul A.; Afnan, Quadri; Rafiq, Rather A.; Sharma, Love; Amin, Shajrul; Kaiser, Peerzada; Sharma, Parduman R.; Tasduq, Sheikh A. Oxidative stress mediated Ca2+ release manifests endoplasmic reticulum stress leading to unfolded protein response in UV-B irradiated human skin cells. *Journal of Dermatological Science* **(2014)**, 75(1), 24-35. DOI:10.1016/j.jdermsci.2014.03.005

62. Venkateswarlu, Vunnam; Kumar, K. A. Aravinda; Balgotra, Shilpi; Reddy, G. Lakshma; Srinivas, M.; Vishwakarma, Ram A.; Sawant, Sanghapal D. C-H oxygenation and N-trifluoroacylation of arylamines under metal-free conditions. A convenient approach to 2- aminophenols and N-trifluoroacyl-ortho-aminophenols. *Chemistry - A European Journal* **(2014)**, 20(22), 6641-6645. DOI:10.1002/chem.201402411

63. Gannedi, Veeranjaneyulu; Ali, Asif; Singh, Parvinder Pal; Vishwakarma, Ram A. Intramolecular aglycon delivery for (1→2)-β-mannosylation: towards the synthesis of phospholipomannan of Candida albicans. *Tetrahedron Letters* **(2014),** 55(18), 2945-2947. DOI:10.1016/j.tetlet.2014.03.099

64. Kumar, Brijesh; Aga, Mushtaq A.; Rouf, Abdul; Shah, Bhahwal A.; Taneja, Subhash C. Common precursor strategy for the synthesis of bestatin, amprenavir intermediate and syn-4-hydroxy-5-phenyl-γ- lactam. *RSC Advances* **(2014)**, 4(33), 17206-17209. DOI:10.1039/c4ra00205a

65. Zilla, Mahesh K.; Nayak, Debasis; Vishwakarma, Ram A.; Sharma, Parduman Raj; Goswami, Anindya; Ali, Asif. A convergent synthesis of alkyne-azide cycloaddition derivatives of 4-α,β-2-propyne podophyllotoxin depicting potent cytotoxic activity. *European Journal of Medicinal Chemistry* **(2014)**, 77, 47-55. DOI:10.1016/j.ejmech.2014.02.030

66. Aga, Mushtaq A.; Kumar, Brijesh; Rouf, Abdul; Shah, Bhahwal A.; Taneja, Subhash C. Vasicine as tridentate ligand for enantioselective addition of diethylzinc to aldehydes. *Tetrahedron Letters* **(2014)**, 55(16), 2639-2641. DOI:10.1016/j.tetlet.2014.03.002

67. Rayees, Sheikh; Satti, Naresh Kumar; Mehra, Rukmankesh; Nargotra, Amit; Rasool, Shafaq; Sharma, Anjna; Sahu, Promod Kumar; Rajnikant; Gupta, Vivek K.; Nepali, Kunal; et al. Anti-asthmatic activity of azepino [2, 1-b] quinazolones, synthetic analogues of vasicine, an alkaloid from Adhatoda vasica. *Medicinal Chemistry Research* **(2014)**, 23(9), 4269-4279. DOI:10.1007/s00044-014-0996-y

68. Munagala, Gurunadham; Yempalla, Kushalava Reddy; Aithagani, Sravan Kumar; Kalia, Nitin Pal; Ali, Furqan; Ali, Intzar; Rajput, Vikrant Singh; Rani, Chitra; Chib, Reena; Mehra, Rukmankesh; et al. Synthesis and biological evaluation of substituted N-alkylphenyl-3,5-dinitrobenzamide analogs as anti-TB agents. *MedChemComm* **(2014)**, 5(4), 521-527. DOI:10.1039/c3md00366c

69. Mudududdla, Ramesh; Sharma, Rohit; Guru, Santosh K.; Kushwaha, Manoj; Gupta, Ajai P.; Bharate, Sonali S.; Aravinda, Subrayashastry; Kant, Rajni; Bhushan, Shashi; Vishwakarma, Ram A.; et al. Trifluoroacetic acid catalyzed thiophenylmethylation and thioalkylmethylation of lactams and phenols via domino three-component reaction in water. *RSC Advances* **(2014)**, 4(27), 14081-14088. DOI:10.1039/c3ra47874b

70. Alam, Noor; Khare, Vaibhav; Dubey, Ravindra; Saneja, Ankit; Kushwaha, Manoj; Singh, Gurdarshan; Sharma, Neelam; Chandan, Balkrishan; Gupta, Prem N. Biodegradable polymeric system for cisplatin delivery: Development, in vitro characterization and investigation of toxicity profile. *Materials Science & Engineering, C: Materials for Biological Applications* **(2014)**, 38, 85-93. DOI:10.1016/j.msec.2014.01.043

71. Lone, Shabir H.; Bhat, Khursheed A.; Bhat, Haroon M.; Majeed, Rabiya; Anand, Rajneesh; Hamid, Abid; Khuroo, Mohd A. Essential oil composition of Senecio

graciliflorus DC: Comparative analysis of different parts and evaluation of antioxidant and cytotoxic activities. *Phytomedicine* (2014), 21(6), 919-925. DOI:10.1016/j.phymed.2014.01.012

72. Najar, Ishtiyaq Ahmad; Johri, Rakesh Kamal. Pharmaceutical and pharmacological approaches for bioavailability enhancement of etoposide. *Journal of Biosciences* (New Delhi, India) **(2014)**, 39(1), 139-144. DOI:10.1007/s12038-013-9399-3

73. Bhat, Wajid Waheed; Rana, Satiander; Dhar, Niha; Razdan, Sumeer; Pandith, Shahzad A.; Vishwakarma, Ram; Lattoo, Surrinder K. An inducible NADPH-cytochrome P450 reductase from Picrorhiza kurrooa - an imperative redox partner of cytochrome P450 enzymes. *Functional & Integrative Genomics* **(2014)**, 14(2), 381-399. DOI:10.1007/s10142-014-0362-7

74. Dar, Bashir Ahmad; Dangroo, Nisar A.; Gupta, Amit; Wali, Aarti; Khuroo, Mohammad Akbar; Vishwakarma, Ram A.; Singh, Baldev. Iodine catalyzed solvent-free cross-dehydrogenative coupling of arylamines and H-phosphonates for the synthesis of N-arylphosphoramidates under atmospheric conditions. *Tetrahedron Letters* **(2014)**, 55(9), 1544-1548. DOI:10.1016/j.tetlet.2014.01.064

75. Lone, Shabir H.; Bhat, Khursheed A.; Majeed, Rabiya; Hamid, Abid; Khuroo, Mohd A. Click chemistry inspired facile synthesis and bioevaluation of novel triazolyl analogs of Ludartin. *Bioorganic & Medicinal Chemistry Letters* **(2014)**, 24(4), 1047-1051. DOI:10.1016/j.bmcl.2014.01.018

76. Chib, Renu; Kumar, Manjeet; Rizvi, Masood; Sharma, Simmi; Pandey, Anjali; Bani, Sarang; Andotra, Samar S.; Taneja, Subhash C.; Shah, Bhahwal A. Anti-inflammatory terpenoids from Boswellia ovalifoliolata. *RSC Advances* **(2014)**, 4(17), 8632-8637. DOI:10.1039/c3ra46412a

77. Yadav, Mahipal; Raghupathy, Riya; Saikam, Varma; Dara, Saidulu; Singh, Parvinder Pal; Sawant, Sanghapal D.; Mayor, Satyajit; Vishwakarma, Ram A. Synthesis of non-hydrolysable mimics of glycosylphosphatidylinositol (GPI) anchors. *Organic & Biomolecular Chemistry* **(2014)**, 12(7), 1163-1172. DOI:10.1039/c3ob42116c

78. Dar, Bashir Ahmad; Singh, Snehil; Pandey, Nalini; Singh, A. P.; Sharma, Priti; Lazar, Anish; Sharma, Meena; Vishwakarma, Ram A.; Singh, Baldev. Clay encapsulated Cu(OH)x promoted homocoupling of arylboronic acids: An efficient and eco-friendly protocol. *Applied Catalysis, A: General* **(2014)**, 470, 232-238. DOI:10.1016/j.apcata.2013.10.048

79. Wani, Naiem Ahmad; Gupta, Vivek Kumar; Kant, Rajni; Aravinda, Subrayashastry; Rai, Rajkishor. Conformation of a terminally protected βγ hybrid dipeptide Boc-Ant-Gpn-OMe stabilized by C6/C7 hydrogen bonds. *Acta Crystallographica, Section C: Structural Chemistry* **(2014)**, 70(1), 46-49. DOI:10.1107/S2053229613033044

80. Bharate, Jaideep Bibishan; Vishwakarma, Ram Ashrey; Bharate, Sandip Bibishan; Kushwaha, Manoj; Gupta, Ajai Prakash. Quantification of Anticancer Polyisoprenylated Benzophenones Garcinol and Isogarcinol Using Multiple reaction monitoring Lc-Esi-Ms-Ms in Ultra-Sound Assisted Extracts of Garcinia Indica Fruits. *Journal of Liquid Chromatography & Related Technologies* **(2014)**, Ahead of Print. DOI:10.1080/10826076.2013.873872

81. Sawant, Sanghapal D.; Hudwekar, Abhinandan D.; Aravinda Kumar, K. A.; Venkateswarlu, Vunnam; Singh, Parvinder Pal; Vishwakarma, Ram A. Ligand- and base-free synthesis of phenols by rapid oxidation of arylboronic acids using iron(III) oxide. *Tetrahedron Letters* **(2014)**, 55(4), 811-814. DOI:10.1016/j.tetlet.2013.12.003

82. Dar, Bashir Ahmad; Pandey, Nalini; Singh, Snehil; Bamezai, R. K.; Sharma, Meena; Vishwakarma, Ram A.; Singh, Baldev. Heterogeneous reusable catalyst, ultrasound energy, and no solvent: a quick and green recipe for one-pot synthesis of β-phosphonomalononitriles at room temperature. *Tetrahedron Letters* **(2014)**, 55(3), 623-628.

DOI:10.1016/j.tetlet.2013.11.095

83. Rayees, Sheikh; Malik, Fayaz; Bukhari, Syed Imran; Singh, Gurdarshan. Linking GATA-3 and interleukin-13: implications in asthma. *Inflammation Research* **(2014)**, 63(4), 255-265. DOI:10.1007/s00011- 013-0700-6

84. Rouf, Abdul; Taneja, S. C. Synthesis of Single-enantiomer Bioactive Molecules: A Brief Overview. *Chirality* **(2014)**, 26(2), 63-78. DOI:10.1002/chir.22268

85. Lone, Ali Mohd; Bhat, Bilal Ahmad. Metal free stereoselective synthesis of functionalized enamides. *Organic & Biomolecular Chemistry* **(2014)**, 12(2), 242-246. DOI:10.1039/C3OB41847B

86. Dar, Bashir Ahmad; Vyas, Dushyant; Shrivastava, Varsha; Farooq, Saleem; Sharma, Amit; Sharma, Sadhana; Sharma, Parduman R.; Sharma, Meena; Singh, Baldev. Oxidative homocoupling of terminal alkynes under palladium-, ligand- and base-free conditions using Cu(II)-clay as a heterogeneous catalyst. *Comptes Rendus Chimie* **(2014)**, 17(4), 316-323. DOI:10.1016/j.crci.2013.07.012

87. Sofi, Shahnawaz N.; Shakeel-u-Rehman; Qazi, Parvaiz H.; Lone, Shabir H.; Bhat, Haroon M.; Bhat, Khursheed A. Isolation, identification, and simultaneous quantification of five major flavonoids in Epimedium elatum by high performance liquid chromatography. *Journal of Liquid Chromatography & Related Technologies* **(2014),** 37(8), 1104-1113. DOI:10.1080/10826076.2013.765465

88. Rather, S. A.; Kumar, Sunil; Rah, Bilal; Arif, Mohammad; Ali, Asif; Qazi, Parvaiz. A potent cytotoxic metabolite from terrestrial actinomycete, Streptomyces collinus. *Medicinal Chemistry Research* **(2014)**, 23(1), 382-387. DOI:10.1007/s00044-013-0640-2

89. Gupta, Devinder K.; Verma, Mahendra K.; Lal, Shankar; Anand, Rajneesh; Khajuria, Ravi K.; Kitchlu, Surinder; Koul, Surrinder. Extraction Studies of Podophyllum Hexandrum using Conventional and Nonconventional Methods by HPLC-UV-DAD. *Journal of Liquid Chromatography & Related Technologies* **(2014)**, 37(2), 259-273. DOI:10.1080/10826076.2012.745134

90. Parveen S; Godara R; Katoch R; Yadav A; Verma P K; Katoch M; Singh N K. In vitro evaluation of ethanolic extracts of Ageratum conyzoides and Artemisia absinthium against cattle tick, Rhipicephalus microplus. *The Scientific World Journal* **(2014)**, 2014858973.

91. Godara R; Katoch R; Yadav Anish; Parveen S; Khajuria Varun; Katoch M; Vij Bhavna; Singh G; Singh Nirbhay K. In vitro acaricidal activity of Atropa belladonna and its components, scopolamine and atropine, against Rhipicephalus (Boophilus) microplus. *The Scientific World Journal* **(2014)**, 2014713170

92. Jaganathan Saravana Kumar; Supriyanto Eko; Mondhe Dilip; Wani Z A. Evaluation of selected honey and one of its phenolic constituent eugenol against L1210 lymphoid leukemia. *The Scientific World Journal* **(2014)**, 2014912051.

93. Ahmad Wani Naiem; Aravinda Subrayashastry; Rai Rajkishor; Gupta Vivek K; Kant Rajni. Conformation and crystal structures of 1-amino-cyclo-hexa-neacetic acid (β(3,3)Ac6c) in N-protected derivatives. *Acta crystallographica. Section E, Structure reports online* **(2014)**, 70(Pt 11), 272-7.

94. Sharma Jyotsana; Gairola Sumeet; Sharma Yash Pal; Gaur R D. Ethnomedicinal plants used to treat skin diseases by Tharu community of district Udham Singh Nagar, Uttarakhand, India. *Journal of ethnopharmacology* **(2014)**, 158 Pt A140-206

95. Zilla Mahesh K; Nalli Yedukondalu; Nayak Debasis; Rah Bilal; Chakraborty Souneek; Amin Hina; Kitchlu Surender; Goswami Anindya; Ali Asif. 4'-Demethyl-deoxypodophyllotoxin glucoside isolated from Podophyllum hexandrum exhibits potential anticancer activities by altering Chk-2 signaling pathway in MCF-7 breast cancer cells. *Chemico-biological interactions* **(2014)**, 224C100-107.

96. Bharate Sonali S; Bharate Sandip B. Non-enzymatic browning in citrus juice: chemical markers, their detection and ways to

improve product quality. *Journal of food science and technology* **(2014)**, 51(10), 2271-88.

97. Qazi Asif Khurshid; Hussain Aashiq; Aga Mushtaq A; Ali Shakir; Taneja Subhash Chandra; Sharma Parduman Raj; Saxena Ajit Kumar; Mondhe Dilip M; Hamid Abid. Cell specific apoptosis by RLX is mediated by NFκB in human colon carcinoma HCT-116 cells. *BMC cell biology* **(2014)**, 1536.

98. Sharma Vishal; Chaudhry Ashun; Arora Rohit; Arora Saroj; Chashoo Gousia; Saxena Ajit K; Ishar Mohan Paul S. β-Ionone derived apoptosis inducing endoperoxides; Discovery of potent leads for anticancer agents. *European journal of medicinal chemistry* **(2014)**, 87228-36.

99. Pandita Archana; Manvati Siddharth; Vaishnavi Samantha; Kumar Bhupender; Bamezai Rameshwar N K; Singh Shashank K. Synergistic combination of gemcitabine and dietary molecule induces apoptosis in pancreatic cancer cells and down regulates PKM2 expression. *PloS one* **(2014)**, 9(9), e107154.

100. Goswami Akshra; Shah Bhahwal Ali; Kumar Ajay; Kumar Suresh; Bhushan Shashi; Malik Fayaz Ahmed; Rizvi Masood Ahmad; Batra Navneet; Joshi Amit; Singh Jagtar. Antiproliferative potential of a novel parthenin analog P16 as evident by apoptosis accompanied by down-regulation of PI3K/AKT and ERK pathways in human acute lymphoblastic leukemia MOLT-4 cells. *Chemico-biological interactions* **(2014)**, 222C60-67.

101. Akindele Abidemi J; Iyamu Endurance A; Adeyemi Olufunmilayo O; Dutt Prabhu; Satti Naresh K. Ameliorative Effect of Hydroethanolic Leaf Extract of Byrsocarpus coccineus in Alcohol- and Sucrose-Induced Hypertension in Rats. *Journal of traditional and complementary medicine* **(2014)**, 4(3), 177-88.

102. Sharma Deepak K; Pandey Jyotsana; Tamrakar Akhilesh K; Mukherjee Debaraj. Synthesis of heteroaryl/aryl kojic acid conjugates as stimulators of glucose uptake by GLUT4 translocation. *European journal of medicinal chemistry* **(2014)**, 85727-36.

103. Sharma Sahil; Kaur Charanjit; Bedi P M S; Budhiraja Abhishek; Nepali Kunal; Gupta Manish K; Saxena A K. Chalcone based azacarboline analogues as novel antitubulin agents: design, synthesis, biological evaluation and molecular modelling studies. *European journal of medicinal chemistry* **(2014)**, 85648-60.

104. Wani Naiem Ahmad; Aravinda Subrayashastry; Rai Rajkishor; Gupta Vivek Kumar; Kant Rajni. An unusual conformation of gabapentin (Gpn) in Pyr-Gpn-NH-NH-Pyr stabilized by weak interactions. *Acta crystallographica. Section C, Structural chemistry* **(2014),** 70(Pt 8), 776-9.

105. Rathore Kalpana; Singh Vijay Kumar; Jain Parag; Rao S Prakash; Ahmed Zabeer; Singh Veena D. In-vitro and in-vivo antiadipogenic, hypolipidemic and antidiabetic activity of Diospyros melanoxylon (Roxb). *Journal of ethnopharmacology* **(2014)**, 155(2), 1171-6.

106. Rizvi Masood Ahmad; Guru Santosh; Singh Shashank K; Bhushan Shashi; Naqvi Tahira; Akhoon Showkat; Banday Shazia; Mustafa Peerzada G; Kumar Manjeet; Kumbhar Navanath; et al. An investigation of in vitro cytotoxicity and apoptotic potential of aromatic diselenides. *Bioorganic & medicinal chemistry letters* **(2014)**, 24(15), 3440-6.

107. Gairola Sumeet; Sharma Jyotsana; Bedi Yashbir Singh. A cross-cultural analysis of Jammu, Kashmir and Ladakh (India) medicinal plant use. *Journal of ethnopharmacology* **(2014)**, 155(2), 925-86.

108. Kumar Shashank; Pandey Abhay K; Pandey Sanjay. In vitro antibacterial, antioxidant, and cytotoxic activities of Parthenium hysterophorus and characterization of extracts by LC-MS analysis. *BioMed research international* **(2014)**, 2014495154.

109. Sudan Rasleen; Bhagat Madhulika; Gupta Sahil; Singh Jasvinder; Koul Anupurna. Iron (FeII) chelation, ferric reducing antioxidant power, and immune modulating potential of Arisaema jacquemontii (Himalayan Cobra Lily). *BioMed research international* **(2014)**, 2014179865.

110. Nigg Jared; Strobel Gary; Knighton W Berk; Hilmer Jonathan; Geary Brad; Riyaz-Ul-Hassan Syed; Harper James K; Valenti Domenic; Wang Yuemin. Functionalized para-substituted benzenes as

1,8-cineole production modulators in an endophytic Nodulisporium species. *Microbiology* (Reading, England) **(2014)**, 160(Pt 8), 1772-82.

111. Saneja Ankit; Dubey Ravindra Dhar; Alam Noor; Khare Vaibhav; Gupta Prem N. Co-formulation of P-glycoprotein Substrate and Inhibitor in Nanocarriers: An Emerging Strategy for Cancer Chemotherapy. *Current cancer drug targets* **(2014)**.

112. Kumar Ashwani; Khan Inshad Ali; Sharma Parduman Raj; Sumathy K; Krishna M Ella. Evaluation of activity of recombinant lysostaphin against isolates of meticillin-resistant Staphylococcus aureus from Indian hospitals. *Journal of medical microbiology* **(2014)**, 63(Pt 5), 763-6.

113. Zilla Mahesh K; Vishwakarma Ram A; Nayak Debasis; Sharma Parduman Raj; Goswami Anindya; Ali Asif. A convergent synthesis of alkyne-azide cycloaddition derivatives of 4-α,β-2-propyne podophyllotoxin depicting potent cytotoxic activity. *European journal of medicinal chemistry* **(2014)**, 7747-55.

114. Qadri Masroor; Rajput Roopali; Abdin Malik Z; Vishwakarma Ram A; Riyaz-Ul-Hassan Syed. Diversity, molecular phylogeny, and bioactive potential of fungal endophytes associated with the Himalayan blue pine (Pinus wallichiana). *Microbial ecology* **(2014)**, 67(4), 877-87.

