वार्षिक प्रतिवेदन
ANNUAL REPORT

2017-2018

सीएसआईआर - भारतीय समवेत औषध संस्थान, जम्मू - 180001 (भारत)
CSIR-Indian Institute of Integrative Medicine
(Council of Scientific and Industrial Research)
JAMMU-180001 (INDIA)

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IIIM

CONTENTS


IIIM

Director's Message....

I take this opportunity to present the Annual Report of CSIR- Indian Institute of Integrative Medicine, Jammu to its readers which highlights the scientific achievements and work done in the institute during the year 2017-2018. This report summarizes the achievements in all facets of natural products research and technology including discovery of novel pharmacologically active natural products from plants and microbial species and translating them into drug leads, preclinical pharmacology and clinical development in both NCE as well as botanical herbal mode. I am indeed happy to inform that the strides of progress have continued unabated towards excellence in research and development of innovative products for societal benefit.

This period has been highly exiting for us as CSIR-IIIM, Jammu. This institute has been ranked 4th within the CSIR Institutes by Scimago Institutions Ranking. We have filed 12 patent applications both in India and in foreign and 11 patents were granted to IIIM. During this period, IIIM published a total of 177 scientific publications with an average impact factor of 2. 93.

Several important events took place during this year. Firstly, CSIR-Indian Institute of Integrative Medicine (IIIM) signed a MoU with Central University of Jammu (CUJ) to cooperate in the diverse areas of biological and chemical science. Secondly, this institute has rich history of working on Research & Development of the high value aromatic crops since last many decades. Under the CSIR– Aroma Mission which aims to provide end-to-end technology and value-addition solutions across the country at a sizable scale. CSIR- Aroma Mission will bring transformative change in the aroma sector through scientific interventions in the areas of agriculture, processing and product development for fuelling the growth of aroma industry and rural employment.

CSIR-IIIM, Jammu as one of the nodal centre for CSIR Mission on phyto-pharmaceuticals who aims to improve the availability (through cultivation) of such medicinal plants which are in high demand by global and domestic industry involved in the preparation of medicines of Indian traditional systems. Under this mission it is proposed to prevent exhaustion of medicinal plants from their native locations by identifying the elite germplasm and conserving it by cultivation and in gene banks. Improved varieties along with their agro-technologies will be developed to increase productivity and profitability per unit land area, and to make use of such areas which are affected by abiotic stresses such as drought, salinity, flood, shade etc. Chemical processes will be developed for the preparation of standardized extracts and enriched fractions of selected medicinal plants to transfer the value- addition technologies to the entrepreneurs to promote use and export of value-added material instead of the raw plant material. Efforts would be

made to translate the potential clinical leads in different CSIR laboratories to develop them into phyto-pharmaceutical drugs which would be affordable and acceptable at global standards.

CSIR-IIIM, Jammu has joined in a Mission Mode Project on Sickle Cell Anaemia through brainstorming and domain expert group discussions. The CSIR Mission on Sickle Cell Anaemia aims at:

- Managing Genetic Burden of Sickle Cell Anaemia and Understanding Genetic Basis of Differential Response to Hydroxyurea Therapy;
- Drug discovery and development for management of SCA;
- Genome editing and stem cell research approach for the treatment of SCA; and
- Development and on-ground implementation of an affordable, accurate and accelerated diagnostic kit.

Institute has launched an Integrated Skill Development Initiative for gainful utilization of its state-of-the-art infrastructure and human resources through specific industry oriented skilling programmes. Under the JIGYASA programme CSIR is collaborated with the Ministry of Human Resource Development. The focus is on connecting school students and scientists so as to extend the classroom learning of students with experiential education based on a very well planned research laboratory environment.

This year NIDHI-TBI "Indian Institute of Integrative Medicine- Technology Business Incubator (IIIM-TBI)" has been established at Indian Institute of Integrative Medicine (CSIR-IIIM, Jammu. The IIIM-TBI has been sanctioned by National S&T Entrepreneurship Development Board (NSTEDB), DST, to cater the demand of business incubators and starts-ups and support innovations and development of technology & prototype/ product development. This year the institute has also been approved as drug testing laboratory (DTL) by Drugs & Food Control Organization Jammu and Kashmir.

As part of CSIR Platinum Jubilee celebration, a three days mega scientific exhibition was launched CSIR-IIIM, Jammu campus from 25-27 September 2017 which stressed upon the needs of imparting practical knowledge along with the theoretical teaching given in the schools, colleges and universities.

In order to bring commercial cultivation of banana in J&K, CSIR- Indian Institute of Integrative Medicine has conceived a new biotechnology driven programme. This work was jointly done by CSIR-IIIM, Jammu and M/s Cadila Pharmaceutical, Ahmadabad. After full trial and established tissue culture and agriculture practice, the institute launched the J&K grown banana fruit.

This year Dr. Inshad Ali Khan, Principal Scientist, was awarded the NASI - Reliance Industries Platinum Jubilee Award (2017) in Biological Sciences.

(Ram Vishwakarma)

1.0 PLANT BIOTECHNOLOGY, BIODIVERSITY AND APPLIED BOTANY

1.1. Plant Survey, Collection and Certification in Janaki Ammal Herbarium

Bikarma Singh

During 2017-2018, many field tours for collection of plant materials were undertaken and plant vouchers were collected for studying plant diversity, ecology, genetic variability, DNA bar-coding, tissue culture, and for isolation of different markers and compounds from different Bio-geographic regions of Himalayas. The proper authentication of raw material is critically important as far as safety and efficacy of herbal medicines are concerned. Plant authentication and identification services are provided to industries and growers by the scientific Staff working in herbarium section. Janaki Ammal Herbarium is recognized as a National Referral Centre for plant identification and authentication. The identities of these plants were confirmed by SOP followed in Janaki Ammal Herbarium.

Table 1.1.1: On-going Plants for research during 2017-2018

Botanical name / Family	Parts supplied	Quantity
Bergenia ciliata (Haw.) Sternb./ Saxifragaceae –Wild collection	Rhizome	1.5 kg dried
Bergenia ciliata (Haw.) Sternb./ Saxifragaceae – purchased	Whole Plant	35.00 kg dried
Boswellia serrata Roxb. ex Colebr./ Burseraceae	Gum	40.00 kg dried
Andrographis paniculata (Burm.f.) Wall. ex Nees/ Acanthaceae	Whole Plant	15.00 kg dried
Terminalia bellirica (Gaertn.) Roxb./ Combretaceae	Fruits	60.00 kg dried
Syzygium aromaticum L. / Myrtaceae	Inflorescence	10.00 dried
Piper nigrum L. / Piperaceae	Fruits	10.00 kg dried
Piper betle L./ Piperaceae	Leaves	6.50 kg dried
Piper longum L./ Piperaceae	Inflorescence	10.00 kg dried
Alkanna tinctoria (L.) Taush / Boraginaceae	Whole plant	10 kg dried
Passiflora incarnata L./ Passifloraceae	Root	200 gram dried
	Leaves	200 gram dried
	Stem	200 gram dried
	Tendril	100 gram dried
Symphytum officinale L. / Boraginaceae	Root	200 gram dried
	Leaves	200 gram dried
	Inflorescence	200 gram dried
Pueraria tuberosa (Willd.) DC. /Fabaceae	Tuber accession 1 of Basholi	100 gram dried
	Tuber accession 2 of Bani	100 gram dried
	Tuber accession 3 of Kathua	100 gram dried
	Tuber accession 4 of Nandini	100 gram dried
Boerhavia diffusa L. /Nyctaginaceae	Root	200 gm dried
	Stem	100 gm dried
	Leaves	100 gm dried
	Inflorescence	100 gm dried
Piper betle L./Piperaceae	Leaves	1.5 kg dried

The details of field tours undertaken during this reporting period is given below:

- **Bani-Sarthal, J&K State:** Five days field tour, *w.e.f.* 11-15 May 2017, were undertaken to Bani and Sarthal for collection of plant samples for studying biodiversity, mapping of medicinal wealth, bulk collection of sample for studying DNA barcoding and for collection of germplasm of critically endangered species. 230 samples collected along with digital photographs and GPS points.
- **Himachal Pradesh State:** Six days field tour, *w.e.f.* 22nd-26thJune 2017, were undertaken to Palampur, Kullu, Manali and Rohtang Pass of Himachal Pradesh for collection of different accessions of *Cannabis sativa, Bergenia ciliata, Trillium govanianum, Cassia tora* and other plants for studying phyto-chemistry and for germplasm maintenance.
- **Uttar Pradesh State:** Four days field tour, *w.e.f.* 18-21 July 2017, were undertaken to Lucknow and adjoining areas for bulk collection of plant samples and herbarium consultation for proper authentication and certification of plants vouchers.
- **Lowang-Kakunu, J&K State:** Five days field tour, *w.e.f.* 4-8 August 2017, were undertaken to Lowang and Kakunu for collection of plant samples for mapping biodiversity, and bulk collection of sample for studying chemistry and taxonomy. 405 plants samples collected along with digital photographs and GPS points.
- **Rajouri, J&K State**: Four days field tours, *w.e.f.* 16-19thAugust 2017, were undertaken for land surveys, farmers meeting and organising training-cum-awareness programme on cultivation, processing and marketing of aromatic crops at Rajouri and adjoining areas under CSIR-Aroma Mission project.
- **Kathua, J&K State:** Five days field tour, *w.e.f.* 5-9 September 2017, were undertaken to Kathua, Basoli, Dharmahanpur and adjoining areas for monitoring, evaluation and upgrading the status of aromatic crops planted under JAAG project in Kathua district for calculating the expected materials to get for completing the target area under CSIR-Aroma Mission Project.
- **Samba, J&KState:**
  - ☞ One day field tour, 9th October 2017, were undertaken to Samba district for organizing one day awareness-cum-training programme for cultivation and processing of aromatic crops suitable for Samba region and adjoining areas.
  - ☞ One day field tour, 29th December 2017, for monitoring and evaluation of planted crops in Uttar behni of Samba district.
- **Basholi, J&K State: O**ne day field tour, 16th October 2017, were undertaken to Samba district for organizing one day awareness-cum-training programme for cultivation and processing of aromatic crops suitable for Samba region and adjoining areas.
- **Amritsar, Punjab State:** Five days field tour, *w.e.f.* 24-27th November 2017, were undertaken to Amritsar Punjab for purchase of bulk quality of plant materials such as *Bergenia cliata, Piper longum, and Boswellia serrata* for GAP project for chemistry and cGMP works of IIIM.
- **Biotech Park Kathua, J&KState:**
  - ☞ One day field tour, 19th December 2017, for land survey, monitoring and evaluation of planted crops in Biotech Park Kathua.
  - ☞ One day field tour, 5thJanuary 2018, evaluation of planted crops CN-5 aromatic crop in Biotech park of Kathua district.
  - ☞ One day field tour, 19th January 2018, were undertaken to Biotech Park Ghati of Kathua district for organizing Value-Addition Stall representing IIIM produced essential oils and to participate in one day awareness-cum-training programme for cultivation, processing and marketing of aromatic crops suitable for Kathua regions and similar adjoining areas.

1.2. Biological Spectrum and Floral Diversity of Western Himalaya-A Case Study of Nandini Wildlife Sanctuary in J&KState

Bikarma Singh, Bishander Singh, Sumit Singh, Rajendra Bhanwaria, Suresh Chandra

Increasingly, land managers are becoming proactive about biodiversity inventories, recognizing that it is cost-effective to document hot spots in advance and incorporate them appropriately into planning, rather than wait until a conflictarises. Utilising parameters for biodiversity mapping, measuring and modelling provides us with the ability to undertake inventory and assessment, which is essential for the establishment of baseline biological data that will aid in the successful management of our environment. Indian Himalaya is rich in biological diversity, and studying the form and structure of plant communities can be explored by classifying the taxa involved in categories reflecting environmental relationships. First time taxonomic inventorying and biological spectrum studies of plant species occurring in Nandini Wildlife Sanctuary (NWLS) were conducted.

Nandini Hills in district Udhampur (J&K) State located 30km from Jammu railway station. This sanctuary was named after an old Nandini village laying on the way to Jammu- Srinagar National highway. This place was famous for dhabas and paneer pakoda prepared by local Gujjar tribe. Later on, the area was notified as wildlife sanctuary by J&K Government in 1990 with total geographic area of 3 3.3 4 square kilo meters NWLS lies between latitude of 32°47'43"- 32°53'23"N and longitudes of 74°56'19"-74°59'39"E, and elevation on the hills varies from 741- 843 m above mean sea level (Figure1.2.1). Earlier, Jammu-Srinagar zigzag road was passing through the middle of this hills and this road was dividing the sanctuary into two identical halves, but construction of underground Chenani- Nashri Tunnel in 2017 completely stopped the earlier route and helping the Forest Department in conservation of biodiversity of this sanctuary. The forest hill terrains are rugged, and the hills characterized with moderate to steep slopes topography. The entire belts represent the Western Shivalik range, and the vegetation components are characterized by typical Himalayan subtropical forests. The NWLS enjoy a great extremity of temperature with June-July recorded as the hottest months, and December- January as the coldest months. The average annual temperature varies from 2°C in winter to 45°C in summer. The annual rainfall varies from 100-400cm. Due to varied topography and suitable climate, the region homed to several rare and endangered species of plants, animals, birds, butterflies, insects and soil microbial community. Investigation of survey revealed 331 species belonging to 249 genera and 84 families, and has been grouped into different life- form classes. Fabaceae was recorded as the most dominant family represented by 24 genera and 51 species, followed by Asteraceae (22 genera and 26 species) and Lamiaceae (14 genera and 16 species). Acanthaceae (13 genera), Scrophulariaceae (10 genera), Apocynaceae (8 genera), Asclepiadaceae (8 genera), Moraceae (8 genera), Malvaceae (7 genera), Rosaceae (7 genera), Rubiaceae (7 genera), Convolvulaceae (6 genera), Solanaceae (5 genera) and Verbenaceae (5 genera) were other major angiosperm families in NWLS. In terms of species diversity, *Desmodium Desv.* (6 spp.) and *Indigofera L.* (6 spp.) were the dominant genera followed by *Cassia L.* (5 spp.), *Crotolaria L.* (5 spp.), *Ipomea L.* (5 spp.), *Ficus* (4 spp.), *Vitis L.* (4 spp.), *Acacia Mill.* (4 spp.), *Alysicarpus Neck.* (4 spp.), *Atylosia Wight.* & *Arn.* (4 spp.), *Corchorus L.* (4 spp.), *Jasminum L.* (4 spp.), (4 spp.), *Justicia L.* (4 spp.), *Leucas R. Br.* (4 spp.), *Medicago L.* (4 spp.), *Tephrosia Dalz.* (4 spp.), and *Trigonella L.* (4 spp.).

The biological spectrum of the whole study area, showed that the most dominant life form are therophytes (120 sp.) represented with 36.254%), followed by 20.846% phanerophytes (69 sp.), and 12.991% chamaephytes (43 sp.) (Table 1.2.1 and Table 1.2.2). Lianas (climbers, vines and scandant under shrubs), and hemicryptophytes (36 sp.) each represented by 10.876% of the total plant diversity of higher groups. Among the flora of Nandini wildlife sanctuary the parasites and saprophytes (1 sp. each) were low and represent about 0.302%. A graphical representation of the biological life form of NWLS is presented in Figure 1.2.2.

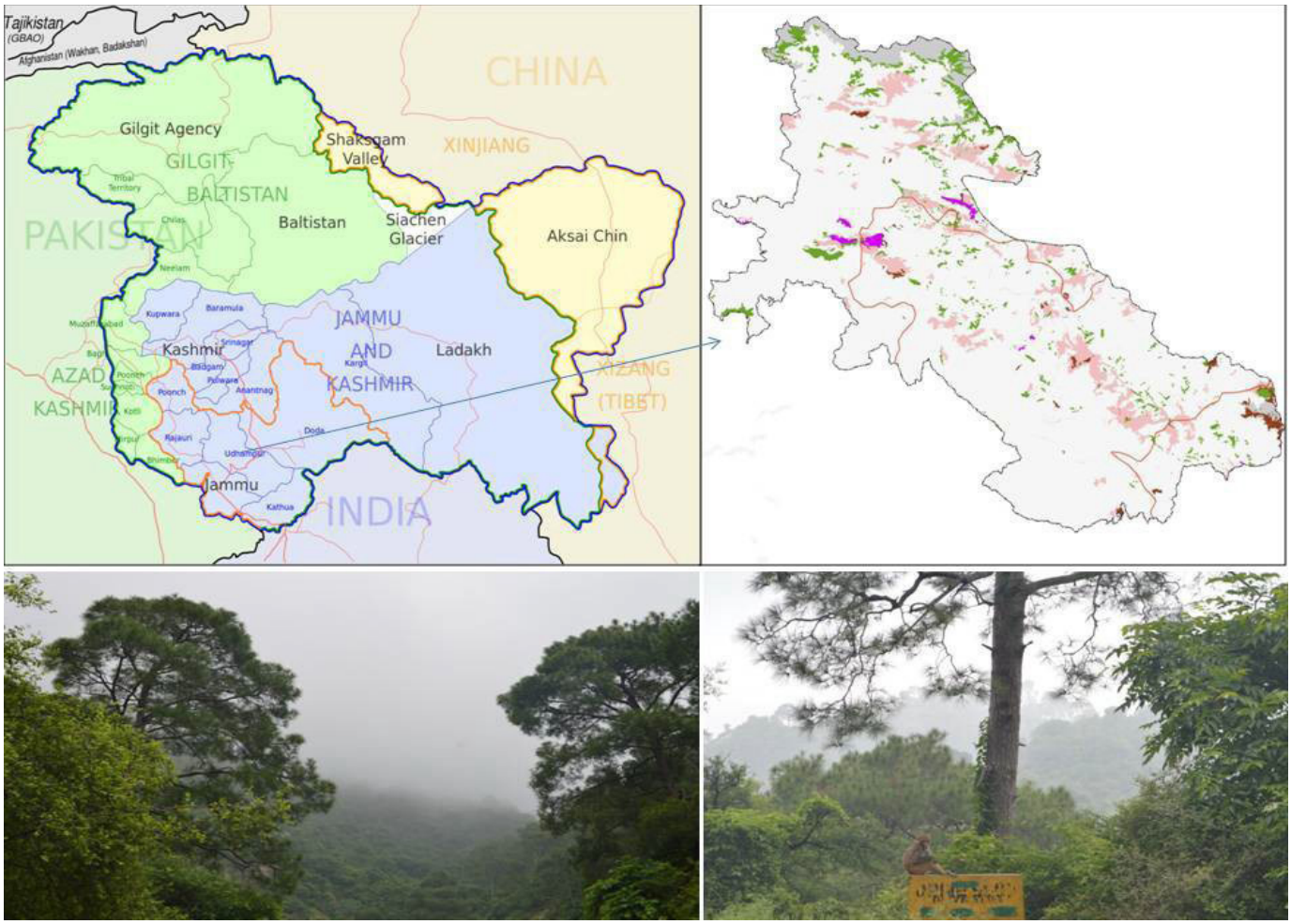


Figure 1.2.1. Floristic inventory, population mapping and bioprospection of Nandini Wildlife Sanctuary

Table 1.2.1. Comparison of biological spectrum of NWLS with Raunkiaer's model

Life- forms	Ph	Ch	Hc	G	He	Hy	Th	L	Ep	P	Sp
Normal biologica l spectrum (%)	46.00	9.00	26.00	4.00	-	26.00	13.00	-	3.00	-	-
NWLS biologica l spectrum (%)	20.846	12.991	10.876	5.136	0.302	0.604	36.254	10.876	1.511	0.302	0.302
Deviation (%)	+25.154	-3.991	+15.124	- 1.136	- 0.302	+25.396	- 23.254	- 10.876	+1.489	- 0.302	- 0.302

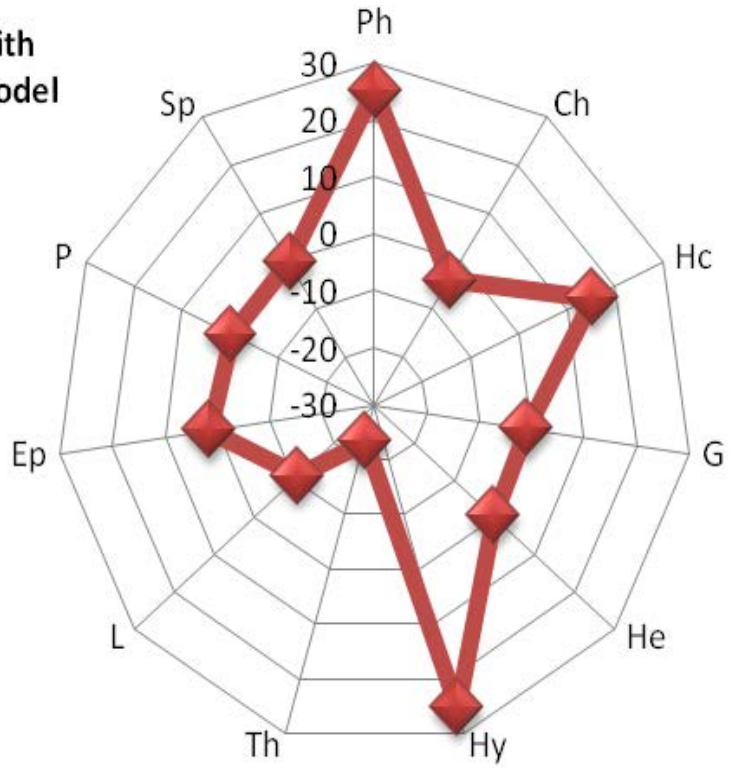


Figure 1.2.2. Biological spectrum of Nandini wildlife sanctuary with respect to normal Raunkiaer's model

Table 1.2.2. Life-form spectrum classes for the flora of Nandini wildlife sanctuary, J&K State

Life-form classes	Abbreviation	No. of Taxa	Biological spectrum (Percentage)
Phanerophytes	Ph	69	20.846
Chamaephytes	Ch	43	12.991
Hemicryptophytes	Hc	36	10.876
Life-form classes	Abbreviation	No. of Taxa	Biological spectrum (Percentage)
Geophytes	G	17	5.136
Helophytes	He	1	0.302
Hydrophytes	Hy	2	0.604
Therophytes	Th	120	36.254
Lianas	L	36	10.876
Epiphytes	Ep	5	1.511
Parasites	P	1	0.302
Saprophytes	Sp	1	0.302
Total		331	100

Economically, the entire hill comprised of several plant species with high economic value. These plants are of economic use in the form of timber, fibre, used as wild food and medicines. Sustainable management of such plants through concerted conservational efforts needed to protect the depleting population of plants and State Forest Department and NGOs can contributes a lot for conserving depleting gene pools of NWLS.

1.3. Indian Folklore Medicinal Herbalism-Contribution of Pharmaceutically Active Himalayan Orchids Traditionally Used As Herbal Medicine

Bikarma Singh

Botanists, conservationists and general public communities are now a day's knowledgeable about the increasing losses of biological diversity from the earth. It is estimated that total 87,40,000 eukaryotic species exist on the earth and of these 2,98,000 species are of Plantae (plants), and 1,24,035 plant species representing 45.9% in hotspot regions are endemics. Orchids, known by the name of mighty miniatures, declared as flagship species grow luxuriantly in the Himalayan regions and attracted author's attention while working in the North-eastern states of India. Considering the rich biodiversity, ethnic Knowledge on plants associated with tribes, and to fill-up the gap in the botanical exploration of the Himalaya, the present study aimed at documenting the medicinal use of orchid plants of Meghalaya state. The objectives of this study were to assess the diversity and utilization pattern of medicinal orchids. The presented investigation recorded the use of 36 Himalayan orchid plant species under 24 genera in traditionally managed primary health care practice by the tribal community of Meghalaya state these include 18 epiphytic species (*Acampe chracea* (Lindl.) Hochr., *Acampe papillosa* (Lindl.) Lindl., *Aerides multiflora* Roxb., *Aerides odoratum* Lour., *Bulbophyllum odoratissimum* (J.E.Sm.) Lindl., *Coelogyne punctulata* Lindl., *Conchidium muscicola* (Lindl.) Rauschert, *Cymbidium aloifolium* (L) Sw., *Cymbidium longifolium* D.Don, *Dendrobium densiflorum* Lindl., *Dendrobium fimbriatum* Hook., *endrobium moschatum* (Buch.-Ham.) Swartz, *Eria pannea* Lindl., *Flickingeria fugax* (Rchb.f.) Seidenf., *Papilionanthe teres* (Roxb.) Schltr., *Rhynchostylis retusa* (L.) Blume., *Vanda coerulea* Griff. ex Lindl. and *Vanda cristata* Lindl.), 12 terrestrial species (*Anoectochilus roxburghii* (Wall.). Lindl., *Arundina graminifolia* (D.Don) Hochr., *Eulophia graminea* Lindl., *Geodorum densiflorum* (Lam.) Schltr., *Habenaria dentata* (Sw.) Schltr., *Habenaria intermedia* D.Don, *Habenaria marginata* Colebr., *Herminium lanceum* (Thunb. ex Sw.) J.Vuijk, *Malaxis acuminate* D.Don, *Malaxis muscifera* (Lindl.) Ktze, *Phaius tankervilleae* (Banks ex L'Her.) Blume, *Satyrium nepalens* D.Don), 4 species epiphytic as well as lithophytic (*Coelogyn corymbosa* Lindl., *Dendrobium nobile* Lindl.,

Plate I: (1) *Acampe ochracea* (Lindl.) Hochr., (2) *Acampe papillosa* (Lindl.) Lindl., (3) *Aerides odoratum* Lour., (4) *Aerides multiflora* Roxb., (5) *Anoectochilusroxburghii* (Wall.) Lindl., (6) *Arundina graminifolia* (D.Don) Hochr.

Pholidata pallid Lindl., *Pholidotar imbricata* Hook.), and 2 species terrestrial as well as epiphytic plant (*Crepidium acuminatum* (D.Don) Szlach., and *Liparis nervosa* (Thunb.) Lindl.) [recorded in Plate I and Plate II.

Plate II: (7) *Bulbophyllum odoratissimum* (J.E.Sm.) Lindl., (8) *Coelogyne corymbosa* Lindl., (9) *Coelogyne punctulata* Lindl., (10) *Conchidium muscicola* (Lindl.) Rauschert, (11) *Crepidium acuminatum* (D.Don) Szlach., (12) *Cymbidium aloifolium* (L) Sw.

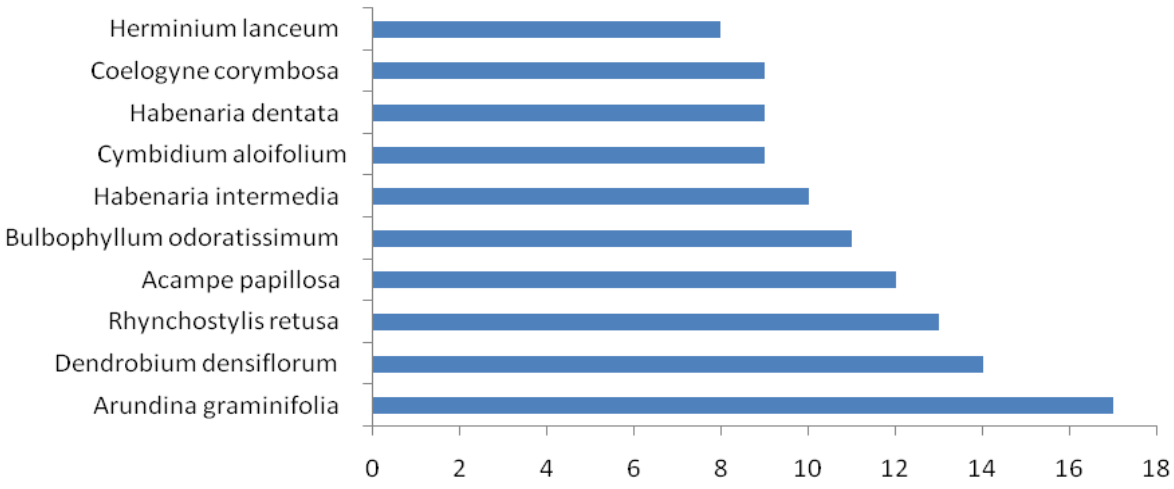


Figure 1.3.1. Frequency of informants per taxa investigated during field. Out of a total of 36 medicinal orchid phytotaxa, only the top ranking taxa accounting for at least 10 informants are shown (n=226)

Orchids are endangered plant group and protected by national or local community laws in many countries including India. International trade and collection of orchids from the wild is banned. Initiate ecological restoration of degraded riverine forests and promote afforestation of suitable host tree species such as *Toona ciliata*, *Engelhardtia spicata* and *Quercus* and *Castanopsis* species, which helps in the conservation programme. The results shows that *Arundina graminifolia*, *Dendrobium densiflorum*, *Rhynchostylis retusa*, *Acampe papillosa*, *Bulbophyllum odoratissimum*, *Habenaria intermedia*, *Cymbidium aloifolium*, *Habenaria dentata*, *Coelogyne corymbosa*, and *Herminium lanceum* were the most commonly medicinal use orchid in the State of Meghalaya (Table 1.3.1, Figure 1.3.1). Such species should be properly documented and steps are required for their conservation. Endemic and near endemic species need special attention, urgent need to conduct a population monitoring program together with study on orchid ecology so that we can use this information to design orchid conservation plans for the intact regions of habitat where orchids still thrive. Establishment of orchid seed bank and germplasm banks promotes orchid conservation. Local people should be made aware of this valuable plant wealth by means of awareness programs.

Table 1.3.1. Use value of medicinal orchid taxa investigated in Himalayas.

Botanical name	Informants	Use value
Arundina graminifolia	17	7.522
Dendrobium densiflorum	14	6.195
Rhynchostylis retusa	13	5.752
Acampe papillosa	12	5.310
Bulbophyllum odoratissimum	11	4.867
Habenaria intermedia	10	4.425
Cymbidium aloifolium	9	3.982
Habenaria dentata	9	3.982
Coelogyne corymbosa	9	3.982
Herminium lanceum	8	3.540
Papilionanthe teres	7	3.097
Aerides multiflora	7	3.097
Cymbidium longifolium	7	3.097
Dendrobium nobile	7	3.097
Flickingeria fugax	7	3.097
Malaxis muscifera	7	3.097
Aerides odoratum	6	2.655
Vanda coerulea	6	2.655
Dendrobium fimbriatum	5	2.212
Eulophia graminea	5	2.212
Habenaria marginata	5	2.212
Vanda cristata	5	2.212
Liparis nervosa	4	1.770
Malaxis acuminata	4	1.770
Pholidota imbricata	4	1.770
Acampe ochracea	3	1.327
Anoectochilus roxburghii	3	1.327

Botanical name	Informants	Use value
Coelogyne punctulata	3	1.327
Dendrobium moschatum	3	1.327
Eria pannea	3	1.327
Geodorum densiflorum	3	1.327
Phaius tankervilleae	3	1.327
Crepidium acuminatum	2	0.885
Pholidata pallida	2	0.885
Satyrium nepalense	2	0.885
Conchidium muscicola	1	0.442

1.4. Eating from raw wild plants in Himalaya: Traditional knowledge documentary on Sheena tribe in Kashmir

Bikarma Singh, Yashbir Singh Bedi

Commonly referred as *Terrestrial Paradise on Earth*, valleys of Kashmir Himalaya are sub-divided into ten districts with a total area of 15,948 sqkm, formed by girding chain of Pir Panjal mountain ranges of Lesser Himalaya in south, Zanskar range of Greater Himalaya in southeast and west. The total forest area is 8,128 sq km (forest cover 50.97 %), and population of Kashmir is 69,07,623, has a density of 433 person per sq km in 2011. The area under study in Kashmir lies between latitudes of 34˚ 31' 34.04"-34˚ 41' 12.03" N an d longitudes 74˚ 15' 42.50"-78˚ 38' 18.50" E. The altitude of the study regions ranges between 2000-3512 m MSL and the valley remains cut-off for five to six months in a year due to heavy snowfall in several places such as Razdan Pass and Purana Tulel. The vegetations and forest types can be categorized into four groups: alpine, sub-alpine scrub, temperate coniferous and temperate broad-leaved. The region is known for rare animals such as Snow Leopard (*Panthera uncia*-IUCN categorized as an endangered C1 species. Hangul Deer (*Cervus canadensis hanglu*- critically endangered Kashmir Stag as per IUCN), Alpine Ibex (*Capra ibex*-a species of wild goat),and Himalayan Monal Pheasant (*Lophophorus impejanus*). The study area is rich in flora and abode to a large number of useful economic and other plant species. While studying ethnobotany, a total of 42 species under 32 genera and 17 families were documented to be consumed by the *Sheena* tribe as raw food. Out of these, roots and tubers of 5 spp., stems and petioles of spp., leaves and young twigs of 9 spp., flowers/ flower- buds of 1 sp., fruits/pods of 21 spp., seeds and kernels of 2 spp., whole parts of 2 spp., were recorded to be consumed by the *Sheena* tribe (Table 1.4.1). The plants documented were categorized in different life-forms like herbs (50.00 %), shrubs (21.43 %), liana (4.76%), and trees (23.81%). The majority of food taxa belong to the family Rosaceae (12 spp.), Polygonaceae (4 spp.), Lamiaceae (3 spp.), Berberidaceae (3 spp.) and Asteraceae (3 spp.); while families such as Apiaceae, Campanulaceae, Fabaceae, Grossulariaceae and Moraceae, represented by 2 species each, and rest of the families like Cyperaceae, Elaegnaceae,Juglandaceae, Liliaceae, Oxalidaceae, and Solanaceae are represented by only1 species each. The genera with by the highest number of REPs species was *Rubus* (5 spp.), followed by *Berberis*, *Codonopsis*, *Elsholtzia*, *Fragaria*, *Prunus*, and *Ribes*, which is represented by 2 species each. The most frequently used parts recorded were fruits, young leaves, and tubers. The results are similar to earlier studies from Ladakh in North Himalaya (India) and from Tibet in Yunnan (China). Collection season of the wild edible plants varied from May to August (for young leaves, tubers and roots) and late August to October (for fruits and seeds). In winter, plants usually die out due to heavy snowfall in higher altitude regions; therefore, people dry the edible parts and store them for use in winter months. Kernel of *Juglans regia* is consumed fresh as well as stored for use in winter. Commonly available fruits of *Berberis lycium*, *Berberis pachyacantha* ssp. *zabeliana*, *Ficus auriculata*, *Fragaria nubicola*, *Morus alba*, *Rubus alceifolius*, *Rubus caesius*, and *Rubus idaeus* are found

to be eaten fresh. Young twigs and leaves of *Gentiana tianschanica, Lactuca sativa,* and *Sonchus oleraceus* were consumed as salad or added to preparation of local home- made soup (Figure1.4.1 & Figure 1.4.2.)

Figure 1.4.1 Ethnobotanical investigation from *Sheena* tribe in Kashmir Himalaya: a)A woman of *Sheena* tribe, b)Plant sample collection, c) *Asparagus racemosus*, d)*Berberis pachyacantha* ssp. *zabeliana*, e) *Berberis lyceum*, f) *Centella asiatica*

Figure 1.4.2 Ethnobotanical investigation from *Sheena* tribe in Kashmir Himalaya: g) *Hippophae rhamnoides*, h) *Juglans regia, i*) *Mentha longifolia*, j) *Oxyria digyna*, k) *Ribes orientale*, l) *Rosa webbiana*, m) *Rubus saxatilis*.