115. Kumar Davender; Parshad Rajinder; Gupta Vijay Kumar. Application of a statistically enhanced, novel, organic solvent stable lipase from Bacillus safensis DVL-43. *International journal of biological macromolecules* **(2014)**, 6697-107.

116. Katoch Meenu; Singh Gurpreet; Sharma Sadhna; Gupta Nidhi; Sangwan Payare Lal; Saxena Ajit Kumar. Cytotoxic and antimicrobial activities of endophytic fungi isolated from Bacopa monnieri (L.) Pennell (Scrophulariaceae). *BMC complementary and alternative medicine* **(2014)**, 1452.

117. Mupparapu Nagaraju; Khan Shahnawaz; Battula Satyanarayana; Kushwaha Manoj; Gupta Ajai Prakash; Ahmed Qazi Naveed; Vishwakarma Ram A. Metal-free oxidative amidation of 2-oxoaldehydes: a facile access to α-ketoamides. *Organic letters* **(2014)**, 16(4), 1152-5.

118. Malik Tauseef Ahmad; Kamili Azra N; Chishti M Z; Tanveer Syed; Ahad Shazia; Johri R K. In vivo anticoccidial activity of berberine [18, 5,6-dihydro-9,10-dimethoxybenzo(g)-1,3-benzodioxolo(5,6-a) quinolizinium]--an isoquinoline alkaloid present in the root bark of Berberis lyceum. *Phytomedicine: international journal of phytotherapy and phytopharmacology* **(2014)**, 21(5), 663-9.

119. Wani Naiem Ahmad; Aravinda Subrayashastry; Rai Rajkishor; Gupta Vivek Kumar; Kant Rajni. Conformation of a terminally protected βγ hybrid dipeptide Boc-Ant-Gpn-OMe stabilized by C6/C7 hydrogen bonds. *Acta crystallographica. Section C, Structural chemistry* **(2014)**, 70(Pt 1), 46-9.

120. Devari Shekaraiah; Deshidi Ramesh; Jaglan Sundeep; Kushwaha Manoj; Gupta Ajai P; Kumar Manjeet; Taneja Subhash C; Vishwakarma Ram A; Guru Santosh; Bhushan Shashi; et al. Capsaicin production by Alternaria alternata, an endophytic fungus from Capsicum annum; LC-ESI-MS/MS analysis. *Phytochemistry* **(2014)**, 98183-9.

121. Suresh Narva; Nagesh Hunsur Nagendra; Renuka Janupally; Rajput Vikrant; Sharma Rashmi; Khan Inshad Ali; Kondapalli Venkata Gowri Chandra Sekhar. Synthesis and evaluation of 1-cyclopropyl-6-fluoro-1,4-dihydro-4-oxo-7-(4-(2-(4-substitutedpiperazin-1-yl)acetyl)piperazin-1-yl)quinoline-3-carboxylic acid derivatives as anti-tubercular and antibacterial agents. *European journal of medicinal chemistry* **(2014)**, 71324-32.

122. Buragohain Pori; Saikia Bishwajit; Surineni Naresh; Barua Nabin C; Saxena Ajit K; Suri Nitasha. Synthesis of a novel series of artemisinin dimers with potent anticancer activity involving Sonogashira crosscoupling reaction. *Bioorganic & medicinal chemistry letters* **(2014)**, 24(1), 237-9.

LIST OF PUBLICATIONS
(Calender Year: 2015 Till 11th June 2015)

1. Reddy, K. Ranjith; Reddy, A. Siva; Shankar, Ravi; Kant, Rajni; Das, Parthasarathi. Copper-Catalyzed Oxidative C-H Amination: Synthesis of Imidazo[1,2-a]-N-Heterocycles from N-Heteroaryl Enaminones. *Asian Journal of Organic Chemistry* **(2015)**, 4(6), 573-583. DOI:10.1002/ajoc.201500052

2. Yadav, Rammohan R.; Sharma, Sadhana; Joshi, Prashant; Wani, Abubakar; Vishwakarma, Ram A.; Kumar, Ajay; Bharate, Sandip B. Meridianin derivatives as potent Dyrk1A inhibitors and neuroprotective agents. *Bioorganic & Medicinal Chemistry Letters* **(2015)**, Ahead of Print. DOI:10.1016/j.bmcl.2015.05.034

3. Majeed, Rabiya; Hussain, Aashiq; Sangwan, Payare L.; Chinthakindi, Praveen K.; Khan, Imran; Sharma, Parduman R.; Koul, Surrinder; Saxena, Ajit K.; Hamid, Abid. PI3K target based novel cyano derivative of betulinic acid induces its signalling inhibition by down-regulation of pGSK3β and cyclin D1 and potentially checks cancer cell proliferation. *Molecular Carcinogenesis* **(2015)**, Ahead of Print. DOI:10.1002/mc.22339

4. Farrukh, Mufti Rana; Nissar, Ul-Ashraf; Kaiser, Peerzada J.; Afnan, Quadri; Sharma, Praduman R.; Bhushan, Shashi; Tasduq, Sheikh A. Glycyrrhizic acid (GA) inhibits reactive oxygen Species mediated photodamage by blocking ER stress and MAPK pathway in UV-B irradiated human skin fibroblasts. *Journal of Photochemistry and Photobiology, B: Biology* **(2015)**, 148, 351-357. DOI:10.1016/j.jphotobiol.2015.05.003

5. Balgotra, Shilpi; Venkateswarlu, Vunnam; Vishwakarma, Ram A.; Sawant, Sanghapal D. Direct C-N bond cleavage of N-vinyl or N-allyl arylamines: a metal-free strategy for N-devinylation and N-deallylation. *Tetrahedron Letters* **(2015)**, Ahead of Print. DOI:10.1016/j.tetlet.2015.05.042

6. Amin, Hina; Nayak, Debasis; ur Rasool, Reyaz; Chakraborty, Souneek; Kumar, Anmol; Yousuf, Khalid; Sharma, Parduman Raj; Ahmed, Zabeer; Sharma, Neelam; Magotra, Asmita; et al. Par-4 dependent modulation of cellular β-catenin by medicinal plant natural product derivative 3-azido Withaferin A. *Molecular Carcinogenesis* **(2015)**, Ahead of Print. DOI:10.1002/mc.22328.

7. Kumar, Manjeet; Devari, Shekaraiah; Kumar, Arvind; Sultan, Shaista; Ahmed, Qazi Naveed; Rizvi, Masood; Shah, Bhahwal Ali. Copper(II)-Triflate-Catalyzed Oxidative Amidation of Terminal Alkynes: A General Approach to α-Ketoamides. *Asian Journal of Organic Chemistry* **(2015)**, 4(5), 438-441. DOI:10.1002/ajoc.201500022

8. Bharate, Jaideep B.; Vishwakarma, Ram A.; Bharate, Sandip B. Metal-free domino one-pot protocols for quinoline synthesis. *RSC Advances* **(2015)**, 5(52), 42020-42053. DOI:10.1039/C5RA07798B

9. Sharma, Rohit; Abbat, Sheenu; Mudududdla, Ramesh; Vishwakarma, Ram A.; Bharatam, Prasad V.; Bharate, Sandip B. Ortho-Quinone methides: TFA-mediated generation in water and trapping with lactams and styrenes. *Tetrahedron Letters* **(2015)**, Ahead of Print. DOI:10.1016/j.tetlet.2015.04.072.

10. Padala, Anil K.; Mupparapu, Nagaraju; Singh, Deepika; Vishwakarma, Ram A.; Ahmed, Qazi Naveed. α-Carbonylimine to α-Carbonylamide: An Efficient Oxidative Amidation Approach. *European Journal of Organic Chemistry* **(2015)**, 2015(16), 3577-3586. DOI:10.1002/ejoc.201500251

11. Baba, Shoib Ahmad; Malik, Aubid Hussain; Wani, Zahoor

Ahmed; Mohiuddin, Tabasum; Shah, Zeeshan; Abbas, Nazia; Ashraf, Nasheeman. Phytochemical analysis and antioxidant activity of different tissue types of Crocus sativus and oxidative stress alleviating potential of saffron extract in plants, bacteria, and yeast. *South African Journal of Botany* **(2015)**, 99, 80-87. DOI:10.1016/j.sajb.2015.03.194

12. Mupparapu, Nagaraju; Vishwakarma, Ram A.; Ahmed, Qazi Naveed. Iodine-DMSO promoted C-H (SP3) functionalization approach to α-ketoamides. *Tetrahedron* **(2015)**, 71(21), 3417-3421.

13. Rayees, Sheikh; Mabalirajan, Ulaganathan; Bhat, Wajid Waheed; Rasool, Shafaq; Rather, Rafiq Ahmad; Panda, Lipsa; Satti, Naresh Kumar; Lattoo, Surrinder Kumar; Ghosh, Balaram; Singh, Gurdarshan. Therapeutic effects of R8, a semi-synthetic analogue of Vasicine, on murine model of allergic airway inflammation via STAT6 inhibition. *International Immunopharmacology* **(2015)**, 26(1), 246-256. DOI:10.1016/j.intimp.2015.03.035

14. Singh, Baljinder; Kumar, Ashok; Joshi, Prashant; Guru, Santosh K.; Kumar, Suresh; Wani, Zahoor A.; Mahajan, Girish; Hussain, Aashiq; Qazi, Asif Khurshid; Kumar, Ajay; et al. Colchicine derivatives with potent anticancer activity and reduced P-glycoprotein induction liability. *Organic & Biomolecular Chemistry* **(2015)**, 13(20), 5674-5689. DOI:10.1039/C5OB00406C.

15. Bharate, Jaideep B.; Batarseh, Yazan S.; Wani, Abubakar; Sharma, Sadhana; Vishwakarma, Ram A.; Kaddoumi, Amal; Kumar, Ajay; Bharate, Sandip B. Synthesis and P-glycoprotein induction activity of colupulone analogs. *Organic & Biomolecular Chemistry* **(2015)**, 13(19), 5488-5496. DOI:10.1039/C5OB00554J.

16. Rehman, Shakeel-u; Rah, Bilal; Lone, Shabir H.; Rasool, Reyaz Ur; Farooq, Saleem; Nayak, Debasis; Chikan, Naveed Anjum; Chakraborty, Souneek; Behl, Akanksha; Mondhe, Dilip Manikaro; et al. Design and Synthesis of Antitumor Heck-Coupled Sclareol Analogues: Modulation of BH3 Family Members by SS-12 in Autophagy and Apoptotic Cell Death. *Journal of Medicinal Chemistry* **(2015)**, 58(8), 3432-3444. DOI:10.1021/jm501942m

17. Bharate, Jaideep B.; Abbat, Sheenu; Sharma, Rohit; Bharatam, Prasad V.; Vishwakarma, Ram A.; Bharate, Sandip B. Cobalt(II) catalyzed C(sp)-H bond functionalization of alkynes with phenyl hydrazines: facile access to diaryl 1,2- diketones. *Organic & Biomolecular Chemistry* **(2015)**, 13(18), 5235-5242. DOI:10.1039/C5OB00419E

18. Venkateswarlu, Vunnam; Balgotra, Shilpi; Aravinda Kumar, K. A.; Vishwakarma, Ram A.; Sawant, Sanghapal D. Metal-Free Chemoselective ortho-C(sp2)-F Bond Hydroxylation and N-Trifluoroacylation of Fluoroarylamines for Domino Synthesis of 2-(N-Trifluoroacyl)aminophenols*Synlett* **(2015)**, 26(9), 1258-1262. DOI:10.1055/s-0034-1379905

19. Bharate, Jaideep B.; Singh, Samsher; Wani, Abubakar; Sharma, Sadhana; Joshi, Prashant; Khan, Inshad A.; Kumar, Ajay; Vishwakarma, Ram A.; Bharate, Sandip B. Discovery of 4-acetyl-3-(4-fluorophenyl)-1-(p-tolyl)-5-methylpyrrole as a dual inhibitor of human P-glycoprotein and Staphylococcus aureus Nor A efflux pump. *Organic & Biomolecular Chemistry* **(2015)**, 13(19), 5424-5431. DOI:10.1039/C5OB00246J

20. Bharate, Jaideep B.; Singh, Samsher; Wani, Abubakar; Sharma, Sadhana; Joshi, Prashant; Khan, Inshad A.;Kumar, Ajay; Vishwakarma, Ram A.; Bharate, Sandip B. Discovery of 4-acetyl-3-(4-fluorophenyl)-1-(p-tolyl)-5-methylpyrrole as a dual inhibitor of human P-glycoprotein and Staphylococcus aureus Nor A efflux pump. *Organic & Biomolecular Chemistry* **(2015)**, 13(19), 5424-5431. DOI:10.1039/C5OB00246J

21. Nayak, Debasis; Amin, Hina; Rah, Bilal; ur Rasool, Reyaz; Sharma, Deepak; Gupta, Ajai Prakash; Kushwaha, Manoj; Mukherjee, Debaraj; Goswami, Anindya. A therapeutically relevant, 3,3'-diindolylmethane derivative NGD16 attenuates angiogenesis by targeting glucose regulated protein, 78 kDa (GRP78). *Chemico-Biological Interactions* **(2015)**, 232, 58-67. DOI:10.1016/j.cbi.2015.03.008

22. Naseer, Syed; Lone, Shabir H.; Lone, Javeed A.; Khuroo, Mohd A.; Bhat, Khursheed A. LC-MS guided isolation, quantification and antioxidant evaluation of bioactive principles from Epimedium elatum. *Journal of Chromatography B: Analytical*

Technologies in the Biomedical and Life Sciences **(2015)**, 989, 62-70. DOI:10.1016/j.jchromb.2015.02.046

23. Pathania, Anup S.; Wani, Zahoor A.; Guru, Santosh K.; Kumar, Suresh; Bhushan, Shashi; Korkaya, Hasan; Seals, Darren F.; Kumar, Ajay; Mondhe, Dilip M.; Ahmed, Zabeer; *et al.* The anti-angiogenic and cytotoxic effects of the boswellic acid analog BA145 are potentiated by autophagy inhibitors. *Molecular Cancer* **(2015)**, 14, 1-27. DOI:10.1186/1476-4598-14-6

24. Sawant, Sanghapal D.; Lakshma Reddy, G.; Dar, Mohd Ishaq; Srinivas, M.; Gupta, Gourav; Sahu, Promod Kumar; Mahajan, Priya; Nargotra, Amit; Singh, Surjeet; Sharma, Subhash C.; *et al.* Discovery of novel pyrazolopyrimidinone analogs as potent inhibitors of phosphodiesterase type-5. *Bioorganic & Medicinal Chemistry* **(2015)**, 23(9), 2121-2128. DOI:10.1016/j.bmc.2015.03.005

25. Wani, Zahoor Ahmed; Ashraf, Nasheeman; Mohiuddin, Tabasum; Riyaz-Ul-Hassan, Syed. Plant-endophyte symbiosis, an ecological perspective. *Applied Microbiology and Biotechnology* **(2015)**, 99(7), 2955-2965. DOI:10.1007/s00253-015-6487-3

26. Lone, Shabir H.; Bhat, Khursheed A. Hemisynthesis of a naturally occurring clinically significant antitumor arglabin from ludartin. *Tetrahedron Letters* **(2015)**, 56(14), 1908-1910. DOI:10.1016/j.tetlet.2015.02.100

27. Mudududdla, Ramesh; Guru, Santosh K.; Wani, Abubakar; Sharma, Sadhana; Joshi, Prashant; Vishwakarma, Ram A.; Kumar, Ajay; Bhushan, Shashi; Bharate, Sandip B. 3-(Benzo[d][1,3]dioxol-5-ylamino)-N-(4-fluorophenyl)thiophene-2-carboxamide overcomes cancer chemoresistance via inhibition of angiogenesis and P-glycoprotein efflux pump activity. *Organic & Biomolecular Chemistry* **(2015)**, 13(14), 4296-4309. DOI:10.1039/C5OB00233H

28. Lone, Shabir H.; Bhat, Khursheed A. Phytosterols as precursors for the synthesis of aromatase inhibitors: Hemisynthesis of testololactone and testolactone. *Steroids* **(2015)**, 96, 164-168. DOI:10.1016/j.steroids.2015.02.011

29. Deshidi, Ramesh; Devari, Shekaraiah; Shah, Bhahwal Ali. Iodine-Promoted Oxidative Amidation of Terminal Alkenes - Synthesis of a-Ketoamides, Benzothiazoles and Quinazolines. *European Journal of Organic Chemistry* **(2015)**, 2015(7), 1428-1432. DOI:10.1002/ejoc.201403547

30. Ashraf, Nasheeman; Jain, Deepti; Vishwakarma, Ram A. Identification, cloning and characterization of an ultrapetala transcription factor CsULT1 from Crocus: a novel regulator of apocarotenoid biosynthesis. *BMC Plant Biology* **(2015)**, 15, 1-24, 24 pp.. DOI:10.1186/s12870-015-0423-7

31. Bharate, Sonali S.; Vishwakarma, Ram A. Thermodynamic equilibrium solubility measurements in simulated fluids by 96-well plate method in early drug discovery. *Bioorganic & Medicinal Chemistry Letters* **(2015)**, 25(7), 1561-1567. DOI:10.1016/j.bmcl.2015.02.013

32. Devari, Shekaraiah; Kumar, Arvind; Deshidi, Ramesh; Shah, Bhahwal Ali. C-H functionalization of terminal alkynes towards stereospecific synthesis of (E) or (Z) 2-methylthio-1,4-ene-diones. *Chemical Communications* (Cambridge, United Kingdom) **(2015)**, 51(24), 5013-5016. DOI:10.1039/C4CC10438B

33. Akindele, Abidemi J.; Mahajan, Girish; Wani, Zahoor A.; Sharma, Sadhana; Satti, Naresh K.; Adeyemi, Olufunmilayo O.; Mondhe, Dilip M.; Saxena, Ajit K. Anticancer activity of the phytomedicine DAS-77. *Integrative Cancer Therapies* **(2015)**, 14(1), 57-64. DOI:10.1177/1534735414555807

34. Mahajan, Vidushi; Sharma, Neha; Kumar, Sunil; Bhardwaj, Vikram; Ali, Asif; Khajuria, R. K.; Bedi, Y. S.; Vishwakarma, Ram A.; Gandhi, Sumit G. Production of rohitukine in leaves and seeds of Dysoxylum binectariferum: An alternate renewable resource. *Pharmaceutical Biology* (London, United Kingdom) **(2015)**, 53(3), 446-450. DOI:10.3109/13880209.2014.923006

35. Munagala, Gurunadham; Yempalla, Kushalava Reddy; Singh, Samsher; Sharma, Sumit; Kalia, Nitin Pal; Rajput, Vikrant Singh; Kumar, Sunil; Sawant, Sanghapal D.; Khan, Inshad Ali; Vishwakarma, Ram A.; *et al.* Synthesis of new generation triazolyl- and

isoxazolyl-containing 6-nitro-2,3-dihydroimidazooxazoles as anti-TB agents: in vitro, structure-activity relationship, pharmacokinetics and in vivo evaluation. *Organic & Biomolecular Chemistry* **(2015)**, 13(12), 3610-3624. DOI:10.1039/C5OB00054H

36. Yusuf, Farnaz; Rather, Irshad Ahmad; Jamwal, Urmila; Gandhi, Sumit G.; Chaubey, Asha. Cloning and functional characterization of nitrilase from Fusarium proliferatum AUF-2 for detoxification of nitriles. *Functional & Integrative Genomics* **(2015)**, Ahead of Print. DOI:10.1007/s10142-014-0430-z

37. Aruri, Hariprasad; Singh, Umed; Sharma, Sumit; Gudup, Satish; Bhogal, Mukesh; Kumar, Sanjay; Singh, Deepika; Gupta, Vivek K.; Kant, Rajni; Vishwakarma, Ram A.; et al. Cross-Dehydrogenative Coupling of Azoles with a-C(sp3)-H of Ethers and Thioethers under Metal-Free Conditions: Functionalization of H-N Azoles via C-H Activation. *Journal of Organic Chemistry* **(2015)**, 80(3), 1929-1936. DOI:10.1021/jo502477r

38. Qazi, Asif Khurshid; Hussain, Aashiq; Khan, Saima; Aga, Mushtaq A.; Behl, Akanksha; Ali, Shakir; Singh, Shashank Kumar; Taneja, Subhash Chandra; Shah, Bhahwal Ali; Saxena, Ajit Kumar; et al. Quinazoline based small molecule exerts potent tumour suppressive properties by inhibiting PI3K/Akt/FoxO3a signalling in experimental colon cancer. *Cancer Letters* (New York, NY, United States) **(2015)**, 359(1), 47-56. DOI:10.1016/j.canlet.2014.12.034

39. Gandhi, Sumit G.; Mahajan, Vidushi; Bedi, Yashbir S. Changing trends in biotechnology of secondary metabolism in medicinal and aromatic plants. *Planta* **(2015)**, 241(2), 303-317. DOI:10.1007/s00425-014-2232-x

40. Rafiq, Rather A.; Ganai, Bashir A.; Tasduq, Sheikh A. Piperine promotes ultraviolet (UV)-B-induced cell death in B16F10 mouse melanoma cells through modulation of major regulators of cell survival. *RSC Advances* **(2015)**, 5(16), 11884-11894. DOI:10.1039/C4RA12860E

41. Rather, Irshad Ahmad; Awasthi, Praveen; Mahajan, Vidushi; Bedi, Yashbir S.; Vishwakarma, Ram A.; Gandhi, Sumit G. Molecular cloning and functional characterization of an antifungal PR-5 protein from Ocimum basilicum. *Gene* **(2015)**, 558(1), 143-151. DOI:10.1016/j.gene.2014.12.055

42. Kumar, Sunil; Pathania, Anoop S.; Satti, Naresh K.; Dutt, Parbhu; Sharma, Neha; Mallik, Fayaz A.; Ali, Asif. Synthetic modification of hydroxychavicol by Mannich reaction and alkyne-azide cycloaddition derivatives depicting cytotoxic potential. *European Journal of Medicinal Chemistry* **(2015)**, 92, 236-245. DOI:10.1016/j.ejmech.2014.12.047

43. Mehra, Rukmankesh; Sharma, Rashmi; Khan, Inshad Ali; Nargotra, Amit. Identification and optimization of Escherichia coli GlmU inhibitors: An in silico approach with validation thereof. *European Journal of Medicinal Chemistry* **(2015)**, 92, 78-90. DOI:10.1016/j.ejmech.2014.12.030

44. Mupparapu, Nagaraju; Battini, Narsaiah; Battula, Satyanarayana; Khan, Shahnawaz; Vishwakarma, Ram A.; Ahmed, Qazi Naveed. Aminocatalytic Cross-Coupling Approach via Iminium Ions to Different C[n.63743]C Bonds. *Chemistry - A European Journal* **(2015)**, 21(7), 2954-2960. DOI:10.1002/chem.201405477

45. Khazir, Jabeena; Ali, Intizar; Khan, Inshad Ali; Sampath Kumar, Halmuthur Mahabalarao. Enzyme mediated-transesterification of verbascoside and evaluation of antifungal activity of synthesized compounds. *Natural Product Research* **(2015)**, 29(8), 727-734. DOI:10.1080/14786419.2014.984181

46. Mohammed, Shabber; Vishwakarma, Ram A.; Bharate, Sandip B. Metal-free DBU promoted regioselective synthesis of isoxazoles and isoxazolines. *RSC Advances* **(2015)**, 5(5), 3470-3473. DOI:10.1039/C4RA14694H

47. Sharma, Rajni; Guru, Santosh K.; Jain, Shreyans K.; Pathania, Anup Singh; Vishwakarma, Ram A.; Bhushan, Shashi; Bharate, Sandip B. 3-(2,6-Dichloro-benzyloxy)-11-oxo-olean-12-ene-29-oic acid, a semisynthetic derivative of glycyrrhetic acid: synthesis, antiproliferative, apoptotic and anti-angiogenesis activity. *MedChemComm* **(2015)**, 6(4), 564-575. DOI:10.1039/C4MD00344F

48. Dar, Bashir Ahmad; Shrivastava, Varsha; Bowmik, Amrita; Wagay, Mohammad Arif; Singh, Baldev. An expeditious N,N-dibenzylation

of anilines under ultrasonic irradiation conditions using low loading Cu(II)-clay heterogeneous catalyst. *Tetrahedron Letters* **(2015)**, 56(1), 136-141. DOI:10.1016/j.tetlet.2014.11.044

49. Mahajan, Vidushi; Rather, Irshad Ahmad; Awasthi, Praveen; Anand, Rajneesh; Gairola, Sumeet; Meena, Siya Ram; Bedi, Yashbir S.; Gandhi, Sumit G. Development of chemical and EST-SSR markers for Ocimum genus. *Industrial Crops and Products* **(2015)**, 63, 65-70. DOI:10.1016/j.indcrop.2014.10.052

50. Kumar, Sunil; Pathania, Anup S.; Nalli, Yedu K.; Malik, Fayaz A.; Vishwakarma, R. A.; Ali, Asif. Synthesis of new O-alkyl and alkyne-azide cycloaddition derivatives of 4'-methoxy licoflavanone: a distinct prenylated flavonoids depicting potent cytotoxic activity. *Medicinal Chemistry Research* **(2015)**, 24(2), 669-683. DOI:10.1007/s00044-014-1177-8

51. Pandotra, Pankaj; Viz, Bhavana; Ram, Gandhi; Gupta, Ajai Prakash; Gupta, Suphla. Multi-elemental profiling and chemo-metric validation revealed nutritional qualities of Zingiber officinale. *Ecotoxicology and Environmental Safety* **(2015)**, 114, 222-231. DOI:10.1016/j.ecoenv.2014.01.021

52. Singh, Bikarma; Borthakur, S. K. Phenology and Geographic Extension of Lycophyta and Fern flora in Nokrek Biosphere Reserve of Eastern Himalaya. *Proceedings of the National Academy of Sciences, India, Section B: Biological Sciences* **(2015)**, 85(1), 291-301. DOI:10.1007/s40011-014-0342-7

53. Battini Narsaiah; Battula Satyanarayana; Ahmed Qazi Naveed; Battini Narsaiah; Battula Satyanarayana; Ahmed Qazi Naveed; Kumar Raju Ranjith. 2-Oxo Driven Unconventional reactions: Microwave Assisted Approaches to Tetrahydrofuro[3,2-d]oxazoles and Furanones. *Organic letters* (2015).

54. Hyder Irfan; Miryala Sreekanth; Yedlapudi Deepthi; Kalivendi Shasi V; Khazir Jabeena; Ismail Tabasum; Nalla Naresh; Sampath Kumar Halmuthur M. Synthesis and Biological evaluation of novel 4b-[(5-substituted)-1,2,3,4-tetrazolyl] podophyllotoxins as anticancer compounds. *Bioorganic & medicinal chemistry letters* **(2015).**

55. Majeed Rabiya; Hussain Aashiq; Sharma Parduman R; Saxena Ajit K; Hamid Abid; Majeed Rabiya; Sangwan Payare L; Chinthakindi Praveen K; Khan Imran; Koul Surrinder; et al. PI3K target based novel cyano derivative of betulinic acid induces its signalling inhibition by down-regulation of pGSK3b and cyclin D1 and potentially checks cancer cell proliferation. *Molecular carcinogenesis* **(2015).**

56. Dar R A; Qazi P H; Saba I; Rather S A; Shiekh A A; Manzoor A; Wani Z A; Qazi A K; Hamid A; Modae D M. Cytotoxic Potential and Molecular Characterization of Fungal Endophytes from Selected High Value Medicinal Plants of the Kashmir Valley – India. *Drug research* **(2015).**

57. Yadav Rammohan R; Vishwakarma Ram A; Khan Shabana I; Singh Samsher; Khan Inshad A; Bharate Sandip B. Synthesis, antimalarial and antitubercular activities of meridianin derivatives. *European journal of medicinal chemistry* **(2015)**, 98160-169.

58. Guru Santosh Kumar; Pathania Anup Singh; Kumar Suresh; Kumar Ajay; Malik Fayaz; Sharma P R; Saxena A K; Bhushan Shashi; Ramesh Deshidi; Kumar Manjeet; et al. Secalonic acid-D represses HIF-1a/VEGF mediated angiogenesis by regulating the Akt/mTOR/p70S6K signaling cascade. *Cancer research* **(2015)**.

59. Mahale S; Chaudhuri B; Bharate S B; Manda S; Joshi P; Vishwakarma R A; Jenkins P R. Antitumour potential of BPT: a dual inhibitor of cdk4 and tubulin polymerization. *Cell death & disease* **(2015)**, 6e1743

60. Singh Aastha; Fatima Kaneez; Singh Arjun; Luqman Suaib; Shanker Karuna; Chanda Debabrata; Behl Akansha; Mintoo M J; Mondhe D M; Hasanain Mohammad; et al. Anticancer activity and toxicity profiles of 2-benzylidene indanone lead molecule. *European journal of pharmaceutical sciences* : official journal of the European Federation for Pharmaceutical Sciences **(2015)**, 7657-67.

61. Raghupathy Riya; Anilkumar Anupama Ambika; Polley Anirban; Singh Parvinder Pal; Yadav Mahipal; Saikam Varma; Sawant Sanghapal D; Vishwakarma Ram A; Johnson Charles; Suryawanshi Sharad; et al. Transbilayer lipid interactions mediate

nanoclustering of lipid-anchored proteins. *Cell* **(2015)**, 161(3), 581-94.

62. Pandita Archana; Manvati Siddharth; Singh Shashank K; Vaishnavi Samantha; Bamezai Rameshwar N K. Combined effect of microRNA, nutraceuticals and drug on pancreatic cancer cell lines. *Chemico-biological interactions* **(2015)**, 23356-64.

63. Kumar Suresh; Guru Santosh Kumar; Venkateswarlu Vunnam; Malik Fayaz; Vishwakarma Ram A; Sawant Sanghapal D; Bhushan Shashi. A novel quinolinebased second-generation mTOR inhibitor that induces apoptosis and disruptsPI3K-Akt-mTOR signaling in human leukemia HL-60 cells. *Anti-cancer agents in medicinal chemistry* **(2015)**.

64. Akindele Abidemi J; Wani Zahoor A; Sharma Sadhana; Mahajan Girish; Mondhe Dilip M; Saxena Ajit K; Satti Naresh K; Adeyemi Olufunmilayo. In Vitro and In Vivo Anticancer Activity of Root Extracts of Sansevieria liberica Gerome and Labroy (Agavaceae). *Evidence-based complementary and alternative medicine*: eCAM **(2015),** 2015560404.

65. Sen A; Sanyal U; Goswami K K; Mallick A; Baral R; Saxena A K. In vitro and in vivo evaluation of 2-chloroethylnitrosourea derivatives as antitumor agents. *Experimental oncology* **(2015)**, 37(1), 23-9.

66. Azam Mohammad; Khan Azmat Ali; Al-Resayes Saud I; Islam Mohammad Shahidul; Saxena Ajit Kumar; Dwivedi Sourabh; Musarrat Javed; Trzesowska-Kruszynska Agata; Kruszynski Rafal. Synthesis and characterization of 2-substituted benzimidazoles and their evaluation as anticancer agent. *Spectrochimica acta. Part A, Molecular and biomolecular spectroscopy* **(2015)**, 142286-91.

67. Kumar Arvind; Kumar Manjeet; Sharma Simmi; Guru Santosh Kumar; Bhushan Shashi; Shah Bhahwal Ali. Design and synthesis of a new class of cryptophycins based tubulin inhibitors. *European journal of medicinal chemistry* **(2015)**, 9355-63.

68. Ashraf Nasheeman; Jain Deepti; Vishwakarma Ram A. Identification, cloning and characterization of an ultrapetala transcription factor CsULT1 from Crocus: a novel regulator of apocarotenoid biosynthesis. *BMC plant biology* **(2015)**, 1525.

69. Agrawal Udita; Vyas S P; Chashoo Gousia; Sharma Parduman Raj; Kumar Ashok; Saxena Ajit Kumar. Tailored polymer-lipid hybrid nanoparticles for the delivery of drug conjugate: dual strategy for brain targeting. *Colloids and surfaces. B, Biointerfaces* **(2015)**, 126414-25.

70. Kumar Suresh; Guru Santosh Kumar; Pathania Anup Singh; Manda Sudhakar; Kumar Ajay; Bharate Sandip B; Vishwakarma Ram A; Malik Fayaz; Bhushan Shashi. Fascaplysin induces caspase mediated crosstalk between apoptosis and autophagy through the inhibition of PI3K/AKT/mTOR signaling cascade in human leukemia HL-60 cells. *Journal of cellular biochemistry* **(2015)**, 116(6), 985-97.

71. Rizvi Masood Ahmad; Peerzada Ghulam Mustafa; Zaki Mehvash; Afzal Mohd; Mane Manoj; Kumar Manjeet; Shah Bhahwal Ali; Srivastav Saurabh; Srikrishna Saripella; Tabassum Sartaj. Nuclear blebbing of biologically active organoselenium compound towards human cervical cancer cell (HeLa): in vitro DNA/HSA binding, cleavage and cell imaging studies. *European journal of medicinal chemistry* **(2015)**, 90876-88.

72. Nisar Albeena; Malik Akhter; Akhter Nayeema; Singh Gurudarshan; Masood Akbar; Banday Basharat; Zargar Mohammed Afzal. Modulation of T-helper cytokines and inflammatory mediators by Atropa accuminata. Royle in adjuvant induced arthritic tissues. *Journal of ethnopharmacology* **(2015)**, 162215-24.

LIST OF PATENTS (2013-2014)

A. Patents Filed In India

Sno	Title	Inventors	NFNO	Application No.	Remarks
1	New Chromone Alkaloid Dysoline For The Treatment Of Cancer And Inflammatory Disorders	Vishwakarma Ram Asrey, Jain Shreyans Kumar, Bharate Sandip Bibishan, Dar Abid Hamid, Khajuria Anamika, Meena Samdarshi, Bhola Sunil Kumar, Qazi Asif Khurdhid, Hussain Aashiq, Sidiq Tabasum, Uma Shaanker Ramanan, Ravikanth Gudasalamani, Vasudeva Ramesh, Mohana Kumara Patel, Ganeshaiah Kotiganahalli	0037NF2013/IN	1077DEL2013 Dt. 10-04-2013	
2	Cyclin-Dependent Kinase Inhibition By 5,7-Dihydroxy-8-(3-Hydroxy-1-Methylpiperidin-4-Yl)-2-Methyl-4h-Chromen-4-One Analogs	Vishwakarma Ram Asrey, Bharate Sandip Bibishan, Bhushan Shashi, Jain Shreyans Kumar, Meena Samdarshi, Guru Santosh Kumar, Pathania Anup Singh, Kumar Suresh	0219nf2012/IN	1142del2013 Dt. 17-04-2013	Provisional Specification
3	Tetrahydro-2h-Pyrano [3,2-C] Isochromene-6-Ones And Analogs For The Treatment Of Inflammatory Disorders	Jain Shreyans Kumar, Sidiq Tabasum, Meena Samdarshi, Khajuria Anamika, Vishwakarma Ram Asrey, Bharate Sandip Bibishan	0063nf2012/IN	1565del2013 Dt. 24-05-2013	
4	Brachiatin D And Process For Their Production Thereof	Deepika Singh, Jai Prakash Sharma, Sundeep Jaglan, Abid Hamid Dar, Anamika Khajuria, Varun Pratap Singh, Ram Asrey Vishwakarma	0038nf2013/IN	2563del2013 Dt. 30-08-2013	Provisional Specification
5	6-Nitro-2,3-Dihydroimidazo[2,1-B]Oxazoles And A Process For The Preparation Thereofanti-Mycobacterial Agents	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	0225nf2012/IN	2954del2013 Dt. 04-10-2013	
6	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	0106nf2013	0281del2014 Dt. 30-01-2014	

Sno	Title	Inventors	NFNO	Application No.	Remarks
7	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	0117nf2013/IN	0554del2014 Dt. 27-02-2014	
8	A Novel Formulation Useful In Cancer Chemotherapy	Dilip Manikrao Mondhe, Subhash Chandra Taneja, Surrinder Koul, Jagdish Kumar Dhar, Ajit Kumar Saxena, Rakesh Kamal Johri, Zahoor Ahmad Wani, Samar Singh Andotra, Subhash Chander Sharma, Surjeet Singh, Prem Narayan Gupta, Ram Asrey Vishwakarma	0088nf2012/IN	Provisional Filed On 17-02-2013 And Completely Filed On 10-02-2014	

B. Patents Filed In Foreign

Sno	Title	Inventors	NFNO	Application No.	Remarks
1	Quinolylpiperazino Substituted Thiolactone Compounds And Process For The Preparation Thereof	Ahmed Kamal, Shaik Azeeza, Ahmed Ali Shaik, M Shaheer Malik, Inshad Ali Khan, Sheikh Tasduq Abdullah, Sandeep Sharma, Anshu Beulah Ram	0073nf2010/US	13/643133 Dt. 10-04-2013	
2	Tetrahydro-2h-Pyrano [3,2-C] Isochromene-6-Ones And Analogs For The Treatment Of Inflammatory Disorders	Jain Shreyans Kumar, Sidiq Tabasum, Meena Samdarshi, Khajuria Anamika, Vishwakarma Ram Asrey, Bharate Sandip Bibishan	0063nf2012/WO	PCT/In2013/000679 Dt. 01-11-2013	

C. Granted Foreign Patents

SNo	Title	Inventors	NFNO	Application No.	Grant Date	Patent No
1	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	0159NF2008/US	13/130702	21-05-2013	8445700
2	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	0159nf2008/EP/DE/FR/ GB	9801288.3	10-07-2013	2361244 Granted In EP/DE/ FR/ GB

SNo	Title	Inventors	NFNO	Application No.	Grant Date	Patent No
3	Substituted 1H-Benz[De]Isoquinoline-1,3-Diones	Qazi Ghulam Nabi, Saxena Ajit Kumar, Muthiah Shanmugavel, Mondhe Dilip Manikrao, Sharma Praduman Raj, Singh Shashank Kumar, Sanyal Utpal, Mukherjee Asama, Hazra Suva, Dutta Sushanta	0006NF2006/DE/GB/FR/EP	7849684.1	14-08-2013	EP2118065 Granted In DE/GB/FR/EP
4	Aromatic Amides As Potentiators Of Bioefficacy Of Anti-Infective Drugs	Koul; Surrinder (Jammu Tawi, IN), Koul; Jawahir Lal (Jammu Tawi, IN), Taneja; Subhash Chandra (Jammu Tawi, IN), Gupta; Pankaj (Jammu Tawi, IN), Khan; Inshad Ali (Jammu Tawi, IN), Mirza; Zahid Mehmood (Jammu Tawi, IN), Kumar; Ashwani (Jammu Tawi, TW), Johri; Rakesh Kamal (Jammu Tawi, IN), Pandita; Monika (Jammu Tawi, IN), Khosa; Anita (Jammu Tawi, IN), Tikoo; Ashok Kumar (Jammu Tawi, IN), Sharma; Subhash Chander (Jammu Tawi, IN), Verma; Vijeshwar (Jammu Tawi, IN), Qazi; Ghulam Nabi (Jammu Tawi, IN)	0472NF2004/US	11/391391	12-11-2013	8580752
5	Spiro Derivatives Of Parthenin As Novel Anticancer Agents;Design And Synthesis	Halmuthur Mahabalarao Sampath Kumar, Saxena Ajit Kumar, Taneja Subhash Chandra, Singh Shashank Kumar, Sethi Vijay Kumar, Qazi Naveed Ahmed, Sawant Sanghapal Damodar, Doma Mahender Reddy, Banday Abid Hussain, Verma Monika, Qazi Ghulam Nabi	0158nf2007/RU	2010140598	27-11-2013	2499798
6	Spiro Derivatives Of Parthenin As Novel Anticancer Agents	Halmuthur; Mahabalarao Sampath Kumar (Jammu Tawi, IN), Saxena; Ajit Kumar (Jammu Tawi, IN), Taneja; Subhash Chandra (Jammu Tawi, IN), Singh; Shashank Kumar (Jammu Tawi, IN), Sethi; Vijay Kumar (Jammu Tawi, IN), Qazi; Naveed Ahmed (Jammu Tawi, IN), Sawant; Sanghapal Damodhar (Jammu Tawi, IN),	0158NF2007/US	12/921061	17-12-2013	8609858
7	Novel 4-Alkyl-5-(Substituted Phenyl)-2(E), 4(E)-Pentadienoic Acid Amide And Its Tetrahydro Analogues As Potentiators Of Bioeficacy Of Antiinfectives	Surrinder Koul,Jawahir Lal Koul,Subhash Chandra Taneja,Inshad Ali Khan,Zahid Mehmood Mirza,Ashwani Kumar Tikoo,Subhash Chander Sharma,Vijeshwar Verma,Ghulam Nabi Qazi	0472nf2004/KR	10-2007-7025170	13-01-2014	1353030

LIST OF PATENTS 2014-2015

A. Patents Filed in India

S. No.	Title	Inventors	NF No.	Application No.
1	10-Substituted Colchicinoids As Potent Anticancer Agents	Vishwakarma Ram, Bharate Sandip Bibishan, Kumar Ajay, Singh Baljinder, Kumar Ashok, Bhushan Shashi, Hamid Abid, Joshi Prashant, Guru Santosh Kumar, Kumar Suresh, Hussain Aashiq, Qazi Asif Khurshid, Bharate Sonali Sandip, Sharma Parduman, Saxena Ajit Kumar, Mondhe Dilip Manikrao, Mahajan Girish, Wani Zahoor	0059NF2014/IN	2929DEL2014 Dated: 10/14/2014
2	N-Substituted Beta-Carbolinium Compounds As Potent P-Glycoprotein Inducers	Bharate sandip, kumar ajay, manda sudhakar, joshi prashant, bharate sonali, vishwakarma ram	0302NF2013/IN	3002DEL2014 Dated: 10/21/2014
3	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	0060NF2014/IN	3004DEL2014 Dated: 10/21/2014
4	Alkylidene Phosphonate Esters As P-Glycoprotein Inducers	Bharate Sandip, Kumar Ajay, Manda Sudhakar, Joshi Prashant, Bharate Sonali, Wani Abubakar, Sharma Sadhana, Vishwakarma Ram	0058NF2014/IN	3010DEL2014 Dated: 10/21/2014
5	Substituted 1,2,3-Triazol-1-Yl-Methyl-2,3-Dihydro-2-Methyl-6-Nitroimidazo[2,1-B]Oxazoles As Anti-Mycobacterial Agents And A Process For The Preparation Thereof	Yempalla Kushalava Reddy, Munagala Gurunadham, Singh Samsher, Sharma Sumit, Khan Inshad Ali, Vishwakarma Ram Asrey, Singh Parvinder Pal	0176NF2014/IN	3009DEL2014 Dated: 10/21/2014
6	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	0036NF2014/IN	3077DEL2014 Dated: 10/29/2014
7	Novel 1,3,5 -Triazine Based Pi3k Inhibitors As Anticancer Agents And A Process For The Preparation Thereof	Thatikonda Thanusha, Kumar Suresh, Singh Umed, Mahajan Priya, Mahajan Girish, Nargotra Amit, Malik Fayaz, Mondhe Dilip Manikrao, Vishwakarma Ram Asrey, Singh Parvinder Pal	0127NF2014/IN	3369DEL2014 Dated: 11/20/2014