Table 1.4.1: Raw wild edible plants used by the *Sheena* tribein Kashmir, Western Himalaya

Sr. No	Plant name / Family/Voucher no.	Kashmiri Name	Life- form	Parts used	Mode of Use	Population status
1	*Anaphalis triplinervis* (Sims) Sims ex C.B.Clarke / Asteraceae/RRLH16190	*Yoktso/ Chikiga*	Herb	Flower buds	Yellowish flower buds are consumed as salads by shepherds	Endemic to Asia; common in Kashmir Himalaya
2	*Asparagus racemosus* Willd. / Liliaceae/ RRLH51548	*Prangoos*	Liana	Tubers	Fresh tubers are eaten raw by shepherds	Endemic to Asia; sparsely distributed in Himalaya belts
3	*Berberis lycium* Royle / Berberidaceae/ RRLH51024	*Daruhaldi*	Shrub	Fruits	Ripe bluish fruits are eaten raw	Endemic to Asia; common in Himalayan belts
4	*Berberis pachyacantha* Koehne ssp. *zabeliana* (C.K.Schneid.) Jafri / Berberidaceae/ RRLH51559	*Phulchopa*	Tree	Fruits	Ripe fruits are eaten raw	Rare and endemic to Kashmir Himalaya
5	*Centella asiatica* (L.) Urban / Apiaceae/ RRLH51017	*Gotu Kola*	Herb	Leaves	Fresh green leaves are eaten as salads	Common throughout Asia, abundant in Himalaya belts
6	*Codonopsis ovata* Benth. / Campanulaceae/ RRLH20920	*Chameli*	Herb	Roots	Fresh roots are consumed raw by shepherds	Rare and endemic to Kashmir Himalaya
7	*Codonopsis rotundifolia* Benth. / Campanulaceae/ RRLH51025	*Kabra/ Bibdi*	Herb	Roots	Raw roots are eaten	Rare and endemic to Kashmir Himalaya
8	*Crataegus rhipidophylla* Gand. / Rosaceae/ RRLH51531	*Shoonat*	Tree	Fruits	Ripe red coloured fruits are	Naturalized growth in Himalaya belts
9	*Cyperus rotundus* L. / Cyperaceae/ RRLH51520	*Chirpeet*	Herb	Tubers	Fresh tubers are eaten raw	Common naturalized growth in Himalaya belts
10	*Elsholtzia densa* Benth. / Lamiaceae/ RRLH21115	*Philongtso*	Herb	Leaves	Young leaves used in preparation of local chutney	Common in Himalaya belts
11	*Elsholtzia eriostachya* (Benth.) Benth. / Lamiaceae/ RRLH50956	*Tsatsa*	Herb	Leaves	Young leaves are used in preparation of local chutney	Common in Himalaya belts
12	*Ficus auriculata* Lour. / Moraceae/ RRLH18981	-	Tree	Fruits	Pinkish ripe fruits are eaten raw	Common in Himalaya belts

Sr. No	Plant name / Family/Voucher no.	Kashmiri Name	Life- form	Parts used	Mode of Use	Population status
13	*Fragaria nubicola* Lindl. ex Lacaita / Rosaceae/ RRLH50905	*Budmewa*	Herb	Fruits	Eaten raw	Common in Himalaya belts
14	*Fragaria vesca* L. / Rosaceae/ RRLH51563	*Budmewa/Jungli strawberry*	Herb	Fruits	Reddish ripe fruits eaten raw	Rare in Kashmir Himalaya belts
15	*Gentiana tianschanica* Rupr. ex Kusn. / Gentianaceae/ RRLH19757	*Wanglo*	Herb	Whole plants	Fresh plant parts are eaten as salad	Common in Kashmir and Ladakh Himalaya belts
16	*Heracleum candicans* Wall. / Apiaceae/ RRLH51027	*Folla / Mirkul*	Shrub	Young twigs	Fresh twigs are eaten by shepherds as salad	Common in Kashmir Himalaya belts
17	*Hippophae rhamnoides* L. / Elaeagnaceae/ RRLH51527	*Kond/ Chacoo*	Shrub	Fruits	Local juice prepared, stored and consumed in winter	Very common in Kashmir and Ladakh Himalaya belts
18	*Juglans regia* L. / Juglandaceae/ RRLH51510	*Akhrot/Achoo*	Tree	Fruits	Kernel of fruits are eaten	Very common in Kashmir and Ladakh Himalaya belts
19	*Lactuca sativa* L. / Asteraceae/ RRLH51026	*Salad*	Herb	Young twigs	Fresh leaves and young twigs are eaten raw as salad	Cultivated in Himalaya belts of Asia
20	*Lathyrus humilis* (Ser.) Fisher ex Spreng. / Fabaceae/ RRLH51536	*Kaown*	Herb	Seeds	Raw seeds are eaten	Common in Kashmir and Ladakh Himalaya belts
21	*Malus domestica* Borkh. / Rosaceae/ RRLH51515	*Pulay*	Tree	Fruits	Ripe fruits are eaten raw, it is cultivated as source of cash income	Cultivated in Kashmir Himalaya belts
22	*Mentha longifolia* L. / Lamiaceae/ RRLH51516	*Breeena/Jungli Phudina*	Herb	Leaves	Fresh leaves are eaten as chutney	Commonly occurs in Kashmir and Ladakh Himalaya belts
23	*Morus alba* L. / Moraceae/ RRLH51514	*Marooth*	Tree	Fruits	Ripe fruits are eaten raw and chutney is prepared from unripe fruits	Common in Asian countries
24	*Oxyria digyna* (L.) Hill / Polygonaceae/ RRLH50985	*Lamanchu/ Tajkiral*	Herb	Leaves	Eaten as salad and chutney	Sparsely occurs in high altitude areas of Kashmir and Ladakh regions

Sr. No	Plant name / Family/Voucher no.	Kashmiri Name	Life- form	Parts used	Mode of Use	Population status
25	*Oxalis acetosella* L. / Oxalidaceae/ RRLH51028	*Gammenuma*	Herb	Tubers	Eaten raw to alleviate thirst by Shepherds	Common in Himalaya belts
26	*Persicaria alpina* (All.) H.Gross / Polygonaceae/ RRLH850985	*Chikro / Maruch phonar*	Herb	Stems	Stem is chewed as well as used in chutney	Common in Kashmir and Arunachal Himalaya belts
27	*Prunus armeniaca* L. / Rosaceae/ RRLH19613	*Chuli*	Tree	Fruits	Kernel of fruits is eaten raw	Common in Himalaya belts
28	*Prunus cornuta* (Wall. ex Royle) Steud. / Rosaceae/ RRLH21785	*Padus*	Tree	Fruits	Ripe fruits are eaten raw	Common in Himalaya belts
29	*Rheum webbianum* Royle / Polygonaceae/ RRLH21343	*Lachhu*	Herb	Petioles	Eaten as salad and chutney	Common in Kashmir and Ladakh Himalaya belts
30	*Ribes alpestre* Wall. ex Decne. / Grossulariaceae/ RRLH50984	*Shatoo*	Tree	Fruits	Ripe fruits are eaten raw	Common in Kashmir Himalaya belts
31	*Ribes orientale* Desf. / Grossulariaceae/ RRLH50988	*Askut*	Tree	Fruits	Ripe fruits are eaten raw	Common in Kashmir and Ladakh Himalaya belts
32	*Rosa webbiana* Wall ex Royle / Rosaceae/ RRLH50989	*Siah*	Shrub	Fruits	Ripe fruits are eaten raw	Common throughout Himalaya belts
33	*Rubus alceifolius* Poir. / Rosaceae / RRLH50985		Liana	Fruits	Ripe fruits are eaten raw	Common throughout Himalaya belts
34	*Rubus caesius* L. / Rosaceae/ RRLH51584	*Akhray*	Shrub	Fruits	Ripe fruits are eaten raw	Common throughout Himalaya belts
35	*Rubus idaeus* L. / Rosaceae/ RRLH51552	*Lalresh*	Shrub	Fruits	Ripe pinkish fruits are eaten raw	Sparsely occurs in Himalay a belts
36	*Rubus niveus* Thunb. / Rosaceae/51550	*Jomy*	Shrub	Fruits	Ripe black fruits are eaten raw	Common throughout Himalaya belts
37	*Rubus saxatilis* L. / Rosaceae/ RRLH59982	*Chhota Akhray*	Shrub	Fruits	Ripe red fruits are eaten	Rare in Himalaya belts
38	*Rumex patientia* L. ssp. *orientalis* (Bernh. ex Schult. & Schult.f.) Danser / Polygonaceae/ RRLH50958	*Shommena*	Herb	Leaves	Eaten as chutney	Common throughout Kashmir and Ladakh Himalaya belts
39	*Sinopodophyllum hexandrum* (Royle) T.S.Ying / Berberidaceae/ RRLH50983	*Chamandi*	Herb	Fruits	Ripe red fruits are eaten raw	Common throughout Northern Himalaya belts

Sr. No	Plant name / Family/Voucher no.	Kashmiri Name	Life- form	Parts used	Mode of Use	Population status
40	*Solanum americanum* Mill. / Solanaceae/ RRLH51590	*Tsigma*	Shrub	Fruits	Black ripe fruits are eaten raw	Common throughout Himalaya belts
41	*Sonchus oleraceus* (L.) L. / Asteraceae/ RRLH51598	*Khala*	Herb	Leaves	Shepherds eat the fresh leaves as salad	Common throughout Kashmir and Ladakh Himalaya belts
42	*Trifolium repens* L. / Fabaceae/ RRLH50958	*Ishpit*	Herb	Whole plants	Fresh plant parts are eaten as salad	Common throughout Himalaya belts

This study was the first ethnobotanical investigation of raw edible plants used by *Sheena* tribe residing along LoC border of Kashmir. As plant resources in Western Himalaya are rather plentiful and under the influence of other ethnic groups such as *Pahari* and *Bakarwals*, the *Sheenas* not only cultivate various crops, but also collect wild edible plants as food. The present study concludes that different parts of the plants were used as food and medicine by the *Sheena* tribe, which sustains their life. The most frequently used parts include fruits, leaves, and tubers. If properly maintained and harvested, wild plants of this region could be the source of additional income for local people. With increased demand for green nutraceuticals, wild raw foods have attracted global interest as they contain numerous micronutrients and pharmacologically active substances. But, due to urbanization and fast modernization activities, the Traditional knowledge on the use of plants is fast vanishing. Therefore, there is an urgent need to document the traditional knowledge associated with a particular tribe, or otherwise such customs and indigenous knowledge will be lost forever. The conservation efforts of the tribal communities need to be recognized and the *in-situ* and *ex-situ* conservation of important documented wild plant species needs to be revitalized.

1.5. Studying eco-taxonomy of unexplored Bani, Sarthal and Malhar regions

Sumit Singh, Bikarma Singh

During the reporting period, three field tours *w.e.f.* 14th- 18th April 2017, 11th -16th May 2017 and 4th-8th September 2017, were carried out for survey and plant collection from the research area. Bani and Kakunu forest area were visited during the first tour and 37 field numbers consisting of 93 plant samples and around 170 digital photographs were taken. Some of the common plant species identified from this tour includes *Prinsepia utilis, Rubus ellipticus, Valeriana jatamansi, Eriophorum comosum, Rubus idaeus, Zanthoxylum armatum, Rhododendron arboreum, Isodon japonicus, Viola odorata, Gallium aparine, Berberis aristata, Lithocarpus henyri, Gerbera gossypiana etc.* During the second field tour, Lowang and Sarthal, area where targeted for plant collection, and 60 field numbers having 132 plant samples were collected *along* with 200 digital photographs. Some of the common plant species which were identified are *Ranunculus scleratus, Ligularia amplexicaulis, Barbarea intermedia, Potentilla sterilis, Pteris cretica, Onychium japonicum, Asplenium alternans, Microlepia hancei, Cheilanthes subvillosa, Polystichum polyblepharum, Leucas ciliata etc.* Third field tour was conducted between 4-8th September 2017, and sites of collection include Bani, Lowang and adjoining areas. Total 160 field numbers were collected having 405 plant samples along with 300 digital photographs and GPS points. Some of the important plant species which were identified are *Pyrus pashia, Mentha piperita, Thymus serpyllum, Nepeta lamiopsis, Colebrookia oppositifolia, Persicaria maculosa, Rumex hastatus, Bergenia ciliata, Rubia cordifolia, Berberis wallichiana, Urtica dioca, Pilea scripta, Woodfordia fruticosa, Trifolium pratense, Paspalum vaginatum, Isachne himalaica, Saccharum spontaneum* etc. GPS location of Bani is 32°52'33.15'' N and 75°48'14.53'' E and elevation is 1525 m ASL; Lowang is 32°46'51.86'' N, 75°44'33.24'' E, and elevation is 3000 m ASL, and Sarthal is 32°49'43.27'' N, 75°43'27.80'' E. Elevation is 3200 m ASL.

1.6. Cytogenetic analysis of diploid and tetraploid cytotypes of *Gentiana kurroo* Royle and evaluation of *in vitro* cytotoxicity in relation to chemotypic diversity

Syed Mudassir Jeelani, Jasvinder Singh, Ajai Prakash Gupta, Shashank Singh and Surrinder K. Lattoo

Gentiana kurroo Royle (Gentianaceae), a critically endangered endemic perennial herb grows between 1600-3500 m altitudes in north-western Himalayas. It is locally called as 'Neelkanth' in Kashmir Himalayas. The key bioactive compounds identified in the species include secoiridoidal glycosides in the form of sweroside, swertiamarin and gentiopicroside. It has been medicinally employed for the treatment of skin diseases, leucoderma, leprosy, bronchial asthma, flatulence, colic, anorexia, helminthiosis, inflammations, amenorrhoea, dysmenorrhoea, strangury, haemorrhoids, constipation and urinary infections. The present investigation was aimed at to investigate chemical diversity in different populations / cytotypes of *G. kurroo* from Kashmir Himalayas (Table 1.6.1). The populations displayed ploidy levels from diploidy to tetraploidy (2*n*=2*x*=26 to 2n=4*x*=52). Detailed investigation of these populations revealed the existence of different chromosomal races *n* =13, 26 (Figure 1.6.1a, b). The chromosome number *n* = 26 is recorded for the first time for the species.

Figure 1.6.1 Wild growing plants of *Gentiana kurroo* at Gurez (Jammu & Kashmir)

These cytological investigations were further corroborated with comparative chemo- profiling of the cytotypes to have an insight regarding the prevalent chemical diversity. Furthermore, anticancer activities of the methanolic herbal extracts were also undertaken. The existence of intraspecific polyploids in the species is indicative of the fact that the genome of such species is still in constant flux, plausibly to increase the adaptive and survival value under diverse ecological niches of Himalayas. Additionally, the morphological comparison of diploids and tetraploids at intraspecific level revealed significant variations in the qualitative characters both at macro and micro levels (Table 1.6.2). Overall assessment showed that the tetraploid species mostly inhabit higher altitudes and generally show stunted growth, fewer leaves and more flowers. Further, the seed production was copious in tetraploids than diploids.

Table 1.6.1: Data on chromosome number, ploidy status and place of collection in different populations of *Gentiana kurroo* Royle from Kashmir Himalayas

S. No.	Observed chromosome number ('*n*')	Ploidy status	Place of collection
GK1	13	Diploid (2*n* = 2*x* = 26)	Tulial (34°37′N, 74°59′E; 2500 m)
GK2	13	Diploid (2*n* = 2*x* = 26)	Gurinullah (34°34′ N, 75°44′ E; 2400 m)
GK 3	13	Diploid (2*n* = 2*x* = 26)	Yosmarg (33º47′N, 74º39'E; 24000 m)
GK 4	13	Diploid (2*n* = 2*x* = 26)	Patalwan (34°35′N, 74◦52′E; 2300 m)
GK 5	26	Tetraploid (2*n* = 4*x* = 52)	Razdan (34°34′N, 75°43′E; 3200 m)
GK 6	26	Tetraploid (2*n* = 4*x* = 52)	Mahadev (34°10′ N, 75°00′ E; 3000 m)

Table 1.6.2: Quantitative morphological comparison of different cytotypes in *Gentiana kurroo*

S. no.	Characters		Diploid cytotypes ($2n = 2x = 26$)	Tetraploid cytotypes ($2n = 4x = 52$)
1.	Plant height (cm)		16-21	13-15
2.	Rhizome	Length (cm) Diameter (cm)	9-12 1.5-2.5	11-16 2.2-3.4
3.	Root	Length (cm) Diameter (cm)	7.5-9 0.2-0.3	8-10 0.25-0.4
4.	Leaves	No. of radical No. of cauline Length of radical (cm) Length of cauline (cm)	33-37 22-25 1-1.5 by 0.9-1 0.5-0.6 by 0.4-0.5	36-40 18-20 2-3 by 1.3-2 0.8-1.2 by 0.6-0.9
5.	Flowering Shoot	Length (cm) No. of floweringshoots/plant No. of flowers/inflorescence No. of flowers/plant	16-18 4-5 4-5 14-16	19-22 6-8 5-6 17-20
6.	Flower	Length (cm) Diameter (cm) Pedicel length (cm)	4-5 2-3 1.5-2.5	5-6 2-3 2-3
7.	Fruit	Length (cm) Weight (g)	4-5 2-2.5	5-6 3-4
8.	Seed	Length (µm) Breadth (µm) Weight of 100 seeds (g)	38-41 13-15 0.015-0.017	40-43 16-17 0.018-0.02

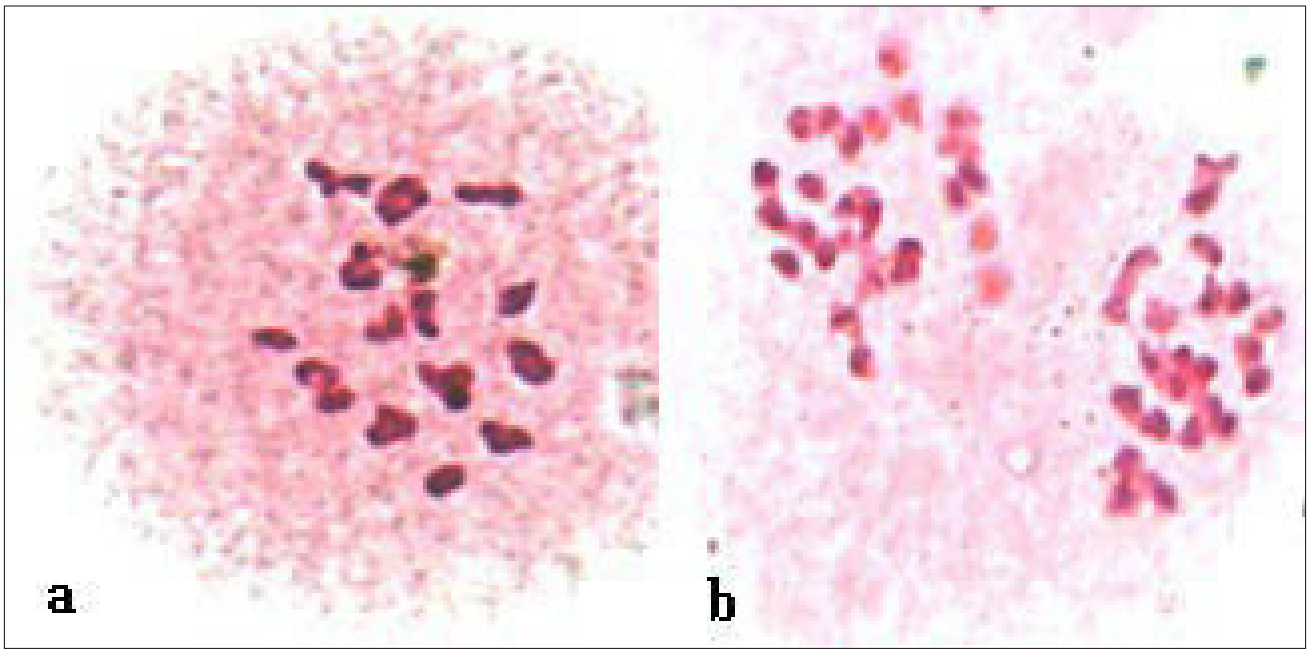


Figure 1.6.1: Meiotic chromosome numbers in two different populations of *Gentiana kurroo*: a) PMC at metaphase-I showing thirteen bivalents ($2n = 2x = 26$); b) PMC at anaphase-I showing twenty six chromosomes ($2n = 4x = 52$).

These cytotypes were examined phytochemically to assess the concentration of major bioactive compounds like sweroside, swertiamarin and gentiopicroside by using standard LC-E-MS technique (Table 1.6.3; Figure 1.6.2 & 1.6.3). Overall, the relative concentration of swertiamarin was highest followed by gentiopicroside and sweroside (Table 1.6.4). On the other hand, the tissue-specific chemo-profiling revealed relative dominance of sweroside, swertiamarin and gentiopicroside in root stock followed by flowers and aerial parts (Table 1.6.4). Root stocks tend to accumulate higher concentration of secondary metabolites in both diploids as well astetraploids.

Table 1.6.3: MRM positive LC-MS/MS optimized operating conditions for the quantification of sweroside, swertiamarin and gentiopicroside

Name of compound and $[M+H]^+$	Retention time (min)	Regression equation	R^2	Linearrange (ng/mL)	LOQ (ng/mL)	LOD (ng/mL)	Fragmentor voltage (V) & Collision energy (eV)
Sweroside [359.2]	2.07	y= 407.964789x-475.080215	0.994	0.97-1000	970	300	100; 07
Swertiamarin [375.1]	2.06	y=76.986232x-28.418210	0.997	0.97-1000	970	350	80; 20
Gentiopicroside [357.1]	2.08	y=25.511086x-12.646409	0.998	0.97-1000	970	400	80; 03

Table 1.6.4. Concentrations on dry weight basis (ng/mg) of major bioactive compounds in different populations/ cytotypes *Gentiana kurroo*

S.no.	Ploidy status & collection site	Plant part	Swertiamarin	Gentiopicroside	Sweroside
GK1	Diploid, Tulial, 34°37′N, 74°59′E; 2500 m	RS* AP** Flower	5.998 ± 0.196 0.223 ± 0.056 3.998 ± 0.202	3.639 ± 0.202 1.541 ± 0.264 0.339 ± 0.023	0.303 ± 0.021 0.374 ± 0.031 0.399 ± 0.019
GK2	Diploid, Gurinullah, 34°34′ N, 75°44′ E; 2400 m	RS AP Flower	5.338 ± 0.196 0.396 ± 0.026 3.436 ± 0.251	3.149 ± 0.202 0.534 ± 0.025 0.778 ± 0.03	0.402 ± 0.03 0.446 ± 0.031 0.238 ± 0.017
GK3	Diploid, Yosmarg, 33°47′N, 74°39’E; 2400 m	RS AP Flower	4.886 ± 0.313 0.554 ± 0.063 1.284 ± 0.173	3.338 ± 0.266 0.094 ± 0.009 2.053 ± 0.407	0.348 ± 0.04 0.240 ± 0.005 1.006 ± 0.191
GK4	Diploid, Patalwan, 34°35′N, 74◦52′E; 2300 m	RS AP Flower	3.542 ± 0.265 0.349 ± 0.023 2.894 ± 0.245	3.403 ± 0.23 0.480 ± 0.023 0.772 ± 0.116	0.503± 0.036 0.390 ± 0.034 0.280 ± 0.023
GK5	Tetraploid, Razdan 34°34′N, 75°43′E; 3200 m	RS AP Flower	6.721 ± 0.17 1.738 ± 0.054 3.191 ± 0.148	3.260 ± 0.103 1.375 ± 0.077 2.181 ± 0.144	0.364 ± 0.023 0.457 ± 0.027 0.130 ± 0.018
GK6	Tetraploid, Mahadev, 34°10′ N, 75°00′ E; 3000 m	RS AP Flower	6.323 ± 0.241 1.576 ± 0.179 3.026 ± 0.158	3.166 ± 0.165 0.493 ± 0.021 1.655 ± 0.147	0.459 ± 0.029 0.406 ± 0.031 0.424 ± 0.014

*RS=Root stock (including adventitious roots and rhizome); **AP= Aerial parts (including flowering shoot, radical and cauline leaves)

The *in vitro* antitumor activity of the diploid and tetraploid herbal extracts was carried out via standard MTT assay on four different human cancer cell lines i.e. lung (A-549), colon (HCT- 116), prostate (PC-3) and breast (MCF-7) cell lines (Table 1.6.5). The percentage of growth inhibition was observed through preliminary cytotoxicity screening of the extracts and was carried out at 50, 25, 10µg/mL concentrations for 48hours. The methanolic extracts (root stock, flower, aerial part) of diploid *G. kurroo* did not display any significant inhibition against any of the cell lines tested except for breast MCF-7 cell line. On the hand extracts of tetraploid cytotype of the same species depicted significant action against the colon HCT-116 cancer cell line with some minor effect on prostrate PC- 3 and breast MCF-7 cancer cell lines.

Among these, root stock extract was the potent representative with 85% growth inhibition against Colon HCT-116 cancer cell line. DAPI staining experiment was carried out at ic-50 concentration (9µg/mL) to assess the apoptosis in colon cancer cell line. The formation of apoptotic bodies and chromatin condensation were observed suggesting that root stock extract of tetraploid cytotype inhibits growth of HCT-116 cells (Figure.1.6.4).

Table 1.6.5: Cytotoxic activity of various extracts of diploid and tetraploid cytotypes of *Gentiana kurroo* against different human cancer cell lines at 50, 25, 10 µg/mL concentrations. Mean ± SD were calculated on the basis of independent triplicate experiments.

Plant part	Tissue Cell line type Conc. (µg/mL)	Colon HCT-116	Prostrate PC-3	Lung A-549	Breast MCF-7
		Growth inhibition(%)			
Diploid cytotype					
Root stock	50	20 ± 1	20 ± 1	41 ± 1	**69 ± 1**
	25	15 ± 2	7 ± 3	40 ± 2	36 ± 2
	10	1 ± 3	6 ± 3	24 ± 3	22 ± 3
Flower	50	17 ± 1	14 ± 1	50 ± 1	66 ± 1
	25	3 ± 3	9 ± 2	47 ± 2	42 ± 2
	10	0	0	40 ± 3	10 ± 3
Aerial parts	50	6 ± 1	21 ± 1	49 ± 2	35 ± 2
	25	4 ± 1	15 ± 2	35 ± 2	12 ± 3
	10	0	9 ± 2	26 ± 3	**66 ± 1**
Tetraploid cytotype					
Root stock	50	**85 ± 1**	**55 ± 1**	28 ± 2	**55 ± 1**
	25	**80 ± 1**	48 ± 1	22 ± 2	39 ± 2
	10	**53 ± 2**	25 ± 2	16 ± 3	19 ± 3
Flower	50	**57 ± 2**	23 ± 2	20 ± 3	32 ± 2
	25	**59 ± 1**	20 ± 1	**51 ± 1**	19 ± 3
	10	16 ± 3	18 ± 3	4 ± 3	0
Aerial parts	50	32 ± 1	24 ± 2	**52 ± 1**	45 ± 1
	25	11 ± 3	11 ± 3	44 ± 1	25 ± 2
	10	0	7 ± 3	41 ± 2	15 ± 2

The bold values indicate >50% growth inhibition of cells.

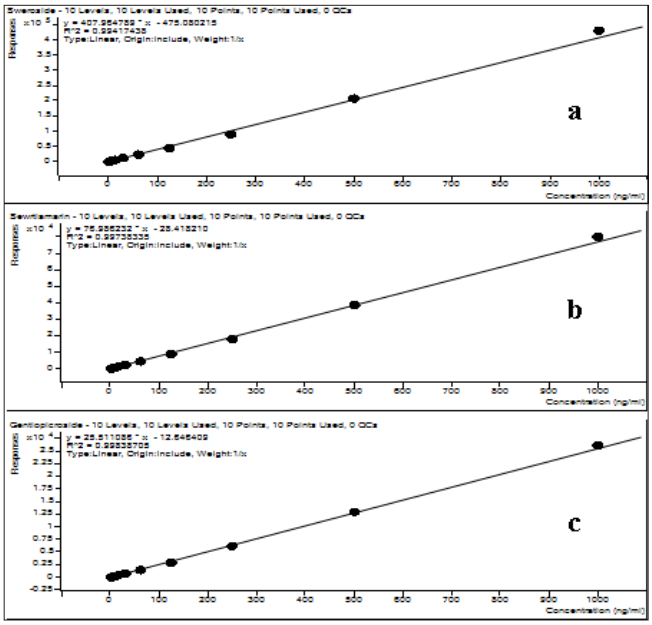


Figure 1.6. 2: Calibration curves of

(a) sweroside
(b) swertiamarin
(c) gentiopicroside

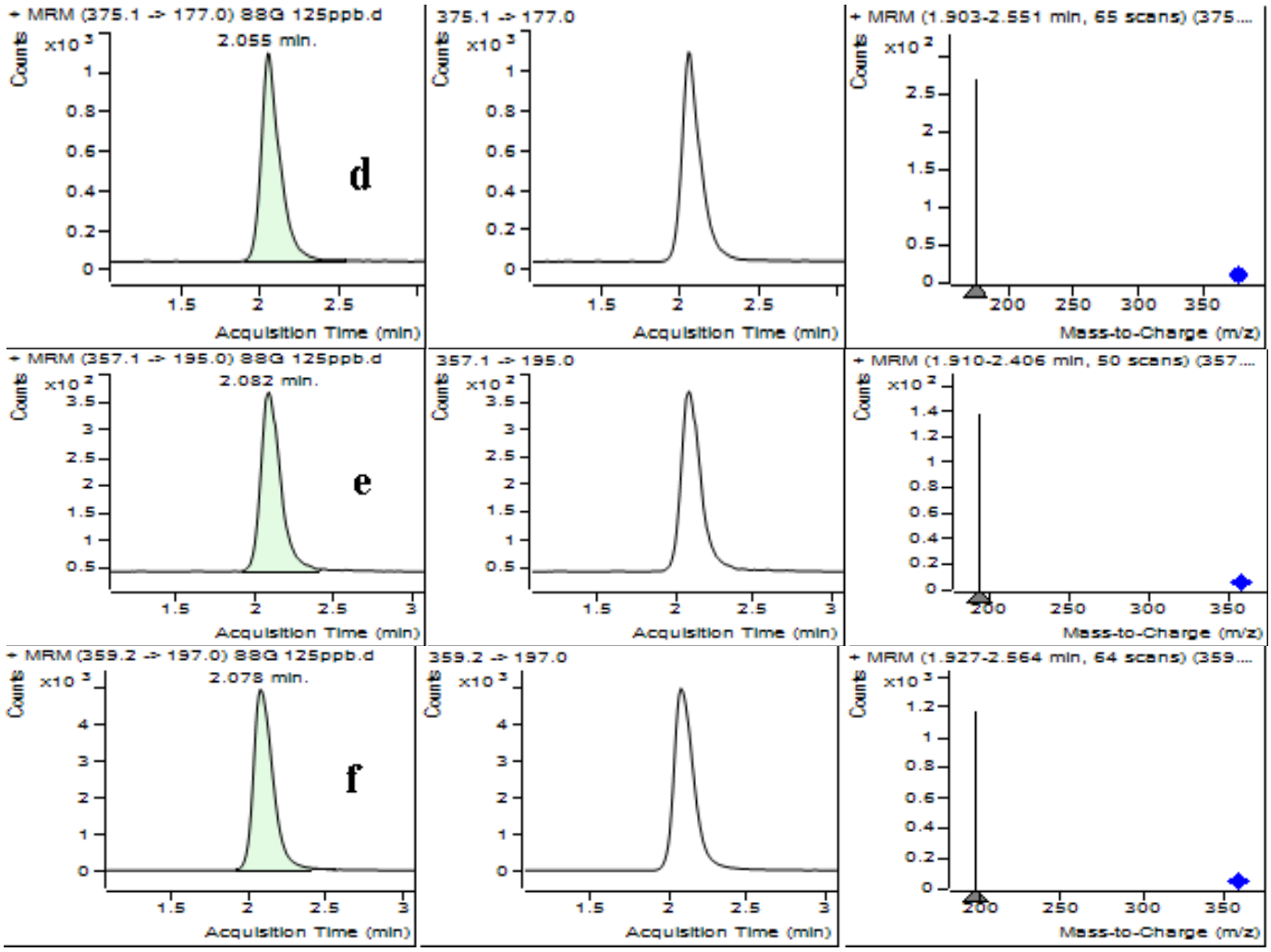
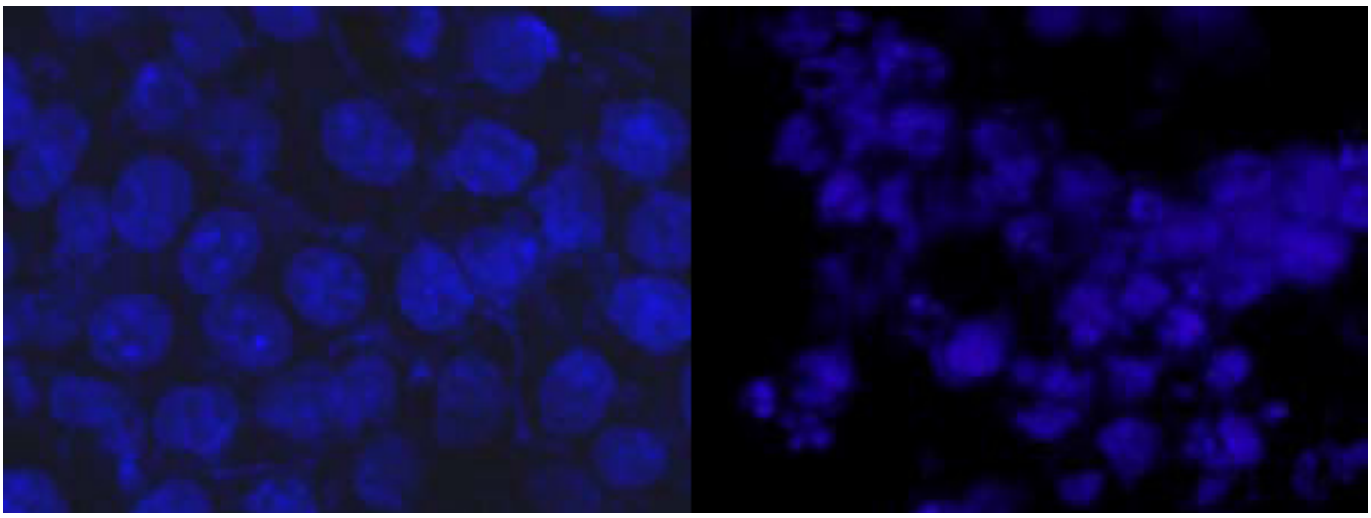


Figure 1.6.3: MRM graph of (a) sweroside, (b) swertiamarin (c) gentiopicroside



Control **9 µM**

Figure 1.6.4: HCT-116 cells were treated with root stock extract (*Gentiana kurroo*) at a concentration of 9µg/mL. Cells were fixed and stained with DAPI (1µg/mL) and visualized on fluorescent microscope (Olympus) at 40 x magnification for nuclear morphology and apoptotic bodies.

In conclusion, the existence of different morphotypes and cytotypes has been re-ordered in *G. kurroo* for the first time. The chemical evaluation (LC- E-MS) of three major bioactive compounds in diverse cytotypes from root stock, flower and aerial parts along different altitudinal gradients presented an appreciable variability in sweroside, swertiamarin and gentiopicroside contents. Besides, the concentrations of bioactive constituents varied among different screened cytotypes for antiproliferative activity. This quantitative deviation is in correspondence with growth inhibition percentage of different cancer cell lines involved. Therefore the study affords an approach for the documentation of elite chemotypes with better pharmacological performance.

1.7 Functional characterization of CYP76B6 and CYP72A1 of unresolved seco-iridoid pathway from *Nothapodytes nimmoniana*.

Gulzar A Rather, Arti Sharma, Deepika Singh, Utpal Nandi, Surrinder K. Lattoo

Seco-iridoids exhibit a diverse array of intriguing structural frameworks with versatile pharmacological properties. *Nothapodytes nimmoniana* is a richest source of a complex pentacyclic pyrroloqinoline alkaloid camptothecin (CPT). It is produced *via* an intricate seco-iridoid pathway whose biosynthetic and regulatory mechanism is still unresolved. Moreover, total synthesis of CPT remains a daunting challenge at the industrial level. Biotechnological production is hampered as few attempts have been made to uncover the enzymatic mechanism involved in CPT biosynthesis. In the present investigation two crucial cytochrome p450s, CYP76B6 and CYP72A1 of seco-iridoid pathway were functionally characterized from *N.nimmoniana* (Figure 1.7.1). The full length *Nn*CYP76B6 and *Nn*CYP72A1 have open reading frames of 1497 and 1566 bp encoding 499 and 522 amino acid residues, respectively.