B. Patents Filed In Foreign

Sno	Country	Lab	Title	Inventors	NFNO	Application No.
1	WO	IIIM	Rohitukine Analogs As Cyclin - Dependent Kinase Inhibitors And A Process For The Preparation Thereof	Vishwa karma Ram Asrey, Bharate Sandip Bibishan, Bhushan Shashi, Mondhe Dilip Manikrao, Jain Shreyans Kumar, Meena Samdarshi, Guru Santosh Kumar, Pathania Anup Singh, Kumar Suresh, Behl Akanksha, Mintoo Mubashir Javed, Bharate Sonali Sandip, Joshi Prashant	0219NF 2012/WO	PCT/IN2014/000239 Dated: 4/16/2014
2	TW	IIIM	6-Nitro-2,3-Dihydroimidazo[2,1-B]Oxazoles And A Process For The Preparation Thereofanti-Mycobacterial Agents	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	0225NF2012/TW	103120596 Dated: 13/Jun/2014
3	WO	IIIM	Brachiatin D And Process For Their Production Thereof	Deepika Singh, Jai Prakash Sharma, Sundeep Jaglan, Abid Hamid Dar, Anamika Khajuria, Varun Pratap Singh, Ram Asrey Vishwakarma	0038NF2013/WO	PCT/IN2014/000557 Dated: 8/29/2014
4	EP	IIIM	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	0195NF2011/EP	13723567.7 Dated: 9/10/2014
5	CA	IIIM	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	0195NF2011/CA	Awaited Dated: 15/Sept/2014

Sno	Country	Lab	Title	Inventors	NFNO	Application No.
6	US	IIIM	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	0195NF2011/US	14/385808 Dated: 9/17/2014
7	JP	IIIM	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	0195NF2011/JP	---
8	WO	IIIM	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	0106NF2013/WO	PCT/IN2014/000662 Dated: 10/20/2014
9	CN	IIIM	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	0195NF2011/CN	Dated: 11/19/2014
10	WO	IIIM	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	0117NF2013/WO	PCT/IN2015/000088 Dated: 2/16/2015

C. Patents – Granted Foreign 2014-2015

Sno	Title	Inventors	NFNO	Comp. Filing Date	Application No.	Patent No.
1	Spiro Derivatives Of Parthenin As Novel Anticancer Agents;Design And Synthesis	Halmuthur Mahabalarao Sampath Kumar, Saxena Ajit Kumar, Taneja Subhash Chandra, Singh Shashank Kumar, Sethi Vijay Kumar, Qazi Naveed Ahmed, Sawant Sanghapal Damodar, Doma Mahender Reddy, Banday Abid Hussain, Verma Monika, Qazi Ghulam Nabi	0158NF2007/EP	22-Sep-10	9717600.2	2265620 Dated: 18-Jun-14
2	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	0159NF2008/AU	24-May-11	2009318789	2009318789 Dated: 11-Sep-14

BOOKS CHAPTER

1. Ajai Prakash Gupta, Pankaj Pandotra, Rajni Sharma,Manoj Kushwaha, and **Suphla Gupta.** (2013). Marine Resource: A Promising Future for Anticancer Drugs Studies in Natural Products Chemistry. 40 Elsevier, The Boulevard, Langford Lane, Kidlington, Oxford, OX5 1GB, UK Radarweg 29, PO Box 211, 1000 AE Amsterdam, The Netherlands First edition 2013.

SEMINARS/ CONFERENCES/ WORKSHOPS/ SYMPOSIUM

1. M. K. Verma, D. K. Gupta, Sunil Kumar, **S. Chandra,** R. A. Vishwakarma. Development and validation of simple, rapid improved RP-HPLC-UV(DAD) method for determination and quantification of curcuminoids in extracts obtained by different extraction methods in Indo-US *Symposium on Botanical Drug Development organized by CSIR-IIIM(J), Medanta Medicity and NCNPR, USA* at Medanta – The Medicity, Gurgaon, Haryana on December 13-14, 2013.
2. Suresh Chandra. Participated in *101th Indian science congress* was held at Jammu this year and a huge stall was set up of CSIR were various CSIR institutions depicted their achievements to general public as well as various delegates who had participated from all across the country.
3. Pankaj Pandotra, Ajai Gupta, Gandhiram, Saima Khan & Suphla Gupta. Prospects of Ginger Cultivation in Jammu & Kashmir: Molecular and Biochemical basis. *Second J&K Women Science Congress* held on Oct. 24 to 26 , 2013.

Award

1. Richa Sharma, Farnaz Yusuf, Chand Raina and Asha Chaubey. Isolation and characterization of *Penicillium* sp. isolated from cold shiwalik region for linolenic acid production. *International conference on Food Technology: Impact on nutrition and health* (ICFIN-2013) held at JNU, N. Delhi during 23-24 Dec 2013.

RESEARCH COUNCIL 2013-2014

Prof. Goverdhan Mehta — **Chairman**
National Research Professor and Lily – Jubilant Chair,
School of Chemistry,
University of Hyderabad, Hyderabad - 500046

Dr. Rajiv I. Modi — **External Member**
Managing Director, Cadila Pharmaceuticals Ltd.
Cadila Corporate Campus, Ahmedabad -382210

Prof. Sudhir K. Sopory — **External Member**
Vice Chancellor
Jawaharlal Nehru University, New Delhi -110067

Prof. Satyajit Mayor — **External Member**
Professor and Dean
National Centre for Biological Sciences, (Tata Institute of Fundamental Research)
Bellary Road, GKVK Campus, Bengaluru -560065

Prof. Y.K. Gupta — **External Member**
Professor and Head
Department of Pharmacology,
All India Institute of Medical Sciences
New Delhi -110029

Dr. Satyajit Rath — **External Member**
Scientist, National Institute of Immunology
Aruna Asaf Ali Marg, JNU Complex, New Delhi -110 067

Dr. T. S. Balganesh — **External Member**
CSIR Distinguished Scientist
CSIR- Fourth Paradigm Institute,
NAL Belur Campus, Bengaluru -560037

Dr. G.J. Samathanam — **Agency Representative**
Adviser
Department of Science & Technology, Technology Bhawan, New Mehrauli Road
New Delhi -110016

Dr. P.K. Biswas — **DG Nominee**
Former Adviser (S&T), Planning Commission
MS-11/905, Kendriya Vihar, Sector 56,Gurgaon, Haryana -122003

Dr. Ramesh V. Sonti — **Sister Laboratory**
Scientist
CSIR0- Center for Cellular and Molecular Biology,
Uppal Road, Hyderabad - 500007

Dr. P.S. Ahuja — **Cluster Director**
Director
CSIR - Institute of Himalayan Bioresource Technology (IHBT)
Palampur -176061

Dr. Ram Vishwakarma — **Director**
Director, Indian Institute of Integrative Medicine
Canal Road, Jammu

Head or his Nominee — **Permanent Invitee**
Planning & Performance Division
Council of Science & Industrial Research
Anusandhan Bhawan, 2, Rafi Marg,
New Delhi -110 001

RESEARCH COUNCIL 2014-2015

Prof. Goverdhan Mehta, FRS — **Chairman**
National Research Professor
CSIR Bhatnagar Fellow,
Department of Organic Chemistry,
Indian Institute of Science, Bangalore – 500012

Dr. Satyajit Rath — **External Member**
Scientist, National Institute of Immunology
Aruna Asaf Ali Marg, JNU Complex, New Delhi -110 067

Prof. Sudhir K. Sopory — **External Member**
Senior Scientist & Coordinator Plant Biology Group Leader
Plant Molecular Biology
International Centre for Genetic Engineering and Biotechnology,
New Delhi -110067

Prof. Dipankar Chatterji — **External Member**
Professor in Molecular Biophysics Unit
Indian Institute of Science, Bangalore – 500012

Prof. Satyajit Mayor — **External Member**
Professor and Dean
National Centre for Biological Sciences,
(Tata Institute of Fundamental Research)
Bellary Road, GKVK Campus, Bengaluru -560065

Prof. Sushil Durani — **External Member**
Department of Chemistry,
Indian Institute of Technology,
Powai, Mumbai -400076

Dr. Raman Govindarajan — **External Member**
Senior Vice President
Discovery Biology,
Development of Translation Medicine
Bengaluru -560022

Dr. R. Brakaspathy — **Agency Representative**
Scientist G
Department of Science & Technology,
Technology Bhawan, New Mehrauli Road
New Delhi -110016

Dr. P.K. Biswas — **DG Nominee**
Former Adviser (S&T), Planning Commission
MS-11/905, Kendriya Vihar, Sector 56,Gurgaon, Haryana -122003

Dr. T.K. Chakraborty — **Sister Laboratory**
Director
CSIR- Central Drug Research Laboratory,
Chattar Manzil Palace, Lucknow - 226001

Prof. Siddhartha Roy — **Cluster Director**
Director
CSIR – Indian Institute of Chemical Biology (IICB)
Kolkatta -700032

Dr. Ram Vishwakarma — **Director**
Director, Indian Institute of Integrative Medicine
Canal Road, Jammu

Head or his Nominee — **Permanent Invitee**
Planning & Performance Division
Council of Science & Industrial Research, New Delhi -110 001

MANAGEMENT COUNCIL 2013 - 2014

Dr. Ram Vishwakarma — **Chairman**
Director, Indian Institute of Integrative Medicine
Canal Road, Jammu

Dr. Girish Sahani — **Member**
Director, Institute of Microbial Technology
Chandigarh

Er. Abdul Rahim **Member**
Principal Scientist /Head, PME Division
Indian Institute of Integrative Medicine, Canal Road, Jammu

Er. Rajneesh Anand **Member**
Sr. Principal Scientist
Indian Institute of Integrative Medicine, Canal Road, Jammu

Dr. Parthasarthi Das **Member**
Principal Scientist
Indian Institute of Integrative Medicine, Canal Road, Jammu

Dr. Dhiraj Kumar Vyas **Member**
Scientist
Indian Institute of Integrative Medicine, Canal Road, Jammu

Dr. Shashank Kumar Singh **Member**
Sr. Scientist
Indian Institute of Integrative Medicine, Canal Road, Jammu

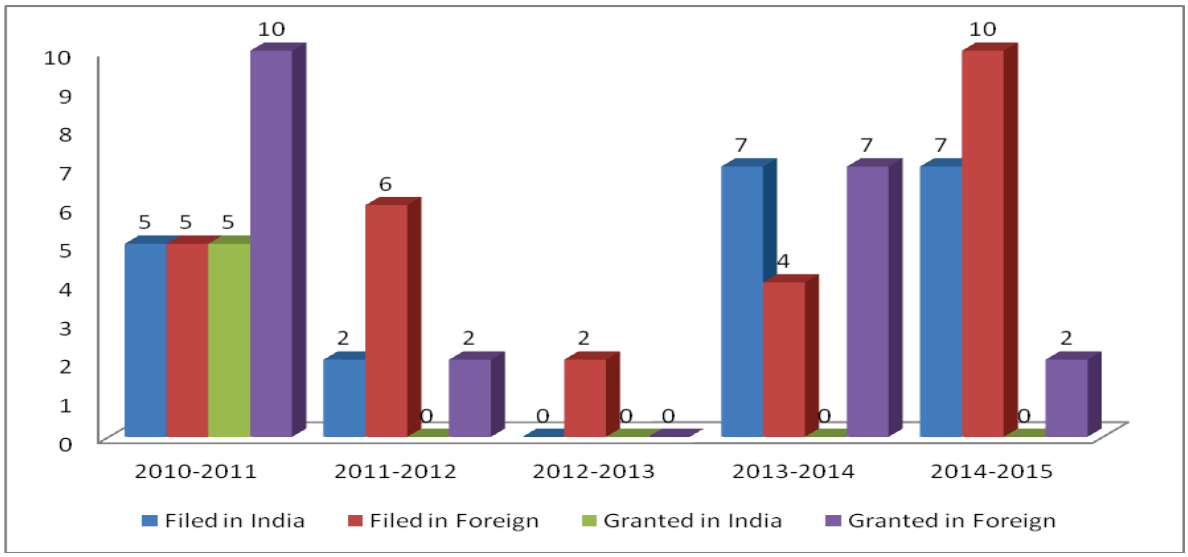
Sh. R K Raina **Member**
F&AO
Indian Institute of Integrative Medicine, Canal Road, Jammu

Sh. Om Prakash **Member**
COA
Indian Institute of Integrative Medicine, Canal Road, Jammu

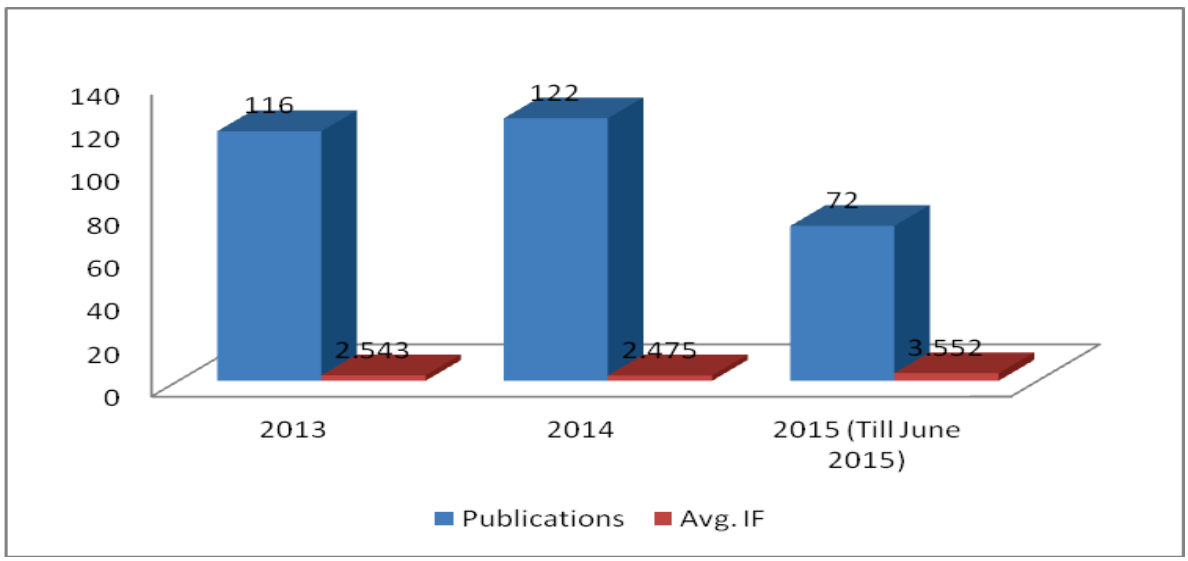
Dr. S.C. Sharma **Member**
Principal Technical Officer
Indian Institute of Integrative Medicine, Canal Road, Jammu.

Performance Parameters

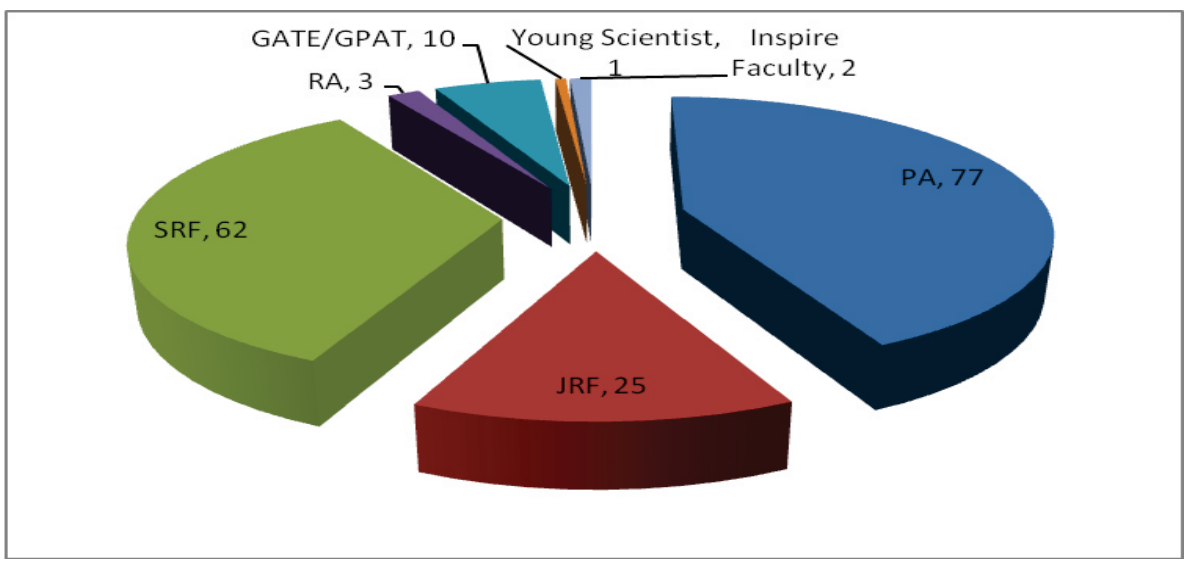
Patents



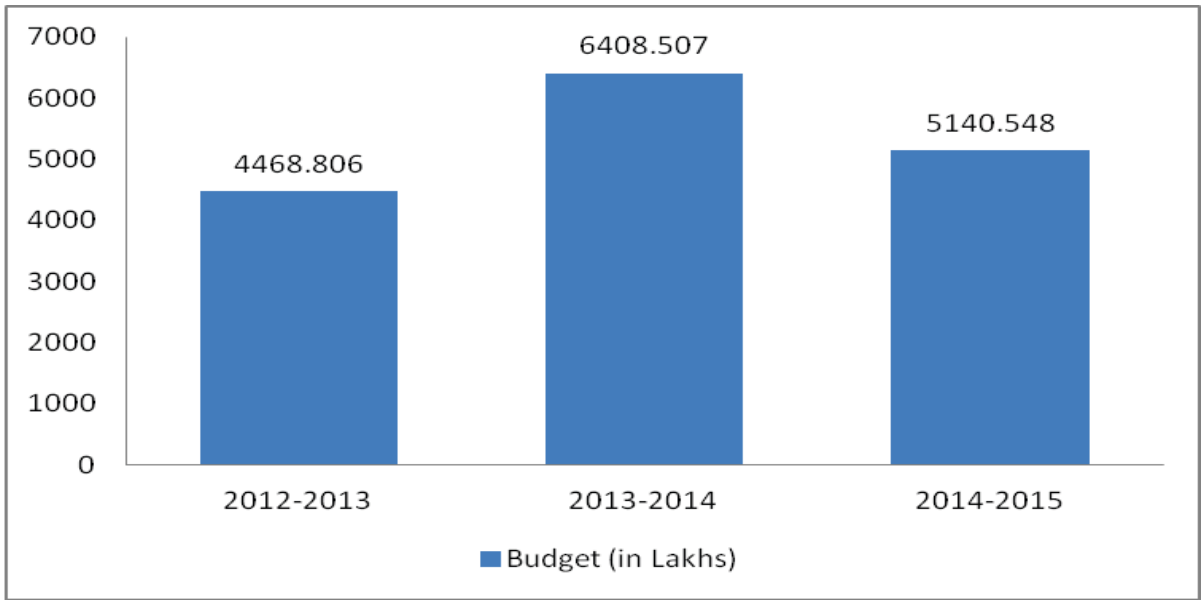
Publications [Calender Year Wise]



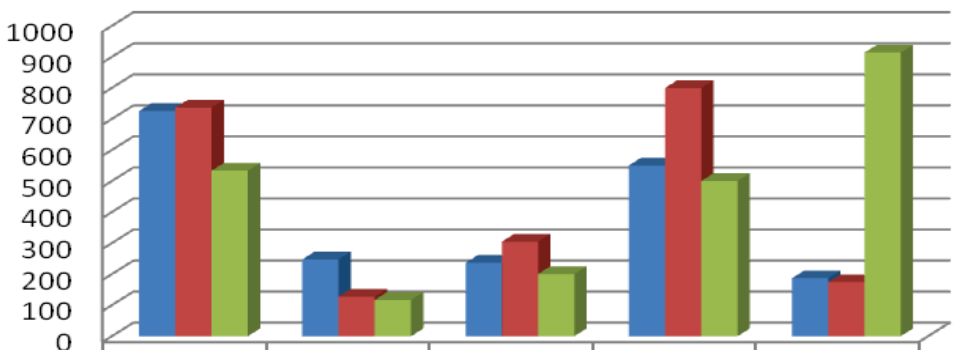
Fellows



Budget (Rs. In Lakhs)

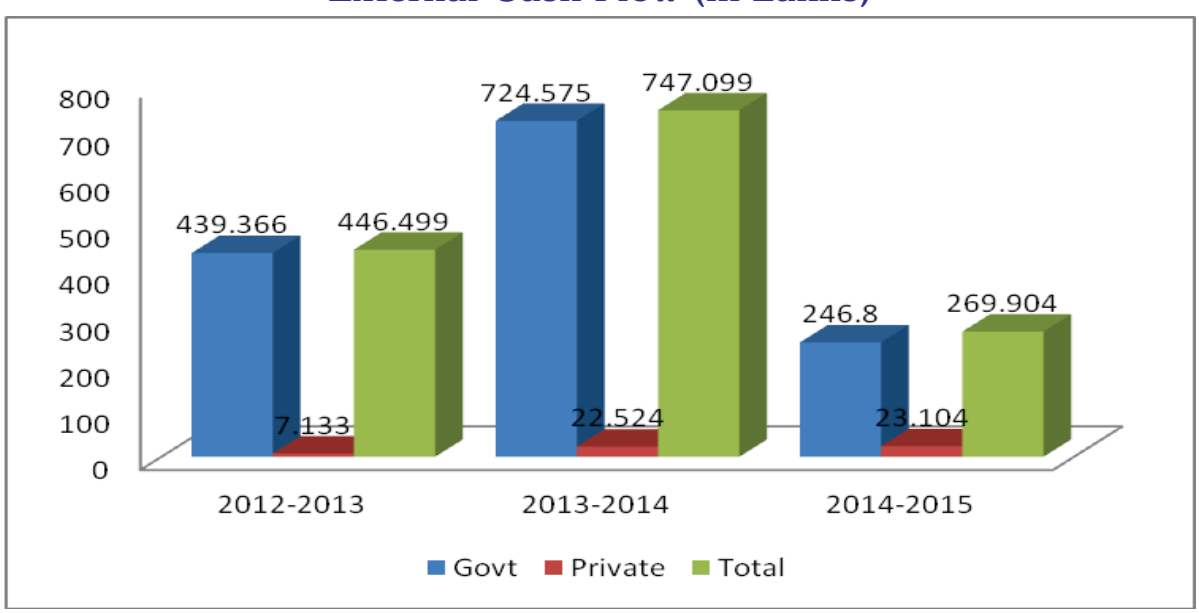


Institute's Reserve (Rs. In Lakhs)



	Open baln.	Gene	Expn	Bal. in TDR	Bal in Inst. A/c
2012-2013	725.667	247.599	236.467	550	186.799
2013-2014	736.799	127.38	304.493	800	174.132
2014-2015	533.484	116.984	200.347	500	913.941

External Cash Flow (in Lakhs)



RURAL DEVELOPMENT AND SOCIETAL ACTIVITIES

Kissan Mela and Flower Show

IIIM has a tradition to organize Annual Flower Show in its campus since 1961. The event has been rechristened as "'Kissan Mela, Flower Show & Entrepreneurship Programme' on 17th. March, 2014 and in which more than 600 farmers/ entrepreneurs / industrial housed participated. National seminar sum exhibition on Kissan Mela, Entrepreneurship programme & Flower Show is going to be organised at IIIM Farm, Chatha on 15th and 16th March, 2015.

Promotion in the cultivation of Phalsa

In order to promote the cultivation of Phalsa in Jammu region a awareness camp was organised at **Jhiri** In June 6, 2013, where bottles of Phalsa juice was distributed among the rural people in order to encourage them to cultivate the same.

Some images of collection of plants/microbes from wild








Blood Donation Camp

In 2014, on 14th November, IIIM in association with Blood Transfusion Department, Govt. Medical College, Jammu had organized a voluntary blood donation camp in its campus premises. Director IIIM, Dr. Ram Vishwakarma inaugurated the camp alongwith Dr. Vijay Sawhney (Prof. & Head, Blood Transfusion Deptt., GMC, Jammu) under the supervision of Chairman Dispensary Dr. D.M. Mondhe and L.M.O. dispensary Dr. Anju Gupta. The scientists as well as the students participated in the donation camp. About 27 students/staff have volunteered in this camp for donating blood.

46th SSBMT A Mega Sport Event Organized by CSIR-IIIM

Sports are a great barometer for a society's state of health. Sporting success requires mental, physical and emotional health and is closely interconnected with the state of development in any field. The success of 46th SSBMT – a multi-CSIR lab sports event, held at CSIR-IIIM, Jammu – has several positive tangible and intangible implications.

This year, 46th SSBMT tournament was organized by CSIR-IIIM Jammu. About 160 participants, from ten different CSIR labs viz., CSIR-CECRI Karaikudi, CSIR-NIIST Trivandrum, CSIR- Madras Complex Chennai, CSIR-SERC Chennai, CSIR-CMERI Durgapur, CSIR-IICT Hyderabad, CSIR-NISTARDS New Delhi, CSIR-CSMCRI Bhavnagar, CSIR-NGRI Hyderabad, CSIR-IITR Lucknow have participated in the event. Various games like Carom, Chess, Table Tennis, Badminton and Bridge were organized by CSIR-IIIM, Jammu. All lodgings and boarding to the players were provided, along with refreshments and other facilities during the tournament. It was a great success. All arrangements were admired by the participants and senior colleagues.

All the events were played within the lab campus except for badminton and table tennis. Badminton was played at J& K police multipurpose indoor complex, Jammu and Table tennis at M. A. stadium whereas; Bridge, carom and chess were played at new student's hostel of IIIM.

A great support was received from the CSIR-Sports Board. The event became more graceful because of the presence of the Honorable minister of Science and Technology and Earth Sciences Dr. Jitendra Singh being guest of honor. More significantly, the quality of competitors was outstanding and we were able to witness a very high level all sports activities.

We the organizers are thank full to all those who helped in make the 46th SSBMT tournament a great success. This includes all our partners, the venues, the sports, patrons, staff, volunteers, of course, the competitors and team management who were the stars.

'Swachh Bharat' Abhiyaan At IIIM, Chatha Farm

Cleanliness drive by Chief Guest, Dr. Jitender Singh

CSIR Relief Camp

CSIR-IIIM Jammu organized 3 days relief camp in flood effected Villages Tawi Island, Sure Chak and Makwal of District Jammu during which Water filtration units of different capacities were installed besides providing the medicines to the inhabitants in these areas.

HUMAN RESOURCE 2013-2015

Director
Dr. Ram A Vishwakarma

Chief Scientist
Dr. Surinder Kaul
[Retd.on 30.06.2013]
Dr. Rajinder Parshad
[Retd. on 30.09.2014]
Dr. R. K Raina
[Retd.on 30.04.2013]
Dr. Y .S. Bedi Dr. J. K. Dhar
[Retd. on 31.01.2014]
Dr. R.K. Johri
Dr. A.K. Saxena
[Retd. on 31.08.2013]
Dr. Sushma Koul
[Retd. on 30.04.2014]
Dr. Suresh Chandra
Dr. R .K. Khajuria
Dr. V.K.Gupta
[Retd. on 31.12.2014]
Dr. D.K. Sultan
[Retd. on 31.10.2013]
Dr. Ashok Ahuja
[Retd. on 30.09.2013]

Sr. Principal Scientist
Mr. Rajneesh Anand
Mr. R.K. Malhotra
[Retd. on 31.08.2014]
Dr. Baldev Singh
[Retd. on 31.01.2015]

Principal Scientist
Dr. Dilip Manikrao Mondhe
Mr. Abdul Rahim
Dr. Anindya Goswami
Dr. Muzamil Ahmad
Mrs. Geeta Mehta
[Retd. on 30.09.2014]
Dr. Inshad Ali Khan
Dr. D.K. Gupta
[Retd. on 31.12.2014]
Dr. Zabeer Ahmed
Dr. Gurdarshan Singh
Dr. Parthasarthi Das

Sr. Scientist
Dr. Rajkishore Rai
Dr. Subash Singh
Dr. P.N. Gupta
Dr. Zahoor Ahmad Parry
Dr. Asha Chaubey
Dr. Shashank Kr. Singh
Dr. Mrs Meenu Katoch
Dr. Abid Hamid Dar
Dr. Mohd. Jamal Dar
Dr. Sandip B. Bharate
Dr. Asif Ali
Dr. Qazi Naveed Ahmad
Dr. Prasoon Kumar Gupta

Scientist
Dr. Shashi Bhushan
Dr. Sheikh Tasduq Abdullah
Dr. Fayaz Ahmad Malik
Dr. Dhiraj Kumar Vyas
Dr. Sumit G Gandhi
Mrs. Deepika Singh
Dr. Govind Yadav
Mr. Anil Kumar Katare
Dr. Bilal Ahamd Bhat
Dr. Qazi Parvaiz Hassan
Dr. Kursheed Ahmad Bhat
Dr. S.D. Sawant
Dr. (Mrs) Suphla Bajpai Gupta
Dr. Debaraj Mukherjee
Dr. Amit Nargotra
Dr. Payare Lal Sangwan
Dr. Syed Riyaz- Ul Hassan
Dr.(Mrs.) Nasheeman Ashraf
Dr. Sumit Gairola
Dr. Prashant Mishra
Mr. Shaghaf Mobin Ansari
Dr. Narendra Kumar
Dr. Vikas Babu
Dr. Bikarma Singh
Dr. Ravi Shankar

Jr. Scientist
Dr. Parvinder Pal Singh
Dr. Dr. Bhahwal Ali Shah
Dr. Sandeep Jaglan

Principal Technical Officer
Dr. Arun Kumar
Mr. M.K. Tikoo
Dr. J.P. Sharma
Mr. Rakesh Bhasin
Dr. Bal Krishan Chandan
Dr. Surjeet Singh
Dr. Surrinder K. Lattoo
Mr. Prabhu Dutt
Dr. Anupurna Kaul
Dr. Anamika Khajuria
[Retd. on 31.05.2013]
Dr. P.R. Sharma
Dr. N.K. Satti

Sr. Technical Officer (III)
Mrs. Kushal Bindu
Dr. S.C. Sharma
[Retired on 30.06.2014]
Dr. Sarojini Johri
Mr. R.K. Thapa
Mrs. Urmila Jamwal
Mr. R.K. Khajuria
Mr. Surinder Kitchlu
Dr. Satya Narayan Sharma
Mr. Vijendra Kumar
Mr. L.R. Manhas
Mr. Chandji Raina
Mr. Shankar Lal
[Retired on 30.06.2014]
Dr. Kanti Rekha
Dr. A K Tripathi
Mrs. Suman Koul
Mr. Vinay Kumar Gupta
Dr. Ajai Prakash Gupta

Sr. Technical Officer (II)
Mrs. Pinki Koul
Mr. Rajinder Kumar

Tech Officer-I
Mrs. Asha Bhagat
Mr. Buddh Singh
Mr. Sunil Kumar
Dr. Phalisteen Sultan

Medical Officer
Dr. Amit Sharma
Dr. Mrs. Anju Gupta

Library Officer
Mr. Sanjay Sharma
Transfer from HRDG, Feb. 2015
Mr. Rakesh Singh Bisen
Transfer to IITR March 2015

E. E (Civil)
Mr. Gurinder Pal Singh

AEE(Elect.)
Mr. Ashwani Chopra

Jr. Engr
Mr. S.N. Bharati

Technical Officer A
Mr. Siya Ram Meena
Mr. Ajit Prabhakaran
Dr. Mahendara Kr. Verma

Technical Assistant
Mrs. Bhavna Vij
Mr. Gourav Sharma
Mr. Manish Kumar
Mr. Vijay Budania
Mr. Kamlesh Singh
Mr. Sumit Kumar
Dr. Shashid Rasool
Mr. Arvind K. Yadav
Mr. Yogesh Kumar
Mr. Amit Kumar
Mr. Brijender Koli
Mr. Rajinder Gochar
Mr. Nitin Ashok Narkhede
Mr. Uma Shankar
Ms. Monika Gupta
Mr. Chandera Pal Singh
Mr. Bikrama Singh
Mr. Durga Prasad Mindala
Mr. Ashok Kumar Bhargava

Sr. Technician
Mr . Sudhir Nanda
Mr. V. K. Khanna
Mr. Manoharlal Sharma
[Retired on 31.10.2014]
Mr. Inderjit Singh
Mr. Vijay Kumar
[Retired on 31.05.2014]
Mr. Ajeet Singh
Mr. Ramesh Kumar
Mr. Sardari Lal
[Retired on 31.07.2013]
Mrs. Raj Kumari
Mr. Nagar Singh
Mr. Kuldip Raj
Mr. Jeet Singh
[Retired on 28.02.2015]
Mr. Ram Rakha
[Retired on 31 July, 2012]
Mr.Gulshan Kumar
Mr. S.K. Rattan
Mr. Ali Mohd. Hajam
[Retired on 31.01.2014]
Mr. Prithi Pal
Mr. Vikram Abrol
Mr. Bhushan Lal
Mr. Nirmal Singh
Mr. Om Singh
Mr. Parshotam Kumar
Mr. T.S. Salathia
[Retired on 30.04.2013]
Mr. Jasbir Singh
Mr. Ravinder Wali
Mrs .Kamlesh Sharma
Mrs. Manju Sambyal
Mrs. Neelam Sharma
Mr A. K. Sharma
Mr .Parshotam Kumar
Mr. Madan Lal
Mr. Kuldeep Singh
Mr. Rajinder Kumar Gupta
Mrs. Sunita Devi
Mr. R. L. Jolly
[Retired on 28.02.2014]
Mr. A.K. Mehra
[Retried on 30.04.2013]
Mr. Vikram Bhardwaj
Mrs. Parveen Sharma
Dr. Ravinder Kour
Mrs. Shabnam Khan

Technician
Mr. Pushap Rattan
Dr. Anil Prabhakar
Mr. Ashwani Sharma
Mr. Partap Chand
Mr. S.K. Ganjoo
Mr. Samar Singh
Mrs. Kiran Koul
Mr. Satya Bhushan
Mrs. Sarla Bhat
Mr. Rajinder Kumar
Mr. Naresh Pal
Ms. Anjum Vashist
Mr. Rajesh Kumar Sahdev
Mr. Surinder Kumar
Mr. Bachitar Singh
[Retired on 31.10.2013]
Mr. Ashok Kumar
Mr. Kewal Singh
Mr. Kasturi Lal
Mr. Girdhari Lal

Lab Assist.
Mrs. Santosh Baigra
Mr. Dilbag Rai
[Retired on 30.09.2013]
Mr. Jita Ram
[Retired on 30.09.2013]
Mr. Shimlu Ram
[Retired on 31.03.2014]
Mr. Girdhari Lal
Mr. Gulam Quadir Sheikh
[Retired on 30.04.2013]
Mr. Chaman Lal
Mr. Bishan Kumar
Mr. Jasbir Singh
Mr. Kuldeep Kumar
Mr. Madan Lal
[Retired on 31.10.2014]
Mr. Moti Ram
[Retired on 31.12.2013]
Mr. Nasibu Ram
Mr. Sham Lal Bhagat
Mr. Sham Lal
[Retired on 31.01.2015]
Mr. V.P. Kohli
[Retired on 30.04.2015]
Mr. Balwant Raj
Mr. Hens Raj
Mr. Kartar Chand
[Retired on 31.03.2014]
Mr. Sham Lal
[Retired on 31.07.2014]
Mr. Ram Pal
Mr. Balwant Raj
Mr. Babu Ram
Mr. Dila Ram
Mr. Gudu Ram
Mr. Abid Hamid Dar
Mr. Karam Chand
Retired on 31.12.2013
Mr. Wali Wani
Retired on 31.07.2014
Mr. Mohd. Wani.
Retired on 31.07.2014
Mr. Rasool Mir
Mr. Neel Kamal
Mr. Rishi Kumar
Mr. Balwinder Singh
Mr. Manoj Kumar
Mr. Ajit Ram
Mr. Lal Chand
Mr. Om Parkash
Mr. Girdhari Lal
Mr. Abdul Ahad Sheikh
Mr. Fayaz Ahmad Dhar
Mr. Bushan Lal
[Retired on 31.07.2013]
Mr. Naranjan Singh
Mrs. Darshana
Mr. Nagar Lal
Mr. Kuldeep kumar

Admn. Officer Gr.(1)
Mr. Om Parkash Transfered.
Mr. Pankaj Bhadur

Finance & Accounts Officer
Mr. Upendra Kumar
Mr. R.K.Raina
Mr. Sunil Kumar
joined on 1.1.2015
transfered from CSIR Headquarters

Store & Purchase Officer
Mr. Ashok Kumar
Mr. Praphul Kumar
[Joined on 02.09.14]
Transfer from CDRI, Lucknow

Sr. Hindi Officer
Dr. Amar Singh
Dr. Rama Sharma

Section Officer
Mr. S.R. Alam
Mr. Rajesh Kumar Gupta

Section Officer
(Store & purchase)
Mr. B.B. Gupta
Mr. Ram Singh

Private Secretary
Mr. Ramesh Kumar

Section Officer(F & A)
Mr. Anil Gupta
Mr. Darshan Singh [Transfered]

Security Officer
Mr. Yashpal Singh

Assistant General Gr(1)
Mrs. Vijay Bajaj
[Retired on 30.04.2013]
Mr. Major Singh
[Retired on 31.10.2014]
Mr. Anil Kumar Gupta
Mr. Romesh Kumar Mottan
Mr. U.S. Thappa
Mrs. Kusum Bali
Mrs. Neelam Razdan
Mr. Ranjeet Kr. Gupta
Mr. Manoj Kumar
Ms. Nisha Vij
Mr. Rajinder Singh
Mrs. Kiran Dutta
[Retired on 30.09.2014]
Mr. Ashok Kumar
Mr. Vivek Parmar

Asst.(F&A) Gr(1)
Mr. Tarsem Lal
Mr. Umesh Malhotra
Mr. H.K Gupta

Asst.(S&P) Gr(1)
Mr. Satish Sambyal
Mr. Y.K. Mishra
Mrs. Rajni Kumari

Senior Stenographer
Mr. V.K. Sharma
Mrs. Phoola Kumari

Security Asstt.
Mr. Mohan Lal
[Retired on 31.07.2013]
Mr. Krishan Lal

Receptionist
Ms. Jyoti Prabha

Asstt. (G) Gr(II)
Mrs. Rekha Gupta
Mr. Benjamin
Mr. Mohd. Ayub Bhat

Asstt (F&A) Gr(II)
Mr. Vinod Kumar Meena
Mrs. Lovely Ganjoo.
Mrs. Saroj Mehta
Mr. Sanchit Kumar Sharma

Asstt (S&P) Gr(II)
Mr. Bua Ditta
Mr. Angrez Singh

Asstt (F&A) Gr(III)
Mr. Roshan Lal

Asstt (G) Gr(III)
Mrs. Sunita Kumari

Record Keeper
Mr. Tilak Raj - Gr. B
[Retired on 31.03.2014]
Mr. Amar Nath - Gr. C

Halwai
Mr. Janak Raj

Work Assist.
Mr. G. M. Mir
[Retried on 31.10.2013]
Mr. Milkhi Ram
Mr. Paras Ram
Mr. Panna Lal
Mr Rahim Mir
[Retired on 31.08.2014]
Mr. Jagdish Singh
Mr. Romesh Kumar
Mr. Chaman Lal
Mr. Parshotam Lal
Mr. Mohd. Farooq Bhat
Mr. Banadic Hans
Mr. Ram Lal
Mr. Ashok Kumar
Mr. Tarseem Kumar
Mr. Pawan Kumar
Mr. Rajesh k. Tandon
Mr. Moses Tegi
Mr. Girdhari Lal.
Mr. Sodhagar Mal
Mr. Rashpal
Mr. Prithvi Raj
Mr. Mangal Dass
Mr. Sham Lal
Mr. Subash Chander
Mrs. Ratna
Mr. Girdhari lal
Mr. Suram Chand
Mr. Bala Ram
Mr. Tara Chand
Mr. Rattan Lal
Mr. Sham Lal
Mr. Kala Ram
Mr. Ashok Kumar
Mrs. Satya Sharma
Mr. Bua Ditta
Mr. Kehar Singh
Mr. Seva Ram
Mr. Sodagar Mal
[Retired on 31.08.2013]
Mr. Madan Lal
Mr. Ram Ditta
Mr. Krishan Chand
Mr. Noor Mohd. Dar
[Retired on 31.12.2014]
Mr. Ashok Kumar
Mr. Munna
Mr. Dev Raj
Mr. Surinder Kumar
Mr. Ashok Kumar
Mr. Karnail Chand
Mr. Bachan Lal
Mr. Kali Das
Mr. Daleep Raj
Mr. Sham Lal
Mr. Sodagar Lal
Mrs.Ram Pyari

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

आजादी की 67वीं वर्षगांठ

15 अगस्त, 2013

आज हम आजादी की 67वीं वर्षगांठ मना रहे हैं इस पावन अवसर पर आप सबको हार्दिक शुभकामनाएं एवं बधाई देता हूँ। यह ऐतिहासिक दिन हमें स्वतंत्रता आन्दोलन के हजारों परवानों की महान कुर्बानियों की याद दिलता है। हम उन देश भक्तों, शहीदों तथा देश की रक्षा में शहीद हुए सेना के जवानों व देश के नागरिकों को श्रद्धासुमन अर्पित करते है। जिन्होंने देश की सीमाओं पर रक्षा करते हुए अपनी जॉन कुर्बान कर दी है मेरा उन्हें शत्-शत् प्रणाम !