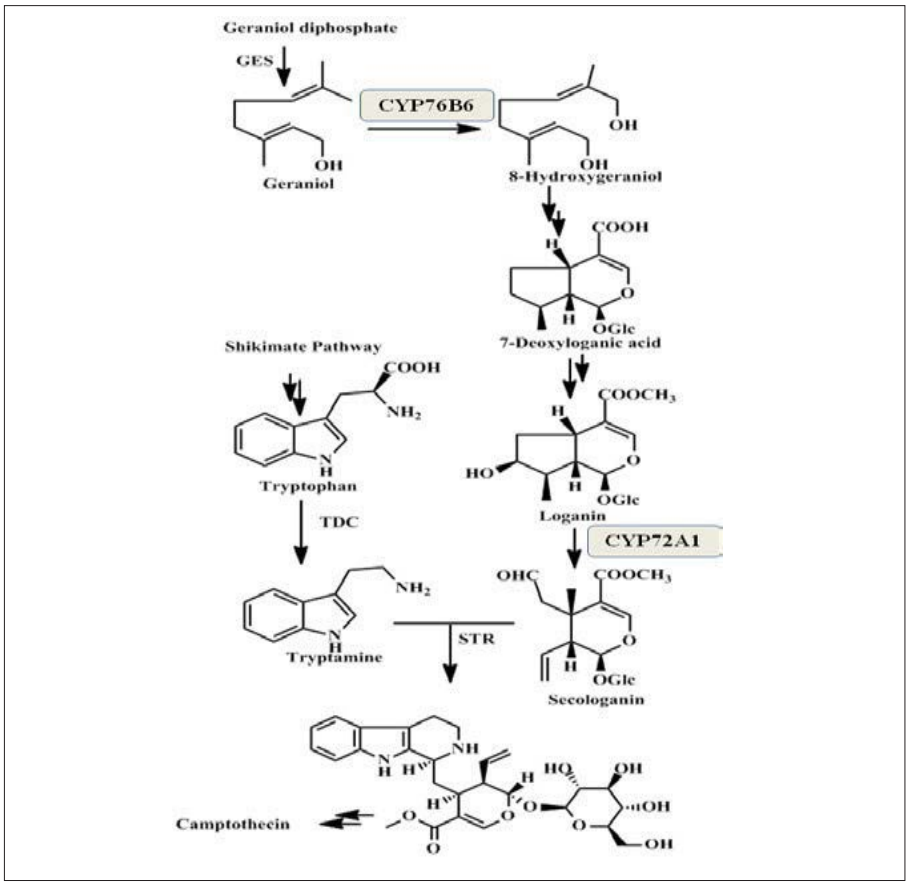


Figure 1.7.1: Putative upstream camptothecin biosynthetic pathway: GES, geraniol synthase; CYP76B6, geraniol 8-hydroxylase; CYP72A1, Secologanin synthase; TDC, tryptophan decarboxylase; STR, strictosidine synthase. Double arrows represents the multiple steps between the intermediates.

To examine the catalytic function of *Nn*CYP76B6 and *Nn*CYP72A1 their open reading frames were transformed in pYeDP60 expression vector and expressed under the control of galactose inducible promoter in *Saccharomyces cerevisiae* Wat11 strain. Expression analysis was carried out at different time periods and the highest expression level for each of the generated constructs was observed with 1M galactose at 18 h and 30 °C. Optimized expression was used as a criterion for isolation of microsomes. Gas chromatography and mass spectrometric analysis revealed that microsomal extract rapidly and efficiently converts geraniol into 8- hydroxy geraniol with a retention time of 19.87 min. as that of the reference standard 19.90 (Figure 1.7.2).

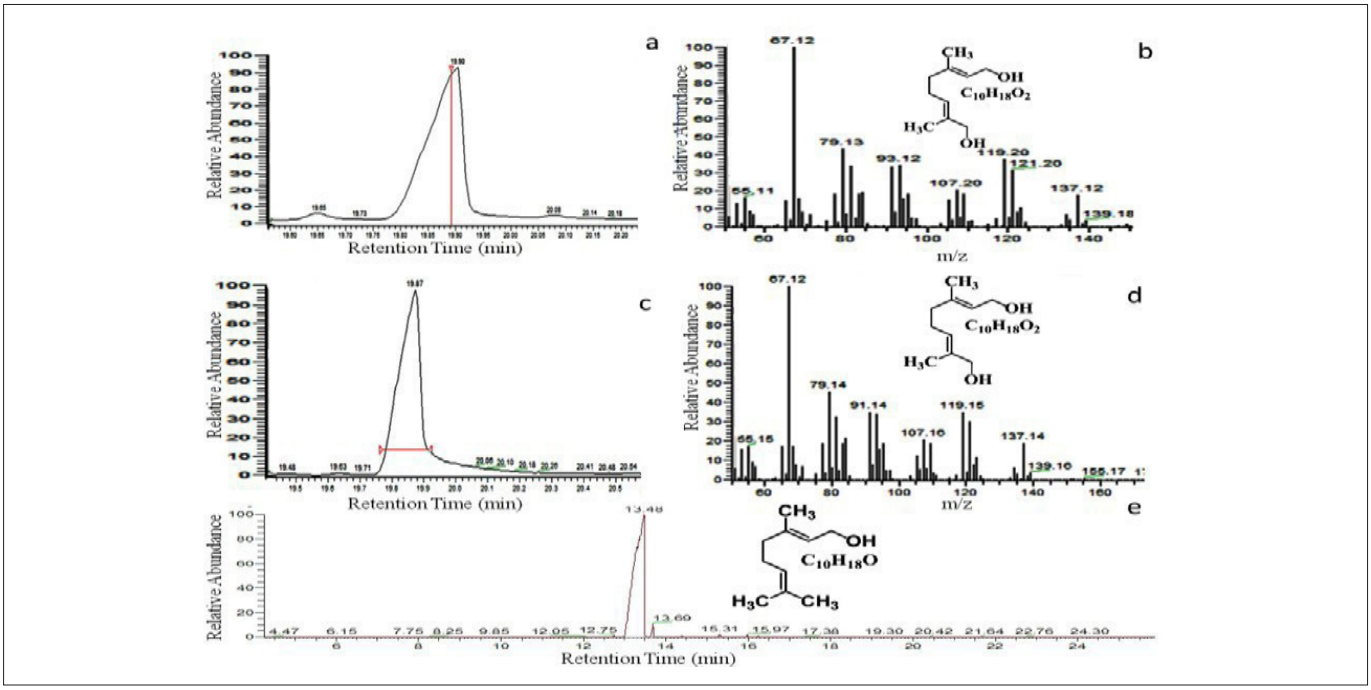


Figure 1.7.2: GC/MS analysis: Metabolism of geraniol by CYP76B6 expressed in yeast and assayed as microsomal protein incubation with geraniol and NADPH. GC-MS chromatogram and MS fragmentation spectra of authentic standard geraniol 8-hydroxylase (a, b). GC-MS chromatogram and MS fragmentation spectra of geraniol 8- hydroxylase generated in enzymatic reaction by *Nn*CYP76B6 (c, d). Chromatogram of geraniol incubated with microsomal preparations from yeast strain transformed with empty vector (e).

While the LC MS/MS analysis was performed to determine secologanin and loganin in the reaction products of *Nn*CYP72A1 where secologanin and loganin was eluted at the retention time of 0.3 and 0.8 min, respectively, as shown in Figure 1.7.3. However, no activity was observed in yeast transformed with the empty vector as control.

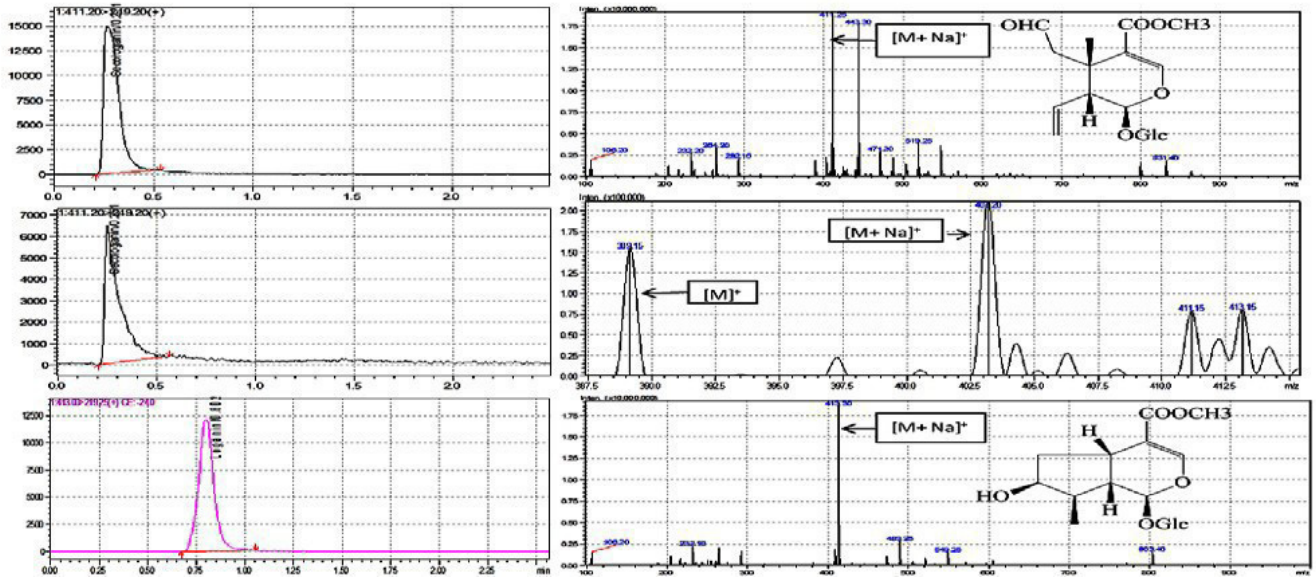


Figure 1.7.3 LC-MS/MS analysis. Multiple reaction monitoring (MRM) chromatograms and Mass spectrometry spectra of the standard compounds of secologanin (a, b). Multiple reaction monitoring (MRM) chromatograms and Mass spectrometry spectra of secologanin which was eluted at about the retention time of 0.3 and 0.8 min and precursor/product ion transition at m/z 411.2/249.2 and 413.0/219.3 for secologanin and loganin respectively.

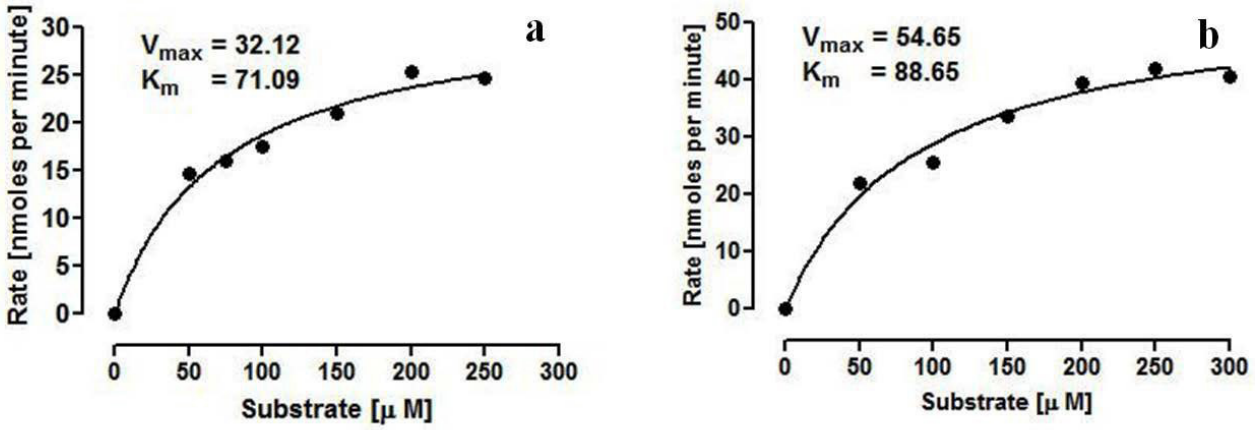


Figure 1.7.4: Kinetic study of NnCYP76B6 and NnCYP72A1. A, Michaelis-Menten plots of NnCYP76B6 and NnCYP72A1 (a,b). The kinetic parameters Km and Vmax were calculated by nonlinear regression analysis using GraphPad Prism 6 software. The activity of NnCYP76B6 and NnCYP72A1 was assayed in 20mM Citrate phosphate buffer. The loganin and geraniol were used as substrates, and the production of 8- hydroxygeraniol and secologanin was quantified as activity (pmol/min).

Further, the purified microsomal proteins of CYP76B6 and CYP72A1 were used for investigating the kinetic properties. The enzyme was kept constant whereas the concentration of the substrate was taken in increasing order. The V_{max} values of CYP76B6 and CYP72A1 for geraniol and loganin, as calculated by non-linear regression analysis, were 32.12 and 54.65 nmol min^{-1}, whereas the apparent K_m values were 71.09 and 88.65 μM, respectively, (Figure 1.7.4, a) explained by Michaelis-Menten plots.

Furthermore, phylogenetic analysis of *Nn*CYP76B6 and *Nn*CYP72A1 were performed for studying evolutionary relationship. A total of 21 amino acid sequences of CYP76B6 and CYP72A1 were retrieved from NCBI belonging to 11 different families. The CYP76B6 and CYP72A1 phylogeny was reconstructed with MEGA-7 software based on neighbor joining method. The CYP76B6 and CYP72A1 are grouped in accord with the amino acid correspondence, constituting two separate phylogenetic clusters. Phylogenetic analysis revealed that *Nn*CYP76B6 share most like common ancestor with recently identified G 8-H from *Camptoteca accuminata* and *Picrorhiza kurroa*. The rapid diversification of CYP71 clan is determinant for the species-specific terpenoid profile. In addition, CYP72A1 analysis revealed that it is closely related to cytochrome of *C.accuminata* as compared to other species. (Figure 1.7.5). Moreover, the divergence of CYPS resulted in chemical diversification of secondary metabolites that has dramatically expanded their role in plant adaptation, protection and, in the broadest sense, interaction of the plant with its biosphere.

Overall, the functional

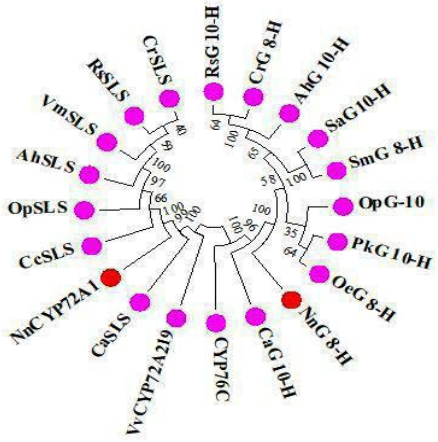


Figure 1.7.5: Phylogenetic tree of NnCYP76B6 and NnCYP72A1: The phylogenetic analysis was performed using the MUSCLE program and MEGA7 software and the tree was reconstructed with neighbor-joining method. The numbers on the nodes indicate the bootstrap values after 1,000 replicate. The analysis involved the alignment of 20 amino acid sequences that were chosen by analyze the available data related to CYP76B6 and CYP72A1 genes from the NCBI data base

characterization of *Nn*CYP76B6 and *Nn*CYP72A1 will be insightful to unravel the hitherto unresolved mechanism and regulation of CPT biosynthesis. It may serve as prognostic tool for metabolic engineering towards enhanced CPT production.

1.8 Role of jasmonate-responsive transcription factor *Ws*MYC2 in regulating the terpenoids biosynthesis in *Withania somnifera* (L.)Dunal

Arti Sharma, Gulzar A. Rathar, Prashant Misra, Surrinder K. Lattoo

Withania somnifera, belongs to Solanaceae family, is a reputed multipurpose medicinal plant from the Ayurvedic medical system used for the treatment of debility, emaciation, inhibition of COX-2 enzyme in various tumour cell lines, Notch-1, NFkB in cancer cells and more recently for the treatment of bronchitis, asthma, ulcerssenile dementia and reverses the pathology and behavioural deficits found in Alzheimer's d i s e a se models etc. Not surprisingly, it has been dubbed the 'Indian ginseng'. It produces 40 different withanolides, 12 alkaloids and several sitoindosides. Although in high demand, these intriguingly valuable compounds accrue in trace amounts in *W. somnifera*. While, much of studies have been done to unravel the biosynthetic pathway, little is known about its regulatory component. Regulatory components include transcription factors that play central role in regulating genes involved likely in all aspects of plant growth and development including secondary metabolism. Several co- ordinately regulated biosynthetic genes are affected at their transcriptionallevel by plethora of transcription factors and result in increased metabolite production. Therefore, over-expression of key pathwaygenes of withanolides biosynthesis through specific transcription factors holds immense promise for improving the withanolides production. Against this backdrop, a jasmonate responsive MYC2 transcription factor was identified and functionally characterized in *W. somnifera*. YC2 transcription factor modulates the biosynthesis of various metabolites by recognizing and binding to the G-box sequence "5′- CAC(G/A) T(G/T)-3′" present in the upstream region (promoter) of several biosynthetic genes. It is also considered as the regulatory hub in JA-signalling pathway channelizing plant growth and development in response to various exogenous as well as endogenous signals.

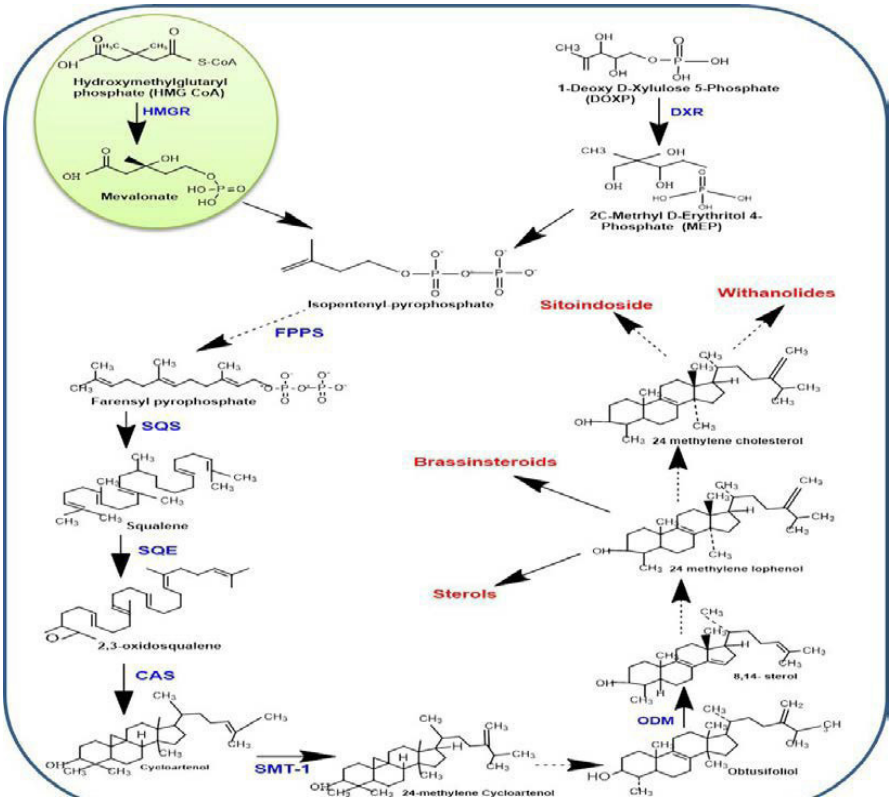


Figure 1.8.1: Overview of proposed withanolide biosynthesis pathway. The abbreviations of the pathway intermediates are as follows: *DXS*: 1-deoxy-D- xylulose 5-phosphate synthase; *DXR*: 1-deoxy-D- xylulose-5-phosphate reductase; F*PPS:* Farensyl pyrophosphate; *SQS*: squalene synthase; *SQE*: squalene epoxidase; *CS*: cycloartenol synthase; ODM: methylase; 24-methylene cholesterol is the major compound that leads to the synthesis of withanolide biosynthesis branch; sterol biosynthesis branch; or sitoindoside biosynthesis branch. One step is represented as dark s*ingle arrows* whereas multiple steps are represented by dotted arrows.

In the present investigation, degenerate primers and the RACE PCR strategy were adopted to isolate the complete coding sequences of *Ws*MYC2 transcription factor. An open reading frame of 2060 bp was obtained which encodes 688 aminoacids protein and showed 79-94% similarity with MYC2 genes of *Capsicum annum* (GenBank accession number PHT92981.1) *Solanum lycopersicum* (GenBank accession number AGZ94899.1) and *Nicotiana tabacum* (GenBank accession number NP_001312960.1). The full-length nucleotides sequence of *Ws*MYC2 was submitted to NCBI GenBank under accession number MG434696. The ORF of *Ws*MYC2 was subjected to online Expasy tool that predicted its molecular weight to be 7.5 kDa with calculated isoelectric point (pI) value of 5.92. Further, the aminoacid sequence was subjected to NCBI conserved domain search tool that revealed the presence of bHLH-MYC_N (pfam14215) and HLH (cd00083) as the superfamily conserved domains (Figure 1.8.2). However, ConSurf server showed the presence of various conserved residues in *Ws*MYC2 (Figure 1.8.3).

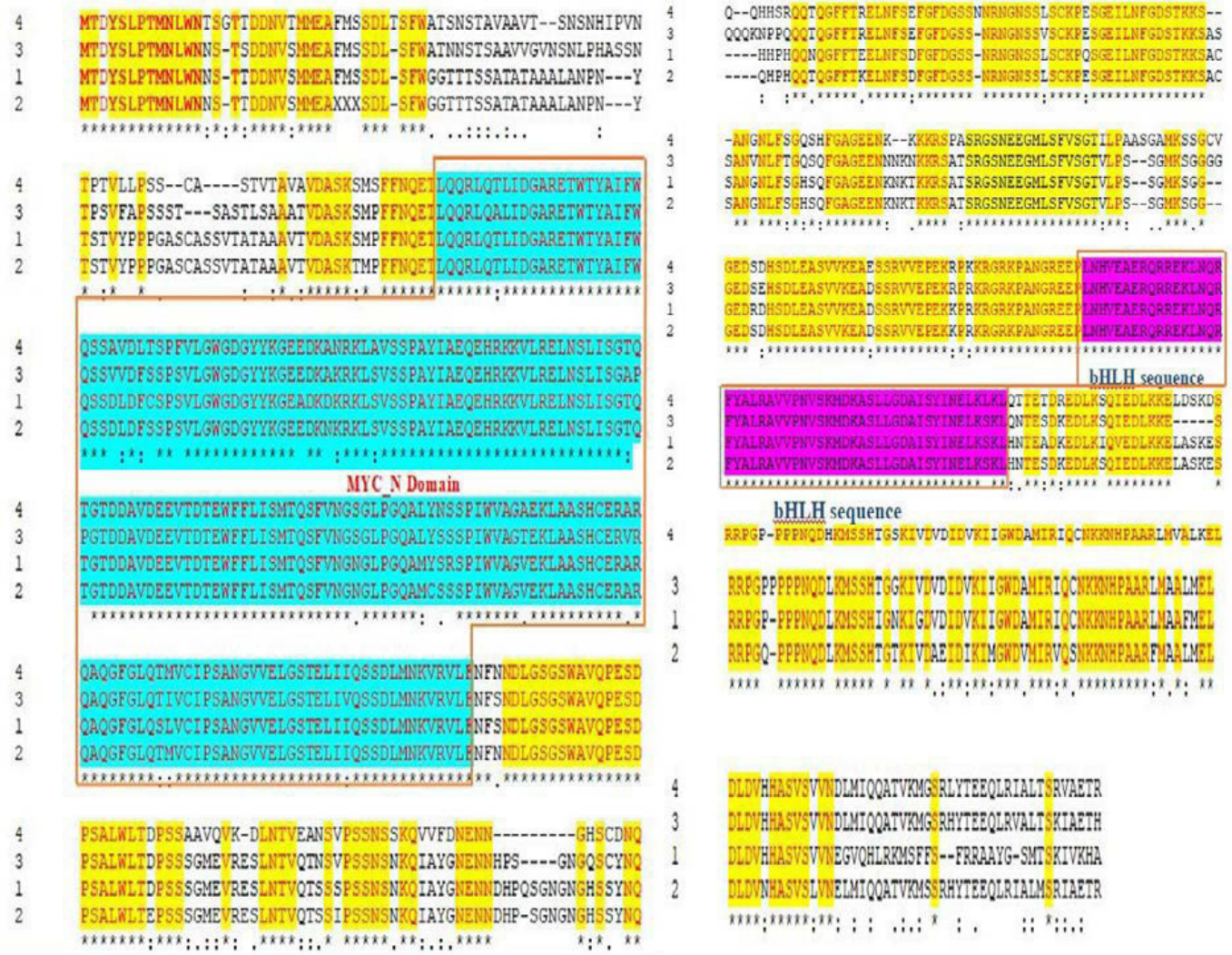


Figure 1.8.2: Multiple sequence alignment of deduced amino acid sequences of *Ws*MYC2 with its respective homologs from different plants using Multalign tool for the comparative analysis. For analysis, sequences were retrieved from NCBI database from four plant species of Solanaceae family: *Withania somnifera* (*Ws*MYC2: HM03679), *Capsicum annuum* (XP_016573059.1), *Solanum lycopersicum* (NP_001311412.1), *Nicotiana tabacum* (NP_001312960.1). Conserved residues are shadedyellow.

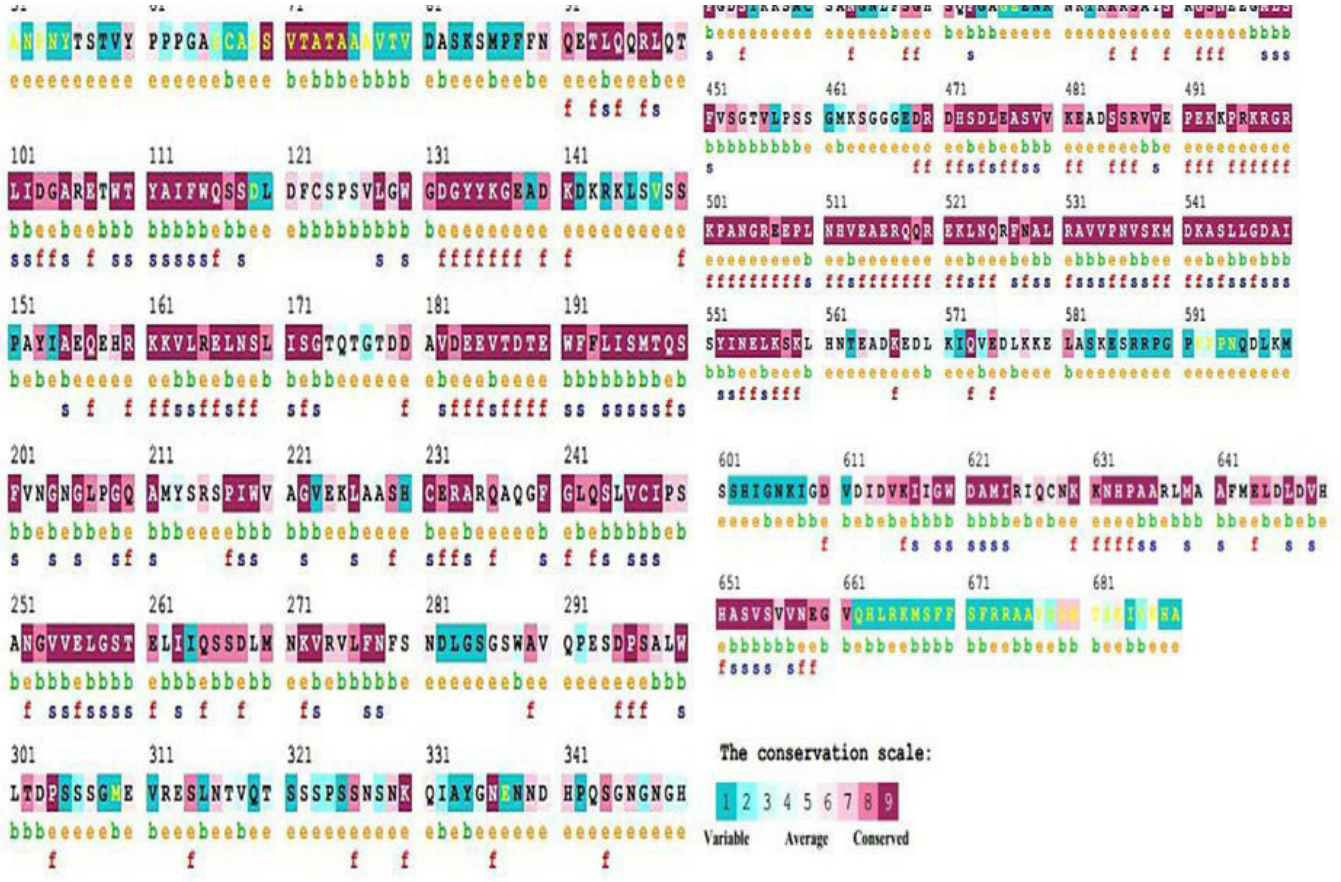


Figure 1.8.3: Prediction of conserved residues of *Ws*MYC2: Analysis of conserved residue of *Ws*MYC2 by using ConSurf and ConSeq web servers. Conserved residues from variable to conserved are presented in blue (1) to purple (9). Abbreviations used are: e= exposed residue according to the neural-network algorithm; b= buried residue according to the neural-network algorithm; f= predicted functional residue (highly conserved and exposed); s= predicted structural residue (highly conserved and buried); and X= insufficient data, the calculation for this site was performed on less than 9% of the sequences.

These entire features substantiate that *Ws*MYC2 belongs to the basic-helix-loop- helix (bHLH) superfamily of transcription factors that mediate the regulation of various secondary metabolites. Furthermore, for the prediction of the secondary structure of *Ws*MYC2, the Self- Optimized Prediction Method with Alignment (SOPMA) online tool was used which revealed *Ws*MYC2 is predominantly an α-helical protein with respective percentage of α- helix (37.21%) and random coils (40.55%), whereas β-turns (4.65%), and extended strands (17.59%) are also present (Figure 1.8.4a). Additionally, Phyre2-based homology modelling was performed to generate the three-dimensional protein model of *Ws*MYC2. The modelling was achieved with 90% confidence level using single highest scoring crystal structure of MYC3 as template having the percentage identity of 80% when 620 residues were aligned for *Ws*MYC2 which gave the coverage score of 98% (Figure 1.8.4b) (Kelley *et al.*, 2015) Furthermore, to analyze the evolutionary degree of relationship, MEGA7.0 software was used. Around 20 amino acid sequences were selected from different plant species. Results showed that Solanaceae MYC2 members exhibited a different evolutionary history. Among different members of Solanaceae family, *N. tabacum* and *N. attenuate* segregate and constitutes a separate clade while *Solanum lycopersicum, W. somnifera* and *C. annum* belong to same clade that revealed the close relatedness among them. Therefore, *Ws*MYC2 showed high homology with MYC2 of *C. annum* and *S. lycopersicum*, all three belonging to the same family (Figure1.8.5).

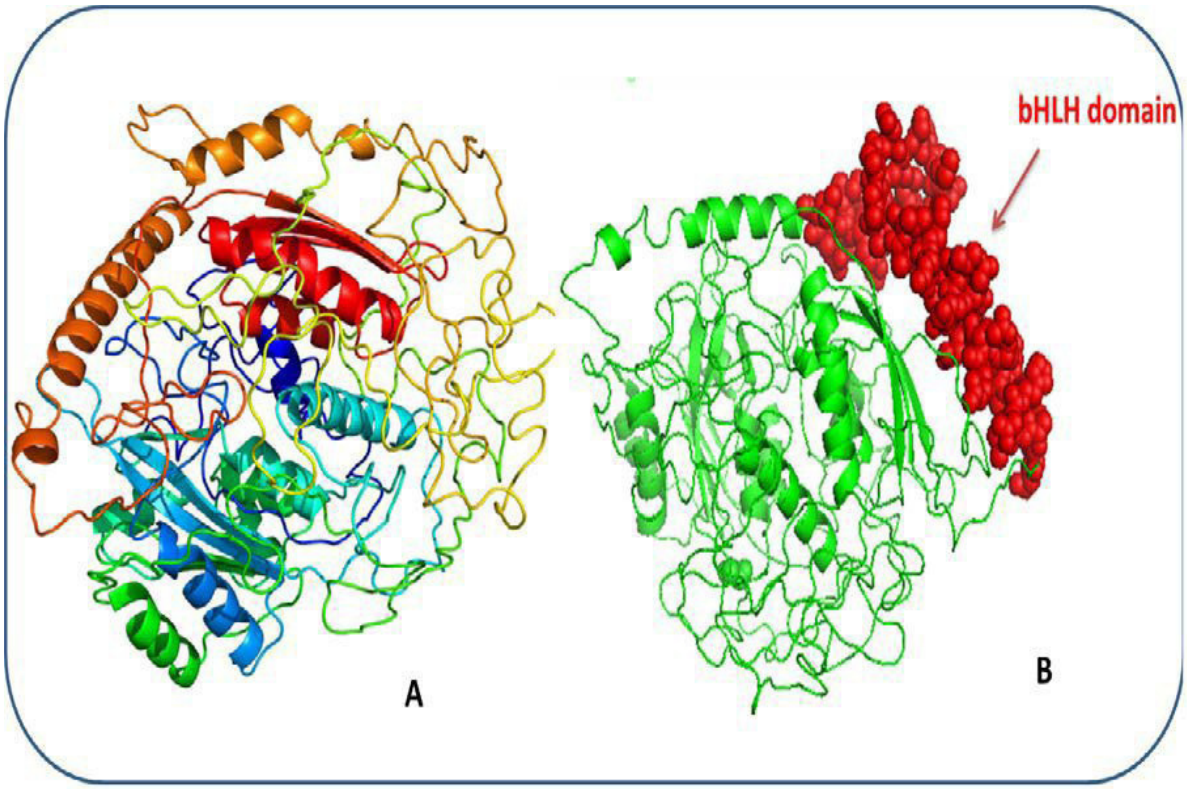


Figure 1.8.4: Phyre2 server based homology modelling of *Ws*MYC2 for the prediction of three dimensional structure. A: Cartoon model of the 3-D structure of *Ws*MYC2 as predicted by Phyre2 using crystal structure of transcription factor MYC 3(5-242) fragment in complex with jaz9(218-2 239) as template. B: Predicted bHLH domain (shown in red) binding sites as predicted by prosite and SMART servers. The site is rich in aliphatic amino acids and is characterised by EPLNHVEAERQQREKLNQRFNALRAVVPNVSKMDASLLGDAISYINEL.

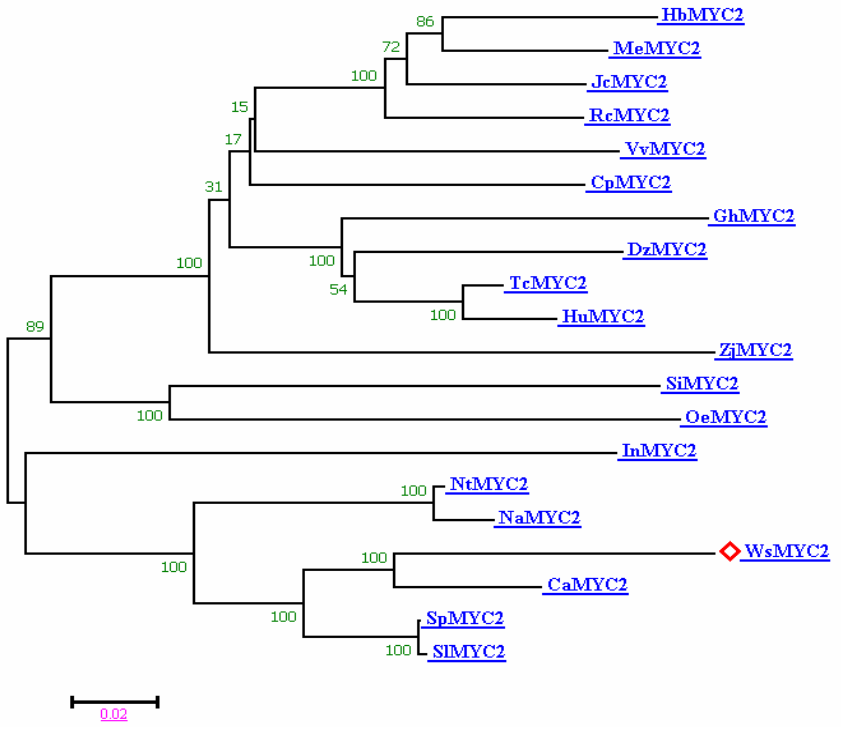


Figure 1.8.5: The evolutionary tree for *Ws*MYC2 was constructed using MUSCLE program of MEGA 7.0 software. The degree of evolutionary relatedness was calculated by aligning amino acid sequences of 20 MYC2 genes belonging to 12 plant families. Poisson correction method was used to estimate the evolutionary distances among the chosen plant species. The numbers on the nodes indicate the bootstrap values after 100replicates.

The *Ws*MYC2 transcription factor was further analyzed at the transcription level to evaluate its role in the differential accumulation of withanolides. The expression pattern of *Ws*MYC2 revealed its highest expression in young leaves followed by inflorescence and berries while roots showed the lowest expression (Figure 1.8.6a). Additionally, phytochemical analysis revealed that young leaves accumulated highest amount of withaferin A (18.137µg/mg on dry weight basis [DWB]) as compared to stem (14.023 µg/mg DWB), inflorescence (9.648 µg/mg DWB), and berries (0.112 µg/mg DWB) (Figure 1.8.6b).