15 अगस्त, 1947 को आज से 66 वर्ष पहले हम आज़ाद हुए थे। यह हमारी आजादी का विशेष महत्वपूर्ण एवं गौरवशाली दिन है। क्योंकि 26 जनवरी, 1930 को रावी नदी के तट पर नेहरूजी की अध्यक्षता में पूर्व स्वतंत्रता प्राप्ति का प्रस्ताव कांग्रेस के अधिवेशन में पास हुआ था। हमें स्वाधीन हुए 66 वर्ष हो गये हैं। अब यह समृद्ध भारत है, हमने इन 66 वर्षों में क्या पाया क्या खोया? हमें आगे और प्रगति के लिए आत्म मन्थन करना होगा, बहु।

आगे भी हमें निरन्तर प्रगति के लिए प्रयास करने होंगे। हमें जो आजादी मिली है उसे और व्यापक बनाने की आवश्यकता है, आजादी हमें कितनी कुर्बानियों से प्राप्त हुई। आजादी हमारे देश की एकता, अखण्डता आज जो स्वतंत्रता हम महसूस कर रहे हैं उसके पीछे हमारे देश-वासियों की एक जुटता ही है। मुझे अपने नये विकसित संगठित भारत पर गर्व है।

अत: इस ऐतिहासिक अवसर पर मैं जाति, वर्ग, भाषा, धर्म और क्षेत्र के तुच्छ भेद-भाव से ऊपर उठकर शान्ति, समृद्धि और प्रगति के मार्ग पर चलते हुए राष्ट्रीय एकता व खण्डता को मजबूत करने के लिए सभी को एकजूट होने का हम संकल्प लेते हैं।

ध्वजारोहण करते हुए संस्थान के निदेशक डॉ. राम विश्वकर्मा

नगर राजभाषा कार्यान्वयन समिति, जम्मू की छमाही बैठक दिनांक 27 अगस्त, 2013 को भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में सम्पन्न हुई।

भारत सरकार, गृह मंत्रालय, राजभाषा विभाग के निर्देशानुसार नगर राजभाषा कार्यान्वयन समिति, जम्मू की छमाही बैठक दिनांक 27 अगस्त, 2013 (मंगलवार) को अपराह्न 3.30 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 एन.एस.मेहरा, अनुसंधान अधिकारी, भारत सरकार, गृह मंत्रालय, राजभाषा विभाग, क्षेत्रीय कार्यान्वयन कार्यालय दिल्ली-1, श्री विजय कुमार गर्ग, वरि. क्षेत्रीय प्रबंधक, इंडियन ऑयल कारपोरेशन, जम्मू, श्री सत्यप्रताप सिंह, संयुक्त नियंत्रक, रक्षा लेखा प्रधान नियंत्रक, उत्तरी कमान, जम्मू, श्री ए.जी. अंसारी, महाप्रबंधक, एन.एच.पी.सी., सलाल परियोजना,

नराकास बैठक की अध्यक्षता करते हुए संस्थान के निदेशक एवं अध्यक्ष, नराकास, जम्मू डॉ. राम विश्वकर्मा

ज्योतिपुरम्, रियासी, श्री आर.एन.मीना, मंडल यातायात प्रबंधक, उत्तरी रेलवे, जम्मू तथा नगर जम्मू के केन्द्रीय कार्यालयों/बैंकों/उपक्रमों से आये सभी कार्यालय अध्यक्ष, हिन्दी अधिकारी/राजभाषा अधिकारी/नोडल अधिकारी/हिन्दी अनुवादक तथा प्रिन्ट एवं इलैक्ट्रॉनिक मीडिया के समस्त संवाददाता एवं अन्य गणमान्य व्यक्ति उपस्थित थे।

सर्वप्रथम बैठक में उपस्थित कार्यालय प्रमुखों एवं सज्जनों का स्वागत डॉ. अमर सिंह, वरि. हिन्दी अधिकारी एवं सचिव, नराकास, जम्मू ने किया। उन्होंने अपने स्वागत संबोधन में कहा कि इस बैठक में प्रथम अक्टूबर, 2012 से 31 मार्च, 2013 के दौरान प्राप्त तिमाही प्रगति रिपोर्टों की समीक्षा तथा आपके कार्यालय में राजभाषा हिन्दी में किये गये कार्यों की समीक्षा तथा इससे संबंधित आपके कार्यालयों में उत्पन्न समस्याओं पर चर्चा की जाएगी। संघ के विभिन्न राजकीय प्रयोजनों में इसके प्रगामी प्रयोग को बढ़ावा देने के लिए राजभाषा विभाग प्रति वर्ष एक वार्षिक कार्यक्रम जारी करता है, जिसके अनुसार हम कार्यालयों में राजभाषा के कार्य सम्पन्न करते हैं। चूंकि सरकारी कामकाज में मूल टिप्पण और प्रारूपण के लिए हिन्दी का ही प्रयोग किया जाए। जिसके अन्तर्गत धारा 3(3) का हम सबको अनुपालन सुनिश्चित करना चाहिए। यही संविधान की मूलभावना के अनुरूप होगा। सभी भारतीय भाषाएं देश की एकता की प्रतीक हैं। भारतीय संविधान में जो प्रावधान किये गये हैं इसी के अनुसार हमें आदेशों/अनुदेशों का पालन करना चाहिए और महामहिम राष्ट्रपति जी के संकल्पों का सम्मान करना चाहिए।

नगर राजभाषा कार्यान्वयन समिति, जम्मू की वेबसाइट www.tolicjammu.org को नराकास की छमाही बैठक में नराकास अध्यक्ष, डॉ. राम विश्वकर्मा ने विमोचन किया। इस अवसर पर सभी सदस्य कार्यालयों के कार्यालय अध्यक्ष उपस्थित थे। अब इस वेबसाइट के माध्यम से समिति के जो भी प्रशिक्षण कार्यक्रम, अखिल भारतीय कवि सम्मेलन, सांस्कृतिक कार्यक्रम तथा अन्य प्रतियोगिताएं, गतिविधियां व कार्यकलाप, राष्ट्रीय स्तर पर देखने हेतु उपलब्ध रहेंगे।

नराकास की वेबसाइट का उद्घाटन करते हुए डॉ. राम विश्वकर्मा एवं अन्य कार्यालय प्रमुख गण।

नराकास बैठक को संबोधित करते हुए नराकास, अध्यक्ष डॉ. राम विश्वकर्मा एवं अन्य सदस्य गण।

संस्थान के निदेशक एवं नराकास, अध्यक्ष डॉ. राम विश्वकर्मा ने कॉन्फ्रेंस हॉल में उपस्थित नगर के कार्यालय प्रमुखों एवं अन्य गणमान्य व्यक्तियों का अपने संस्थान की ओर से व नराकास मंच की ओर से सबका हार्दिक स्वागत करते हुए अपने अध्यक्षीय संबोधन में कहा, ''कि समिति की इस वेबसाइट के माध्यम से आपके द्वारा एवं समिति के माध्यम से जो कार्यक्रम आयोजित किए जायेंगे वे सभी उपलब्ध रहेंगे। अब जो होगा वह अच्छा ही होगा आपके माध्यम से कवि सम्मेलन,

प्रशिक्षण कार्यक्रम, संसदीय राजभाषा समितियों के निरीक्षण के समय यह निर्णय लिया गया था कि इस बैठक में आप सभी समय रहते प्रतिभागिता करें और यह मैंडेटरी (अनिवार्य) है।

आपके द्वारा जो आर्थिक सहयोग दिया जा रहा है। इस सहयोग की अपेक्षा करते हैं सदस्यों की उपस्थिति और योगदान करने वाले सदस्यों के नाम वेबसाइट पर उपलब्ध रहेंगे। जो कार्यालय प्रमुख बैठक में भाग लेते हैं उनकी उपस्थिति वेबसाइट पर डाली जाए व एक प्रति संसदीय समिति को प्रेषित की जाए योगदान करने वालों के नाम भी होम पेज पर उपलब्ध रहेंगे। उन्होंने नराकास, जम्मू की अगली बैठक के लिए तिथि 28 नवम्बर, 2013 को निर्धारित कर दी और स्वच्छपत्र एवं कार्यसूची सबको परिपत्र जारी करने के आदेश दिए साथ ही

उन्होंने अपने संस्थान के पुस्तकालय में उपलब्ध हिन्दी पुस्तकों की सूची समिति की वेबसाइट पर डालने का सुझाव दिया तथा स्वयं की आई.डी. ई-मेल पर डालने को कहा और उन्होंने अन्त में कहा कि हिन्दी का कार्य और इसके प्रयोग में हमें अपना योगदान करना चाहिए। आज हर बच्चा हिन्दी समझता है। हर व्यक्ति हिन्दी बोलता है और आपके जो भी विचार एवं सुझाव सब वेबसाइट पर उपलब्ध होंगे।

अन्त में संस्थान के प्रशासनिक अधिकारी, श्री ओम प्रकाश ने संस्थान के निदेशक एवं समिति के अध्यक्ष डॉ. राम विश्वकर्मा जी का धन्यवाद करते हुए कहा कि बैठक के लिए उन्होंने अपना कीमती समय दिया हम उनका हार्दिक आभार व्यक्त करते है। श्री ए.जी. अंसारी, महाप्रबंधक, सलाल पावर स्टेशन, श्री विजय कुमार गर्ग, वरि. क्षेत्रीय प्रबंधक, इंडियन ऑयल कारपोरेशन तथा श्री सत्य प्रताप सिंह, संयुक्त नियंत्रक, सी.डी.ए. ने बैठक में अपना बहुमूल्य समय दिया हम उनका आभार सहित धन्यवाद करते हैं। बैठक में उपस्थित नराकास, जम्मू के सभी कार्यालय प्रमुख एवं प्रिन्ट व इलैक्ट्रानिक मीडिया दूरदर्शन के सभी संवाददाताओं का आभार व्यक्त किया। संस्थान के सभी संकाय सदस्यों का जिन्होंने इस बैठक के आयोजन में अपना योगदान दिया और इस सहयोग के लिए सबका धन्यवाद किया।

हिन्दी सप्ताह, 2013 का कार्यक्रम

संघ की राजभाषा हिन्दी में सरकारी कामकाज तथा हिन्दी के प्रति रूचि जागृति करने के उद्देश्य से संस्थान में दिनांक 03-17 सितम्बर, 2013 के दौरान हिन्दी सप्ताह का आयोजन किया गया। जिसमें निबन्ध लेखन, श्रुतलेख, अनुवाद/टिप्पण एवं प्रारूपण, स्टॉफ सदस्यों के बच्चों के लिए सामान्य ज्ञान प्रतियोगिता, राजभाषा एवं विज्ञान प्रश्नोत्तरी, अन्तरविभागीय भाषण प्रतियोगिता तथा 17 सितम्बर, 2015 को रंगारंग सांस्कृतिक कार्यक्रम विभिन्न भारतीय भाषाओं में भी प्रतियोगिताएं आयोजित की गयीं। जिसमें हिन्दी के प्रयोग एवं प्रगति की दिशा में विभिन्न प्रतियोगिताओं में संस्थान के 250 स्टॉफ सदस्यों ने प्रतियोगी के रूप में प्रतिभागिता की, जिससे उनके कार्य संस्कृति में इज़ाफा निश्चित् हुआ है। समारोह की अध्यक्षा संस्थान के निदेशक डॉ. राम विश्वकर्मा ने की।

सांस्कृतिक कार्यक्रम का शुभारम्भ संस्थान के निदेशक डॉ. राम विश्वकर्मा ने दीप प्रज्ज्वलन करते हुए आर.आर.एल.हाई स्कूल के बच्चों द्वारा सरस्वती वंदना वाचन से प्रारम्भ हुआ।

संस्थान में हिन्दी सप्ताह के दौरान प्रतियोगिताओं में भाग लेते हुए प्रतियोगी।

तत्पश्चात् संस्थान के स्टॉफ सदस्यों तथा बच्चों द्वारा रंगारंग सांस्कृतिक कार्यक्रम आयोजित किए गए।

इसी उपलक्ष्य में दिनांक 08 अक्टूबर, 2013 (मंगलवार) संस्थान के कॉन्फ्रेंस हॉल में पुरस्कार वितरण समारोह का आयोजन किया गया। कार्यक्रम की अध्यक्षता संस्थान के निदेशक डॉ. राम विश्वकर्मा ने की तथा विजयी प्रतियोगियों को नकद राशि के पुरस्कार एवं प्रमाण पत्र प्रदान किए। इस अवसर पर संस्थान के सभी स्टॉफ सदस्य एवं प्रिन्ट एवं इलैक्ट्रॉनिक मीडिया के सभी संवाददाता उपस्थित थे।

अन्त में उपस्थित सज्जनों का स्वागत डॉ. अमर सिंह, वरि. हिन्दी अधिकारी एवं सदस्य-सचिव, नराकास, जम्मू ने किया।

हिन्दी सप्ताह के दौरान सांस्कृतिक कार्यक्रम की झलकियाँ

नगर राजभाषा कार्यान्वयन समिति, जम्मू की छमाही बैठक दिनांक 28 नवम्बर, 2013 को सायं 3.00 बजे भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में सम्पन्न हुई।

भारत सरकार, गृह मंत्रालय, राजभाषा विभाग के निर्देशानुसार नगर राजभाषा कार्यान्वयन समिति, जम्मू की छमाही बैठक दिनांक 28 नवम्बर, 2013 (वृहस्पतिवार) को अपराह्न 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 शैलेश कुमार सिंह, उपनिदेशक (कार्या.), भारत सरकार, गृह मंत्रालय, राजभाषा विभाग, क्षेत्रीय कार्यान्वयन कार्यालय दिल्ली, श्री टोनेश चतुर्वेदी, प्रादेशिक प्रबंधक (रिटेल), भारतीय पेट्रोलियम कारपोरेशन लिमिटेड, क्षेत्रीय कार्यालय, जम्मू, श्री एस.कालगांवकर, कार्यपालक निदेशक, एन.एच.पी.सी.लिमिटेड, क्षेत्रीय कार्यालय (क्षेत्र-1), जम्मू, श्री ए.जी.अंसारी, महाप्रबंधक, एन.एच.पी.सी. सलाल पावर परियोजना, रियासी, श्री आर.एन.मीना, मंडल यातायात प्रबंधक, उत्तर रेलवे, जम्मू, श्री सत्यप्रताप सिंह, संयुक्त नियंत्रक, रक्षा लेखा प्रधान नियंत्रक, उत्तरी कमान, जम्मू, संस्थान के श्री अब्दुल रहीम अध्यक्ष, पी.एम.ई. एवं नराकास के केन्द्रीय कार्यालयों/बैंकों/उपक्रमों के सभी कार्यालय प्रमुख/हिन्दी अधिकारी/नोडल अधिकारी/हिन्दी अनुवादक/राजभाषा अधिकारी/ प्रिन्ट व इलैक्ट्रॉनिक मीडिया के सभी संवाददाता तथा अन्य गणमान्य व्यक्ति उपस्थित थे।

बैठक को संबोधित करते हुए संस्थान के निदेशक एवं अध्यक्ष नराकास डॉ. राम विश्वकर्मा ।

सर्वप्रथम बैठक में उपस्थित कार्यालय प्रमुखों का स्वागत डॉ. अमर सिंह, वरि. हिन्दी अधिकारी एवं सचिव, नराकास, जम्मू ने किया। उन्होंने अपने स्वागत संबोधन में कहा कि इस बैठक में प्रथम अप्रैल, 2013 से 30 सितम्बर, 2013 के दौरान प्राप्त तिमाही प्रगति रिपोर्टों की समीक्षा तथा आपके कार्यालय में राजभाषा हिन्दी में किये गये कार्यों की समीक्षा एवं इससे संबंधित आपके कार्यालयों में उत्पन्न समस्याओं पर चर्चा की जाएगी। संघ के विभिन्न राजकीय प्रयोजनों में इसके प्रगामी प्रयोग को बढ़ावा देने के लिए राजभाषा विभाग के वार्षिक कार्यक्रम पर विस्तार से चर्चा हुई। जिसके अनुसार हम कार्यालयों में राजभाषा के कार्य सम्पन्न करते हैं। चूंकि सरकारी कामकाज में मूल टिप्पण और प्रारूपण के लिए हिन्दी का ही प्रयोग किया जाए। जिसके अन्तर्गत धारा 3(3) का हम सबको अनुपालन सुनिश्चित करना चाहिए। यही संविधान की मूलभावना के अनुरूप होगा। भारतीय संविधान में जो प्रावधान किये गये हैं इसी के अनुसार हमें आदेशों/अनुदेशों का पालन करना चाहिए और महामहिम राष्ट्रपति जी के संकल्पों का सम्मान करना चाहिए।

तत्पश्चात् बैठक में उपस्थित सदस्यों के परिचय के साथ ही बैठक की कार्रवाई आरम्भ हुई। सचिव ने गत बैठक के कार्यवृत्त पर चर्चा के दौरान कहा कि सम्माननीय सदस्यों की कोई प्रतिक्रिया, सुझाव अथवा आपत्ति हो तो वे विचार रखें, लेकिन माननीय उपस्थित सदस्यों की ओर से कोई आपत्ति एवं प्रतिक्रिया न मिलने पर सचिव ने अध्यक्ष महोदय के अनुमोदन पर गत बैठक के कार्यवृत्त की पुष्टि की।

नराकास, जम्मू की ज्ञानवार्ता अंक: 4 के गृह पत्रिका का विमोचन करते हुए संस्थान के निदेशक एवं अध्यक्ष नराकास, डॉ. राम विश्वकर्मा एवं सदस्य गण।

वर्ष 2012-2013 के राजभाषा नीति के श्रेष्ठ निष्पादन के लिए सदस्यों को राजभाषा शील्ड एवं प्रमाण पत्र प्रदान करते हुए समिति के अध्यक्ष डॉ. राम विश्वकर्मा ।

बैठक में नगर राजभाषा कार्यान्वयन समिति की गृह पत्रिका 'ज्ञानवार्ता' अंक: 4 का संस्थान के निदेशक एवं अध्यक्ष, नराकास, जम्मू डॉ. राम विश्वकर्मा ने विमोचन किया। इस अवसर समिति के सभी सदस्य कार्यालयों के कार्यालय प्रमुख उपस्थित थे।

वर्ष 2012-2013 के दौरान समिति के सदस्य कार्यालयों में राजभाषा नीति के श्रेष्ठ निष्पादन के लिए सदस्य कार्यालयों के 39 कार्यालय प्रमुखों को राजभाषा शील्ड एवं संबंधित राजभाषा अधिकारियों को प्रमाण-पत्र प्रदान किये।

बैठक में राजभाषा नीति कार्यान्वयन पर चर्चा एवं सदस्यों की प्रतिक्रियाएं उनके महत्वपूर्ण सुझाव जो इस प्रकार हैं:-

सदस्य-सचिव डॉ. अमर सिंह ने ज्ञानवार्ता के अंशदान हेतु सभी केन्द्रीय कार्यालय/बैंकों/उपक्रमों से रू.2000/-अंशदान के रूप में चैक या ड्रॉफ्ट अध्यक्ष, नगर राजभाषा कार्यान्वयन समिति, जम्मू Chairman, Town Official Language Implemenation Committee, Jammu कार्यालय के पक्ष में देय होंगे। जो पहले से ही प्रस्तावित है। सभी सदस्यों से अनुरोध है कि जिन सदस्य कार्यालयों ने यह अंशदान राशि समिति के सभी सदस्य कार्यालयों से पहले भी गत बैठकों में पत्रिका के प्रकाशन हेतु उच्च स्तरीय लेख / रचनाएं / कविताएं / कहानियां प्रकाशन हेतु मांग की जाती रही है। कृपया पत्रिका के प्रकाशन हेतु सामग्री भिजवाएं जिसे ज्ञानवार्ता के अंक: 5 में उनके लेख प्रकाशित किये जा सके। सचिव ने समिति को जानकारी देते हुए कहा कि सभी सदस्य कार्यालय अपने स्तर से प्रकाशन हेतु सामाग्री भिजवाएं। क्योंकि यह पत्रिका आप सभी के सहयोग से प्रकाशित की जा रही है और इसमें सभी सदस्य कार्यालयों के स्टॉफ सदस्य अपने लेखन सामग्री भिजवाना सुनिश्चित करें। सचिव ने कहा कि सदस्य कार्यालयों से कम संख्या में लेख प्राप्त होते हैं और प्रकाशन के लिए हम बाहर से लेख आमंत्रित करते हैं। यदि इस बारे में आपके सुझाव हो तो रखें। समिति के अध्यक्ष एवं निदेशक, भारतीय समवेत औषध संस्थान, जम्मू डॉ. राम विश्वकर्मा ने समिति की वेबसाइट ूण्जवसपबरंउउनण्वतह पर एक ब्लॉग बनाने का सुझाव दिया। इस ब्लॉग पर राजभाषा हिन्दी से संबंधित विशेष जानकारी एवं हिन्दी का महत्वपूर्ण साहित्य उपलब्ध रहेगा जो अगली बैठक में तैयार होगा।