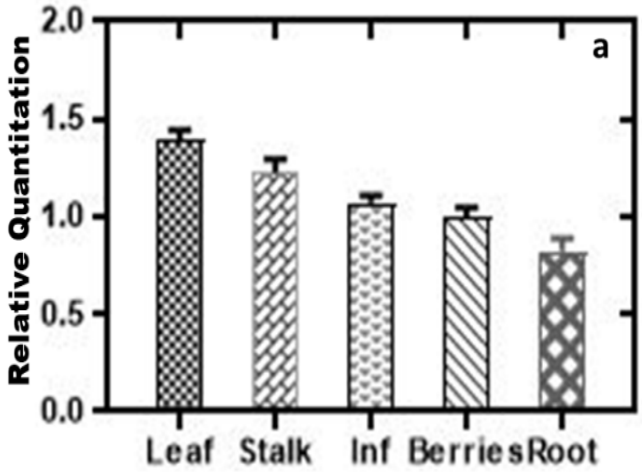


Figure 1.8.6: a) Tissue- specific quantitative real time expression analysis. Quantitative detection of the expression of *Ws*MYC2 in different parts (leaf, stalk, inflorescence, berries and roots) of *W. somnifera*. Obtained data were compared and examined with analysis of variance (ANOVA). The values are means with standard errors indicated by *bars*, representing three technical replicates. Differences were scored as statisticalsignificance at *p* 0.05 (*) and *p* 0.01 (**).

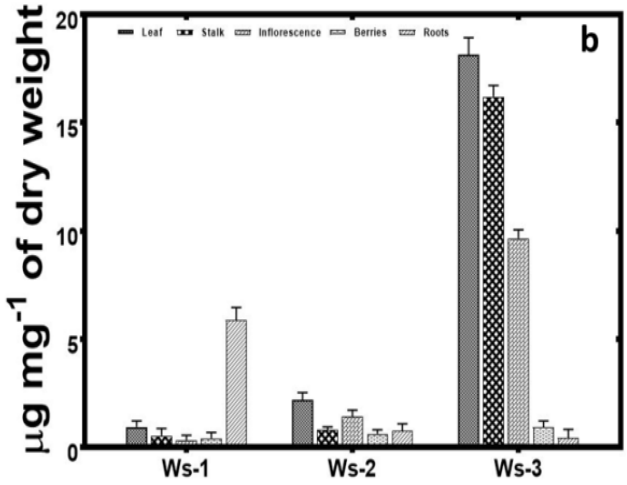


Figure 1.8.6b) Phytocemical analysis of withanolides content in different parts (leaf, stalk, inflorescence, berries and root) of *W. somnifera*. Variation in three key withanolides viz. withanolide A (WS-1), withanone (WS-2) and withaferine A (WS-3) was confirmed by HPLC. All values obtained were means of triplicate with standard errors. Differential accumulation of WS-1, WS-2 and WS-3 was statistically significant at *p < 0.05, **p < 0.01 and ***p < 0.001 levels.

Moreover, for the investigation of the role of *Ws*MYC2 in regulating the expression of triterpenoid biosynthetic genes, transient over-expression assay was performed. *W. somnifera* leaves were transformed by *A. tumefaciens* Gv3l01 strain harboring empty pBI121 vector and pBI121-*Ws*MYC2 construct under the control of 35S-CaMV promoter (Figure 1.8.7a). Transformed leaf samples were harvested after 2nd and 4th day of post-infiltration for GUS assay, qRT-PCR and chemoprofiling. Histochemical GUS assay of transformed leaves was performed after 12 h, 24 h and 48 h of post-infiltration. Harvested infiltered leaves showed blue color only after 48 h compared to control (Figure 1.8.7b).Therefore, 2nd day (after 48 h) was chosen for further analysis. qRT-PCR analysis of transformed leaves harvested at 2nd and 4th day of post- infiltration showed 2.7-fold and 2.2-fold increase in *Ws*MYC2 transcript levels respectively as compared to control (Figure 1.8.8a and 8b). Moreover, phytochemical analysis of transformed leaves showed a significant increase in withanolides content. The highest accumulation of withaferin A (2.984 fold) was observed in overexpressed MYC2 transformed leaves followed by withanolide A (2.93 fold) and withanone (2.81 fold) in comparison to control (Figure 1.8.8c and 1.8.8d). Similarly, stigmasterol accumulation was also analysed in the transformed

leaf samples using HPLC method. A 2.03 fold increase in stigmasterol was detected in transformed leaf samples (Figure 1.8.8e and 1.8.8f).

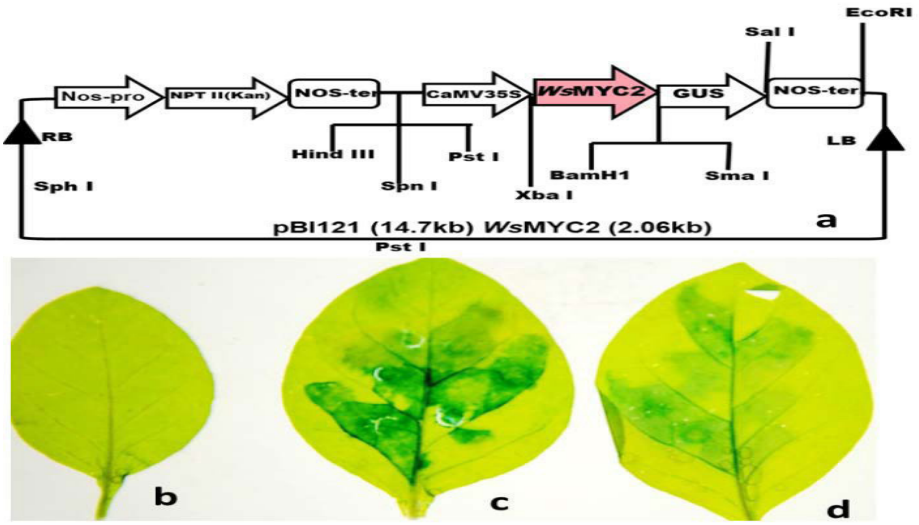


Figure 1.8.7: a) Construct of *Ws*MYC2 in pBI121 under the control of 35S-CaMV promoter for transformation in *Agrobacterium tumefaciens* Gv391 strain used for agroinfilteration. Histochemical GUS assay in control leaf (b) and in agroinfiltered leaf (c and d) for confirmation of expression. Infiltered leaf showed blue colour in response to the 5- bromo, 4-chloro, 3-indolyl glucuridine (X-GlcU) substrate for glucuridine synthase confirming the expression after 48 h.

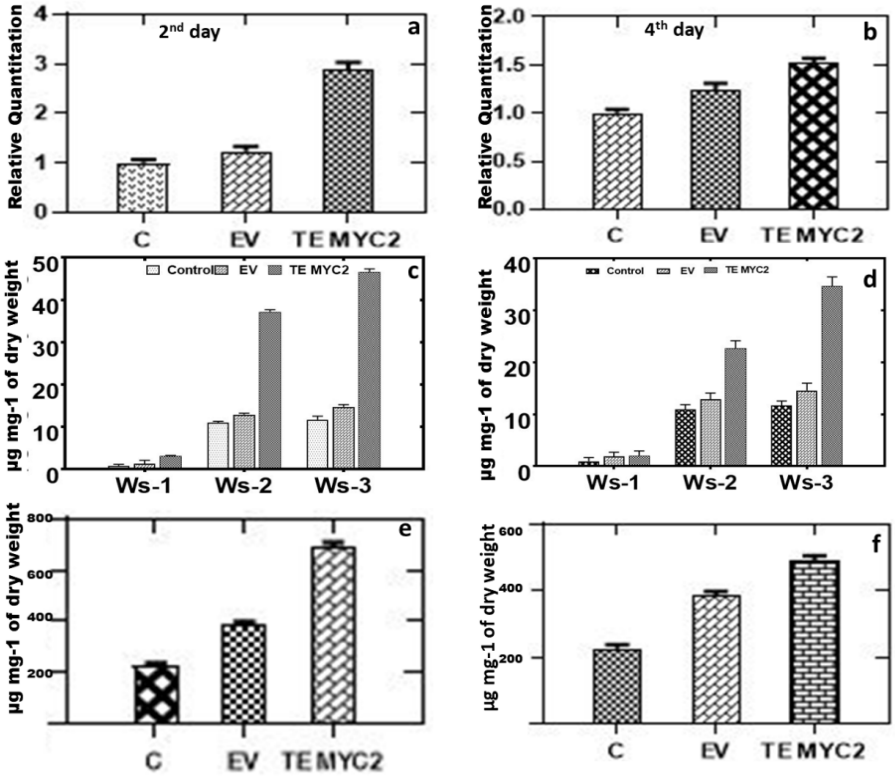


Figure 1.8. 8: Transient over-expression of *Ws*MYC2 in *W. somnifera* leaves. (a, b) qRT-PCR expression analysis of *Ws*MYC2 in leaves transformed with *Ws*MYC2-pBI121 construct after 2nd and 4th day (c, d) HPLC analysis of transformed leaves for elevated levels of withanolides showing 2.34 fold increase in WS-1 levels, 2.8 fold increase in WS-2 levels and 2.984 fold increase in WS-3 levels compared to control after 2nd day and 1.8, 2.5 and 2.68 fold increase in WS-1, WS-2 and WS-3 levels after 4th day (e, f) HPLC analysis of transformed leaves showing 2.03 and 1.81 fold increase in stigmasterol on 2nd and 4th day respectively.

In addition to these, artificial micro RNA (aMIR) mediated down-regulation of *Ws*MYC2 was also performed to confirm its functional role in withanolides biosynthesis. *A. tumefaciens* Gv391 strain harbouring aMIR constructs (aMIR1, aMIR2, aMIR3) were agro-infiltered in *W. somnifera* leaves. After agro-infiltration samples were harvested at 2nd and 4th day of the treatment for RT-PCR analysis vis-à-vis withanolides (WS-1,WS-2,WS-3) content. From qRT PCR analysis, aMIR2 construct was found to be most effective as compared to aMIR1 and aMIR3 constructs in down- regulating the transcript levels of *Ws*MYC2 (Figure 1.8.9a and 9b). aMIR2 construct showed 0.62 and 0.34 fold reduction in *Ws*MYC2 transcript levels on 2nd and 4th day respectively. Similarly aMIR3 showed 0.57 fold (2nd day) and 0.29 fold (4th day) reduction in transcript levels of *Ws*MYC2 whereas aMIR1 showed 0.43 fold (2nd day) and 0.25 fold (4th day) reduction as compared to control. Further, chemo- profiling of aMIR transformed leaves showed 0.43 fold decrease in withaferin A, 0.52 fold in withanolide A and 0.47 fold in withanone content was observed at 2nd day (Figure 1.8.9c). The contents were slightly recovered ~20-30% after 4th day (Figure 1.8.9d). Similarly, chemo-profiling of filtered leaves also showed a reduction of 0.475 fold in stigmasterol content at 2nd day (Figure1.8.9e).

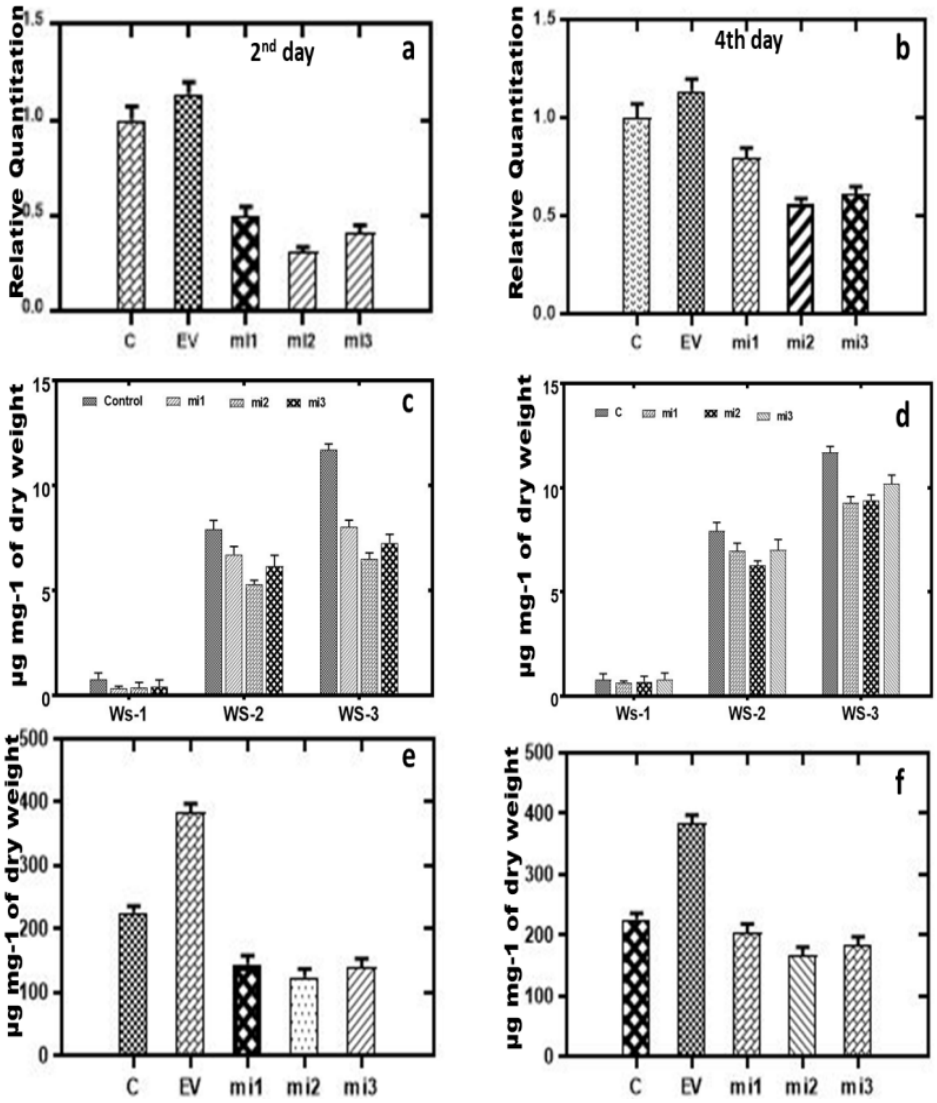


Figure 1.8.9: aMIR mediated suppression of *Ws*MYC2 in *W. somnifera* (a, b) aMIR (aMIR1-*Ws*MYC2, aMIR2- *Ws*MYC2 and aMIR3- *Ws*MYC2) constructs in leaves showing reduced mRNA transcript levels of *Ws*MYC2 compared to control after 2nd and 4th day of agro- infiltration; **(c, d)** Analysis of reduced levels of withanolides in transformed leaves via HPLC on 2nd and 4th day **(e, f)** HPLC analysis of reduced levels of stigmasterol in agro-infiltered leaves.

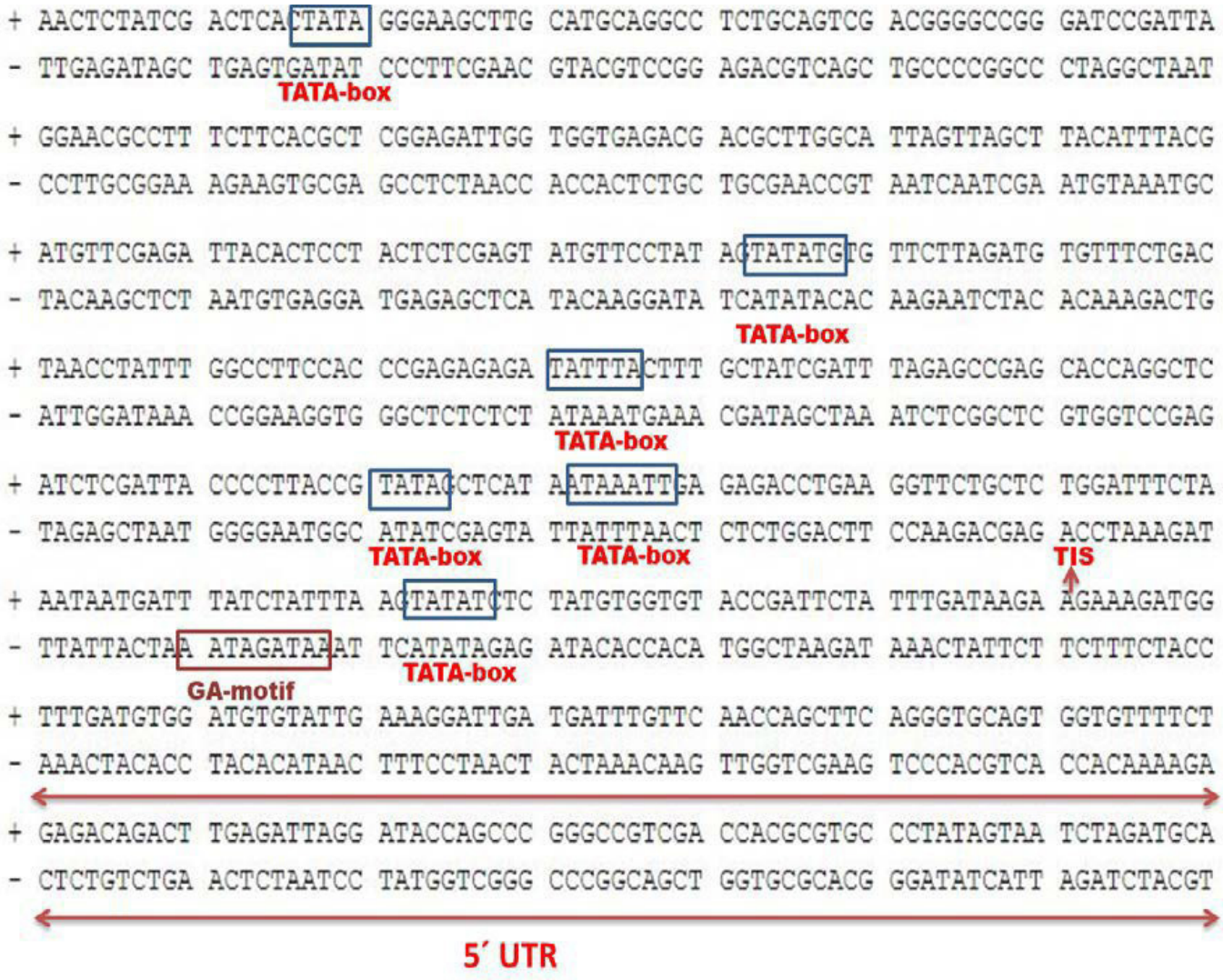


Figure . 1.8.10: Promoter region of WsMYC2 showing the presence of various putative cis-regulatory components.

To study the transcriptional regulation of *Ws*MYC2, its upstream 5′ flanking region was isolated and *in silico* tools were used to examine and analyze the presence of various putative *cis*-regulatory which revelaed the presence of six MYB binding region, three E-boxes, five W-boxes, GA_3 responsive element, light- responsive, hormone-responsive elements and various otherstress-related elements. These regions are implicated in the control of *Ws*MYC2 transcription factor to accomplish diverse functions in terms of regulating other genes and various transcription factors.Elicitor treatments offer the distinctive clue regarding the inducible/repressible nature of the promoter. Therefore, to understand the regulatory nature of *Ws*MYC2 in response to MeJA, SA and GA_3 elicitors, *Ws*MYC2 transcript levels were examined and further corroborated with the metabolite accumulation. MeJA elicitation resulted in higher accumulation of withaferin A when compared with the effect of SA and GA_3 treatments (Figure 1.8.11).

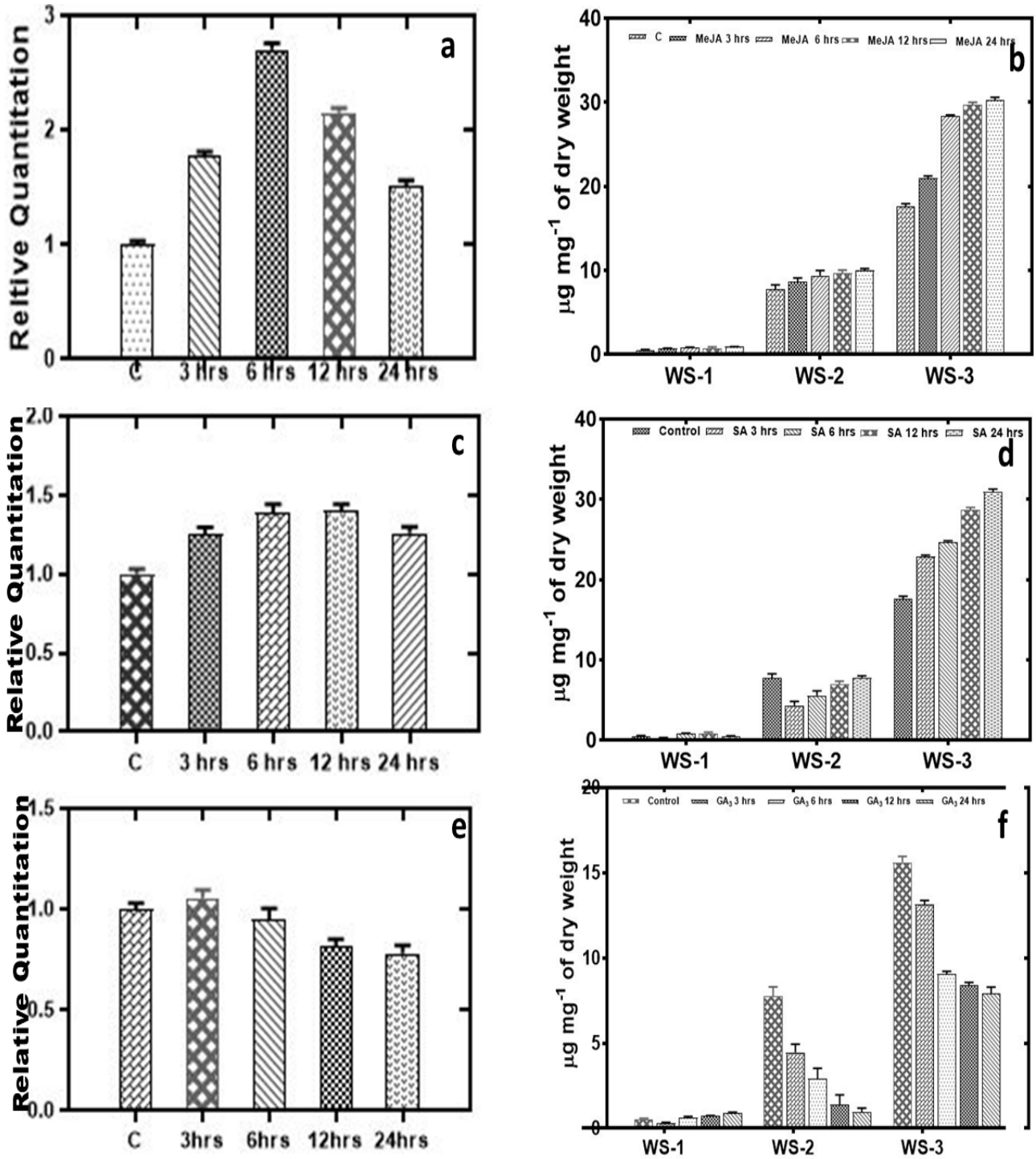


Figure 1.8.11: Transcript profiles of *Ws*MYC2 in response to (a) MeJA (0.1 mM), (c) SA (0.1 mM) and (e) GA_3 (0.1 mM) elicitor treatments. Time courses profiling of *Ws*MYC2 in response to elicitors and actin was used as endogenous control. Similar results were obtained in triplicates; error bars indicate standard deviation of the mean. HPLC profile of withanolides in response to elicitors (b) elevated levels of withanolides in repose to MeJA (3, 6, 12 and 24 h) (d) elevated levels of SA (3, 6 12 and 24 h) (f) decline in withanolides content in response to GA_3 (3, 6, 12 and 24 h)

1.9 Full Length cloning and in-silico characterization of five genes (Squalene synthase, squalene epoxidase, β amyrin synthase, CYP88D6, CYP72A154) related to glycyrrhizin biosynthesis.

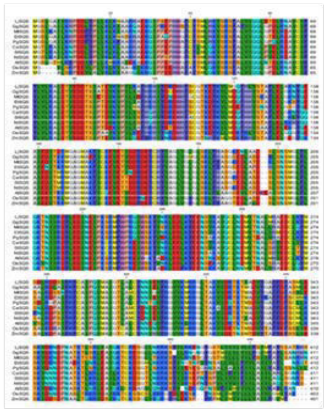
Pankaj Pandotra, Malik Muzafar Manzoor, Pooja Goyal, Prashant Mishra, Ajai P Gupta, Ram Vishwakarma & Suphla Gupta

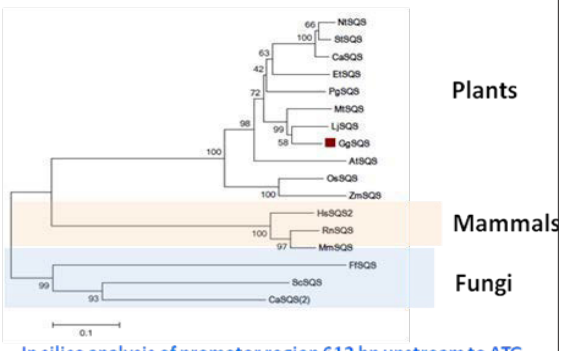
The genus Glycyrrhiza (liquorice/ licorice) is a perennial herbal legumes commonly used in Chinese and Japanese traditional and asnatural sweetener. Experimental and clinical studies have demonstrated liquorice having wide range of pharmacological properties such as anti- inflammatory, antiviral, antimicrobial, antioxidative, antidiabetic, antiasthma and anticancer activities. Triterpene saponins and flavonoids are predominantly present in the licorice root and major ly contribute to the various bioreactivities. Nearly 300 flavonoids and more than 20 triterpenoids have been isolated from liquorice species. Despite the commercial importance and growing demand of liquorice, the lack of information on the secondary metabolite biosynthesis the enhancement of bioactive traits and productivity through molecular breeding has been hampered. Here, we have cloned and characterized five genes contributing to glycyrrhizin biosynthesis. A substantial collection of genes involved in various aspects of plant secondary metabolism will provide a useful gene resource for designing non-natural pathways, as well as enzymes for the generation of novel compounds in synthetic biology. Degenerate oligonucleotide primers were designed by assembling the conserved protein sequences of the respective known genes from other plant species submitted in NCBI. RNA was extracted using Trizol method. One µg of RNA was used for the first strand cDNA synthesis using the Primescript RT reagent kit (Takara, China) as per the protocol recommendedby the manufacturer. First strand cDNA synthesis for 5' and 3' RACE was carried out using SMARTer RACE cDNA amplification kit (Clonetech, USA) according to manufacturer's instructions. The fragments were subsequently used for designing gene specific primers (GSP) for the amplification of 5' and 3' ends by RACE-PCR. The initial 5' & 3' RACE-PCR reaction were carried using GSP and UPM primer (Universal Primer A Mix). Primary PCR product obtained in the reaction was used as template for nested 5' & 3' RACE-PCR reaction in which GSP 2 was used along with NUP. The region amplified by 3' and 5' RACE were cloned in pJET cloning vector and transformed in DH5α cells (Invitrogen, USA). The core DNA fragment amplified was gel eluted and cloned into the pJET cloningvector (Fermentas, USA). Each plasmid with its respective gene was sequenced and subjected to nucleotide BLAST analysis. The ORF region and protein translation studies were performed using ORF Finder and Swissprot tools of NCBI. The open reading frame (ORF), sequence length, BLAST results and predicted amino acid sequences were deduced as presented in Table 1.9.1

Table 1.9. 1: Seven genes cloned and characterized in Glycyrrhiza glabra plant

S N0.	GENE	ORF length	Amino acid residues	Mass (kDa)
1	Squalene synthase	1.239 kb	413	47
2	Squalene epoxidase	1.59 kb	530	58.30
3	B-amyrin synthase	2.067 Kb	765	87.516
4	CYP72	1.572 kb	524	57.6
5	CYP88	1.482 Kb	494	54.34
6	Cycloartenol synthase	2.274 kb	758	83.38
7	Lupeol synthase	2.277 Kb	759	83.49

Cloning of Squalene synthase (GgSQS) cDNA and promoter region





35S P | *GgSQS* | NOS T

Plant expression vector pBI121

↓

Hairy root transformation underway

In silico analysis of promoter region 612 bp upstream to ATG

626 bp usptream of GgCYP72 promoter

GgCYP72deduced amino acid sequence

-- 35SP NOST -

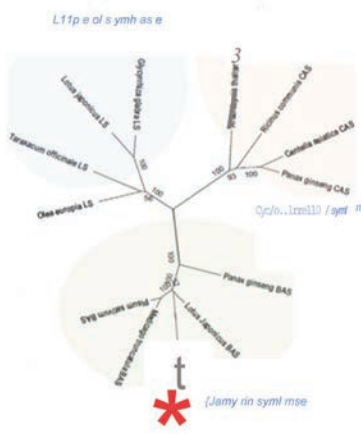
Plantexpression vectorpBI121

!

Hairyroottransfonnationunderway RNAiconstruct

Gg BAS CDS .. 2067 bps

Pro m ot er reg ion = 394 b ps up str ea m to ATG



35SP *GgBAS* NOST

Plantexpression vectorpB1121

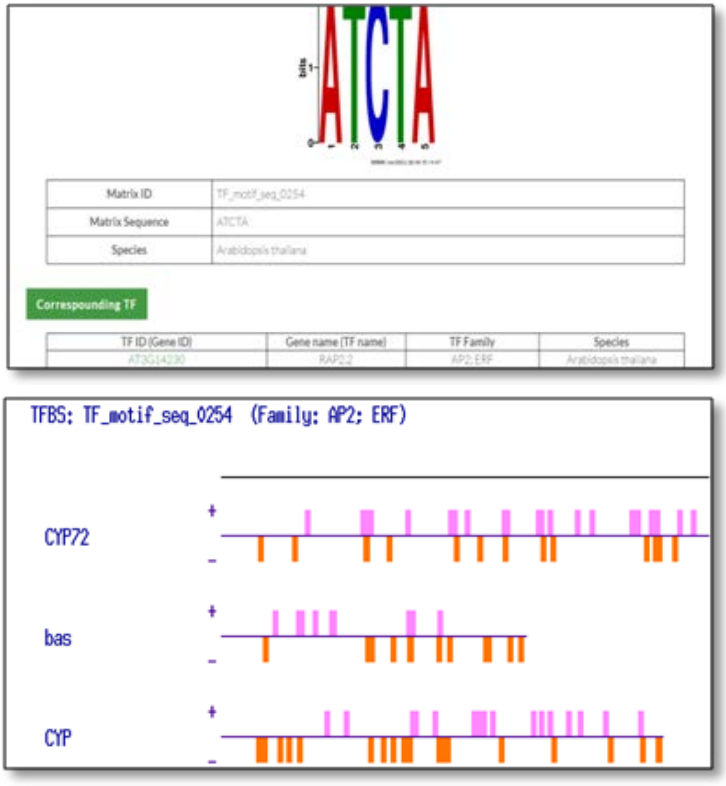
!

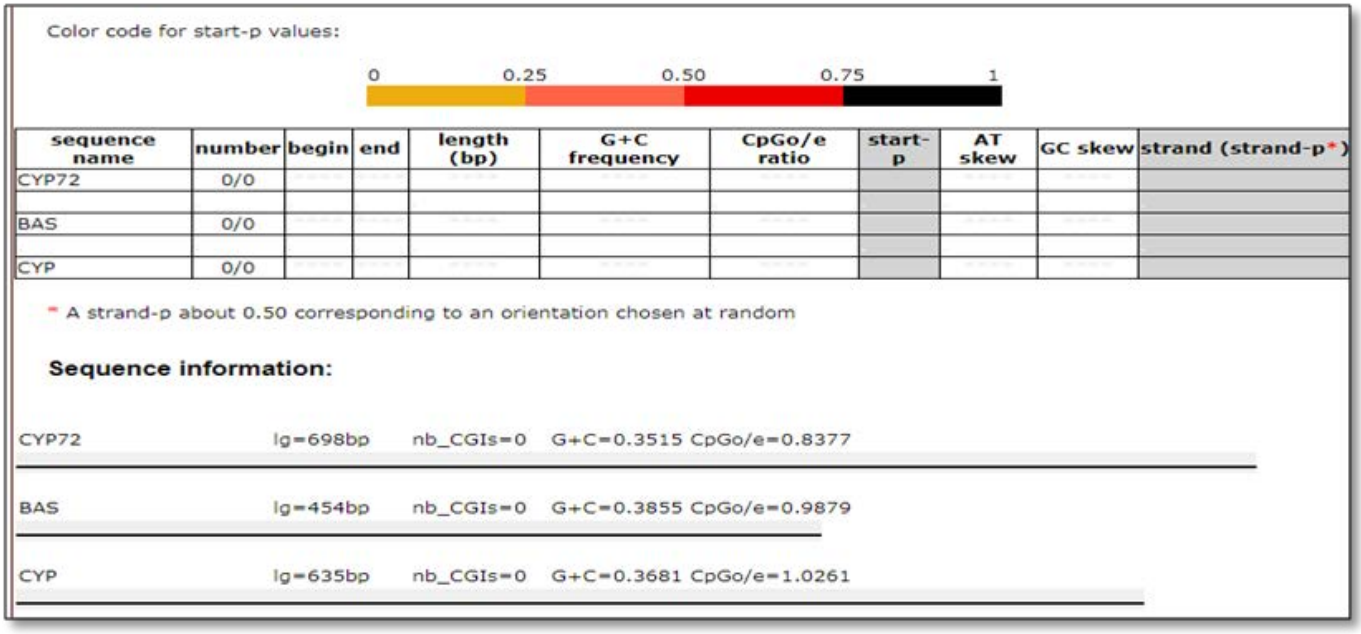
Hairyroottransfonnationundeiway

1.10 Cloning and Promoter Analysis of the genes encoding enzymes for the glycyrrhizin biosynthesis.

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

Controlled transcription of biosynthetic genes is one of the foremost mechanisms regulating secondary metabolism in plants. Primary metabolites are essential for plant growth and development, while secondary metabolites act as defense molecules and protect plants in various adverse conditions. Several transcription factor families such as MYC, MYB, WRKY and AP2/ERF have been found to be involved in the regulation of secondary metabolism in different medicinal plants. These regulating elements control the biosynthesis and accumulation of secondary metabolites in a spatial and temporal manner. These processes are influenced by number of biotic and abiotic factors. The spatiotemporal transcriptional regulation of metabolic pathways is controlled by a complex network involving many regulatory proteins known as transcription factors (TFs). TFs are sequence- specific DNA-binding proteins that interact with the regulatory regions of the target genes and modulate the rate of transcriptional initiation by RNA polymerase. Literature cites their roles in regulating biosynthetic pathways at the transcriptional level. TFs encode proteins that initiate and regulate the transcription of several genes depending on tissue type and in response to external and internal signals. Here, we studied the 5' upstream region of three genes namely, β- amyrin synthase, CYP 88D6 & CYP72A154 to identify regulating element sequences that may be exploited for regulating their respective expression in manipulating the pathway. The 5'upstream region of all the genes involved in glycyrrhizin biosynthesis were cloned using Genome walker kit (Invitrogen) as per the instructions. *In-silico* analysis of the upstream region was performed using Translate tool (http://www.expasy.ch/tool s/ dna. html) and the properties of damino acid sequence were estimated using ProtParam (http://www. expasy.ch/ tools/protparam. html).Structural and functional important regions were identified in deduced protein sequence by SMART tool. Also, secondary structure was determined by SOPMA (http://npsa-pbil.ibcp.fr) program. Hydrophobicity analysis was done by using KyteDoolittle (http://gcat.davidson. edu/DGPB/kd/kyte-doolittle.htlm) and TMHMM (http://www.cbs.dtu.dk/ services/) web tools.





Color code for start-p values:

0 0.25 0.50 0.75 1

sequence name	number	begin	end	length (bp)	G+C frequency	CpGo/e ratio	start-p	AT skew	GC skew	strand (strand-p*)
CYP72	0/0									
BAS	0/0									
CYP	0/0									

* A strand-p about 0.50 corresponding to an orientation chosen at random

Sequence information:

CYP72 lg=698bp nb_CGIs=0 G+C=0.3515 CpGo/e=0.8377

BAS lg=454bp nb_CGIs=0 G+C=0.3855 CpGo/e=0.9879

CYP lg=635bp nb_CGIs=0 G+C=0.3681 CpGo/e=1.0261

The putative cis-acting regulatory elements of the three genes i.e cyp72, cyp88 and BAS were identified about 350-700 bp upstream to the start codon using Plant cis-Regulatory DNA Elements (PLACE) http://www.dna.affrc.go.jp/PLACE. The PLACE database mainly contains plant motifs extracted from the published reports in the literature. TATA box sequence elements required for the critical and precise transcription initiation were found at position 546(+) region of the cyp72 promoter sequence. TSS where RNA polymerase binds and initiate the process of transcription were found at positions 587(+), 283(+) region of the cyp72 upstream sequence. Two promoters was predicted in cyp 72 upstream region. In case of cyp 88 and BAS only one promoter was predicted, having TSS at position 415(+) in cyp88 upstream region or 378(+) in BAS.

Table 1.10.2. The conserved region, signal sequence and their putative functions predicted through in-silico analysis.

CRE's	signal sequence	putative function
AMYBOX1	5'TAACARA3'	amylase box conserved sequence found in promoter sequence of α-amylase gene
MYBCORE	5'CNGTTR3'	binding site for MYB proteins that are responsive to water stress
SEF4MOTIFGM7S	5'RTTTTTR3'	enhancer present in promoter of soyabean beta-conglycinin genes
B1HD1DS	5'TCGTCA3'	binding site of OsB1HD1 a rice BELL homeodomain transcription factor
GT1GMSCAMY	5'GAAAAA3'	involved in gene expression induced by salt and pathogen.It can also stabilize the transcription initiation complex
CAAT Box1	5'CAAT3'	conserved sequence responsible for the tissue specific promoter activity
WRKY710S	5'TGAC3'	WRKY TFB's also known as w-box.Binding site of rice WRKY71.A transcription repressor in the gibrellin signaling pathway

The promoter regions of the three genes showed the presence of 27 regulatory sites. Among these 27 cis- regulatory elements (CREs), two CREs- CACTFTPPCA1 and DOFCOREZM were abundantly present, having duplication frequency in the range of 7 to 16 in case of CACTFTPPCA1 and 5 to 12 in case of other DOFCOREZM. The CACTFTPPCA1 is a tetra- nucleotide motif which is responsible for the expression of C4 phosphoenolpyruvate gene in C4 plants. C4 phosphoenolpyruvate is a mesophyll specific gene. It is a key component of Mem1 (mesophyll expression module 1) in Flaveria trinervia but might have a different role in C3 plants, such as rice. Second, most duplicated CRE DOFCOREZM is the target binding sites of Dof DNA binding proteins associated with the expression of different multiple genes in plants. Diverse promoters in a variety of plant tissues are differentially regulated by Dof proteins. GATABOX, which have GATA motifs are required for light regulated and tissue specific gene expression. This transcription factors are a type of DNA binding proteins, containing a zinc finger motif, which have been implicated in nitrate and light dependent transcription control. GATA transcription factors are reported to bind the CaMV 35S promoter. ARR1AT is a ARR1-binding element, is found in Arabidopsis. ARR1 and ARR2 are transcriptional activators involved in cytokinin response regulation. CAATBOX1, having CAAT consensus motif sequence that is responsible for the tissue specific promoter activity of the pea legumin gene LegA. GT1CONSENSUS are conserved in plant nuclear genes. GT-1 proteins, which have tri-helix DNA binding domains have recognized by GT1CONSENSUS. GT Elements are expresses and show complex regulatory features of plant gene transcription. GTGANTG10, having GTGA conserved motif found in the promoter of tobacco late pollen gene g10. This gene is maximally expressed in mature pollen only and shows homology to tomato gene lat56. ROOTMOTIFTAPOX1 is a motif found in Agrobacterium rhizogenes rolD promoter region. The rolD-GUS genes expression was found in roots. EBOXBNNAPA is a E- box sequence. This CRE factor is responsible for light responsiveness and regulated by MYB transcription factor. MYCCONSENSUSAT, this CRE regulates the transcription of Arabidopsis genes under cold conditions with recruiting a MYC like bHLH transcriptional activator. Also few signal sequences were identified which are known to predict the functionality of the native sequence (s). Several transcription factors were identified which reflects the role of the gene. For example, binding site of MYB gene which are known to play role in water stress were identified. W-box sequences which have shown to regulate secondary metabolite biosynthesis were also found (Table 1.10.2).

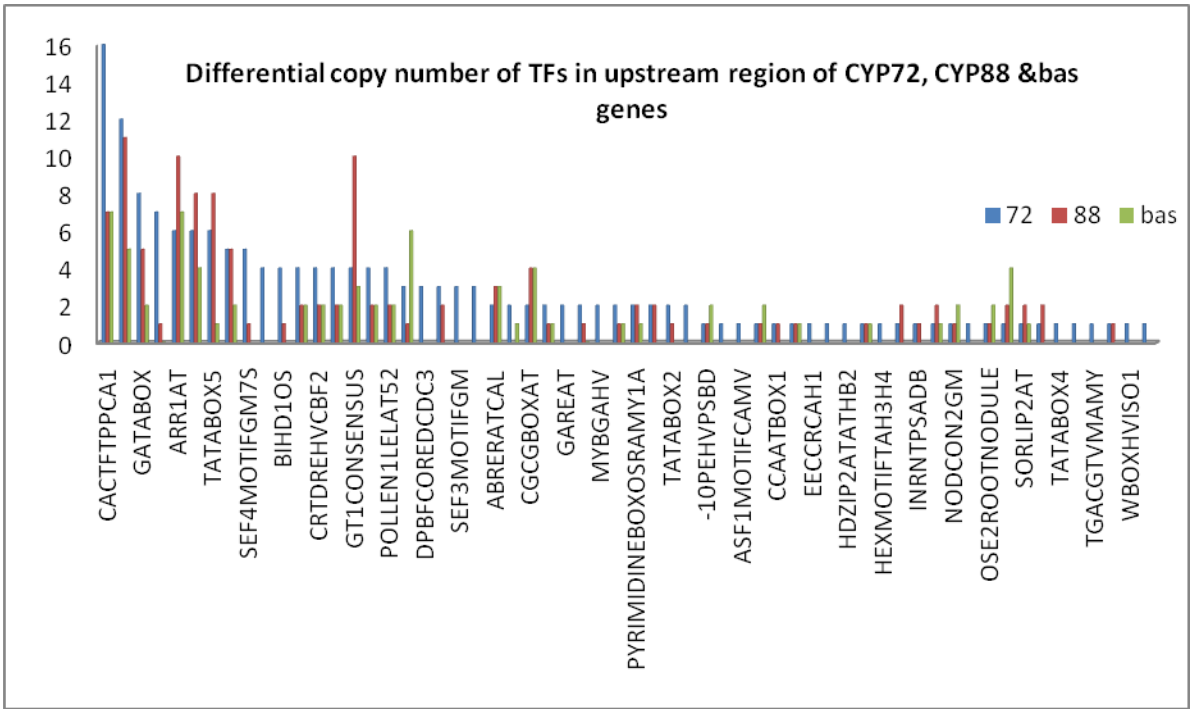
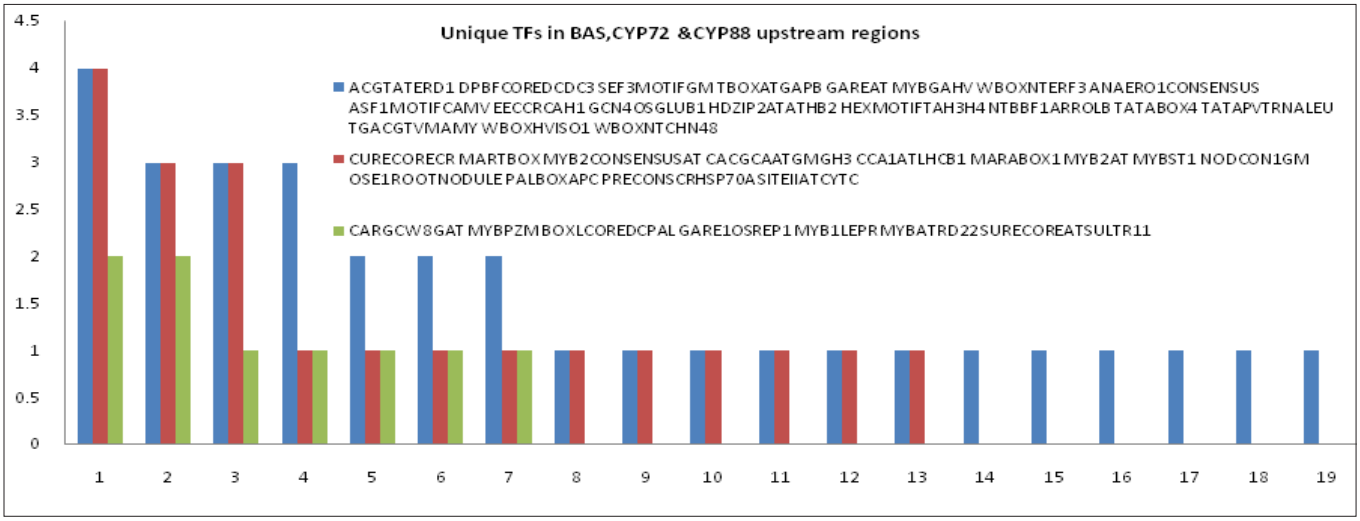


Figure 1.10.1. *In silico* analysis of CYP72 upstream region displaying Transcription factor and their copy number

The copy number of the transcription factors identified in the promoter regions of two CYPs and β- amyrin synthase were calculated and compared with each other. In all. 21, 15 & 9 different regulatory elements binding sites were identified in CYP88, CYP72 and β-amyrin synthase. Maximum (16) binding sites (CACTFTPPCA1) were present in CYP72 promoter region. Fourteen transcription binding sites were common between CYP72 &CYP 88 while 3 and 1 binding sites respectively were common between CYP88- β-amyrin synthase and CYP72- β-amyrin synthase.



1.11 Morphological studies and meiotic chromosome analysis of Epimediumelatum (Morr&Decne) Rare endemic medicinal plant of the Northwestern Himalayas in India

Sajad Ahmad Lone, Qazi Pervaiz Hassan*, Suphla Gupta, SaleemMushatq, Phalisteen Sultan, Yashbir Singh Bedi

Epimediumelatum (Berberidaceae) is a rare endemic medicinal herb of the Northwestern Himalayas in India. Recent ethnopharmacological reports have demonstrated its traditional medicinal use against various bonerelated diseases in the Kashmir Himalayas. It owes its pharmaceutical importance due to high concentration of flavonoid glycosides like Epimedin A, B, C and Icariin which are known mainly for aphrodisiac, antiosteoporosis, anticancer, antioxidant, antiaging, antifatigue, and antiviral activities. It is a neglected medicinal plant in the Northwestern Himalayan region and may fall in the list of endangered species due to continuous anthropogenic pressures in its native habitats. In this study, we investigated distributional and altitudinal range of this prized species from 20 diverse eco- geographical zones of Kashmir Himalayas for the first time. We also report here its diversity in morphological attributes both in wild and captive cultivation. The species has a very small population size in most of the surveyed habitats with no natural protection. Under cultivation it showed increased plant height (63.09± 4.9 cm), more number of leaves (95.53 ±11 cm) and flowers (160.76± 20 cm), indicating importance of high altitude medicinal garden for its immediate ex situ conservation. Further, the acetocarmine staining and squashing of young anthers confirmed it as a diploid species (2n = 12) like other Epimedium species. Chromosome number and meiotic abnormalities are also reported for the first time in the species. Finally, constant anthropogenic pressures in the Northwestern Himalayas demand immediate in situ and ex situ conservation programs for E. elatum.

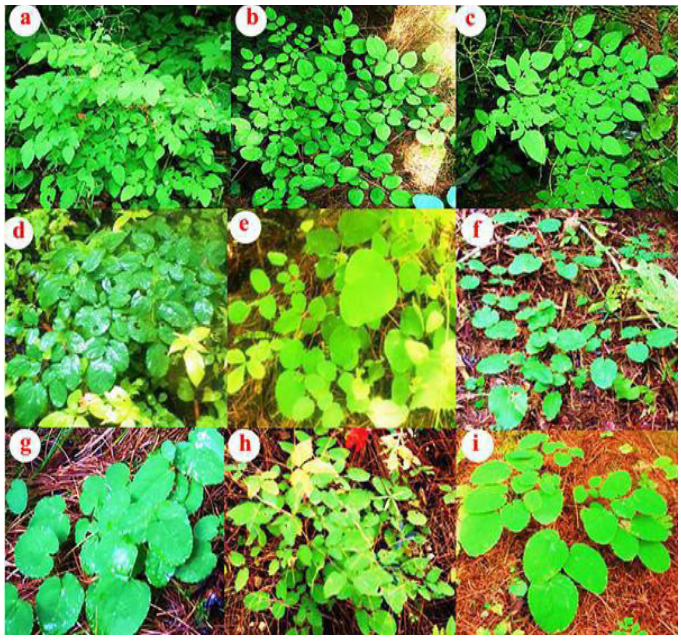


Figure 1.11.1: Representative populations of E.elatum growing in wild (eco-geographical zones) habitats of Kashmir Himalayas in India (a) Aharbal (b) Verinag (c) Naranag (d) Gulmarg (e) Boniyar (f) Khillanmarg (g) Pahalgam (h) Sheikhpora (i) Chaknala.

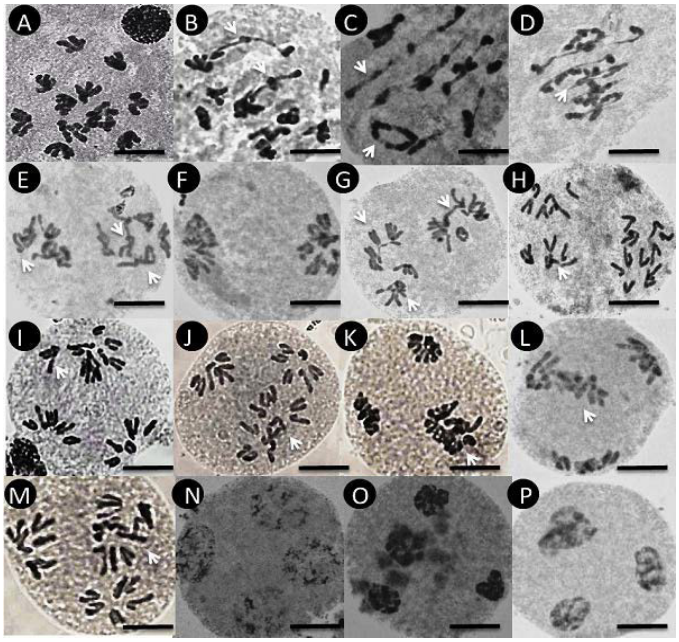


Figure 1.11.2. Various meiotic abnormalities observed during cytological characterization of Epimediumelatum (a-d)- Metaphase II with prominent irregularities like inter-bivalent connections and ring bivalents (white arrows) (e)- Anaphase II with chromosomal connections (f)- Anaphase II with congested chromosomes (g)- Anaphase II with inter- bivalent connections (h)- Anaphase II with scattered chromosomes at three poles (i-m)- Anaphase II with abnormalities like stickiness, interbivalent connection and abnormal segregation (white arrows) (n-p)- Telophase II

1.12 Antimicrobial investigation of selected soil actinomycetes isolated from unexplored regions of Kashmir Himalayas, India

AabidManzoor Shah, Shakeel-u-Rehman, Aehtesham Hussain, SaleemMushtaq, Muzafar Ahmad Rather, Aiyatullah Shah, Zahoor Ahmad, Inshad Ali Khan, Khursheed Ahmad Bhat, Qazi Parvaiz Hassan*

The aim of the present study was to isolate and evaluate the antimicrobial potential of soil actinomycetes of Kashmir Himalayas. The secondary metabolites of actinomycetes are the prominent source of antibiotics. A total of 121 morphologically different actinomycete strains were isolated and screened for antimicrobial activity against various human pathogens. The ethyl acetate extract of fermented broth an actinomycete strain, identified as Streptomyces pratensis exhibited significant antimicrobial activity against Staphylococcus aureus ATCC 29213 with MIC 0.25µg/ml and Mycobacterium tuberculosis Strain H37Rv with MIC 0.062µg/ml. The strain S. pratensis IIIM06 was grown on large scale and their broth was extracted with ethyl acetate. The extract was subjected to various chromatography techniques which led to the isolation of four compounds whose structures were established as actinomycin C1, actinomycin C2, actinomycin C3 and actiphenol on the basis of spectral data analysis. Actinomycin C1, C2 and C3 exhibited potent antimicrobial activity against S. aureus as well as M. tuberculosis. The isolated indigenous actinomycetes exhibited good antibacterial activity and the study reveals that IIIM06 is a promising strain and could be of great potential for industrial applications.

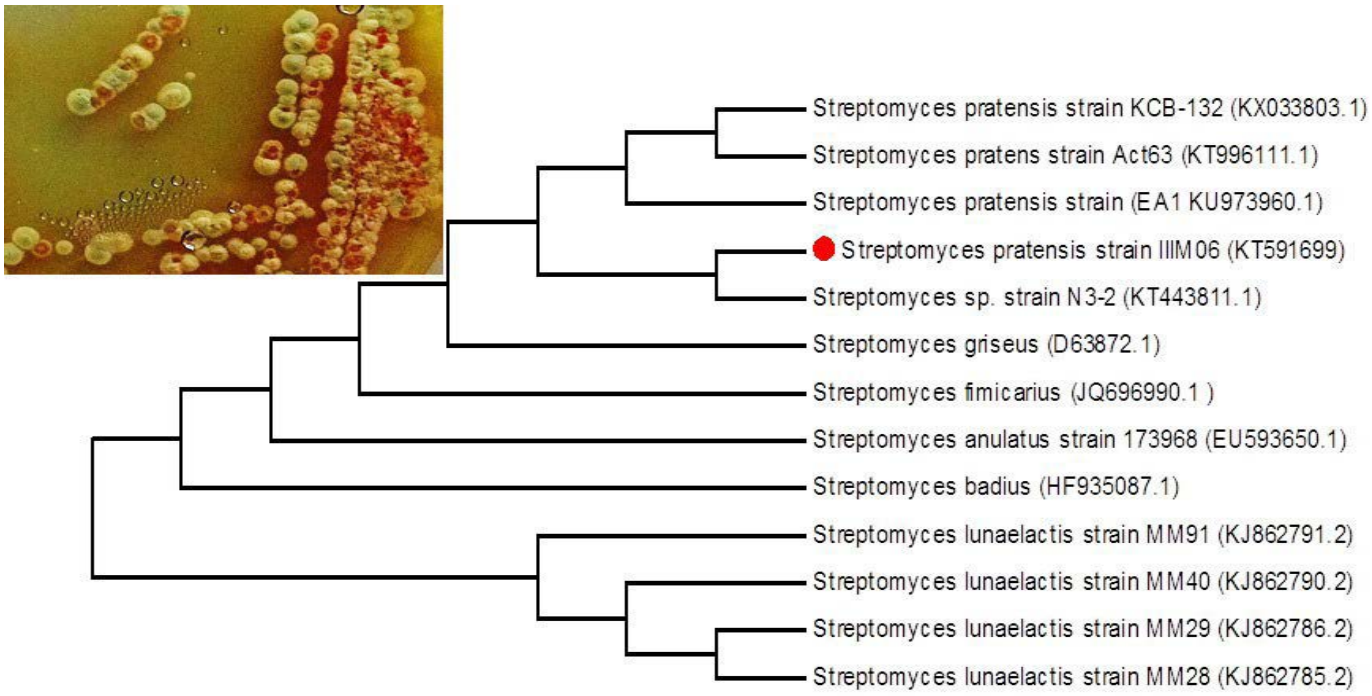


Figure 1.12.1. Culture photograph and Neighbor-joining phylogenetic tree of strain IIIM06 based on 16S rRNA gene sequence generated by Mega 6.0.

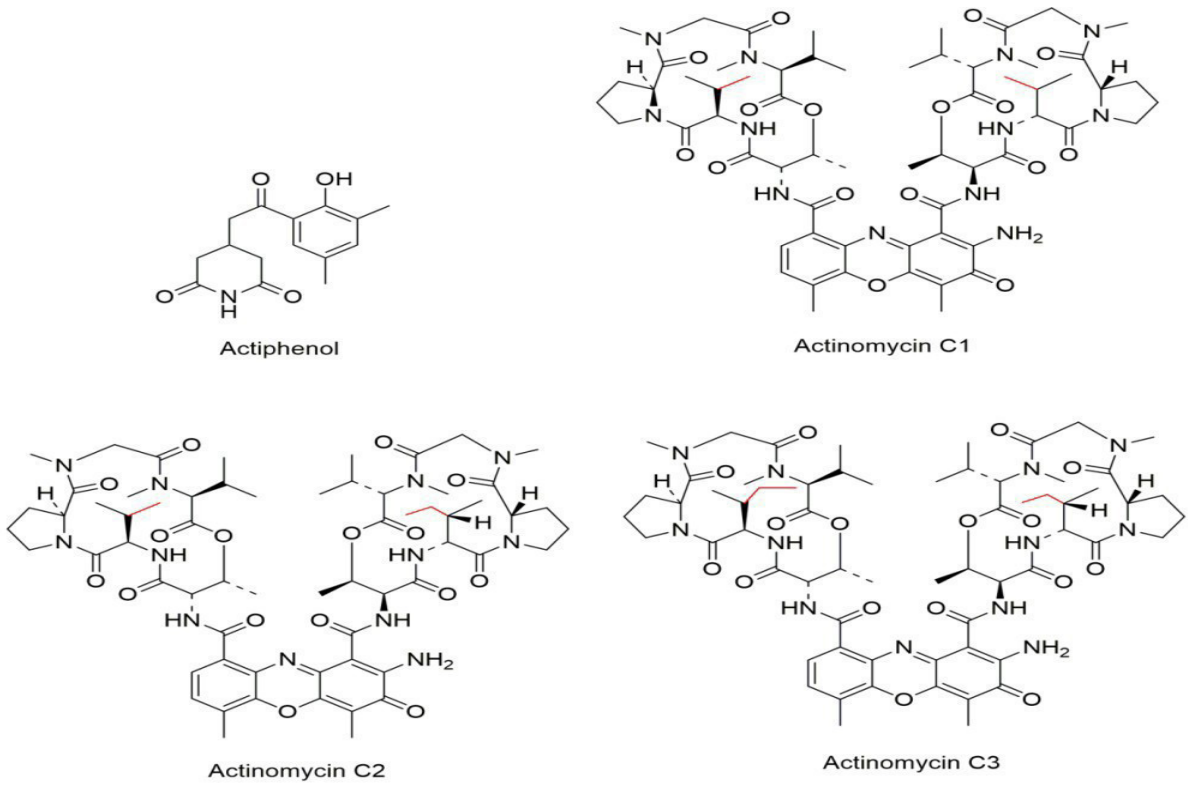
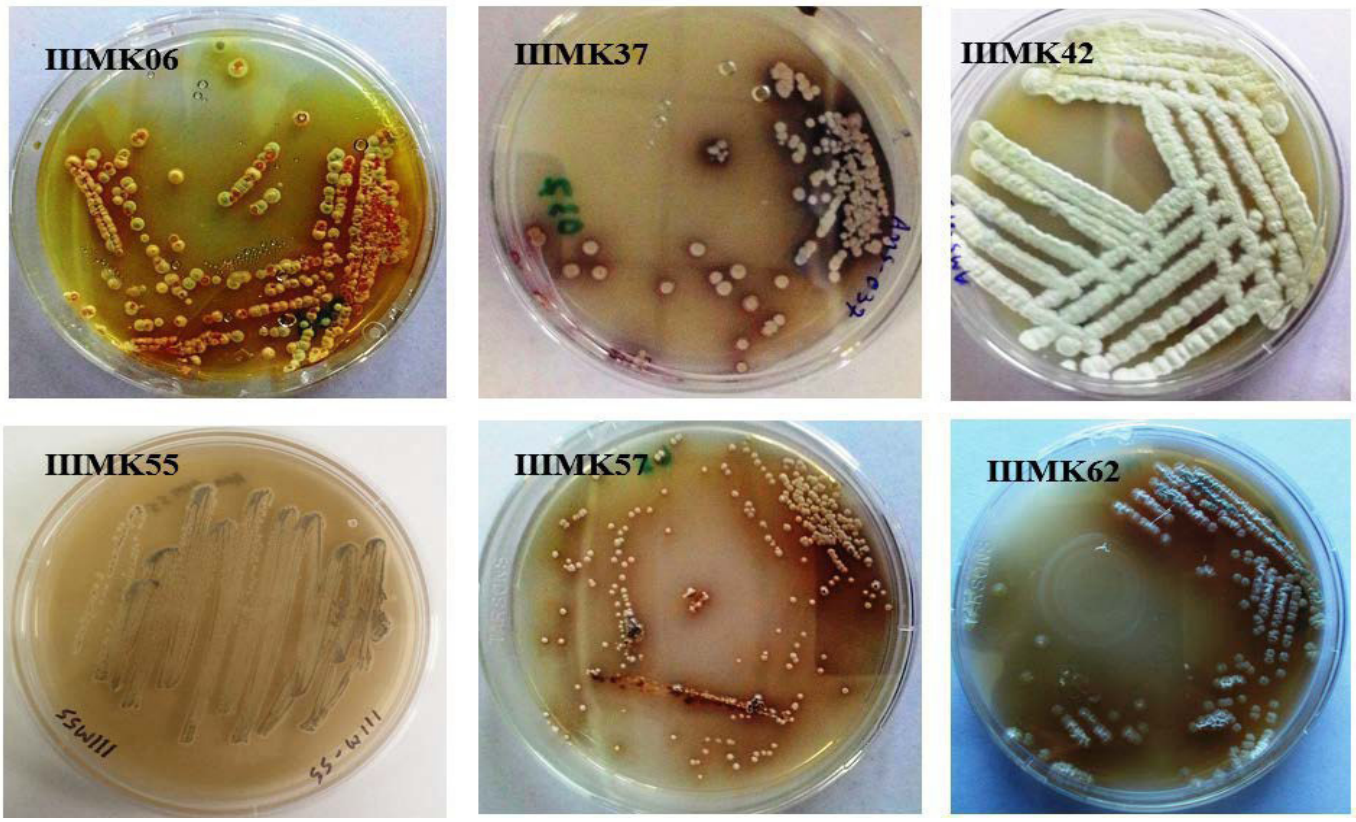


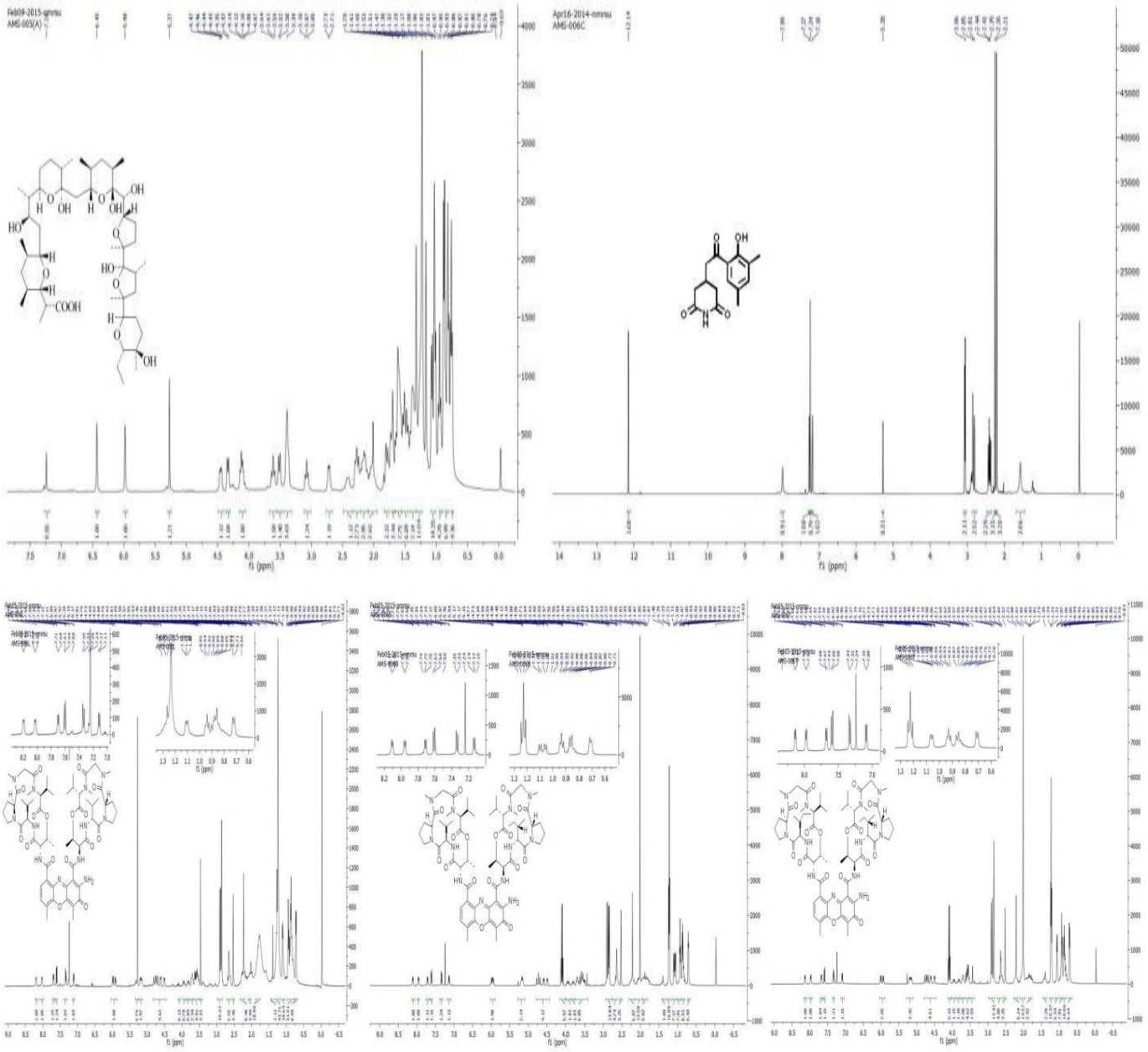
Figure 1.12.2. Structure of compounds isolated from ethylacetate extract of the broth of strain IIIM06

1.13 Streptomyces puniceus strain AS13., Production, characterization and evaluation of bioactive metabolites: A new face of dinactin as an antitumor antibiotic.

Hussain A, Rather MA, Dar MS, Dangroo NA, Aga MA, Qayum A, Shah AM, Ahmad Z, Dar MJ, Hassan QP

A highly active actinobacterial strain isolated from untapped areas of Northwestern Himalayas and characterised as Streptomyces puniceus strain AS13 by 16S rRNA gene sequencing was selected for production of bioactive metabolites. The bioassay- guided fractionation of microbial cultured ethyl acetate extract of the strain, led to isolation of macrotetrolide compound 1 (Dinactin) and compound 2 (1-(2,4-dihydroxy-6-methylphenyl)-ethanone). Structures of the isolated compounds were elucidated interpretation of NMR and other spectroscopic data including HR-ESI-MS, FT- IR. These compounds are reported for first time from Streptomyces Puniceus. Compound 1 exhibited strong anti-microbial activity against all tested bacterial pathogens including Mycobacterium tuberculosis. The MIC values of compound 1 against Gram negative and Gram positive bacterial pathogens ranged between 0.019 - 0.156µgml-1 and 1µgml-1 against Mycobacterium tuberculosis H37Rv. Dinactin exhibited marked anti-tumor potential with IC50 of 1.1- 9.7µM in various human cancerous cell lines and showed least cytotoxicity (IC50~80µM) in normal cells (HEK-293). Dinactin inhabited cellular proliferation in cancer cells, reduced their clonogenic survival as validated by clonogenic assay and also inhabited cell migration and invasion characteristics in colon cancer (HCT-116) cells. Our results expressed the antimicrobial potential of dinactin and also spotted its prospective as an antitumor antibiotic.





1.14 Genetic diversity, LCMS based chemical fingerprinting and antioxidant activity of Epimediumelatum Morr & Decne

Sajad Ahmad Lone, ManojKushwaha, AbubakarWani, Ajay Kumar, Ajai P. Gupta b, Qazi Parvaiz Hassan , Suresh Chandra , Suphla Gupta

EpimediumelatumMorr & Decne is a perennial herb, endemic to shady coniferous forests of north-western Himalayas, India. It owes its pharmaceutical importance to high concentration of flavonoid glycosides par- ticularly epimedins and Icariin. A lot of medicinal properties are attributed to them like aphrodisiac (PDE- 5 inhibition), anti-osteoporosis, anticancer, antioxidant, anti-fatigue and antiviral activities. In the present study, twenty accessions of E. elatum were investigated for their genetic diversity and chemo-profiling through molecular markers and fingerprinting, respectively. Further, their phyto-chemical variation and related antioxidant activities are also being reported. Molecular fingerprinting resulted in 277 total loci, out of which 254 were polymorphic, displaying an overall polymorphism of 91.1%.

Moreover, fourteen unique bands were amplified, maximum (6) were amplified in GL accession from 3 primers (UBC900, UBC834 &UBC823). The dendrogram topology indicated moderate to high genetic diversity corrobo- rating with diversity index (0.36). Chemo-profiling revealed epimedic B and epimedin C as the major prenylated flavonoids in leaves, while Icariin was found highest in underground parts. However, no cor-relation could be deduced between molecular and prenylated flavonoid profiling in the present study. Furthermore, ethanolic extracts of rhizomes exhibited stronger antioxidant ability. The study has great implications as the wild resource conservation, germplasm assessment; quality resource explorations have become critical for the sustainability of the species. Efforts are thus needed to conserve the elite.

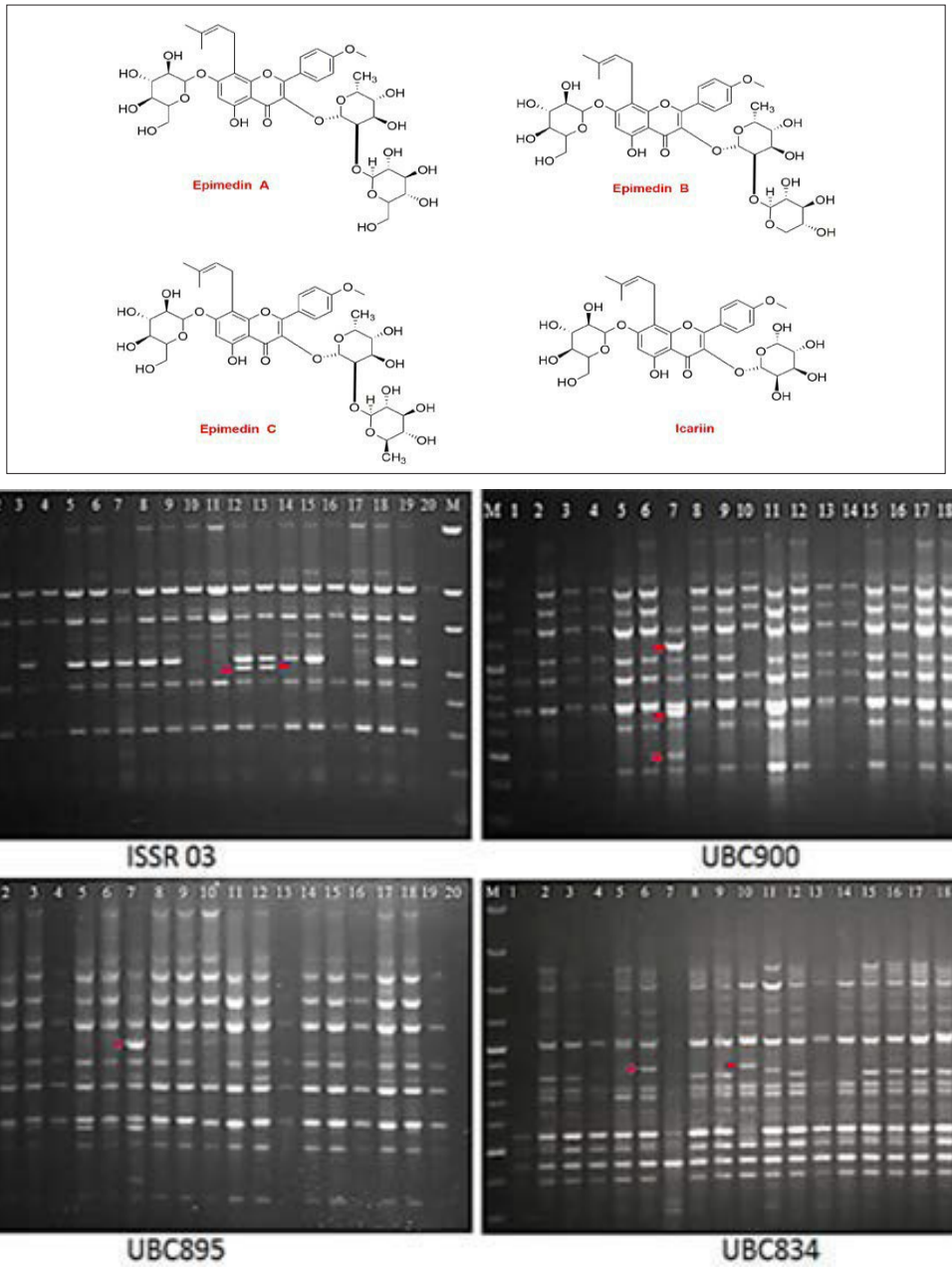


Figure 1.14.1 Results of PCR amplification of unique bands (ISSR-03/ UBC900/ UBC895/ UBC834) in E.elatum genotypes via ISSR fingerprinting. {M: DNA ladder (100bp plus}. Red arrows show the unique bands. [Position of gel lanes (1-20) showing twenty accessions; 1-BY (Boniyar); 2-KZG (KanzalwanGurez); 3- DGM (Dachigam); 4-YS (Yusmarg); 5-DR (Drang); 6-PGM (Pahalgam); 7-GL (Gulmarg); 8-KNG (Kokernag); 9-VNG (Verinag); 10-SPG (SheikhporaGurez); 11-AB (Aharbal); 12-HP (Hirpora); 13-KMG (Khillanmarg); 14-DP (Dodipathri); 15-GG (Gagangir) 16-BDG (BadwanGurez) 17-CNG (ChecknalaGurez); 18-NAR (Naranag); 19-BR (Babareshi); 20-DG(Dangarpora].