बैठक में श्री शैलेश कुमार सिंह, उपनिदेशक (कार्या.), क्षेत्रीय कार्यान्वयन कार्यालय-1 (दिल्ली) राजभाषा विभाग से प्रतिनिधि के रूप में उपस्थित थे। उन्होंने अपने संबोधन में राजभाषा विभाग द्वारा अभिनव प्रौद्योगिकी एवं अभिनव पहल के बारे में सदस्य कार्यालयों द्वारा ऑनलाइन तिमाही प्रगति रिपोर्ट राजभाषा विभाग को भेजने संबंधी ऑनलाइन डेमो दिया। उन्होंने कहा कि अब ऑनलाइन ही आपकी तिमाही प्रगति रिपोर्ट भेजने का प्रस्ताव हैं, उन्होंने बताया कि अधिकांश सदस्य कार्यालयों द्वारा ऑनलाइन रिपोर्ट भेजी जा रही हैं और शेष कार्यालय भी ऑनलाइन ही रिपोर्ट भिजवाएं। इसके लिए उन्होंने ई-मेल आई.डी. प्रत्येक कार्यालय अपना पंजीकरण करवाएं। श्री सिंह ने कहा कि नराकास, जम्मू समिति राजभाषा कार्यान्वयन के लिए उत्तर क्षेत्र के 'ग' क्षेत्र में उत्कृष्ट कार्य कर रही है। बैठकों का आयोजन नियमित रूप से हो रहा है। राजभाषा गृह पत्रिका 'ज्ञानवार्ता' का प्रकाशन तथा समिति की वेबसाइट इस दिशा में एक महत्वपूर्ण उपलब्धि है। समिति के तत्वावधान में सदस्यों का सहयोग उनके द्वारा कंप्यूटर प्रशिक्षण कार्यक्रम, अखिल भारतीय कवि सम्मेलन का आयोजन आदि राजभाषा की प्रगति में अत्यधिक महत्वपूर्ण है। इसके लिए उन्होंने समिति के अध्यक्ष महोदय का आभार व्यक्त करते हुए उनका धन्यवाद किया। इसी प्रकार राजभाषा नीति के श्रेष्ठ निष्पादन के लिए सदस्यों को राजभाषा शील्ड व हिन्दी सेवी कर्मियों के लिए मैरिट सर्टिफिकेट देने का प्रस्ताव अध्यक्ष महोदय की कार्य कुशलता, उनके उत्कृष्ट प्रयासों तथा राजभाषा नीति कार्यान्वयन के लिए उनकी प्रतिबद्धता का अच्छा द्योतक है।

दूरदर्शन केन्द्र, जम्मू के निदेशक श्री शवीर मुज़ाहिद ने बैठक में अपने विचार व्यक्त करते हुए कहा कि हिन्दी, उर्दू, अरबी, फारसी एवं अन्य भारतीय भाषाएं जो सम्पूर्ण व्यक्ति बोली और क्षेत्रीय बोलियों का आपस में कंट्रास्ट है। जब हमारे दूरदर्शन केन्द्र, जम्मू और कश्मीर तथा अन्य इलाकों से समाचार सुनने पर भाषाओं की अलग-अलग ध्वनियां सुनने को मिलती है। उन्होंने अपने केन्द्र की भाषा संबंधी उच्चारण विधियों को प्रस्तुत किया है।

संस्थान के निदेशक एवं नराकास, अध्यक्ष डॉ. राम विश्वकर्मा ने कॉन्फ्रेंस हॉल में उपस्थित

नगर के कार्यालय प्रमुखों एवं अन्य गणमान्य व्यक्तियों का अपने संस्थान की ओर से व नराकास मंच की ओर से सबका हार्दिक स्वागत करते हुए अपने अध्यक्षीय संबोधन में कहा, 'कि हमने अपने संस्थान के आई.टी. विभाग के माध्यम से समिति की वेबसाइट तैयार की है और बैठक की कार्रवाई समिति के अन्य कार्यक्रम वेबसाइट पर उपलब्ध रहेंगे। जो विश्व में पढ़ी जाए और इसका प्रयोग क्षेत्रीय स्तर पर भी उपलब्ध है सभी सदस्य कार्यालय ई-मेल के माध्यम से अपने कार्यक्रम भेजे अपने संस्थान की पुस्तकालय में जो पुस्तकें क्रय की गयी है। वे संस्थान की वेबसाइट पर उपलब्ध हैं। उन्होंने एक ब्लॉग बनाने के आदेश दिये। अगली बैठक तक समिति की वेबसाइट पर ब्लॉग तैयार हो जायेगा। जिसमें साहित्य से संबंधित देश के एवं अन्तर्राष्ट्रीय स्तर के उत्कृष्ट साहित्यकारों के महत्वपूर्ण जानकारी उनकी लेखन एवं रचनाएं उपलब्ध रहेंगी'।

अन्त में संस्थान के सदस्य-सचिव डॉ. अमर सिंह ने संस्थान के निदेशक एवं समिति के अध्यक्ष डॉ. राम विश्वकर्मा जी का धन्यवाद करते हुए कहा कि बैठक के लिए उन्होंने अपना कीमती समय दिया हम उनका हार्दिक आभार व्यक्त करते है। श्री शैलेश कुमार सिंह, उपनिदेशक (कार्या.), भारत सरकार, गृह मंत्रालय, राजभाषा विभाग, क्षेत्रीय कार्यान्वयन कार्यालय (दिल्ली), श्री ए.जी. अंसारी, महाप्रबंधक, सलाल पावर स्टेशन, श्री एस.कालगांवकर, कार्यपालक निदेशक, एन. एच.पी.सी.लिमिटेड, क्षेत्रीय कार्यालय (क्षेत्र-1), जम्मू, श्री सत्यप्रताप सिंह, संयुक्त नियंत्रक, रक्षा लेखा प्रधान नियंत्रक, उत्तरी कमान, जम्मू, श्री आर.एन.मीना, मंडल यातायात प्रबंधक, उत्तर रेलवे, जम्मू, श्री शब्बीर मुज़ाहिद निदेशक, दूरदर्शन केन्द्र, जम्मू तथा संस्थान के श्री अब्दुल रहीम, अध्यक्ष, पी.एम.ई.प्रभाग ने बैठक में अपना बहुमूल्य समय दिया हम उनका भी आभार सहित धन्यवाद करते हैं। बैठक में उपस्थित नराकास, जम्मू के सभी कार्यालय प्रमुख एवं प्रिन्ट व इलैक्ट्रानिक मीडिया दूरदर्शन के सभी संवाददाताओं का आभार व्यक्त किया। संस्थान के सभी संकाय सदस्यों का जिन्होंने इस बैठक के आयोजन में अपना योगदान दिया और तकनीकी सहयोग के लिए अपने आई.टी अनुभाग का आभार व्यक्त करते हुए धन्यवाद किया।

64वाँ गणतंत्र दिवस का आयोजन

26 जनवरी, 2014

गणतंत्र दिवस की 64वीं वर्षगांठ मना रहे है इस पावन अवसर पर आप सबको हार्दिक शुभकामनाएं एवं बधाई देते हुए कहा कि आज के दिन हमारे देश का संविधान लागू हुआ था। 26 जनवरी, 1950 को हमने एक अन्तर्विरोधों के जीवन में प्रवेश किया था। 26 जनवरी गणतंत्र दिवस जो आजादी को याद करने का दिन है क्योंकि इसी दिन हमारा संविधान लागू हुआ था और अंग्रेजों के समय से चले आ रहे नियम/कानूनों से हमें मुक्ति मिली थी। इस राष्ट्रीय प्रस्ताव पर चिन्तन करना होगा। हमें गणतंत्र दिवस पर कुछ नये संकल्प लेने होंगे जिन पर अमल कर आप एक अच्छे नागरिक बने रहें ताकि आप राष्ट्र निर्माण में आपकी भूमिका रहे। किसी लोकतांत्रिक/ प्रजातांत्रिक देश में विधि मानव जीवन का आधार होता है जबकि किसी देश के कानून का ज्ञान सभी नागरिकों को हो ताकि वे अनेक प्रकार के जूल्मों से बच सकें। भारत में नई विधि व्यवस्था एवं मौलिक अधिकारों की पूर्ण स्थापना संविधान में 26 जनवरी, 1950 को लागू होने के साथ हो चुकी थी, हालाँकि उसका आंशिक रूप में प्रारम्भ 26 नवम्बर, 1949 को ही हो गया था जब संविधान को संविधान सभा ने

ध्वजारोहण करते हुए संस्थान के निदेशक डॉ. राम विश्वकर्मा

अधिनियमित किया था। सामाजिक, आर्थिक, न्यायायिक तथा राजनैतिक दृष्टि से भारतीय परम्परा में यह एक नये युग का सूत्र पात हुआ, क्योंकि हमारी विधि व्यवस्था में वे काले कानून और अमानुषिक व्यवहार निषिद्ध हो गये थे, जिन्होंने आदमी की गरिमा प्रतिष्ठा तथा मान-सम्मान को नष्ट-भ्रष्ट कर दिया था। संविधान विधि का संबंध प्राय: किसी देश के शासन एवं कानून व्यवस्था से होता है। संविधान लिखित प्रारूप, प्रलेखों या नियमों, लोकाचारों, परम्पराओं और व्यवहारों पर आधारित हो सकता है। इसमें उन विविध नियमों का संग्रह होता है जिनके अनुसार उस देश की शासन व्यवस्था संचालित की जाती है। वह शासन के संरचनात्मक एवं कार्यात्मक पक्षों का विस्तृत स्वरूप तथा संगठन निर्धारित करता है।

जब नये संविधान का निर्माण संविधान सभा की प्रथम बैठक 9 दिसम्बर 1946 को आरम्भ हुई तब यह उम्मीद नहीं थी कि डॉ. अम्बेडकर की भूमिका इतनी सार्थक एवं निर्णायक रहेंगी जितनी की कालांतर में सिद्ध हुई। इन्हें संविधान प्रारुप (ड्राफ्ट) समिति का अध्यक्ष बनाया गया जिन्होंने नये संविधान की समस्त निर्माण प्रक्रिया में उनके विचार-विमर्श तथा मौलिक संशोधन में महत्वपूर्ण निर्णय स्वयं लिए और संविधान सभा से पारित करवाए संविधान 25 नवम्बर 1949 को बनकर तैयार हुआ तब उनके पूर्व अनेक सदस्यों ने डॉ. अम्बेडकर की बौद्धिक क्षमता, लगन, ज्ञान, सहभागिता तथा रचनात्मक भूमिका की विशेष सराहना की और उन्हें संविधान का मुख्य शिल्पकार तथा आधुनिक मनु की संज्ञा दी। नि:सन्देह डॉ. अम्बेडकर संविधान के मुख्य निर्माता निर्देशक कहे गये।

आज प्रतिस्पर्दा का युग है हम प्रतियोगी बनकर सफलता प्राप्त कर सकते है हमें निराश नहीं होना चाहिए यह मूवमेन्ट हमें सिखाता है कि हमें निरन्तर प्रयास करने होंगे सूचना और प्रौद्योगिकी, कृषि, स्वास्थ, शिक्षा विज्ञान के क्षेत्र में भारत आगे बढ़ा है। हम भारत के लोग सत्यनिष्ठा पूर्वक संकल्प लें कि भारत को एक संप्रभु, समाजवादी, पंथनिर्पेक्ष, लोकतांत्रिक, गणतंत्र में विश्वास स्थापित करें, लेकिन हमें यह भी देखना है कि संविधान के आदर्श किस रूप में वास्तविकता में रूपान्तरित हुए हैं। हमें संप्रभुता की अभिव्यक्ति सार्थक बनानी होगी। मानव मूल्यों की श्रेणी में आने वाले प्रमुख आदर्श प्रजातंत्र, न्याय, स्वतंत्रता, समानता, भाई-चारा, करूणा, मित्रता, अहिंसा, धर्म-निरपेक्षता और साहस का निर्भीकता, जो विधिक एवं प्रासंगिकता जो एक ओर संस्थागत होने की क्षमता रखते हैं तो दुसरी ओर नागरिकों के आचारण संहिता के लिए मानक भी हैं इनकी रक्षा करनी होगी।

नगर राजभाषा कार्यान्वयन समिति, जम्मू की छमाही बैठक दिनांक 11 जून, 2014 को भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में सम्पन्न हुई ।

नराकास की बैठक को संबोधित करते हुए संस्थान के निदेशक एवं अध्यक्ष, नराकास डॉ. राम विश्वकर्मा ।

भारत सरकार, गृह मंत्रालय, राजभाषा विभाग के निर्देशानुसार नगर राजभाषा कार्यान्वयन समिति, जम्मू की छमाही बैठक दिनांक 11 जून, 2014 (बुधवार) को अपराह्न 3.00 बजे भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में आयोजित हुई। बैठक की अध्यक्षता संस्थान के निदेशक एवं नराकास अध्यक्ष डॉ. राम विश्वकर्मा ने की। इस अवसर पर अतिथि के रूप में भारत सरकार, गृह मंत्रालय दिल्ली के श्री एन.एस.मेहरा, अनुसंधान अधिकारी (कार्यान्वयन), श्री सत्यप्रताप सिंह, रक्षा लेखा प्रधान नियंत्रक, संयुक्त नियंत्रक, उत्तरी कमान, जम्मू, श्री ए.जी.अंसारी, महाप्रबंधक, सलाल पावर स्टेशन, रियासी, श्री अरविन्द भट्ट, महाप्रबंधक, दुलहस्ती पावर स्टेशन, किश्वाड़, श्री किशोर कुमार, महाप्रबंधक, भारतीय खाद्य निगम, क्षेत्रीय कार्यालय, जम्मू/श्रीनगर, श्री सुनील खोसा, मुख्य प्रबंधक, पंजाब नेशनल बैंक, मंडल कार्यालय, जम्मू/श्रीनगर, श्री प्रहलाद किशोर, महाप्रबंधक, होटल अशोक, जम्मू, संस्थान के श्री अब्दुल रहीम अध्यक्ष,

पी.एम.ई. एवं तथा नगर जम्मू के केन्द्रीय कार्यालयों/बैंकों/उपक्रमों से आये सभी कार्यालय अध्यक्ष, हिन्दी अधिकारी/राजभाषा अधिकारी/ नोडल अधिकारी/हिन्दी अनुवादक तथा प्रिन्ट एवं इलैक्ट्रॉनिक मीडिया के समस्त संवाददाता एवं उनके साथ अन्य गणमान्य व्यक्ति उपस्थित थे।

सर्वप्रथम बैठक में उपस्थित कार्यालय प्रमुखों एवं सज्जनों का स्वागत डॉ. अमर सिंह, वरि. हिन्दी अधिकारी एवं सचिव, नराकास, जम्मू ने किया। उन्होंने अपने स्वागत संबोधन में कहा, ''कि इस बैठक में प्रथम अक्टूबर, 2013 से 31 मार्च, 2014 के दौरान तिमाही प्रगति रिपोर्टों की समीक्षा तथा आपके कार्यालय में राजभाषा हिन्दी में किये गये कार्यों की समीक्षा तथा इससे संबंधित आपके कार्यालयों में उत्पन्न समस्याओं पर चर्चा की जाएगी। संघ के विभिन्न राजकीय प्रयोजनों में इसके प्रगामी प्रयोग को बढ़ावा देने के लिए राजभाषा विभाग प्रति वर्ष एक वार्षिक कार्यक्रम जारी करता है, जिसके अनुसार हम कार्यालयों में राजभाषा के कार्य सम्पन्न करते हैं। चूंकि सरकारी कामकाज में मूल टिप्पण और प्रारूपण के लिए हिन्दी का ही प्रयोग किया जाए। जिसके अन्तर्गत धारा 3(3) का हम सबको अनुपालन सुनिश्चित करना चाहिए। यही संविधान की मूलभावना के अनुरूप होगा। सभी भारतीय भाषाएं देश की एकता की प्रतीक हैं। भारतीय संविधान में जो प्रावधान किये गये हैं इसी के अनुसार हमें आदेशों/अनुदेशों का पालन करते हुए महामहिम राष्ट्रपति जी के संकल्पों का सम्मान करना चाहिए''।

तत्पश्चात् बैठक में उपस्थित सदस्यों के परिचय के साथ ही बैठक की कार्रवाई आरम्भ हुई। सचिव ने गत बैठक के कार्यवृत्त पर चर्चा के दौरान कहा कि सम्माननीय सदस्यों की कोई प्रतिक्रिया, सुझाव अथवा आपत्ति हो तो वे विचार रखें, लेकिन माननीय उपस्थित सदस्यों की ओर से कोई आपत्ति एवं प्रतिक्रिया न मिलने पर सचिव ने अध्यक्ष महोदय के अनुमोदन से गत बैठक के कार्यवृत्त की पुष्टि की।

संस्थान के निदेशक एवं अध्यक्ष, नराकास, जम्मू डॉ. राम विश्वकर्मा ने सभागार में उपस्थित सभी कार्यालय प्रमुखों तथा उपस्थित गणमान्य व्यक्तियों का अपने संस्थान की ओर तथा नराकास मंच की ओर से सबका हार्दिक स्वागत करते हुए अपने अध्यक्षीय संबोधन में कहा, 'कि हमारे आई.टी. विभाग के सहयोग से हमने समिति की वेबसाइट ई-मेल आई.डी. तैयार की है, उन्होंने वेबसाइट के माध्यम से ब्लॉक भी तैयार किया गया है। जिसके माध्यम से हिन्दी साहित्य का लेखन और हिन्दी में महत्वपूर्ण साहित्यिक उपलब्धियां पढ़ी जा सकती हैं। उन्होंने आगे बताया कि निकट भविष्य में संसदीय राजभाषा निरीक्षण समिति निरीक्षण के लिए अपना कार्यक्रम भेज सकती है। इसलिए हम सबको तैयार रहना चाहिए और अपने कार्यालय स्तर पर राजभाषा के कार्यान्वयन को और प्रगति की दिशा में बढ़ाना होगा। हमारे नराकास की बैठकें नियमानुसार आयोजित की जा रही हैं। उन्होंने हिन्दी टंकण व हिन्दी टाइपराइटर और हिन्दी से जुड़े कुशल टंककों का पैनल बनाने के बारे में सुझाव दिया। क्योंकि हमने स्वयं अनुभव किया है कि जब हमारे प्रधानमंत्री या अन्य कोई भारत सरकार के कार्यक्रम आयोजित किये जाते हैं। तो उनके द्वारा जम्मू संभाग में टंकण कार्य में दक्ष टंककों/हिन्दी अनुवादक की आवश्यकता होती है। इसके लिए एक पैनल बनाने का सुझाव दिया ताकि इस अवसर पर उनकी सेवाएं ली जा सकें। हम सब राजभाषा कार्यान्वयन को एक नई दिशा की ओर अग्रसर हो रहे हैं। एक देश दूसरे देश में अंग्रेजी के माध्यम से एस.एम.एस. के माध्यम से अपने देश की विभिन्न सभी प्रान्तीय भाषाएं एक दूसरे से जुड़ी हैं। उनके साथ-साथ हिन्दी का विकास एवं देश की समस्त भाषाओं का विकास संभव है। उन्होंने सुझाव दिया कि हमारे संस्थान में जो महत्वपूर्ण हिन्दी पुस्तकें पुस्कालय में उपलब्ध हैं। आप सभी लाभान्वित हो सकते हैं। उन्होंने इन पुस्तकों की सूची वेबसाइट पर ऑनलाइन डालने को कहा।

अन्त में संस्थान के श्रीमती रजनी कुमारी ने अध्यक्ष महोदय तथा बैठक में उपस्थित श्री एन.एस.मेहरा, अनुसंधान अधिकारी तथा नराकास जम्मू के सभी केन्द्रीय कार्यालयों/बैंकों/ उपक्रमों के कार्यालय प्रमुखों, वरि. हिन्दी अधिकारियों/हिन्दी अनुवादकों एवं नगर के प्रिन्ट व इलैक्ट्रानिक मीडिया के सभी संवाददाताओं का आभार व्यक्त करते हुए कहा कि मीडिया का सदैव इस बैठक में सहयोग रहा है। बैठक के आयोजन में प्रबंधन के लिए संस्थान के वरिष्ठ हिन्दी अधिकारी एवं सदस्य सचिव, डॉ. अमर सिंह तथा समस्त स्टॉफ सदस्यों का आभार सहित धन्यवाद करता हूँ।

नगर राजभाषा कार्यान्वयन समिति, भारतीय समवेत औषध संस्थान, जम्मू को वर्ष 2012-2013 के दौरान राजभाषा नीति के श्रेष्ठ निष्पादन के लिए 'प्रथम' राजभाषा पुरस्कार ।

नगर राजभाषा कार्यान्वयन समिति, भारतीय समवेत औषध संस्थान, जम्मू को राजभाषा हिन्दी के प्रगामी प्रयोग को बढ़ाने की दिशा में व राजभाषा नीति के श्रेष्ठ निष्पादन के लिए केन्द्रीय सरकार के कार्यालयों/उपक्रमों/बैंकों में राजभाषा के प्रचार-प्रसार हेतु भारत सरकार, गृह मंत्रालय द्वारा राजभाषा नीति के अनुरूप प्रतिवर्ष राजभाषा पुरस्कार प्रदान किये जाते हैं। इसी परिप्रेक्ष्य में वर्ष 2012-2013 के लिए अध्यक्ष, नगर राजभाषा कार्यान्वयन समिति, जम्मू कार्यालय को 'प्रथम' राजभाषा पुरस्कार प्रदान किया गया है।