2.0 VALUE ADDITION

2.1 Echinacea purpurea, an exotic plant as a source of herbal nutraceuticals

Bikarma Singh, Kiran Koul

Herbal nutraceuticals used as a powerful instrument in maintaining health and act against nutritionally induced acute and chronic diseases, thereby promoting optimal health, longevity, and quality of life. The food sources used as nutraceuticals are all natural and can be dietary fibers, probiotics, prebiotics, polyunsaturated fatty acids, antioxidant vitamins, polyphenols and spices. The genus *Echinacea* Moench comprised of ca 9 species, and plants are generally perennial herbs whose distribution ranges from eastern to southern North America. *Echinacea purpurea* (L.) Moench, a native species to North America is a perennial herb. Flowering time is usually early July to August. It is a member of flowering plant family Asteraceae. This species has herbaceous perennial habit, prefers to grows in rocky open woods and prairies. Echinacea phytopharmaceuticals represent the most popular group of immunostimulants in Europe and USA, and more than 800 containing drugs are currently in German market. Echinacea products rank the top ten best selling drugs in USA. Medicinally, it is oftenly used externally for wounds, insect bites, stomach pain, and toothace and throat infections. Phenolic compound are the main constituent of this plant represent by cynarin, cichoric acid, caftaric, chlorogenic and isochlorogenic acids. Major flavonoid is rutoside. All parts of the plant are harvested for polysaccharides, polyacetylenes, caffic acid, cichoric acid and alkyamides. These constituents are implicated in theimmunostimulatory effect of this species. Besides, it also prevents cold, flu and other infections particularly of upper respiratory infections. It is used externally for snake or insect bites and burns. Hot water extract of the dried leaf is taken orally for inflammations. CSIR-IIIM Jammu has started captive cultivation of this species and has undertaken step towards development of its agrotechnology for future product development and bulk production.

2.2. Orientation Programme under CSIR-Aroma Mission Project

Bikarma Singh, Suresh Chandra

A Five Days Orientation Programme was conducted by CSIR-Indian Institute of Integrative Medicine Jammu for Project Staffs appointed and working under CSIR Aroma Mission project with effect from 23rd-30th January 2018 after the instruction and approval of Director. The programme includes invited talks on "captive cultivation, processing, marketing and value addition of aromatic crops" by Suresh Chandra, Bikarma Singh, VP Rahul, Suphla Gupta, Rajendra Bhanwaria, Sougat Sarkar, SR Meena, SK Lattoo, Anil Katare, Parvaiz Qazi, Nasheeman Ashraf, Phalisten Sultan, Ravi Shankar and Deepika Singh. The details of the programme day-wise are given below:

Day 1: 23rd January 2018:

- The programme was inaugurated by Dr. Suresh Chandra, PI and Er. Abdul Rahim, PME division. The welcome speech was presented by Dr. Bikarma Singh.
- First day PIs & Co-PIs interacted with all the project assistants working under CSIR Aroma Mission project. During his inauguration talk. Dr. Chandra gave introduction of the approved project as well as aims and objectives to be covered under this mission documents. Reason for funding and base line projects like JAAG, K5000, CSIR 800 etc. were discussed by Dr. Suresh Chandra.
- The first session presentation began with lecture of Dr. Suresh Chandra on CSIR- AROMA MISSION project and CSIR-IIIM Jammu roles, aims and objectives. The detail description of the project were presented.
- It was followed by presentation of Dr. Bikarma Singh on Role of Survey, collection, identification and Herbarium in relation to Aromatic Crops and variety developed by IIIM, which enlighted all the participants. This was then followed by presentation of Dr. V. P. Rahul on Importance of Genetics and Plant Breeding for improvement in MAPs with special reference to the targeted 10 aromatic crops under CSIR Aroma Mission: Scopes and methods of improvement in aroma bearing crops of industrial importance.

- The second session was started with visits to IIIM institutional three referal centres: Tissue culture, where Mr. Yaduvan Sen delivered importance of tissue culture in conservation of biodiversity and fast multiplication method called micropropagation of aromatic crops. It was then followed by visit to crude drug repository under leadership of Dr. Bikarma Singh and explanation of CDR, its role in discovery of different system of medicines like Ayurvedic, Allopath, Amchi, etc. were discussed. Final visit to internationally recognised Janaki Ammal Herbarium visit was conducted by Dr. Bikarma Singh along with his associated staff Mr. Sudhir Nanda. Different system of plant classification, species concept, variety concept, identification and preservation techniques were discussed among the participants. The 200 old herbarium specimens were shown to all PAs and discussions were done on its importance.
- Both these sessions were very interactive and fruitful.

Day 2: 24th January 2018

- Day 2, first session began with welcome address of Dr. Bikama Singh in continuation of day 1 programme. It was then followed by first presentation of Dr. Sougat Sarkar on Cultivation techniques and methods of breeding, where Dr. Sarkar nicely explained the breeding technique, compared the CSIR developed varieties of CIMAP and IIIM aromatic crops. Mr. Asif Ashraf Shah PA level II gave his valuable comments and concerns regarding the other important conventional and molecular breeding strategies to be applied in addition to already discussed by Dr. Sarkar. It was then followed by presentation of Dr. Rajinder Bhawaria on Soil science based experimental studies (soil physical characteristics, soil chemical characteristics, soil enrichment methods) of aromatic crops.
- In continuation, this session was then followed by presentation of Dr. Bikarma Singh on CN-5 Rosagrass and end to end technology for rural prosperity and industrial perspective. Taxonomy, chemistry, economic, agrotechnology tranfers to different states and its importance in aroma mission projects were nicely explained by Dr. Singh. Value addition and product dvelopment from aromatic crops particularly lemongrass and rosagrass were discussed in detail among the PAs and otherparticipants.
- Day 2 second session was held at Chatha under supervision of Dr. Bikama Singh, Dr. Sougat Sarkar, Mr. K.K. Sharma (consultant Jammu) and Mr. Farooq Ahmad Mir (consultant Srinagar). The programme starts at 2 pm and continues till 5:30pm.
- At Chatha, visit to different aromatic field were conducted under supervsion of Dr. S.R. Meena, Dr. Bikaarma Singh and Rajendra Gochar. Field authentication and taxonomy of aromatic crops and other medicinal plants were carried out under supervision of Dr. Bikarma Singh. The session ends with refreshment of tissue culture raised banana distributed to PAs working under the project, followed by light refreshment of snackes.

Day 3: 25th January 2018

- In continuation of the programme, day 3 first sessions started with welcome speech of Dr. Bikarma Singh, followed by first presentation of Dr. Suphla Gupta on cultivation practices of Ocimum species, followed by presentation of Dr S K Lattoo on cultivation practices of Geranium. It was then followed by presentation of Dr. Suresh Chandra on plant specific released varieties: Lemongrass, and its extension in India and role in industry. This session ends with lecture of Dr S R Meena on Cultivation Practices seed based multiplication and propagation.
- The second session start with lab visit programme of cGMP where Er Anil Kumar Katare, Head cGMP delivered lecture on clevenger type distilation method in laboratory condition and pilot scale by fixed and mobile distillation unit and role in different drug preparations.
- It was then followed by field visit programme for authentication of aromatic crops under supervision of Dr. Bikarma Singh where different aromatic, medicinal and nutraceutical germplasm were discussed

with all project fellows. RET and other IIIM germplasm planted in IIIM Jammu experimental farms, greenhouse and glass house were discussed in details.

- It was then followed by Lab visit to Value Addition Centre under Supervsion of Dr. Bikarma Singh, where Dr. Singh explained lab scale extraction techniques of essential oils among the particiants. Twenty different types of essential oils extracted from captive field and wild collection were shown to the participants. This session ends with vote of thanks by Dr Singh, followed by distribution of small sample of lemongrass oil to all project fellows.

Day 4: 29th January 2018

- The first session was started with welcome speech of Dr. Suphla Gupta, whereby explanation of ongoing programme was discussed. It was then followed by first presentation of Dr. Ravi Shankar on Value Addition of essential oils, demonstration of value addition of thymol analysis. Agrotechnolgy and Chemistry of Jammu monarda was discussed along with GCMS data and its applications in aromaindustry.
- It was then followed by presentation of Dr. Parvaiz Qazi on cultivation practices of lavender, one of the high value high altitude aromatic crops growing in Kashmir regions. It was then followed by presentation of Dr. Phalisteen Sultan on cultivation practices of Rosemary and Tagetes.
- Lab visit programme was organized in the second session under supervision of Dr. Ravi Shankar. Techniques for thymol experimentation and crystal formation from Jammu Monarda at lab scale were discussed along with live demonsration of thymol crystal. The presentation Dr. Nazia Abhas was not undertaken and presentation of Dr. Nasheem shifted to 5th day.

Day 5: 30th January 2018

- In continuation of the programme, first session was started with welcome speech of Dr. Bikarma Singh, followed by first presentation of Mrs Deepika Singh on Physio- chemical properties and Quality assessment of aromatic oils, followed by presentation of Dr. Nasheeman Ashraf on cultivation practices of Sclerea.
- It was then followed by student-interaction programme with scientists working under aroma mission project. Dr. Suresh Chandra also gave valedictory lecture, and purpose of the programme.
- The second session lab visit programme was organized to QC/QA under supervision of Er. Rajneesh Anand, Mrs. Deepika Singh, Dr. A.P. Gupta and Dr. Bikarma Singh. HPLS, TLS, GC/MS, titration, role of NABL etc. related to analysis of chemicals from plants were briefed in the session. Live practical demonstrations were made by different staff's members working in QC/QA division. Lots of discussions on different machines, working parameters etc. were held indetails.
- The vote of thanks was presented by Dr. Bikarma Singh, highlighting national level importance of Aroma Mission Project, and role of individuals towards country prosperity.

Five days sessions were highly interactive and all the Project Assistants, PIs/Co-PIs `took part in discussion and gave their valuable inputs. These days were very interesting and informative as all students gets chance to look and visualize the facilities and work carried out at CSIR laboratories. All the Scientists /Technical Assistants who were associated with the Aroma Mission Presented their best work/expertise.

Photos: Snapshots of Orientation Programme under Aroma Mission

3.0 MICROBIAL BIOTECHNOLOGY

3.1 A strain of Streptomyces sp. isolated from rhizospheric soil of *Crataegus oxycantha* producing Nalidixic acid, a synthetic antibiotic

A strain of *Streptomyces* sp. (C-7) was isolated from rhizospheric soil of *Crataegus oxycantha*. The 16S rRNA gene sequence of strain C-7 displayed 99% sequence similarity with different *Streptomyces* species. The highest score was displayed for *Streptomyces* sp. strain Chy2-8 followed by *Streptomyces violarus* strain NBRC13104 and *Streptomyces arenae* strain ISP5293. Position of C-7 in phylogenetic tree suggested uniqueness of the strain. Nalidixic acid (**1**), a quinolone antibiotic, was isolated from *Streptomyces* sp. strain **(**C-7) for the first time and characterized by NMR and chemical analysis. Compound **1** exhibited antimicrobial activity against *Escherichia coli* and *Pseudomonas aeruginosa*. The production of compound **1** was also validated by repeating fermentation of strain C-7 and compound isolation in a separate natural product laboratory without informing method and result. Further, Compound 1 showed cytotoxic effect against human prostate cancer cell line PC3 with an IC_{50} 11 µg/mL. To the best of our knowledge, this is the first report showing production of nalidixic acid naturally by a strain of *Streptomyces* sp.

Table 3.1.1 : Comparison of the 16s rRNA gene sequence of C-7 among isolates of *Streptomyces*

Species	Strain	Similarity (%)	Total score	Gen Bank accession number
Streptomyces sp.	Chy2-8	99	1310	GQ222221
Streptomyces violarus	NBRC13104	99	1304	NR041116
Streptomyces arenae	ISP5293	99	1304	NR_025494
Streptomyces kunmingensis	NRRLB16240	98	1240	NR043823
Streptomyces flavovariabilis	cfcc3160	98	1264	FJ792572
Streptomyces fimbriatus	Cfcc3155	98	1260	GQ258688
Streptomyces pseudovenezuelae	REA17	98	1247	JN167527
Streptomyces chartreusis	L1105	98	1247	HM149781
Actinobacterium	HW3	98	1243	HQ696524
Streptomyces hawaiiensis	NRRL15010	98	1242	EU624140

Table 3.1.2: Antimicrobial activity (µg/mL) of the extract of *Streptomyces* sp. (Strain C-7), compound **1** and commercial nalidixic acid against *K. pneumoniae*, *P. aeruginosa* and *E. coli*.

Extract/ Compound	*Klebsiella pneumoniae*		*Pseudomonas aeruginosa*		*Escherichia coli*	
	MIC	MBC	MIC	MBC	MIC	MBC
Extract of *Streptomyces* sp. (Strain C-7)	25	25	25	25	15.62	15.62
Compound **1**	>100	>100	6.25	6.25	3.125	3.125
Commercial Nalidixic acid	>100	>100	6.25	6.25	3.125	3.125
Ciprofloxacin	-	0.75	0.3125	0.3125	0.046	0.046

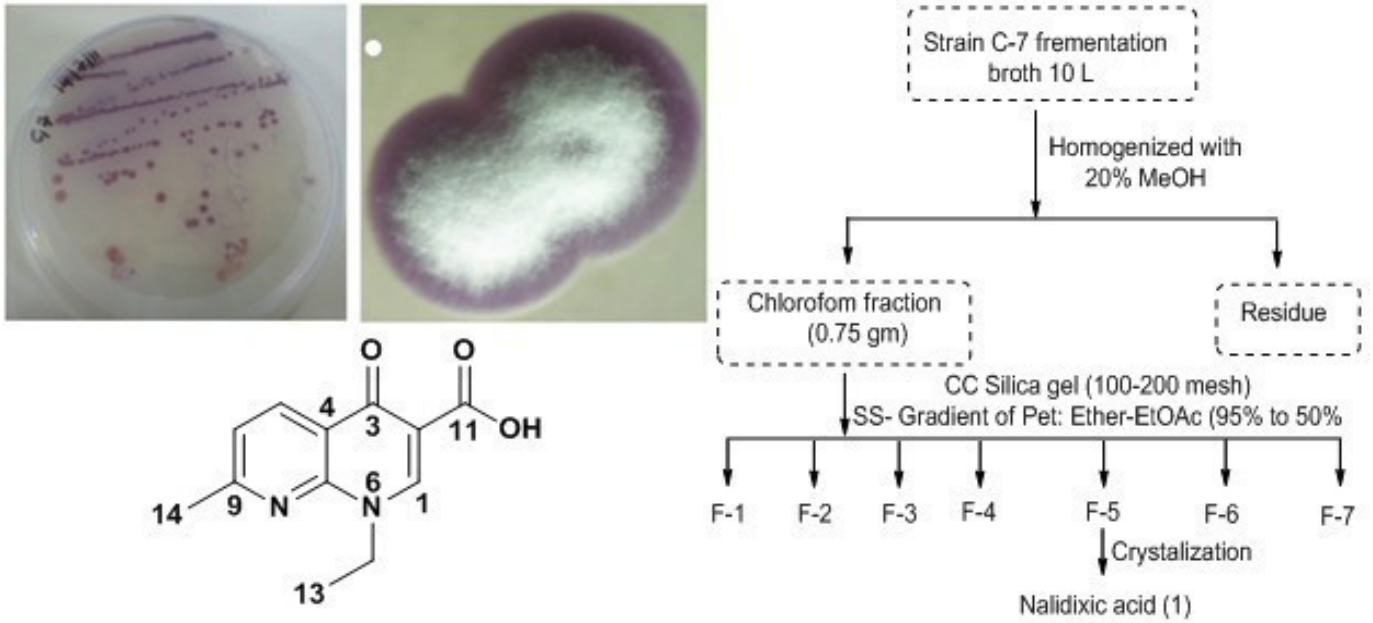


Figure 3.1.1 : Morphology of strain C-7, an actinomycete, associated in nature with the rhizospheric soil of *Crataegus oxycantha*, identified as *Streptomyces* sp. A) Growth of strain C-7 on starch casein agar plate B) Colony under stereomicroscope C) Structure of NA D) Flow chart to isolate NA from Strain C-7 fermentation broth.

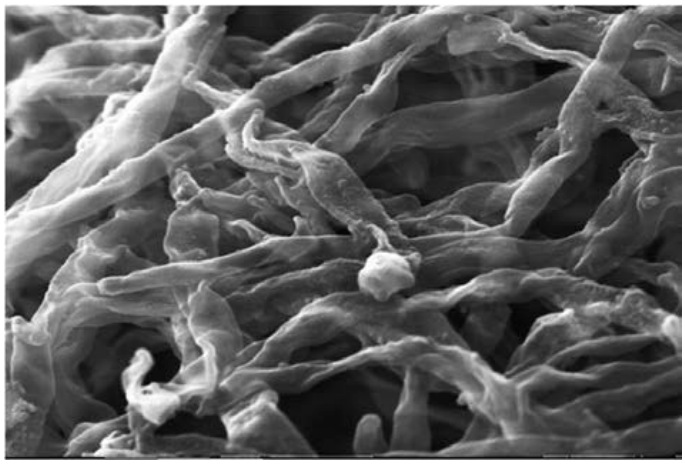


Figure 3.1.2: Surface electron microscopy of strain C-7 C-7 showing aerial mycelia with simple branchingand straight spore bearing hyphae.

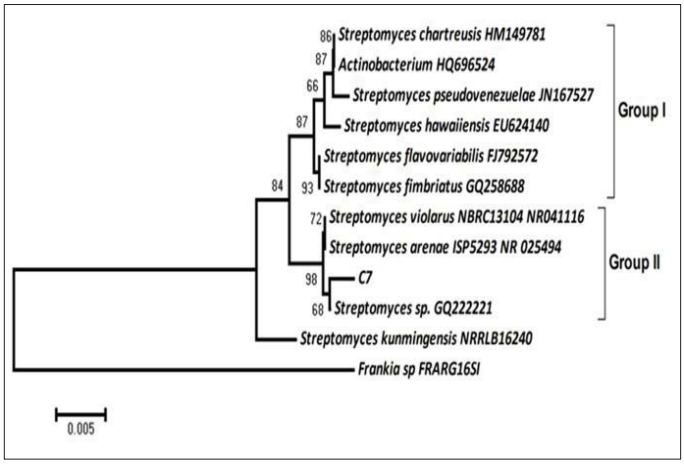


Figure 3.1.3: Phylogenetic position of strain C-7

3.2 Endophytic fungi associated with *Monarda citriodora,* an aromatic and medicinal plant and their biocontrol potential

The Food and Agriculture Organization has estimated that every year considerable losses of the food crops occur due to plant diseases. Although, fungicides are extensively used for management of plant diseases, they are expensive and hazardous to the environment and human health. Alternatively, biological control is the safe way to overcome the effects of plant diseases and to sustain agriculture. Since *Monarda citriodora* Cerv. Ex Lag. (Lamiaceae/Labiatae) is known for its antifungal properties, it was chosen for the study. The study isolates the endophytic fungi from *M. citriodora* and assesses their biocontrol potential. The isolated endophytes were characterized using ITS-5.8S rDNA sequencing. Their biocontrol potential was assessed by using different antagonistic assays against major plant pathogens. Twenty-eight endophytes representing 11 genera were isolated, of which, around 82% endophytes showed biocontrol

potential against plant pathogens. MC-2L (*Fusarium oxysporum*), MC-14F (*F. oxysporum*), MC- 22F (*F. oxysporum*) and MC- 25F (*Fusarium redolens*) displayed significant antagonistic activity against all the tested pathogens. Interestingly, MC-10L (*Muscodor yucatanensis*) completely inhibited the growth of *Sclerotinia* sp., *Colletotrichum capsici*, *Aspergillus flavus* and *Aspergillus fumigatus* in dual culture assay, whereas MC-8L (*Aspergillus oryzae*) and MC-9L (*Penicillium commune*) completely inhibited the growth of the *Sclerotinia* sp. in fumigation assay. Endophytes MC-2L, MC- 14F, MC-22F and MC-25F could effectively be used to control broad range of phytopathogens, while MC- 10L, MC-8L and MC-9L could be used to control specific pathogens. Secondly, endophytes showing varying degrees of antagonism in different assays represented the chemo- diversity not only as promising biocontrol agents but also as a resource of defensive and bioactive metabolites.

Table 3.2.1: Biocontrol Potential of endophytes against plant pathogens using dual culture assay in terms of percent growth inhibition

S No.	Endophyte	*Fusarium solani*	*Sclerotinia* sp.	*Colletotricum capsici*	*Aspergillus flavus*	*Aspergillus fumigatus*
1	MC-1-L	-	47.6	-	-	-
2	MC-2-L	**59.6**	**69.9**	**78.4**	**73.4**	**74**
3	MC-3-L	-	22.8	**53.2**	-	-
4	MC-4-L	-	43	-	-	**66.2**
5	MC-5-L	39.1	-	**73.2**	-	-
6	MC-6-L	-	-	-	-	-
7	MC-8-L	-	-	-	-	-
8	MC-9-L	-	-	-	-	-
9	MC-10-L	-	**100**	**100**	**98**	**100**
10	MC-12-L	-	-	**78.2**	-	-
11	MC-14-L	9.5	17.3	-	40.2	28.2
12	MC-15-L	11.5	11.3	-	17.07	4.8
13	MC-16-L	15.07	41	**78.1**	29.7	41.5
14	MC-17-L	-	-	-	-	-
15	MC-18-L	-	-	**78.7**	-	-
16	MC-20-L	-	42	20	-	35
17	MC-24-L	26.9	**50**	-	3.5	36.8
18	MC-25-L	31.2	-	-	28.6	29.4
19	MC-13-R	-	**78.9**	**51**	**62.7**	43.1
20	MC-20-R	41.6	39.8	-	-	-
21	MC-7-F	5.2	-	-	0.61	44.15
22	MC-14-F	**56.2**	34	**52.6**	-	-
23	MC-17-F	-	40	15.09	**62.4**	-
24	MC-21-F	24.6	40	22	46.8	0.6
25	MC-22-F	-	-	**59.4**	-	-
26	MC-23-F	-	3.4	-	-	38.4
27	MC-25-F	**52.3**	**64.1**	**72.3**	-	-
28	MC-26-F	6.3	24.05	**54.12**	10.08	42.9

Table 3.2.2: Biocontrol Potential of endophytes against plant pathogens using culture filtrate assay in terms of percent growth inhibition

S No.	Endophyte	*Fusarium solani*	*Sclerotinia* sp.	*Colletotricum capsici*	*Aspergillus flavus*	*Aspergillus fumigatus*
1	MC-1-L	25	15	14.28	10	35
2	MC-2-L	4	20	50	50	50
3	MC-3-L	25	20	21.42	15	30
4	MC-4-L	**50**	**69.56**	**63.15**	**80**	44
5	MC-5-L	33.33	**65.21**	**68.42**	**65**	44
6	MC-6-L	**50**	**56.52**	**73.68**	**60**	22.22
7	MC-8-L	**50**	**60.87**	21.05	**50**	22.22
8	MC-9-L	**56.66**	**56.52**	47.36	30	**55**
9	MC-10-L	25	20	14.28	15	40
10	MC-12-L	29.16	10	**50**	20	10
11	MC-14-L	**66**	**75**	28.57	**75**	25
12	MC-15-L	**56.66**	34.78	21.05	35	**50**
13	MC-16-L	16	25	21.42	**55**	20
14	MC-17-L	33.33	47.82	**57.89**	10	44
15	MC-18-L	**56.66**	**65.21**	5.2	**75**	5
16	MC-20-L	25	10	7.1	5	5
17	MC-24-L	**53.33**	43.47	**52.63**	**55**	22.22
18	MC-25-L	46.66	**65.21**	47.36	**50**	11
19	MC-13-R	16	40	21.42	**90**	20
20	MC-20-R	16	0	28.57	25	35
21	MC-7-F	29.16	**50**	42.85	**50**	40
22	MC-14-F	**66.66**	**69.56**	**63.15**	**65**	**72.2**
23	MC-17-F	25	15	42.85	**60**	10
24	MC-21-F	25	20	0	10	**50**
25	MC-22-F	**56.66**	**65.21**	**57.89**	**65**	**61.1**
26	MC-23-F	25	40	7.1	20	20
27	MC-25-F	**56.66**	**60.87**	**57.89**	**60**	**55**
28	MC-26-F	**50**	**73.91**	10.52	**65**	27

Table 3.2.3 : Biocontrol Potential of endophytes against plant pathogens using fumigation assay in terms of percent growth inhibition

S No.	Endophyte	*Fusarium solani*	*Sclerotinia* sp.	*Colletotricum capsici*	*Aspergillus flavus*	*Aspergillus fumigatus*
1	MC-1-L	2	47.91	33.33	**71.05**	**71.11**
2	MC-2-L	0	16.67	27.77	26.82	37.77
3	MC-3-L	33.33	39.58	27.77	22.22	39.74
4	MC-4-L	16	20.83	33.33	4.87	**68.88**
5	MC-5-L	23.33	21.05	0	0	48.88

S No.	Endophyte	*Fusarium solani*	*Sclerotinia* sp.	*Colletotricum capsici*	*Aspergillus flavus*	*Aspergillus fumigatus*
6	MC-6-L	6	0	16.66	46.34	**55.55**
7	MC-8-L	10	**100**	**60**	**75.61**	**66.66**
8	MC-9-L	33.33	**100**	**72.22**	**51.22**	**55.55**
9	MC-10-L	40	0	**83.33**	**88**	**68.88**
10	MC-12-L	16	**68.75**		34.14	**51.11**
11	MC-14-L	27.08	**73.68**	22.22	36.58	40
12	MC-15-L	40	41.67	33.3	**56.09**	33.33
13	MC-16-L	6	43.75	**72.22**	26.82	46.66
14	MC-17-L	0	**52.08**	27.77	0	33.33
15	MC-18-L	20.8	26.31	**72.22**	39.02	**51.11**
16	MC-20-L	23.33	31.15	44.44	7.31	0
17	MC-24-L	47.91	36.84	44.44	37.5	40
18	MC-25-L	36.6	**50**	**0**	**52**	24.44
19	MC-13-R	10.41	8.33	27.77	43.9	11.11
20	MC-20-R	0	35.41	44.44	21.95	**55.55**
21	MC-7-F	10	10.52	33.33	26.82	48.88
22	MC-14-F	10	36.84	38.88	7.3	40
23	MC-17-F	10	0	55.55	39.02	26.66
24	MC-21-F	3	**58.33**	**61.11**	39.02	0
25	MC-22-F	25	0	27.77	**60**	28.88
26	MC-23-F	0	35.41	44.44	25	33.33
27	MC-25-F	6	47.91	**88.88**	26.82	40
28	MC-26-F	75	33.33	16.66	39.02	22.22

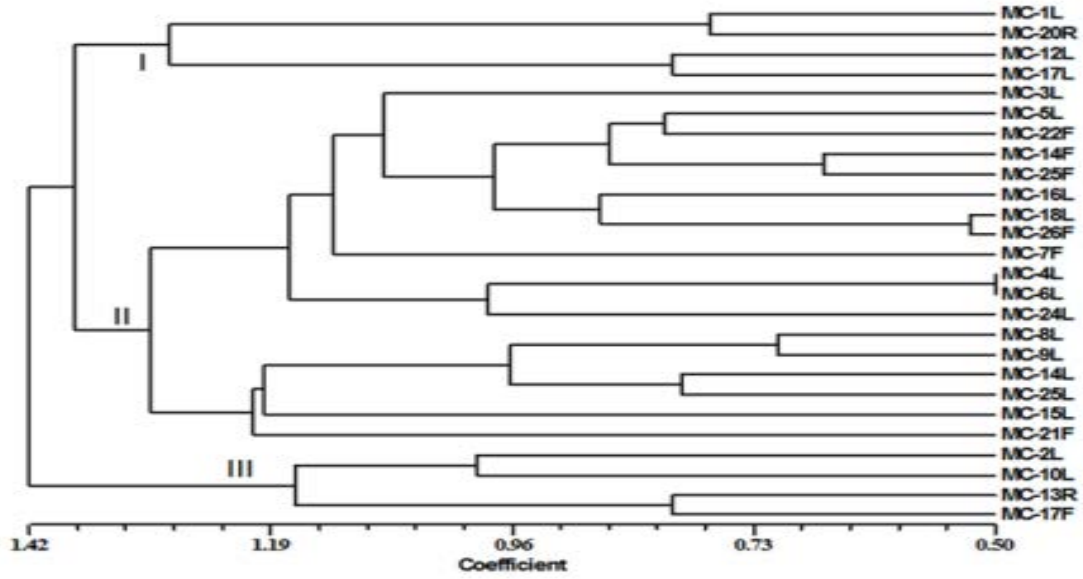


Figure 3.2.1: Phylogenetic tree generated by using NTSYS program showing the clustering of endophytes with varying degree of antagonism

3.3 Unraveling the bacterial endophytic microbiome of saffron

In India, Saffron is cultivated only in Kashmir in a very limited area. But, poor agronomic practices and disease management together with lack of breeding approaches has led to declining trend in saffron production and quality. The area of cultivation has drastically decreased due to low productivity and incidence of corm rot disease. Endophytes play various indispensable roles in nature that help the plants to adapt to different environmental conditions, and also influence plant nutrition, growth, development, survival, and distribution. Therefore, our work on saffron is aimed to isolate endophytes from this plant growing in Kashmir and develop a microbial formulation for corm rot inhibition, increased productivity and enhancement of apocarotenoid content for sustainable saffron cultivation. The work on plant-microbe interactions on *Crocus* may help to improve the quality of the crop through establishment of favourable plant-microbe associations. This work has advanced our knowledge of the preference of symbiotic associations developed by the saffron plant with endophytes and how they may be involved in favouring the growth and development of the plant, and which others may be turning into pathogens in adverse conditions. An endophyte of saffron *Mortierella alpina* has shown promising results as a potential plant growth promoting fungal culture. The fungus is known to be very safe for the environment as well as for humans and animals. The bacterial endophytic microbiome has also yielded lead microbes for plant growth promotion and corm rot inhibition in the host. Thus, our focus is to develop an endophyte- based biofertilizer and biocontrol agent for the sustainable growth of *Crocus sativus.* This formulation may be a single organism or a consortia of two or more endophytes. The technology will lead to an industrial process as well as an agrotechnology beneficial for saffron growers. M/S Globil's Agri and Food Enterprise, a company dealing in agricultural services has shown keen interest in these organisms/products. Diverse microorganisms have been isolated from unexplored environmental niches, characterized and conserved *ex situ.* The microbial resources and their natural products are maintained in the Microbial and chemical repository of the institute.

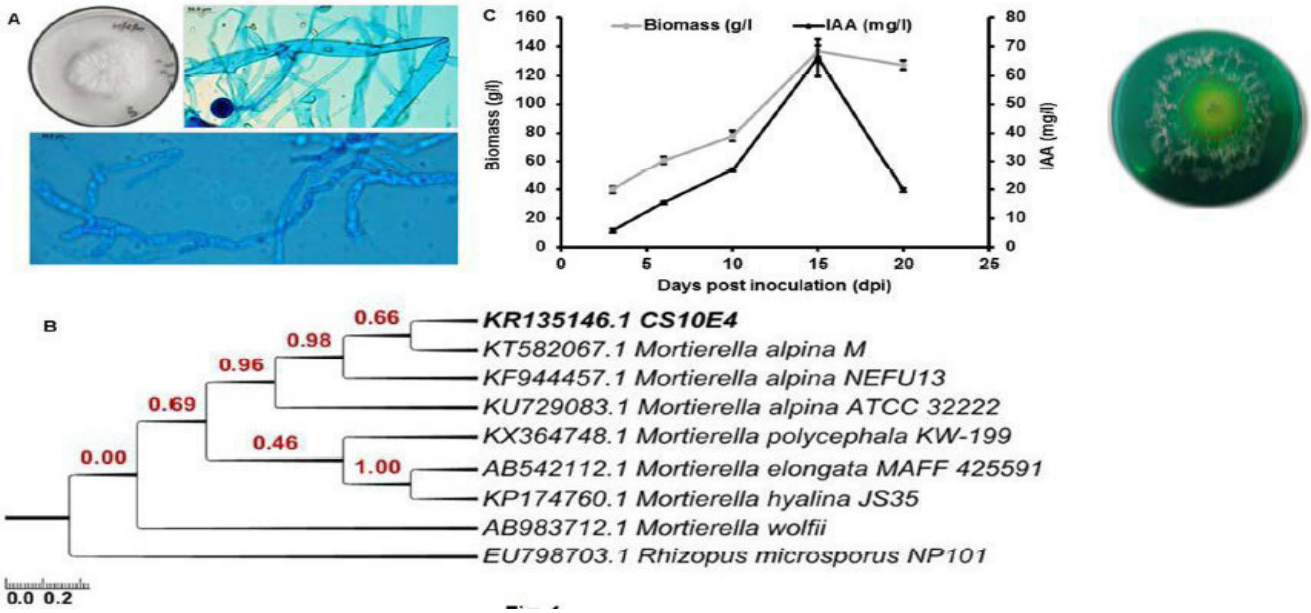


Figure 3.3.1: (A) Whitish colonies with zonate growth pattern on PDA plate. The mycelia are ceonocytic from which arise erect sporangiophores bearing terminal globose saporangia, (B) the evolutionary history based on ITS1-5.8S- ITS2 ribosomal gene sequence, (C) time course accumulation of biomass and phytohormone (indole acetic acid) produced by the endophyte, and (D) Yellow color of the media shows siderophore production by the endophyte CS10E4.

4.0 DISCOVERY INFORMATICS

4.1 Computer aided drug discovery methods for the identification of potent CDK2 inhibitors

Priya Mahajan, Amit Nargotra, Gousia Chashoo, Parvinder Pal Singh

Cyclindependentkinasesplayacentral role in cell cycle regulation which makes them a promising target with multifarious therapeutic potential. CDK2 regulates various events of the eukaryotic cell division cycle and the pharmacological evidences indicate that over expression of CDK2 causes abnormal cell-cycle regulation, which was directly associated with hyper proliferation of cancer cells. Therefore, CDK2 is regarded as a potential target molecule for anti-cancer medication. Thus to decline CDK2 activity by potential lead compounds has proved to be an effective treatment for cancer. The availability of a large number of X-ray crystal structures and known inhibitors of CDK2 provides a gateway to perform computational studies on this target. With the aim to identify new chemical entities from commercial libraries with increased inhibitory potency for CDK2, ligand and structure based computational drug designing approaches were applied. A drug like library of 50,000 compounds from ChemDiv and ChemBridge database was screened against CDK2 and 110 compounds were identified using the parallel application of these models. On in vitro evaluation of 40 compounds, 7 compounds were found to have more than 50% inhibition at 10µM. MD studies of the hits revealed the stability of these inhibitors and pivotal role of Glu81 and Leu83 for binding with CDK2. The overall study resulted in the identification of 4 new chemical entities possessing CDK2 inhibitory activity. The overall activity is summarized in figure 4.1.1.

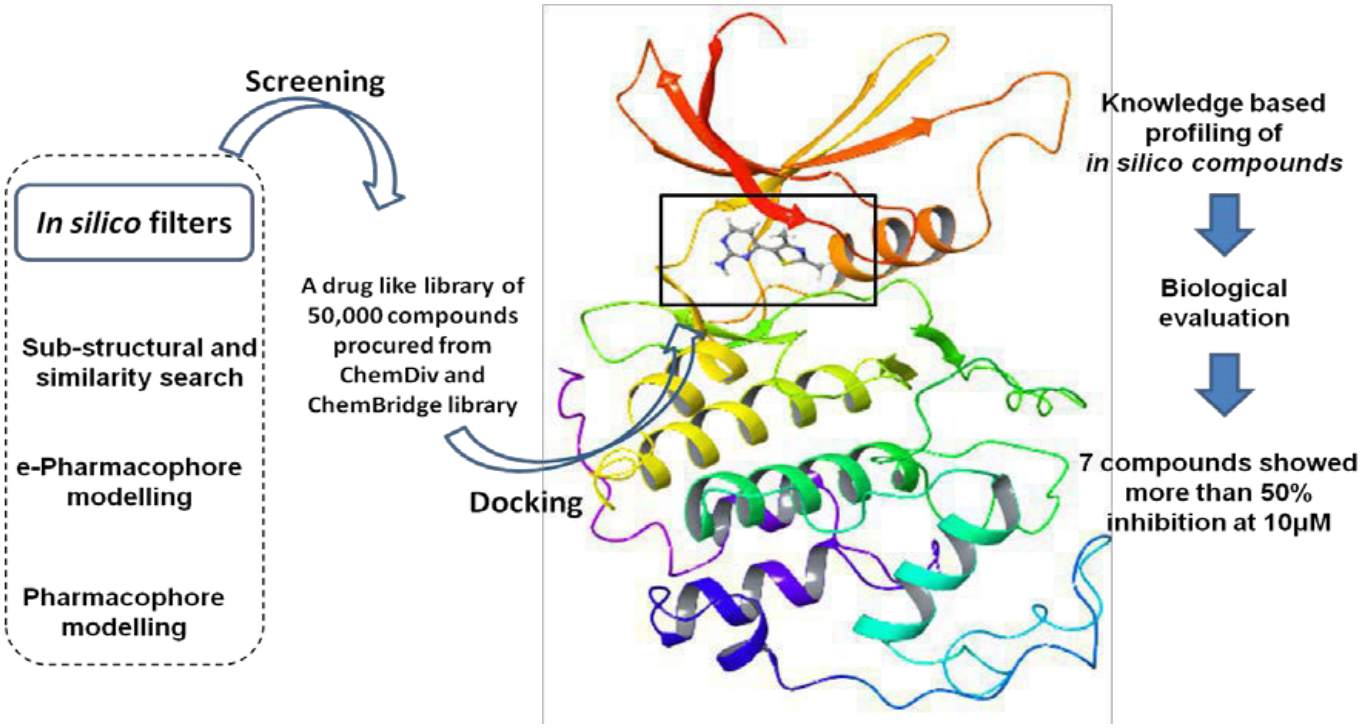


Figure 4.1.1. In silico filtering critera for the identification of potent CDK2 inhibitors.

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

Harshita Tiwari, Amit Nargotra, Smriti Sharma, Inshad Ali Khan

Bacterial diseases are the leading cause of death worldwide. Emerging resistance to the existing antibacterial therapy isthe major problem in present scenario, leading to an urgent requirement for identification of novel drug targets. MurA catalyses the first committed step in peptidoglycan biosynthesis. MurA catalyses the transfer of an enolpyruvyl group from Phosphoenolpyruvate (PEP) to UDP-N-acetyl glucosamine (UNAG) to form UDP-N-acetyl glucosamine enolpyruvate (UNAGEP). Enzyme MurA is composed of 119 amino acids. A surface loop (Pro111–Pro121, *E. coli* numbering) undergoes a large conformation change upon the binding of first substrate UDP- N-acetyl glucosamine (UNAG) which brings substrate Phosphoenol- pyruvate close enough to UNAG, so that reaction can be carried forward. Fosfomycin (an epoxide chemically) is the only approved drug which can target enzyme MurA.Fosfomycin undergoes ring opening reaction and binds covalently with Cys115. Mutation of Cys115Asp leads to complete resistance to drug fosfomycin. In this study, a library of 50,000 drug like molecules and in-house library of compounds was screened for potential MurA inhibitors by using a combination of ligand based and structure based molecular modelling approaches. In this study MurA inhibitors are classified in three major categories:

- Inhibitors which target PEP bindingsite.
- Inhibitors which target Arg91 and brings conformational change inMurA.
- Inhibitors which mimics transitionstate.

4.3 Development Sickle Cell database

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

This database has been designed to provide comprehensive information useful for the management of sickle cell disease. Accordingly, all the information about various targets involved in SCA have been collected and arranged in order in this database. Identified targets have been classified into two groups viz. validated and experimental, according to integrity database. The database also contains the information on all the plants which are reported for the treatment/ management of this disease. This portal also contains information about the phytochemicals present in the plants used for the management of sickle cell disease along with their associated references. The plants reported in this database are selected on the basis of literature survey. The database also includes synonym details of selected plants which have been collected from authenticated database 'The Plant List Ver 1.1'. Another very useful link in the database is the information about all the compounds in clinical trial for the management of sickle cell disease. The database further contains the list of publications related to this disease. The 'News' section has also been included in the database to keep the user up- to-date about the various latest happenings on this disease. The main page of the database portal is shown in Figure 4.3.1

4.4 Molecular modeling studies on sickled haemoglobin(HbS)

Harshita Tiwari, Amit Nargotra

Molecular modeling studies to target the HbS structure have been initiated in order to avoid polymerisation. Since, 3D crystal structure is available for this target, and interactive residues are reported we can apply structure based methods for identification of potent HbS binders, which forms a reversible covalent bond with Val1 and brings conformational change to the structure which increases oxygen affinity (figure 4.4.1). GBT440, a small molecule which binds (reversible covalent bond) to the N- terminal A chain of Hb, increases HbS affinity for oxygen, delays in vitro HbS polymerization and prevents sickling of RBCs.

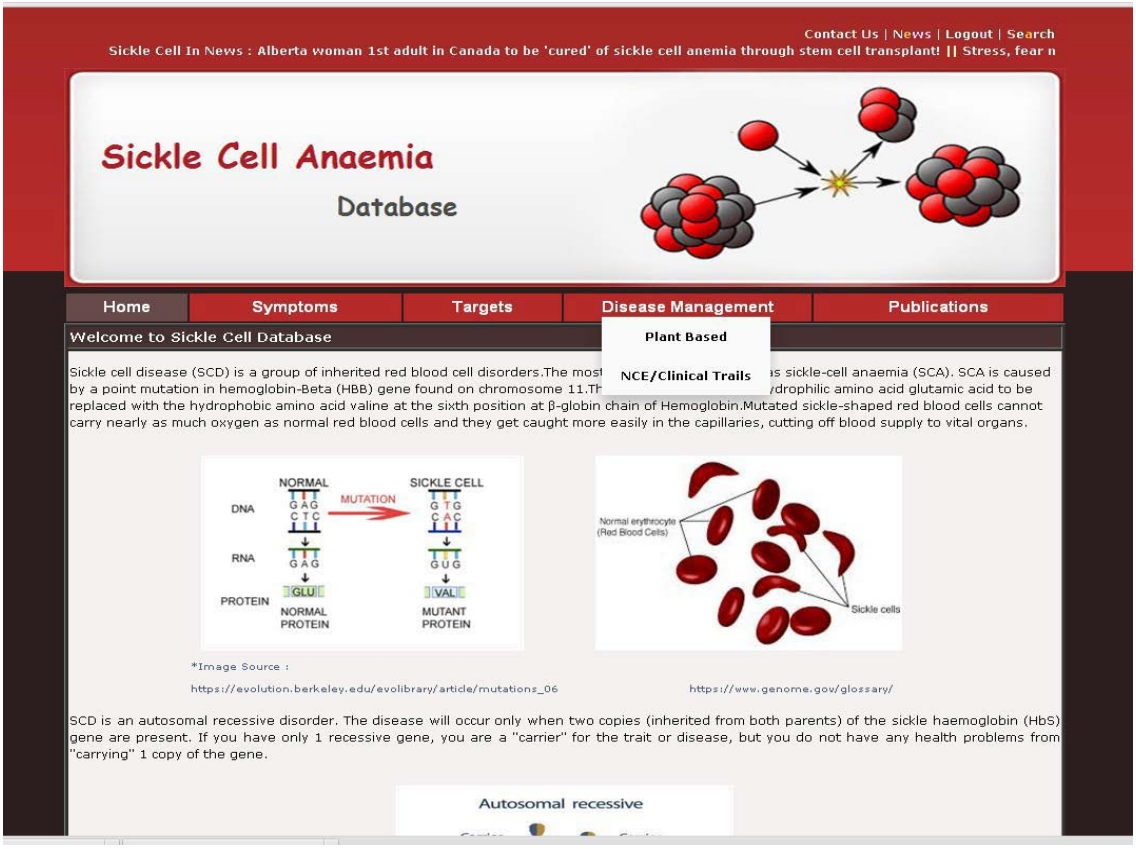


Figure 4.3.1. Snapshot of the main page of the Sickle Cell Database portal.

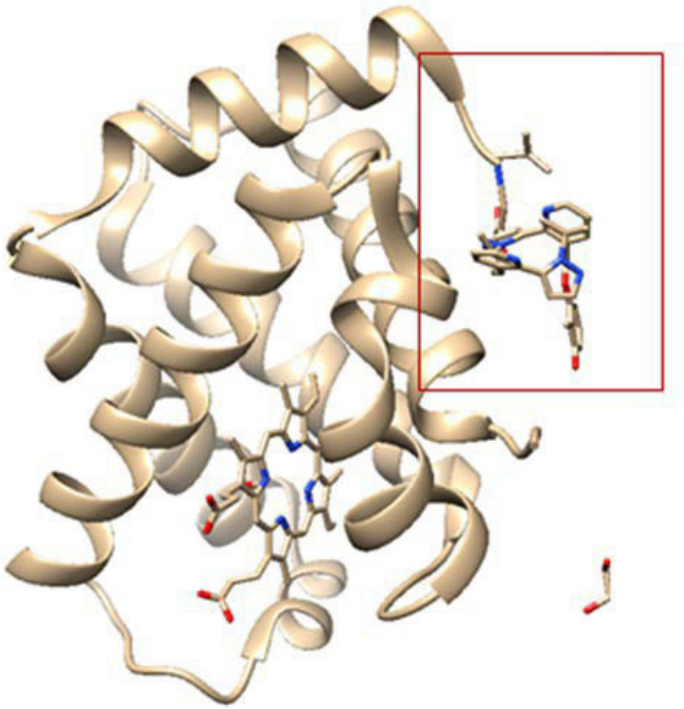


Figure 4.4.1 . 3D ribbon structure of HbS bound with GBT440.

4.5 Development of database on an important Ayurvedic formulation

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

The database of the chemical constituents of the Zandu Pancharishta ingredients was prepared at the Discovery Informatics Division of IIIM Jammu. The entire list of ingredients was first searched for synonyms from The Plant List Ver. 1.1. A total of 357 synonyms were obtained for 34 ingredients. The accepted names and their synonyms as per The Plant List Ver. 1.1, was searched thoroughly for their reported chemical constituents in i) Dictionary of Natural Products (DNP 25.2 Copyright ©2017 Taylor & Francis Group) and ii) KNApSAcK Core System (Plant Cell Physiol.53(2): e1(1–12) (2012). In total, there were close to 2200 chemical constituents found for allthe ingredients. Datasheet for each compound/chemical constituent based on Name, *CAS-ID, MW, Mol Formula, MP, BP, Biological source; Biological Importance and Class* have been prepared and incorporated. Wherever available, IUPAC names and common names have been added. The database, which has been developed using a 3- tier architrecture, has a very strong 'Search' feature which would help the end-user to search the entire content of the database as per his/her subject of interest. The user can search across the database Plant name, compound name, compound class, CAS ID and Molecular weight range.

The entire information of the database is categorized under following tabs (as shown in figure):

i. About the Database
ii. Zandu Pancharishta
iii. Database
iv. Search
v. Project Docs

Figure 4.5.1. Snapshot of the main page

4.6 Updation of Stem cell database(MedchemDB)

Rakhi Talwar, Monika Gupta, Amit Nargotra, Ram Vishwakarma

Regular updation and enrichment of the stem cell portal was carried out. During the reported period about 324 compounds, 16 publications and one target was added in the database. The portal is accessible over Internet at http://medchemdb.iiim.res.in/

4.7 Repository database updation and compound flow management

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

Updation of Institutional compound repository, which comprise of the Institutional pure natural compounds, new chemical entities as an outcome of all medchem projects and the externally procured library of drug like compounds is being regularly carried out. A total of 32 Natural Products and 130 new chemical entities from the med chem projects have been added in the reporting period to the repository along with the HPLC/HPTLC profile. All these compounds are also incorporated into the database for sub-structural search. Further the mother and daughter library was also prepared for the additional 30,000 compounds procured last year. This year a total of 1613 compounds were issued for biological evaluation through this

repository within and outside the Institute. The outcome of the compound repository from the discovery programs at IIIM is shown in Figure 4.7.1.

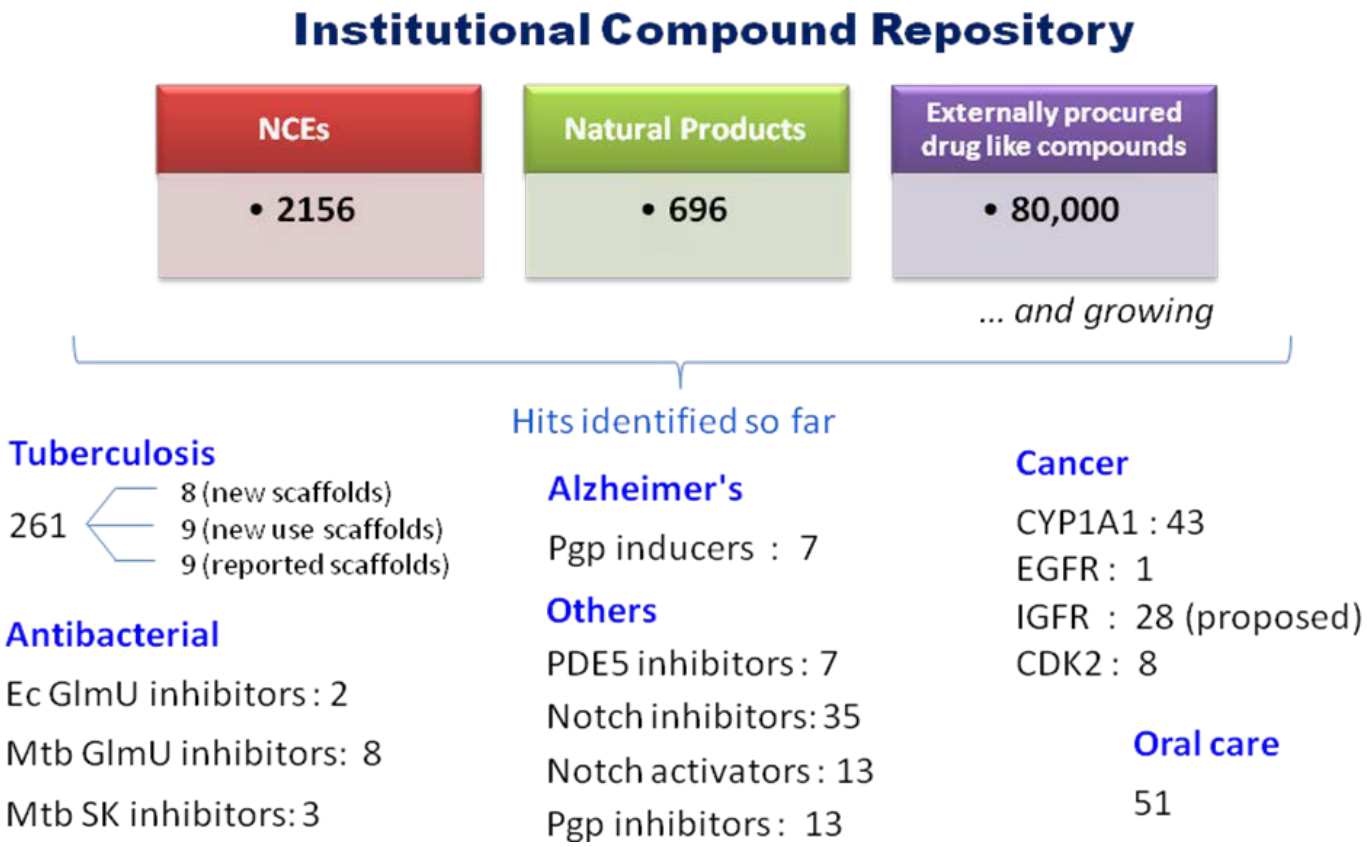
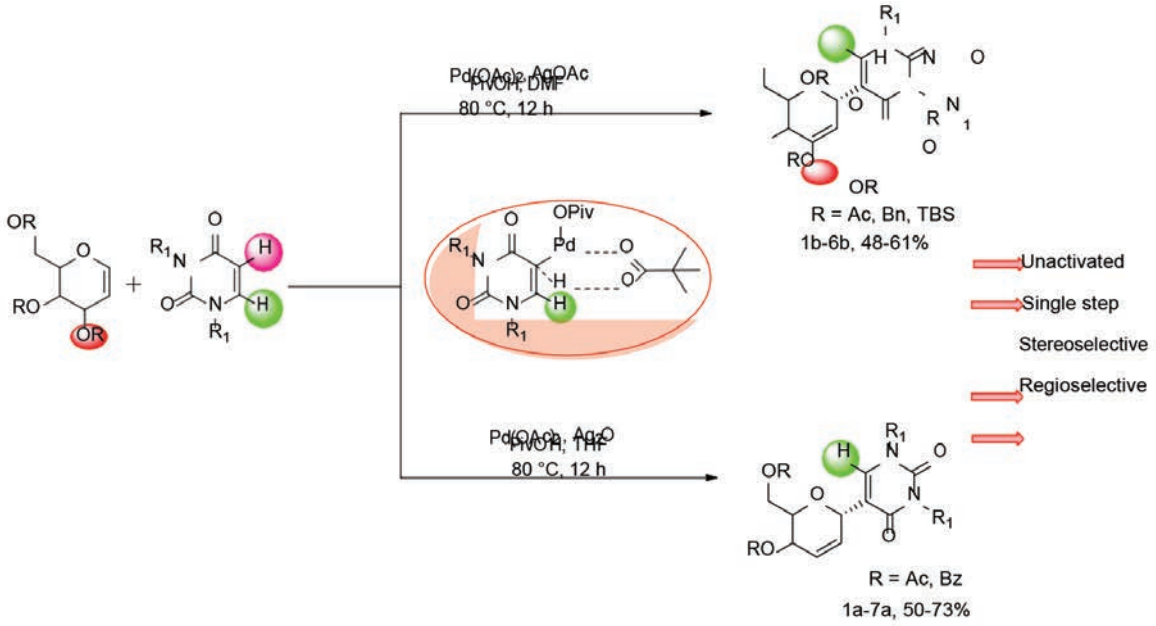


Figure 4.7.1. Discovery outcome of the Institutional compound repository

5.0 BIO ORGANIC CHEMISTRY

5.1 Pd-Catalyzed Regio- and Stereoselective C-Nucleoside Synthesis from Unactivated Uracils and Pyranoid Glycals:

C-nucleosides unlike their N-analogues are more stable to acid and enzyme catalysed hydrolysis. Several bioactive *C*- nucleosides are naturally occurring antibiotics, like Pseudouridine, a *C*- nucleoside present in all types of RNAs increase the protein expression level in synthetic RNA and mediates the nonsense to sense codon conversion. Although there are number of efficient strategies available for the synthesis of N-nucleosides, only a handful of methods are available for their *C*- analogues. One of the most important method for the synthesis of *C*-nucleosides is Pd catalysed direct coupling of pyranoid and furanoid glycals, but these require preactivtion of uracil at C-5 position employing mercuration, stannation or iodination. Besides preactivation of uracilthey require stoichiometric amount of expensive Pd catalyst and handling of toxic reagents like mercury. Taking clue from the biomimetic synthsis of pseudouridine from uridine which proceeds via glycal intermediate, we anticipated that C- nucleosides can be formed regio-and stereoselectivelly directly from unactivated protected uracil and pyranoid glycals under oxidative Pd catalysis.

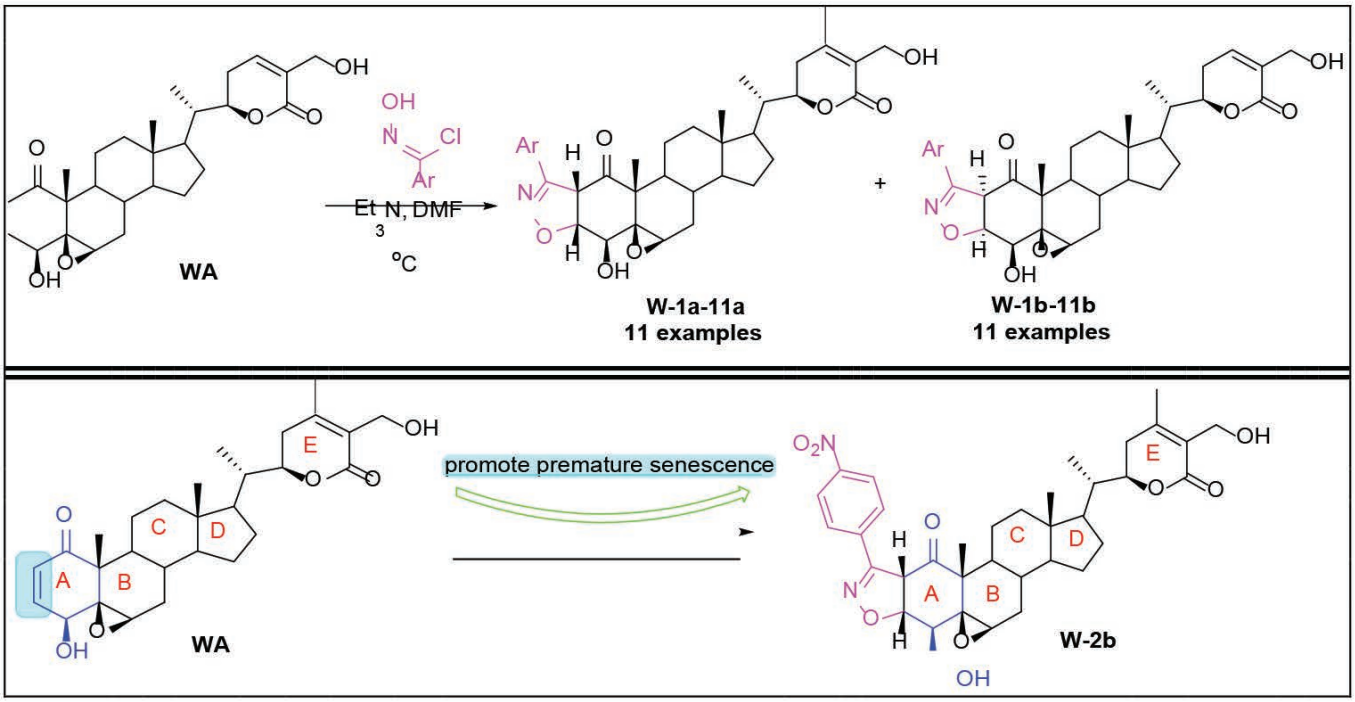


Major outcome of the study:

- ✓ Synthesis of *C*-nucleosides proceeds regio- andstereoselectivelly.
- ✓ No preactivation of uracilrequired.
- ✓ No toxic metal required.
- ✓ Pd required in catalytic amount.
- ✓ Can be extended to furanoidglycals

5.2 Regiospecific Synthesis of Ring A Fused Withaferin A Isoxazoline Analogues: Induction of Premature Senescence by W-2b in Proliferating Cancer Cells

Natural products, particularly steroids, have been employed as a powerful tool for deciphering new biological targets. Indeed, transforming parent bioactive natural steroids to more/new bioactive ones via semisynthetic approach has enlightened researchers for paving way of drug development.Withaferin A (**WA**), a naturally occurring steroidal lactone, has attracted the attention of chemists as well as biologists due to its interesting structure and wide range of biological activities especially its anti-cancer activity. Among the five-membered heterocyclic compounds, 2-isoxazolines are important structural building blocks of biologically active molecules and versatile intermediates in organic synthesis. The importance of isoxazolines also stem from their utility as precursors in the synthesis of 1,3-aminoalcohols, which are excellent starting materials for a wide variety of natural products and related compounds such as alkaloids and nucleoside antibiotics. Thus, the isoxazoline ring system could be semi-synthetically manipulated in presence of bioactive natural product **WA** for the discovery of novel leads with anticancer therapeutic potential. Induction of premature senescence represents a novel functional strategy to curb the uncontrolled proliferation of malignant cancer cells. Senescent cells possess characteristic features including growth arrest, flattened cellular morphology, SA-β-gal activity, and augmentation of cell-cycle specific marker such as cyclin-dependent kinase inhibitor p21. Checkpoint kinase-2 (Chk2) is an essential component to induce bothreplicative and premature senescence through cell-cycle arrest by activating p21 in a p53 dependent manner. However, studies also found that Chk2 can activate senescence in cancer cells by inducing p21, independent of the p53 status of the cell. Hence, Chk2 is a lucratic target that can be manipulated to promote senescence in proliferating cancer cells. Though small molecule natural products such as doxorubicin, camptothecin, resveratrol,triptolide etc., are reported to induce senescence by augmenting p21 through various mechanisms in humancancer cells, the effect of **WA** and its derivatives on induction of premature senescence is yet to be examined. In this endeavour, we sought to examine the potential of fused 2-isoxazoline derivatives of **WA** to induce cytotoxicityin human cancer cells by abrogating cell proliferation through the induction of premature senescence.Using 1,3-dipolar cycloaddition, we synthesized 24 novel isoxazoline derivatives condensed to the ring A of **WA** regiospecifically where the regioselectivity is governed by favourable large-large HOMO-LUMO orbital interactions. Further the attack of dipole from β side of **WA** is less favourablebecause of steric hindrance caused by the substituents at 4, 5 and 10 positions forming the stereoisomer having β,β-ring juncturein major quantity. The synthesized isoxazoline derivatives were screened against proliferating human breast cancer MCF7 and colorectal cancer HCT-116 cell lines. Intrestingly, the *cis* fused products with β-oriented hydrogen exhibited excellent cytotoxic activities against MCF7 and HCT-116 cells. The most potent derivative **W-2b** triggered premature senescence along with increase in senescence-associated β-galactosidase activity, G2/M cell cycle arrest,and induction of senescence-specific marker p21Waf1/Cip1 at its sub-toxic concentration.**W-2b** conferred a robust increase in phosphorylation of mammalian Chk2 in cancer cellsin a dose-dependent manner. Silencing of endogenous Chk2 by siRNA divulged that the amplification of p21 expression and senescence by **W-2b** was Chk2-dependent. In addition,**W-2b** showed excellent *in vivo* efficacy with 83.8% inhibition of tumor growth at a dose of 25 mg/kg, b.w. in mouse mammary carcinoma model.

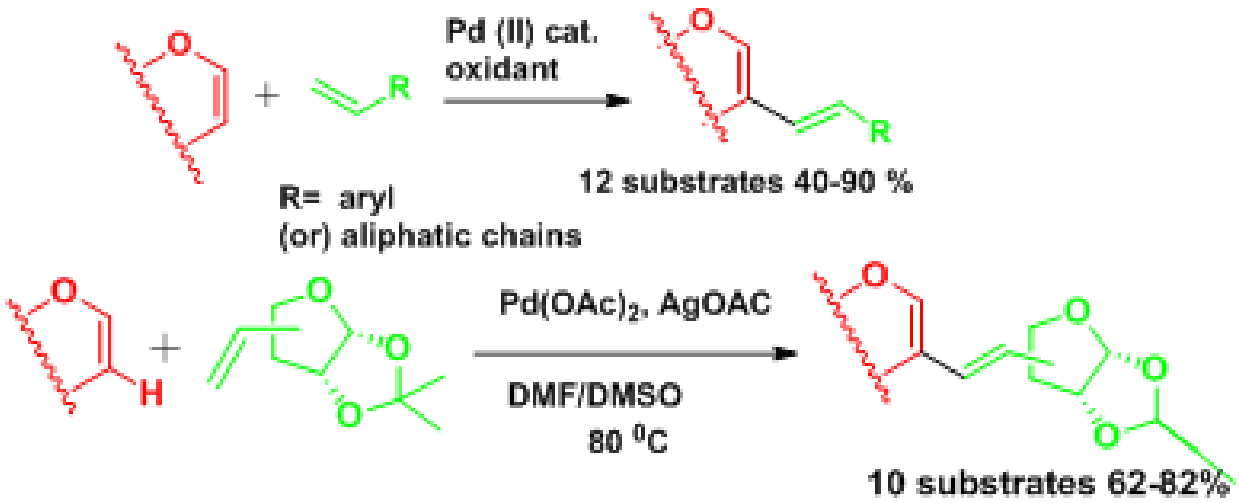


Major outcome of the Work:

- 24 isoxazoline derivatives condensed to ring A of **WA** synthesized in goodyield.
- Regiospecific 1,3-dipolar cycloaddition where the regioselectivity governed by favourable large-large HOMO-LUMO orbitalinteractions.
- *cis*fused products with β-oriented hydrogen exhibited excellent cytotoxic activities against MCF7 and HCT-116 cells than the products having α-oriented hydrogens.
- Potential lead **W-2b** induces premature senescence as an antitumor safeguard mechanism against proliferating cancer cells through activation of tumorsuppressor Chk2.
- **W-2b** show strong *in vivo* efficacy and tolerability.

5.3 Cross dehydrogenative coupling of sugar enol ethers with terminal alkenes in the synthesis of pseudo disaccharides, chiral oxadecalin and conjugated triene

C-glycosides, in which two monosaccharide units are linked carbon to carbon instead of an oxygen atom, are highly stable towards enzymatic hydrolysis and hence can act as carbohydrate mimics. Pseudo-C- disaccharides bearing double bond stitching Monosaccharide units together are of great synthetic and biochemical prominence as double bond sets the stage for several chemical modifications. For example reduction of bridging double bond may lead to C- disaccharide having methylene, or ethylene linkage. Synthetically the major difficulty associated with the synthesis of a pseudo-C-saccharides is the elaborate building block strategies of two coupling monosaccharides units. Cross dehydrogenative coupling approach can be utilized to stich two SP2 hybridized carbon unit by activating C-H bond under palladium catalysis. Utilizing CDC approach we couple sugar enol ether with terminal alkenes both sugar based and non-sugar based under palladium catalysis results Pseudodisaccharides and C-2 branched sugars.

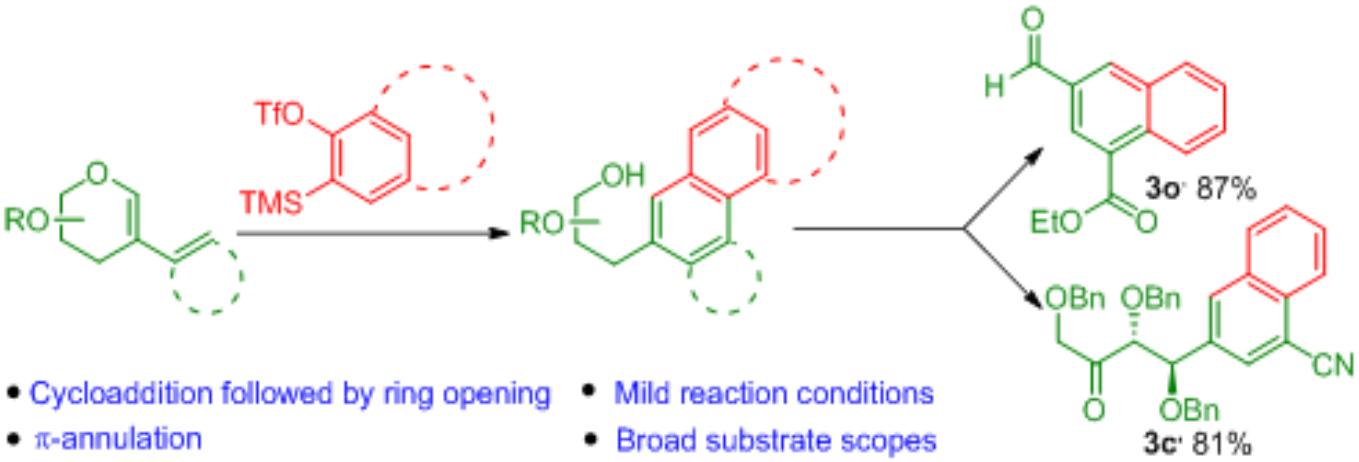


Major Outcome:

- mild reagent system
- sp2-sp2 bond formation with activated/unactivated alkenes
- board substrate scope
- functional group tolerance
- completely *E*-selective
- application in oxadecaline synthesis

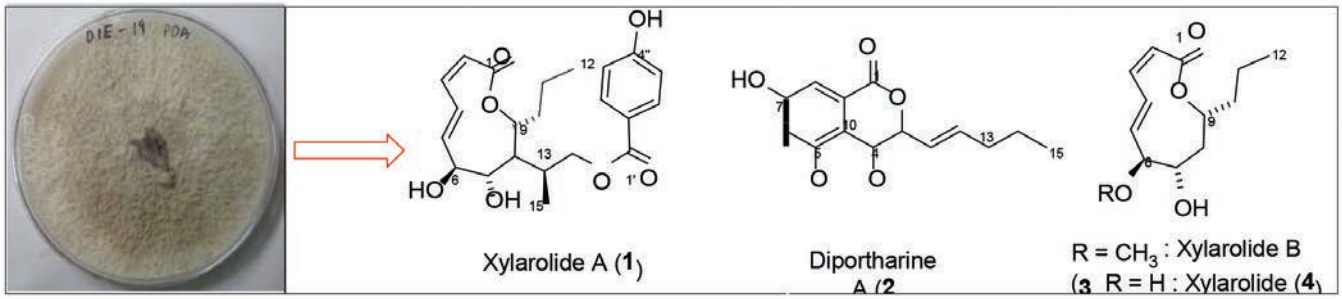
5.4 Tranformation of Substituted Glycals to Chiral Fused Aromatic Cores via Annulative π–Extension Reactions with Arynes

Linearly fused aromatic ring systems can be found in various bioactive natural products and π- conjugated functional materials. Densely substituted fused aromatic cores with chiral side chains are of particular interest because of their ability to bind with receptor biomolecules via p-stacking and chiral recognition. Further, chiral naphthalenes such as BINAP, BINOL, or BINAM have attracted great attention as ligands in transition metal-catalyzed cross-coupling reactions, or as building blocks for the construction of chiral supramolecular and polymeric materials. The annulative p-extension reaction (APEX) using arynes is recognized to have tremendous potential as it facilitates a one-pot π–extension without the requirement for prefunctionalization. Arynes are very suitable candidate for annulative π–extension reactions. Glycals based diene reacted well with arynes results Diels-Alder adduct under basic conditions. Once this Diels- Alder adduct formed aromatic driven annulation takes place results aromatization and opening of sugar ring.



5.5 Valproic Acid Induces Three Novel Cytotoxic Secondary Metabolites in *Diaporthe* sp., an Endophytic Fungus from *Datura inoxia* Mill.

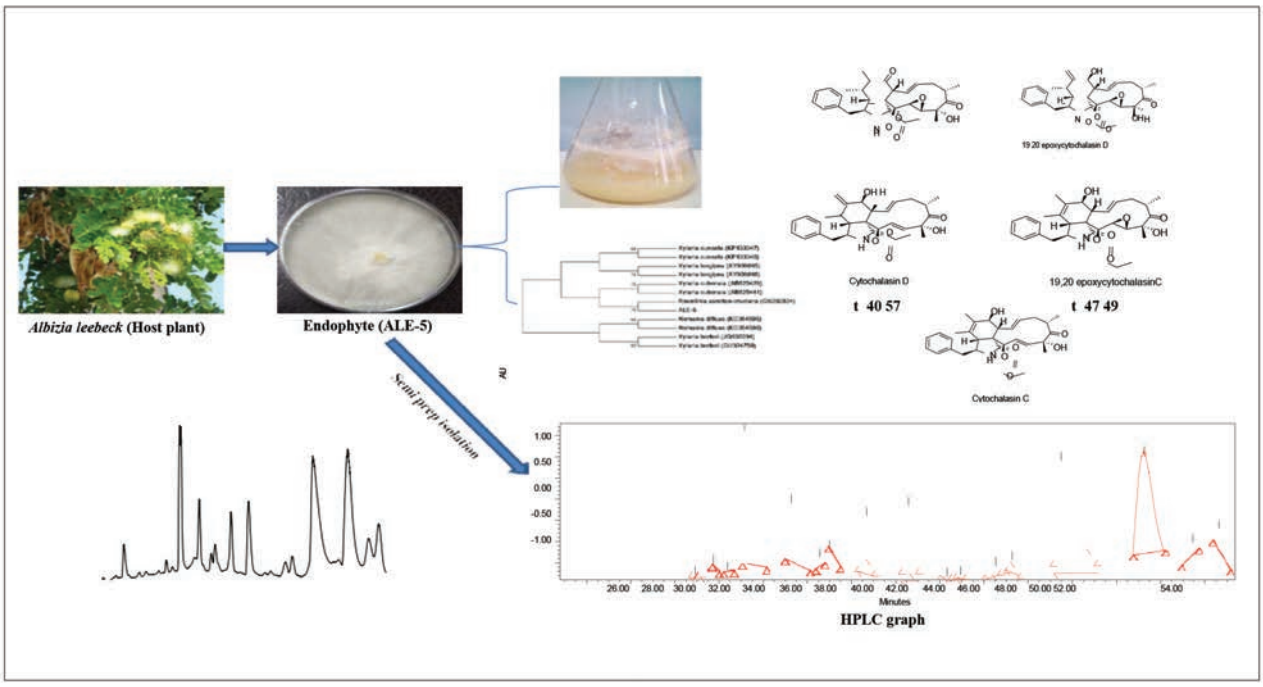
Vishal Sharma, Venugopal Singamaneni, Nisha Sharma, Amit Kumar, Divya Arora, Manoj Kushwaha, Shashi Bhushan, Sundeep Jaglan, Prasoon Gupta



Addition of the valproic acid (histone deacetylases inhibitor) to a culture of an endophytic fungus *Diaporthe* sp. harbored from *Datura inoxia* significantly altered its secondary metabolic profile and resulted in the isolation of three novel compounds, identified as xylarolide A (**1**), diportharine A (**2**) and xylarolide B (**3**) along with one known compound xylarolide (**4**). The structures of all the compounds (**1-4**) were determined by detailed analysis of 1D and 2D NMR spectroscopic data. The relative configurations of compounds **1-3** were determined with the help of NOESY data and comparison of optical rotations with similar compounds with established stereochemistry. All the isolated compounds were screened for antibacterial, antioxidant and cytotoxic activities. Xylarolide A(**1**) and xylarolide(**4**) displayed significant growth inhibition of MIAPaCa-2 with an IC_{50} of 20 and 32 μM respectively and against PC-3 with an IC_{50} of 14 and 18μM respectively. Moreover, compound **1** displayed significant DPPH scavenging activity with EC_{50} of 10.3µM using ascorbic acid as a positive control.