यह पुरस्कार भारत सरकार, गृह मंत्रालय, राजभाषा विभाग द्वारा उत्तर क्षेत्र-1 जिसमें उत्तर क्षेत्र के 8 राज्यों का यह पुरस्कार वितरण समारोह/सम्मेलन दिनांक 05 जून, 2014 को स्नातकोत्तर चिकित्सा शिक्षा एवं अनुसंधान संस्थान, (पीजीआई), चण्डीगढ़ के भार्गव ऑडिटोरियम में माननीय राज्यपाल, पंजाब एवं प्रशासक चण्डीगढ़ श्री शिवराज पाटिल जी एवं सचिव, राजभाषा सुश्री नीता चौधरी के कर कमलो द्वारा नगर राजभाषा कार्यान्वयन समिति, जम्मू के अध्यक्ष डॉ. राम विश्वकर्मा एवं निदेशक, भारतीय समवेत औषध संस्थान, की ओर से समिति के सदस्य-सचिव, डॉ. अमर सिंह, नराकास, जम्मू ने शील्ड एवं प्रमाण-पत्र प्राप्त किए ।

नराकास जम्मू को प्रथम राजभाषा पुरस्कार प्रदान करते हुए माननीय राज्यपाल (पंजाब) श्री शिवराज पाटिल एवं सचिव राजभाषा सुश्री नीता चौधरी

हिन्दी दिवस/सप्ताह, 2014 का कार्यक्रम

हिन्दी दिव/सप्ताह के दौरान प्रतियोगिताओं में भाग लेते हुए प्रतियोगी

स्टॉफ सदस्यों ने प्रतियोगी के रूप में प्रतिभागिता की, जिससे उनकी कार्य संस्कृति में इज़ाफा निश्चित् हुआ है और कुल 28 विजयी प्रतियोगियों को पुरस्कार निदेशक महोदय के कर-कमलों द्वारा प्रदान किये गये।

अन्त में उपस्थित सज्जनों का स्वागत डॉ. अमर सिंह, वरि. हिन्दी अधिकारी एवं सदस्य-सचिव, नराकास, जम्मू ने किया। इस अवसर पर भारत सरकार, गृह मंत्रालय के गृहमंत्री का संदेश श्री ओम प्रकाश, प्रशासनिक अधिकारी द्वारा पढ़ा गया ।

संघ की राजभाषा हिन्दी में सरकारी कामकाज तथा हिन्दी के प्रति रूचि जागृति करने के उद्देश्य से संस्थान में दिनांक 01-16 सितम्बर, 2014 के दौरान हिन्दी सप्ताह का आयोजन किया गया। जिसमें निबन्ध लेखन, श्रुतलेख, स्टॉफ सदस्यों के बच्चों के लिए सामान्य ज्ञान प्रतियोगिता, राजभाषा एवं विज्ञान प्रश्नोत्तरी, अन्तरविभागीय भाषण प्रतियोगिता, हिन्दी कार्यशाला, अनुवाद/टिप्पण एवं प्रारूपण आदि प्रतियोगिताएं आयोजित की गयीं। इस दौरान हिन्दी के प्रयोग एवं प्रगति की दिशा में विभिन्न प्रतियोगिताओं में संस्थान के 300

हिन्दी दिव/सप्ताह के दौरान विजयी प्रतियोगियों को पुरस्कार प्रदान करते हुए संस्थान के निदेशक डॉ. राम विश्वकर्मा।

हिन्दी कार्यशाला

संघ की राजभाषा हिन्दी में सरकारी कामकाज तथा हिन्दी के प्रति रूचि जागृति करने के उद्देश्य से केन्द्र सरकार के कार्यालयों में हिन्दी दिवस/सप्ताह/ पखवाड़ा/मास के अवसर पर हिन्दी कार्यशाला का आयोजन किया गया। जिसमें संस्थान के निदेशक डॉ. राम विश्वकर्मा ने अपने विचार व्यक्त करते हुए कहा कि प्रशासन के सभी स्टॉफ सदस्यों एवं वैज्ञानिकों को हिन्दी कार्यशाला में निष्ठापूर्वक भाग लेना चाहिए। ताकि वैज्ञानिक एवं प्रशासनिक क्षेत्र में हिन्दी की प्रगति हो सके।

श्री प्रफूल कुमार, भण्डार एवं क्रय अधिकारी ने केन्द्र सरकार के कार्यालयों में हिन्दी के प्रयोग व द्विभाषी प्रकाशन की स्थिति पर विचार व्यक्त करते हुए कहा कि हिन्दी कार्यान्वयन को बढ़ाया जा सकता है और प्रशासन के सभी का इसमें सहयोग होना चाहिए साथ ही अपने अनुभाग में सभी स्टॉफ सदस्यों से फाइलों पर हिन्दी में ही कार्य करने के लिए प्रेरित किया।

श्री रमेश कुमार रैणा, वित्त एवं लेखा अधिकारी ने विचार व्यक्त करते हुए कहा, कि प्रशासन व वैज्ञानिक क्षेत्रों में लोगों को हिन्दी में कार्य करने की रूचि जागृति हुई है और लोग बहुत ही अच्छे ढंग से अपनी फाइलों पर हिन्दी में नोटिंग/टिप्पण कर रहे हैं। उन्होंने कहा कि हमने अपने अनुभाग में हिन्दी में कार्य करने के लिए कार्यक्रम बनाया है, जिसके अन्तर्गत ही कार्य सम्पन्न होंगे।

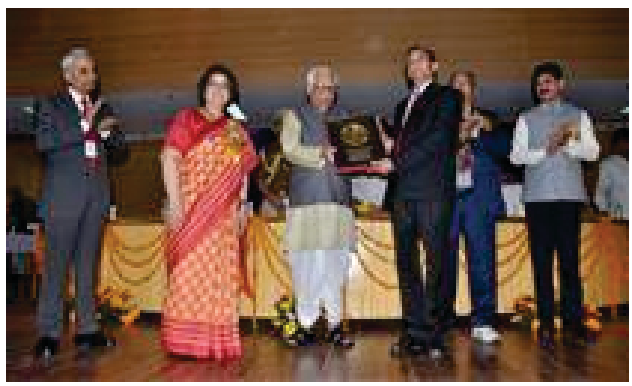
हिन्दी कार्यशाला को संबोधित करते हुए संस्थान के निदेशक डॉ. राम विश्वकर्मा।

श्री ओम प्रकाश, प्रशासन नियंत्रक ने प्रशासनिक कार्यों में हिन्दी का प्रयोग एवं प्रशासनिक दायित्व विषय पर अपने विचार व्यक्त करते हुए कहा कि हमने प्रशासन के सभी अनुभागों में प्रत्राचार को बढ़ाने में सभी स्टॉफ सदस्यों से संविधान के नियमों के अन्तर्गत ही सम्पूर्ण कार्य हिन्दी में ही सम्पन्न करने के लिए उनसे सहयोग की अपेक्षा की है। भारत सरकार द्वारा दिए गए नियमों के अनुसार ही संस्थान में हिन्दी कार्यान्वयन सुनिश्चित हो, जिसके लिए हम प्रतिबद्ध हैं।

अन्त में डॉ. अमर सिंह, वरिष्ठ हिन्दी अधिकारी ने कार्यशाला में सभी सहयोगियों को आभार सहित धन्यवाद किया।

नगर राजभाषा कार्यान्वयन समिति, भारतीय समवेत औषध संस्थान, जम्मू को वर्ष 2013–2014 के दौरान राजभाषा नीति के श्रेष्ठ निष्पादन के लिए 'प्रथम' राजभाषा पुरस्कार ।

नगर राजभाषा कार्यान्वयन समिति, भारतीय समवेत औषध संस्थान, जम्मू को राजभाषा हिन्दी के प्रगामी प्रयोग को बढ़ाने की दिशा में एवं राजभाषा नीति के श्रेष्ठ निष्पादन के लिए केन्द्रीय सरकार के कार्यालयों/उपक्रमों/बैंकों एवं नगर राजभाषा कार्यान्वयन समितियों को भारत सरकार के राजभाषा नीति के अनुरूप प्रतिवर्ष राजभाषा पुरस्कार प्रदान किये जाते हैं। इसी परिप्रेक्ष्य में वर्ष 2013–2014 के लिए अध्यक्ष, नगर राजभाषा कार्यान्वयन समिति, जम्मू कार्यालय को 'प्रथम' राजभाषा पुरस्कार प्रदान किया गया है।यह पुरस्कार भारत सरकार, गृह मंत्रालय, राजभाषा विभाग द्वारा उत्तर क्षेत्र-1 जिसमें उत्तर क्षेत्र के 8 राज्यों का यह पुरस्कार वितरण समारोह/सम्मेलन दिनांक 19 नवम्बर, 2014 को



नराकास जम्मू को प्रथम राजभाषा पुरस्कार प्रदान करते हुए माननीय राज्यपाल (उ.प्र.) श्री राम नाईक एवं सचिव राजभाषा सुश्री नीता चौधरी।

वी.के.एस.वरदन ऑडिटोरियम, भारतीय भू-वैज्ञानिक सर्वेक्षण, लखनऊ में महामहिम राज्यपाल, उत्तर प्रदेश श्री राम नाईक जी एवं सचिव, राजभाषा सुश्री नीता चौधरी के कर कमलो द्वारा नगर राजभाषा कार्यान्वयन समिति, जम्मू के अध्यक्ष डॉ. राम विश्वकर्मा एवं निदेशक, भारतीय समवेत औषध संस्थान, की ओर समिति के सदस्य-सचिव, डॉ. अमर सिंह, नराकास, जम्मू ने शील्ड एवं प्रमाण-पत्र प्राप्त किए ।

नगर राजभाषा कार्यान्वयन समिति, जम्मू की छमाही बैठक दिनांक 27 जनवरी, 2015 को 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 27 जनवरी, 2015 मंगलवार को अपराह्न 3.00 बजे भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में आयोजित हुई। बैठक की अध्यक्षता संस्थान के निदेशक एवं नराकास अध्यक्ष डॉ. राम विश्वकर्मा ने की। इस अवसर पर श्री ए.जी.अंसारी, महाप्रबंधक, एनएचपीसी, सलाल परियोजना, रियासी, श्री सत्यप्रताप सिंह, संयुक्त नियंत्रक, रक्षा लेखा प्रधान नियंत्रक, उत्तरी कमान, जम्मू, श्री एम. एल.मीर, उपमहाप्रबंधक, पंजाब नेशनल बैंक, क्षेत्रीय कार्यालय, जम्मू/श्रीनगर, श्री चन्द्रप्रकाश, मुख्य पोस्टमास्टर, जनरल, जम्मू व कश्मीर, श्री मनीष टंडन, वरिष्ठ क्षेत्रीय प्रबंधक, हिन्दुस्तान पेट्रोलियम कारपोरेशन, क्षेत्रीय कार्याल, जम्मू तथा नगर जम्मू के केन्द्रीय कार्यालयों/बैंकों/ उपक्रमों से आये सभी कार्यालय प्रमुख, वरि.हिन्दी अधिकारी/हिन्दी अधिकारी/राजभाषा अधिकारी/नोडल अधिकारी/वरि.हिन्दी अनुवादक/हिन्दी अनुवादक तथा प्रिन्ट एवं इलैक्ट्रॉनिक मीडिया के समस्त संवाददाता एवं अन्य गणमान्य व्यक्ति उपस्थित थे।

सर्वप्रथम बैठक में अध्यक्ष महोदय एवं उपस्थित कार्यालय प्रमुखों का स्वागत डॉ. अमर सिंह, वरिष्ठ हिन्दी अधिकारी एवं सदस्य-सचिव, नराकास, जम्मू ने किया। उन्होंने अपने स्वागत संबोधन में कहा, ''कि इस बैठक में प्रथम अप्रैल, 2014 से 30 सितम्बर, 2014 के दौरान तिमाही प्रगति रिपोर्टो तथा आपके कार्यालय में राजभाषा हिन्दी में किये गये कार्यो की समीक्षा तथा इससे संबंधित आपके कार्यालयों में उत्पन्न समस्याओं पर चर्चा की जाएगी। संघ के विभिन्न राजकीय प्रयोजनों में इसके प्रगामी प्रयोग को बढ़ावा देने के लिए राजभाषा विभाग प्रति वर्ष एक वार्षिक कार्यक्रम जारी करता है, जिसके

नराकास की बैठक में संस्थान के निदेशक एवं अध्यक्ष, नराकास डॉ. राम विश्वकर्मा एवं अन्य अधिकारी गण।

बैठक को संबोधित करते हुए संस्थान के निदेशक एवं नराकास, अध्यक्ष, डॉ. राम विश्वकर्मा एवं उपस्थित कार्यालय प्रमुख गण।

अनुसार हम कार्यालयों में राजभाषा के कार्य सम्पन्न करते हैं। चूंकि सरकारी कामकाज में मूल टिप्पण और प्रारूपण के लिए हिन्दी का ही प्रयोग किया जाए जिसके अन्तर्गत धारा 3(3) का हम सबको अनुपालन सुनिश्चित करना चाहिए। यही संविधान की मूलभावना के अनुरूप होगा। सभी भारतीय भाषाएं देश की एकता की प्रतीक हैं। भारतीय संविधान में जो प्रावधान किये गये हैं इसी के अनुसार हमें आदेशों/अनुदेशों का पालन करते हुए महामहिम राष्ट्रपति जी के संकल्पों का सम्मान करना चाहिए''।

तत्पश्चात् बैठक में उपस्थित सदस्यों के परिचय के साथ ही बैठक की कार्रवाई आरम्भ हुई। सचिव ने गत बैठक के कार्यवृत्त पर चर्चा के दौरान कहा कि सम्माननीय सदस्यों की कोई प्रतिक्रिया, सुझाव अथवा आपत्ति हो तो वे विचार रखें, लेकिन माननीय उपस्थित सदस्यों की ओर से कोई आपत्ति एवं प्रतिक्रिया न मिलने पर सचिव, ने अध्यक्ष महोदय के अनुमोदन से गत बैठक के कार्यवृत्त की पुष्टि की।

नराकास, जम्मू की वर्ष 2013-2014 में राजभाषा नीति के श्रेष्ठ निष्पादन के लिए पुरस्कृत कार्यालय/बैंकों/ उपक्रमों के नाम निम्न प्रकार है:-

निदेशक, भारतीय समवेत औषध संस्थान, जम्मू, रक्षा लेखा प्रधान नियंत्रक, उत्तरी कमान, जम्मू, आयुक्त आयकर, आयकर कार्यालय, जम्मू/श्रीनगर, प्रभारी, क्षेत्रीय आयुर्वेद अनुसंधान संस्थान, जम्मू, महानिरीक्षक, सीमान्त मुख्यालय, सीमा सुरक्षा बल, पलौड़ा, जम्मू, कार्यालय महालेखाकार (लेखा परीक्षा), जम्मू, उपायुक्त, केन्द्रीय विद्यालय संगठन, गांधी नगर, जम्मू, उप महानिरीक्षक, केन्द्रीय रिजर्व पुलिस बल बनतलाव, जम्मू, उप महानिदेशक, राष्ट्रीय प्रतिदर्श

सर्वेक्षण कार्यालय, क्षेत्रीय कार्यालय, जम्मू, मंडल यातायात प्रबंधक, उत्तर रेलवे, जम्मू, उपमहाप्रबंधक, पंजाब नेशनल बैंक (मंडल कार्यालय) जम्मू, उपमहाप्रबंधक, भारतीय स्टेट बैंक (प्रशासनिक कार्यालय), जम्मू, मुख्य महाप्रबंधक, राष्ट्रीय कृषि और ग्रामीण विकास बैंक, क्षेत्रीय कार्यालय, जम्मू, सहायक महाप्रबंधक, आई.डी.बी.आई.बैंक, जम्मू, कार्यपालक निदेशक, एन.एच.पी.सी.लिमिटेड, क्षेत्रीय कार्यालय (क्षेत्र-1), जम्मू, कार्यपालक निदेशक, पावर ग्रिड कारपोरेशन ऑफ इण्डिया लिमिटेड (उ.क्षेत्र-।।), जम्मू, महाप्रबंधक, एनएचपीसी लिमिटेड, दुलहस्ती पावर परियोजना किश्तवाड़, जम्मू व कश्मीर, महाप्रबंधक, एनएचपीसी, सलाल पावर स्टेशन, रियासी, जम्मू व कश्मीर, निदेशक, भारतीय प्रसारण निगम, दूरदर्शन केन्द्र, जम्मू, महाप्रबंधक, भारतीय खाद्य निगम, क्षेत्रीय कार्यालय, जम्मू, स्टेशन प्रबंधक, एअर इंडिया लिमिटेड, जम्मू, वरिष्ठ मंडल प्रबंधक, दि ओरिएण्टल इंश्योरेंश कम्पनी लिमिटेड, मंडलीय कार्यालय, जम्मू, वरिष्ठ क्षेत्रीय प्रबंधक, हिन्दुस्तान पेट्रोलियम कारपोरेशन लिमिटेड, क्षेत्रीय कार्यालय, जम्मू आदि ।

संस्थान के निदेशक एवं अध्यक्ष, नराकास, जम्मू डॉ. राम विश्वकर्मा ने सभागार में उपस्थित सज्जनों का अपने संस्थान की ओर से व नगर राजभाषा कार्यान्वयन समिति के मंच से उपस्थित कार्यालय प्रमुखों व अन्य गणमान्य व्यक्तियों का स्वागत करते हुए अपने अध्यक्षीय संबोधन में कहा, 'कि हमें छः माह के बाद आपसे राजभाषा नीति कार्यान्वयन पर चर्चा के लिए एक अच्छा अवसर मिलता है। हम सब मिलकर राजभाषा नीति कार्यान्वयन की दिशा में महत्वपूर्ण हल निकालें। उन्होंने संसदीय राजभाषा समिति के विषय में संक्षेप में बताया कि समिति के निरीक्षण से राजभाषा कार्यान्वयन के लिए महत्वपूर्ण मार्गदर्शन मिलते हैं। आपके माध्यम से राजभाषा के कार्यान्वयन में जो समस्याएं उत्पन्न होती हैं। उनका समाधान भी आसानी से निकाला जा सकता है। जिसमें धारा 3(3) के अन्तर्गत जो मद निर्धारित हैं उन पर कार्रवाई आवश्यक रूप से करने का प्रयत्न करें साथ ही हिन्दी पुस्तकों की खरीद 50 प्रतिशत करने का प्रावधान है। इसी प्रकार विज्ञापन भी क्षेत्रीय भाषाओं व हिन्दी/अंग्रेजी में बराबर खर्च किया जाए। उन्होंने वार्षिक कार्यक्रम के अन्तर्गत दिए गये लक्षयों को प्राप्त करना है। गृह पत्रिकाओं के प्रकाशन भी महत्वपूर्ण प्रयास हैं साथ ही इस बैठक में कार्यालय प्रधानों को आवश्यक रूप

से भाग लेना चाहिए। ताकि बैठक में लिए गये निर्णयों को प्रभावी बनाया जाए। हम चाहते है कि ई-मेल के माध्यम से पत्राचार में वृद्धि हो जैसाकि आपने अनुभव किया होगा कि ई-मेल के माध्यम से हमने पत्राचार को सुगम बनाया है और समिति की वेबसाइट पर समिति की गतिविधियां उपलब्ध हैं और ब्लॉक पर अपने सुन्दर विचार प्रेषित करने का माध्यम है। अध्यक्ष महोदय ने सुझाव दिया कि यदि समिति के माध्यम से कंप्यूटर प्रशिक्षण कार्यक्रम आयोजित किए जा सकते हैं। क्या इसकी आवश्यकता है। हमारे कई सदस्य कार्यालयों ने हिन्दी के महत्व पर अपने सुन्दर विचार दिए हैं साथ ही कई सदस्य कार्यालयों द्वारा काव्य के माध्यम से अपने संवाद को सुन्दर ढंग से प्रस्तुत किया है। आप सब बैठक में उपस्थित हुए और राजभाषा की प्रगति के लिए आपने विचार व्यक्त किए उन्होंने सभी का हृदय से आभार सहित धन्यवाद किया।

अन्त में धन्यवाद प्रस्ताव संस्थान की श्रीमती रजनी कुमारी ने बैठक में अध्यक्ष महोदय एवं उपस्थित नराकास जम्मू के सभी केन्द्रीय कार्यालयों/बैंकों/उपक्रमों के कार्यालय प्रमुखों एवं नगर के प्रिन्ट व इलैक्ट्रानिक मीडिया के सभी संवाददाताओं का आभार व्यक्त किया। बैठक में दूरदर्शन तथा मीडिया का सदैव सहयोग रहा है। बैठक के आयोजन में संस्थान के सभी संकाय सदस्यों ने सहयोग प्रदान किया। प्रबंधन के लिए संस्थान के वरि. हिन्दी अधिकारी एवं सदस्य सचिव, डॉ. अमर सिंह तथा समस्त स्टॉफ सदस्यों का आभार सहित धन्यवाद किया।

CSIR-IIIM

सीएसआइआर–भारतीय समवेत औषध संस्थान, जम्मू–180001 (भारत)
CSIR-INDIAN INSTITUTE OF INTEGRATIVE MEDICINE
JAMMU-180001 (INDIA)