5.5 New Cytochalasin from Rosellinia sanctae-cruciana, an Endophytic Fungus of Albizia lebbeck

Nisha Sharma, Manoj Kushwaha, Divya Arora, Shreyans Jain, Venugopal Singamaneni, Sonia Sharma, Ravi Shankar, Shashi Bhushan, Prasoon Gupta, Sundeep Jaglan



To explore the potential of *Rosellinia sanctae-cruciana* an endophytic fungi associated with *Albizia lebbeck* was investigated for pharmaceutically important cytotoxic compounds. One novel cytochalasin, named Jammosporin A (**1**) and four known analogues (**2-5**) were isolated from the culture of the endophytic fungus *Rosellinia sanctae-cruciana*, harbored from the leaves of medicinal plant *Albizia lebbeck*. Their structures were elucidated by extensive spectroscopic analyses including 1D and 2D NMR data along with MS data and by comparison with literature reports. In preliminary screening the ethyl-acetate extract of the fungal culture was tested for the cytotoxic activity against a panel of four cancer cell lines (MOLT-4, A549, MIA PaCa- 2 and MDA-MB-231), was found to be active against MOLT-4 with IC_{50} value of 10 μg/mL. Owing to the remarkable cytotoxic activity of the extract the isolated compounds (**1-5**) were evaluated for their cytotoxicity against MOLT-4 cell line by MTT assay. Interestingly, compounds **1-2, 4** and **5** showed considerable cytotoxic potential against the human leukemia cancer cell line (MOLT-4) with IC_{50} values of 20.0, 10.0, 8.0 and 6.0μM, respectively, while compound **3** showed IC_{50} value of 25 μM. This is the first report of existence of this class of secondary metabolites in *Rosellinia sanctae- cruciana* fungus. This study discovered a novel compound, named ammosporin A, isolated for the first time from *Rosellinia sanctae-cruciana*, an endophytic fungi of *Albizia lebbeck* with anticancer activity against MOLT-4 cell line. *R. sanctae-cruciana* represents an interesting source of a novel compound with a potential to be used as a therapeutic agent against human leukemia cancer cell line (MOLT-4).

5.6 Bacillus amyloliquefaciens induces production of a novel blennolide K in coculture of Setophomaterrestris

Arora D, Chashoo G, Singamaneni V, Sharma N, Gupta P, Jaglan S.

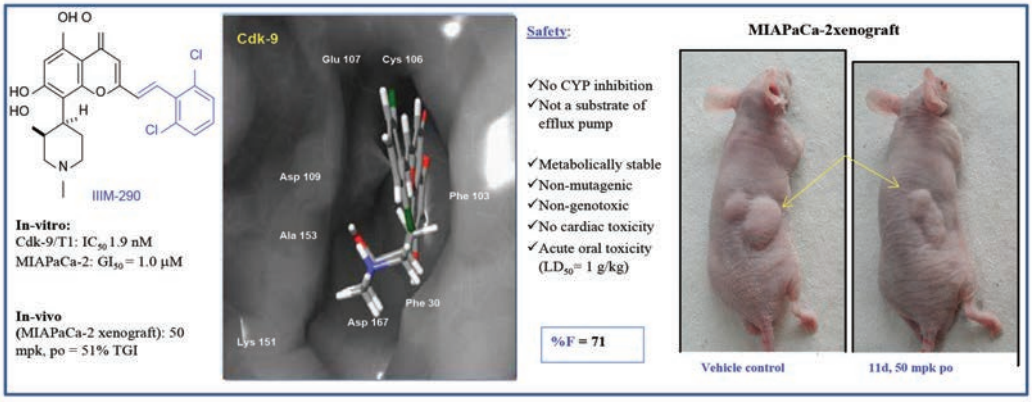
The discovery of known bioactive chemical leads from microbial monocultures hinders the efficiency of drug discovery programmes. Therefore, in recent years, the use of fungal–bacterial co- culture experiments has gained considerable attention due to their ability to generate new bioactive leads. In this work, fungal strain *Setophoma terrestris* was co- cultured with *Bacillus amyloliquifaciens* to discover novel bioactive compounds. The bioactive methanolic coculture extracts waschosen for the isolation of compounds by chromatographic methods. The isolated compounds were characterized by NMR and mass spectrometric techniques. Co-culture extract has resulted in the production of five blennolides. The novel compound, blennolide K was found active against PC-3 (prostate) and MCF-7 (breast) cell lines with an IC50 value of 3.7±0_6 and 4.8±0.4 µmol l^{-1} respectively. Furthermore, the nuclear morphology study in PC-3 cells after treatment with blennolide K, demonstrated chromatin condensation, formation of apoptotic bodies and shrinkage of cells. To our knowledge, only few studies have reported the induction of bioactive compounds by co- culture having long distance inhibition morphology. This is principally due to the low occurrences of such morphology. Our study demonstrates the impact of co-culture on production of new chemical leads in drug discoveryprogrammes.

6.0 MEDICINAL CHEMISTRY

6.1 Discovery and Preclinical Development of IIIM-290, an Orally Active Potent Cyclin- dependent Kinase Inhibitor (J Med Chem. 2018, 61,1664-1687)

Vikas Kumar, Shreyans K. Jain, Mubashir J. Mintoo, Santosh K. Guru, Vijay K. Nuthakki, Mohit Sharma, Sonali S. Bharate, Sumit G. Gandhi, Dilip M. Mondhe, Shashi Bhushan, Ram A. Vishwakarma, Sandip B. Bharate

Rohitukine (**1**), a chromone alkaloid isolated from Indian medicinal plant *Dysoxylum binectariferum* has inspired the discovery of flavopiridol and riviciclib, both of which are bioavailable only via IV route. With the objective to address oral bioavailability issue of this scaffold, four series of rohitukine derivatives were prepared and screened for Cdk inhibition and cellular anti proliferative activity. The 2,6-dichloro-styryl derivative IIIM-290 (**11d**) showed strong inhibition of Cdk-9/T1 (IC_{50} 1.9 nM) kinase and Molt- 4/MIAPaCa-2 cell growth (GI_{50} < 1.0 µM) and was found to be highly selective for cancer cells over normal fibroblast-cells. It inhibited the cell growth of MIAPaCa-2 cells via caspase-dependent apoptosis. It achieved 71% oral bio availability with in- vivo efficacy in pancreatic, colon and leukemia xenografts at 50 mg/kg, po. It did not have CYP/ efflux- pump liability, was not mutagenic/genotoxic or cardiotoxic and was metabolically-stable. The preclinical data presented herein indicates the potential of **11d** for advancement in clinical studies.

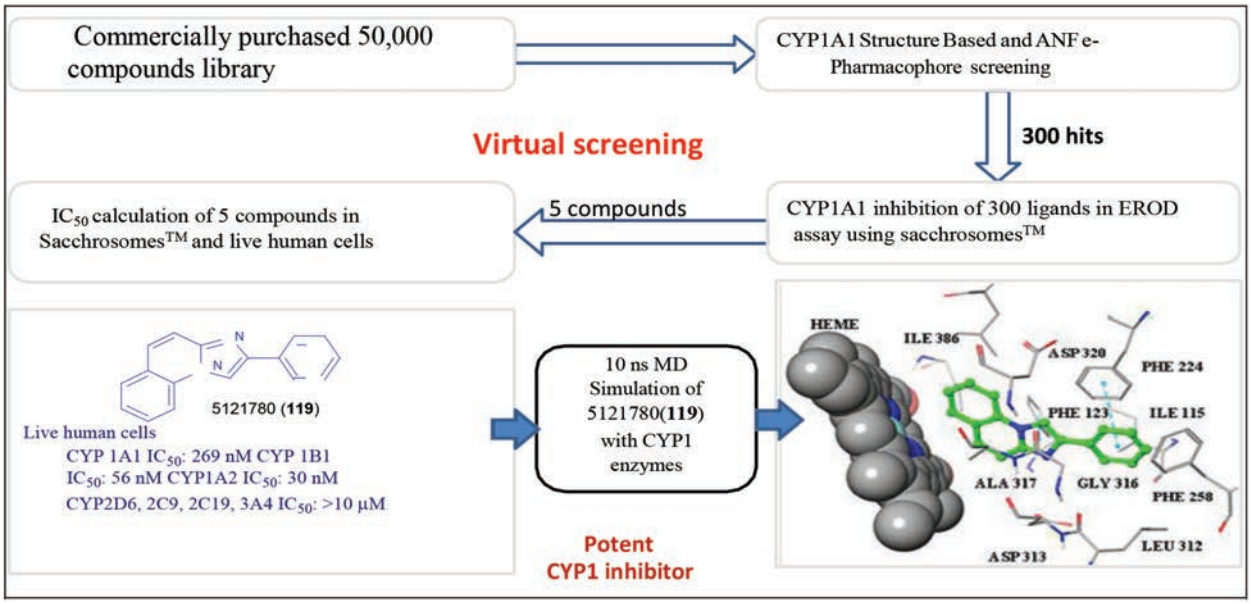


6.2 Identification of Potent & Selective CYP1A1 Inhibitors via Structure Based Virtual Screening and their *in-vitro* Validation (J Chem Inf Model. 2017, 57,1309-1320)

Prashant Joshi, Glen J.P. McCann, Vinay R. Sonawane, Ram A. Vishwakarma, Bhabatosh Chaudhuri, Sandip B. Bharate

Target structure-guided virtual screening (VS) is a versatile, powerful and inexpensive alternative to experimental high- throughput screening (HTS). In order to discover potent CYP1A1 enzyme inhibitors for cancer chemo prevention, a commercially library of 50,000 small molecules was utilized for VS guided by both ligand and structure- based strategies. For experimental validation, 300 ligands were proposed based on combined analysis of fitness scores from ligand based e-pharmacophore screening and docking score, prime MMGB/SA binding affinity and interaction pattern analysis from structure-based VS. These 300 compounds were screened, at 10 µM concentration, for in-vitro inhibition of CYP1A1- Sacchrosomes (yeast-derived microsomal enzyme) in the ethoxyresorufin-*O*-deethylase assay. Thirty-two compounds displayed >50% inhibition of CYP1A1 enzyme activity at 10 µM. 2-Phenylimidazo-[1,2- a]quinoline (5121780, **119**) was found to be the most potent with 97% inhibition. It also inhibited ~95% activity of CYP1B1and CYP1A2, the other two CYP1 enzymes. The compound 5121780 (**119**) showed high selectivity towards inhibition of CYP1 enzymes with respect to CYP2 and CYP3 enzymes (i.e. there was no detectable inhibition of CYP2D6/ CYP2C9/ CYP2C19 and CYP3A4 at 10 µM). It

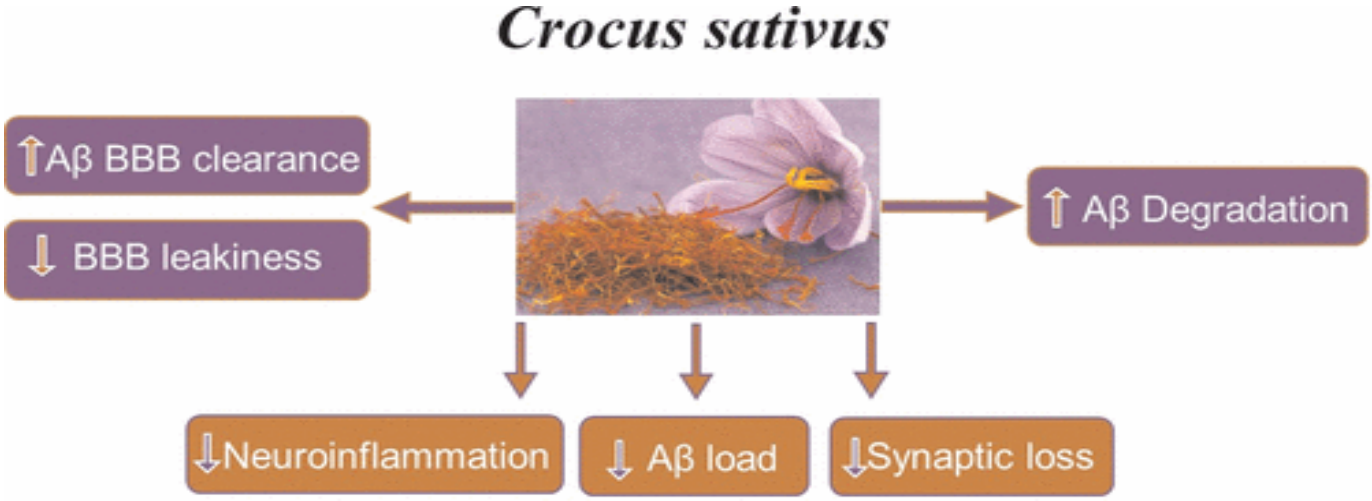
was further investigated in live CYP-expressing human cell system which confirmed that compound 5121780 (**119**) potently inhibited CYP1A1, CYP1A2, CYP1B1 enzymes with IC_{50} values of 269, 30 and 56 nM, respectively. Like in Sacchrosomes, inhibition of CYP2D6/ CYP2C9/ CYP2C19 and CYP3A4 enzymes, expressed within live human cells, could hardly be detected at 10 µM. The compound **119** rescued CYP1A1 over- expressing HEK293 cells from CYP1A1 mediated B[a]P toxicity and also overcame cisplatin resistance in CYP1B1 over-expressing HEK293 cells. Molecular dynamics simulations of 5121780 (**119**) with CYP1enzymes was performed to understand the interaction pattern to CYP isoforms. Results indicate that VS can successfully be used to identify promising CYP1A1 inhibitors, which may have potential in the development of novel cancer chemo- preventive agents.



6.3 *Crocus sativus* Extract Tightens the Blood-Brain Barrier, Reduces Amyloid β Loadand Related Toxicity in 5XFAD Mice

Batarseh YS, Bharate SS, Kumar V, Kumar A, Vishwakarma RA, Bharate SB, Kaddoumi A.

Crocus sativus, commonly known as saffron or Kesar is used in Ayurveda and other folk medicines for various purposes as an aphrodisiac, antispasmodic, and expectorant. Previous evidence suggested that Crocus sativus is linked to improvingcognitive function in Alzheimer's disease (AD) patients. The aim of this study was to in vitro and in vivo investigate the mechanism(s) by which Crocus sativus exerts its positive effect against AD. The effect of Crocus sativus extract on Aβ load and related toxicity was evaluated. In vitro results showed that Crocus sativus extract increases the tightness of a cell-based blood-brain barrier (BBB) model and enhances transport of Aβ. Further in vivo studies confirmed the effect of Crocus sativus extract (50 mg/kg/day, added to mice diet) on the BBB tightness and function that was associated with reduced Aβ load and related pathological changes in 5XFAD mice used as an AD model. Reduced Aβ load could be explained, at least in part, by Crocus sativus extract effect to enhance Aβ clearance pathways including BBB clearance, enzymatic degradation and ApoE clearance pathway. Furthermore, Crocus sativus extract upregulated synaptic proteins and reduced neuroinflammation associated with Aβ pathology in the brains of 5XFAD mice. Crocin, a major active constituent of Crocus sativus and known for its antioxidant and anti- inflammatory effect, was also tested separately *in vivo* in 5XFAD mice. Crocin (10 mg/kg/day) was able to reduce Aβ load but to a lesser extent when compared to Crocus sativus extract.Collectively, findings from this study support the positive effect of Crocus sativus against AD by reducing Aβ pathological manifestations.


Crocus sativus
Aβ BBB clearance
BBB leakiness
Aβ Degradation
Neuroinflammation
Aβ load
Synaptic loss

7.0 FERMENTATION TECHNOLOGY

7.1 Antagonistic potential of a psychrotrophic fungus: Trichoderma velutinumACR-P1

Richa Sharma, Ankita Magotra, Ravi S. Manhas and Asha Chaubey

Trichoderma species are extensively studied as potential sources of biocontrol agents, enzymes (cell wall degrading enzymes, CWDEs) and bioactive peptides. Thus these fungi have been extensively studied and commercializedas biofungicides, biofertilizers and soil amendments. Mycoparasitic activity and antibiotic production in *Trichoderma*was established as probable mechanisms for their present day biotechnological applications of these fungi as biocontrol agents. Fungal phytopathogens constitute the major threat to the crop plants and other plantations. Most phytopathogens belong to the genera *Fusarium, Verticillium, Aspergillus, Collechotrichum, Alternaria* etc. Antagonistic behavior of *Trichoderma* species has been attributed to hyper parasitism, although some species and strains also produce potential bioactive metabolites that enhance their antagonistic potential. Antagonistic potential of *Trichoderma velutinum* ACR-P1 has been evaluated against the important phytopathogens, that is, *Fusarium oxysporum, Verticillium dahliae, Alternaria alternata* and *Collechotrichum capsici* was demonstrated by the dual culturing experiments. Dual cultures of *T. velutinum* ACR-P1and phytopathogenic test fungi were grown from inoculants (*Trichoderma* as well as test fungus) placed at the distance of 1 cm from the corners of the petridish about 5cm apart on potato dextrose agar at 28°C for determination of production of diffusible antifungal metabolites. Control consists of single culture grown in the centre of petridishes. Rate of growth of fungal colonies was measured as radii of colonies which have been recorded daily after 3rd day when the growth corresponded to the exponential growth phase. The efficiency of *T. velutinum* ACR-P1 in suppressing radial growth of the phytopathogens under study was calculated as follows: (C-T/C) X 100, where C is radial growth of the pathogen in the control and T is radial growth of the pathogen in the presence of *velutinum* ACR-P1.

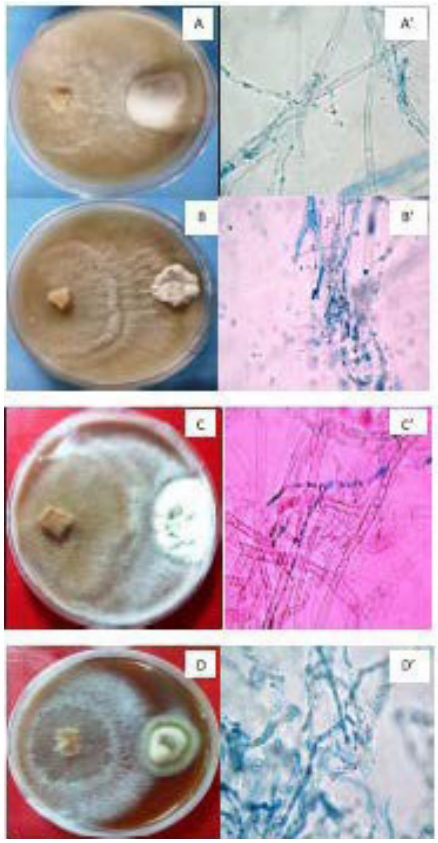


Figure 7.1.1: In-vitro assays for antagonistic interactions and abnormalities in respective phytopathogenic fungi as observed morphologically and microscopically (40X magnification) in plate assays between *T. velutinum* ACR- P1 and *F. oxysporum* (A, A'), *V. dahliae* (B, B'), *C. capsici* (C, C') and *A. alternata* (D, D') respectively

In-vitro antagonism assays of *T. velutinum* ACR-P1 against four phytopathogenic test fungi demonstrated the antagonistic potential of the strain ACR-P1 against *Fusarium oxysporum, Verticillium dahliae, Collechotrichum capsici* and *Alternaria alternata* respectively. Antagonistic potential of *T. velutinum* ACR- P1 against these pathogens has been shown in Table7.1.1. Microscopic examination (at 40x magnification) of the antagonistic strains revealed the induction of deformities and abnormalities in test phytopathogenic fungus, that is, mycelial, hyphal and inhibition of conidiation in phytopathogenic fungi as induced by the potent mycoparasitic strain ACR- P1 at the point of interaction of the two strains thus inhibiting and limiting its mycelial growth (Fig7.1.1). At the interaction point of *T. velutinum* ACR-P1 and *Fusarium oxysporum*, thick mycelial hyphae of ACR-P1 coiled around the thin filamentous hyphae of *Fusarium* and almost completely inhibited the growth of the pathogen thus restricting it to one corner of the petridish. In case of interaction with *Verticillium dahliae*, *T. velutinum* ACR- P1 exhibited extensive coiling and sporulation and completely restricted the growth of the pathogen at almost around the point of the inoculation. *T. Velutinum* ACR-P1 upon interaction with *Collechotrichum capsici* exhibited so extensive hyphenation that there was hardly any hyphal extension of

the pathogen beyond interaction point and the pathogen growth was completely restricted from that point. Also, upon interaction with *Alternaria alternata*, *T. velutinum* ACR- P1 caused inhibition of conidiation in otherwise highly sporulating strain of the pathogen, also the hyphal filaments of the pathogen were deformed with hardly any depiction of sporulation so that no further growth an expansion of the colony occurred.

Table 7.1.1 Antagonistic potential of *T. velutinum* ACR-P1

Phytopathogens	*T. velutinum* ACR-P1 (% inhibition in radial growth (mm)
Fusarium oxysporum	64.2 ± 0.5
Verticillium dahliae	75.0 ± 0.75
Collechotrichum capsici	71.4 ± 0.66
Alternaria alternata	62.5 ± 0.5

7.2 Production of bio-cellulose membranes under the purview of development and application of topical antibiotic based transdermal patches

Successful in development of antibiotic impregnated bacterial cellulose membranes for the developing transdermal patches

1. **Kojic acid production**

   A high kojic acid producing fungus has been isolated from rice husk. The strain is identified as Aspergillus sojae. The culture sequence has been submitted toNCIM.

2. **CYP BasedBiotransformation**

   Biotransformation of industrially important monoterpenes and drug metabolites using Human CYPs450. The biotransformation experiments were carried out with different monoterpenes i.e α-pinine, linalool, Thymol, Geraniol, Limonene and drug intermediates i.e AZD-0328, omeprazole, clochicine , chrysin and khellin etc.

3. **Nutraceutical : Production of DHA Powder as dietarysupplement**

   Preparation of DHA power as nutritional supplement. The process for making DHA based nutritional tablet is under preparation under cGMP facility. The process is under technology transfer with the company

4. **Screening, Isolation and Production and purification of Serratiopeptidase enzymes**

   Isolated a potent serratiopeptidases enzyme producing bacterium from silk moth gut, subsequently isolated organism was identified as Serratia marcescens. Process engineering for maximum production of Serratia sp. is in progress.

5. **Bioprospecting microbial species from unexplored ecological nichesfornovel molecules andenzymes**

   Screening of 70 newer bacteria and 45 newer fungi was carried under this project. Organisms are under screening for potential enzymes production.

6. **CSIR-Aroma Mission Project**

   Biotransformation of Monoterpenes using CYPs enzyme

7. **Zandu PancharishtaProject**

   Process improvement of Zhandu Pancharishta formulations (Emami Project) with relation to reducing the fermentation time and less use of preservatives.

7.3 Service to Industry

Chanakaya Pharma
Cadila Pharmaceuticals Pvt Ltd.
(Agro Division)

Amidase or amidohydrolase is an enzyme that catalyzes the hydrolysis of amides to release free carboxylic acids and ammonia. In recent years, amidases have gained considerable interest in industries for the synthesis of wide variety of carboxylic acids which find applications in commodity chemicals synthesis, pharmaceuticals agrochemicals and waste water treatments, etc. Apart from amide hydrolysis activity, some amidases also exhibit an acyl transferase activity which leads to the formation of pharmaceutically important hydroxamic acids according to the followingreaction: RCONH2 +

NH2OH → RCONHOH + NH3

An amidase producing culture has been isolated from soil sample of hot water springs of Himachal Pradesh. On the basis of 16S r DNA, isolated culture has been designated as Bacillus sp. IIIMB2907. It has been found that amidase from the isolated strain is exhibiting amide hydrolase as well as acyl-transferase activity with benzamide (as shown in figure 7.3.1). Therefore, currently this enzyme is being used in the synthesis of benzohydroxamic acid and other pharmaceutically important aromatic hydroxamicacids.

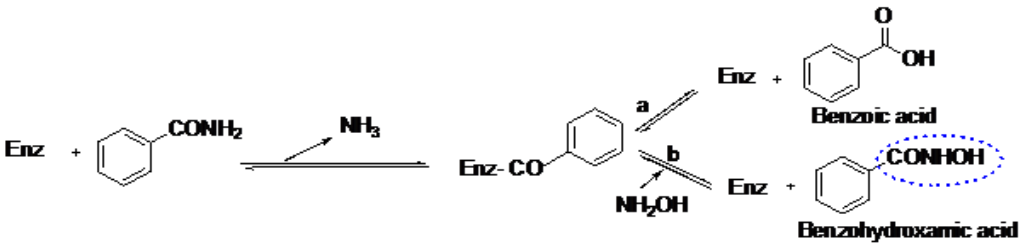
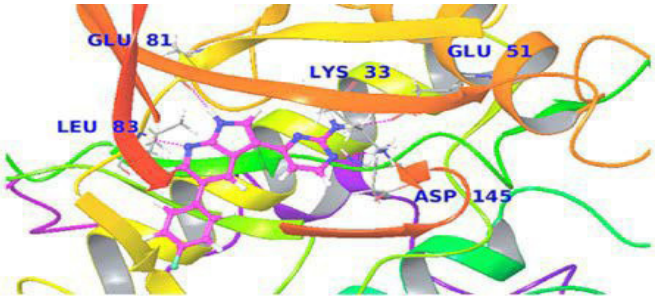


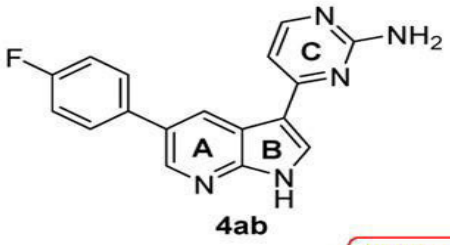
Figure 7.3.1. Reaction of amidase (Enz) with benzamide Pathway (a), amidase catalyzes the hydrolysis of benzamide to the corresponding benzohydroxamic acid. Pathway (b) acyltransferase activity of amidase (in presence of hydroxylamine) for the synthesis of benzohydroxamic acid

8.0 CANCER PHARMACOLOGY

8.1 Identification of Novel 3-Pyrimidinylazaindole CDK2/9 Inhibitors targeting TN breast Cancers

In the present study, a novel series of 3- pyrimidinylazaindoles were designed and synthesized targetting cyclin-dependent kinases CDK2 and CDK9 having critical roles in the cell cycle regulation of cell proliferation. Based on marine scaffold meroline, the study led to the identification of the alternative lead candidate 4ab with a nanomolar potency against CDK2 and CDK9 and potent antiproliferative activities against a panel of tested tumor cell lines along with a better safety ratio of ~33 in comparison to reported leads. In addition, the identified lead 4ab demonstrated a good solubility and an acceptable in vivo PK profile. The identified lead 4ab showed an in vivo efficacy in mouse triple-negative breast cancer (TNBC) syngeneic models with a TGI (tumor growth inhibition) of 90% without any mortality growth inhibition in comparison to reported leads.

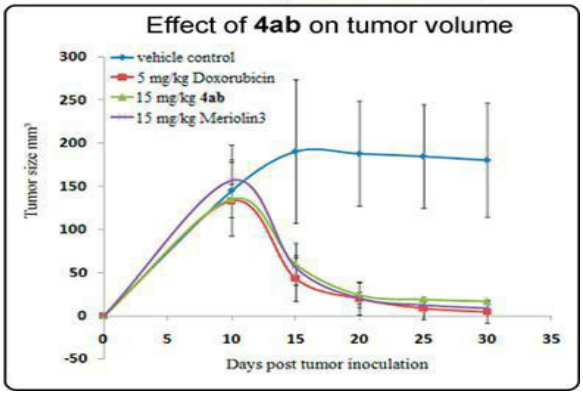




4ab

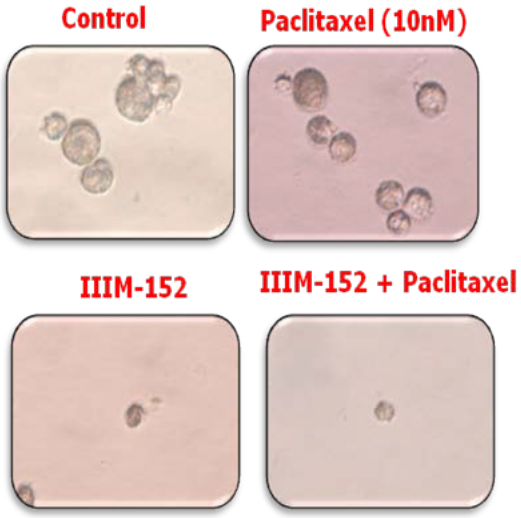
In-vitro biochemical assay	CDK2/cyclinA, IC_{50} = 0.0055 µM CDK9/cyclinT, IC_{50} = 0.024 µM
In-vitro cell line assay	HCT-116, IC_{50} = 0.2 µM SH SY5Y, IC_{50} = 0.8 µM
Safety ratio	~ 33 (IC_{50} HEK/IC_{50} MCF-7)
Solubility profile	Water = 72.467µg/ml PBS = 98.250 µg/ml SGF = 53.733 µg/ml SIF = 138.233 µg/ml
Pharmacokinetic	$t_{1/2}$ = 2.5 h, AUC(0-t) = 437.1 ng*hr/ml, AUC(0-inf.) = 794.6 ng*hr/ml

In-vivo profile



8.2 Identification of Novel small molecule targeting Cancer Stem Cells in TN breast Cancers.

Tumors consist of a mixture of heterogeneous cell types. Cancer stem cells (CSCs) are a minor sub-population within the tumor cell mass that are known for resistant to chemotherapy and radiotherapy. These are considered as the seeds of tumor recurrence, driving force of tumorigenesis and metastases. During Screen against CSCs of breast origin, We have identified small molecules (IIIM152) selectively targeting CSCs by impeding their self renewal capacity and properties of invasion and migration



Cancer stem cell self-renewal assay.

8.3 Cyclodipeptidec(Orn-Pro) Conjugate with 4-Ethylpiperic Acid (EPA)Abrogates Cancer Cells Metastasis through Modulating MDM2

Sudha Shankar, Mir Mohd Faheem, Debasis Nayak, Naiem Ahmad Wani, Saleem Farooq, Surrinder Koul, Anindya Goswami, and Rajkishor Rai.

The cyclodipeptides scaffolds have been substantially investigated in the search for new class of MDM2/p53 inhibitors. The essential molecule that could perturb the MDM2/p53 interaction is being considered as a conscientious topic in the field of emerging anti- metastasis therapeutics. Herein, we synthesized the cyclic dipeptides c(Orn- Pro), **P1**; c(Lys-Pro), **P2** and their conjugates with piperic acid (PA) and 4- ethylpiperic acid (EPA), PA-c(Lys-Pro),**C1**; PA-c(Orn-Pro),**C2**; EPA- c(Lys- Pro), **C3** and EPA-c(Orn- Pro),**C4**. The conjugates **C1- C4** were synthesized based on the novel strategy to conjuate the diketopiperazine scaffold derived from 52RR with piperic/4-ethylpieric acid in order to selectively explore the p53-MDM2 interaction. 52RR has been developed by the side chain modification of the 2,5-DKP's scaffold and exhibited the inhibition of MDM2-p53 interaction with IC50 31µM. Among all the synthesized conjugates, **C4** exhibited promising cytotoxic activity against multiple cancer cell lines of various origins. **C4** evolved as most potent conjugate in terms of cytotoxicity and exhibited IC50 values: 1.3 µM in MDA- MB-231; 3.5 µM in PC-3, 8.9 µM in MCF-7 and 9.6 µM in Miapaca-2 cells. Importantly, against normal breast epithelial cell line fR-2, C4 showed minimum toxicity (IC50 value of 74.3 µM), indicating a higher therapeutic index. Further, we checked the effect of **C4** on MDM2 expression in MDA-MB-231 and PC-3 cells and the western blot results showed a steady decline of MDM2 in a dose-dependent as well as time-dependent manner (**Figure 8.3.1A** & **1B**). However, negligible reduction in the expression of MDM2 was noted in Miapaca-2cells. Additionally, the immunecyto-chemistry results (**Figure 8.3.2C**) were in accordance with the western blots results showing a marked decrease in MDM2 expression at 3 µM (24 h) concentration of **C4** in both the cell lines tested.. To determine the *in vivo* efficacy of C4, the 4T1 spontaneous/orthotopic mouse mammary carcinoma model was employed. A dose of 20 mg/kg b.w. was found to be tolerable and non-toxic and was selected or further experimentation We observed a considerable reduction (52%) in the primary tumor weight of C4 treated group ascompared to the control group (**Figure 8.3.2**). 5-FU was used as a positive control and showed a reduction of 64% in the tumor weights as compared to the control group. Correspondingly, the tumor volume was reduced by 67% in 5-FU treated group and 65% in C4 treated group. The percent reduction in the number of metastatic nodules was 75% and 65% in 5-FU and C4 treated groups, respectively. Taken together, these results confirm the antimetastatic potential of C4 *in vivo* in breast cancer model at a safe and tolerable dose of 20mg/kg b.w.

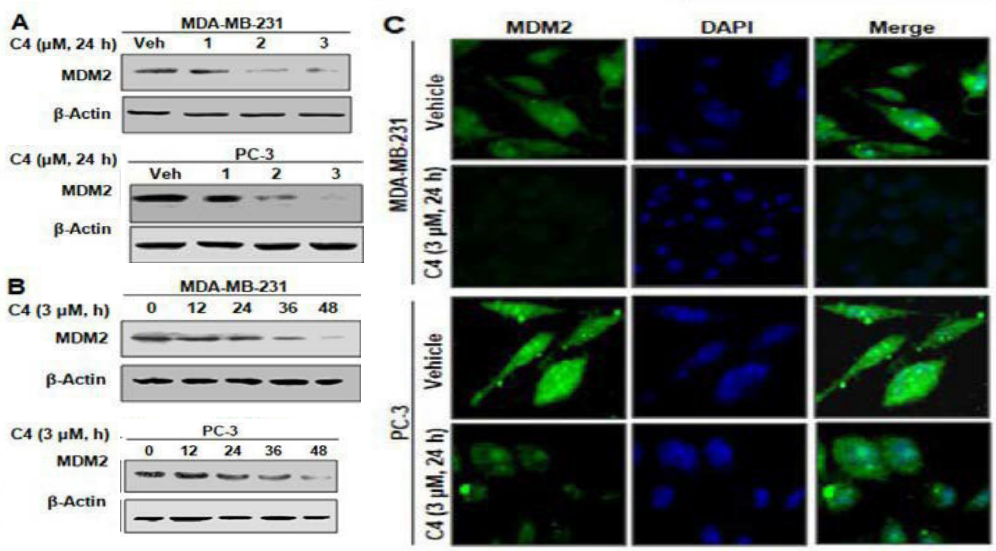


Figure 8.3.1. Downregulates the expression of MDM2 in MDA-MB-231 and PC-3 cells. (A) Dose dependent inhibition of MDM2 by C4 in MDA-MB-231 and PC-3 at 24h observed by western blotting. (B) Time dependent inhibition of MDM2 by C4 (3µM) in MDA-MB-231 and PC-3 cells analysed by western blotting. β-Actin expression was considered to ensure equal loading. (C) Immunocytochemistry images depicting the down modulation ofMDM2 by C4 (3µM) at 24h in MDA- MB-231 and PC-3 cells. The data represents three independent experiments performed separately.

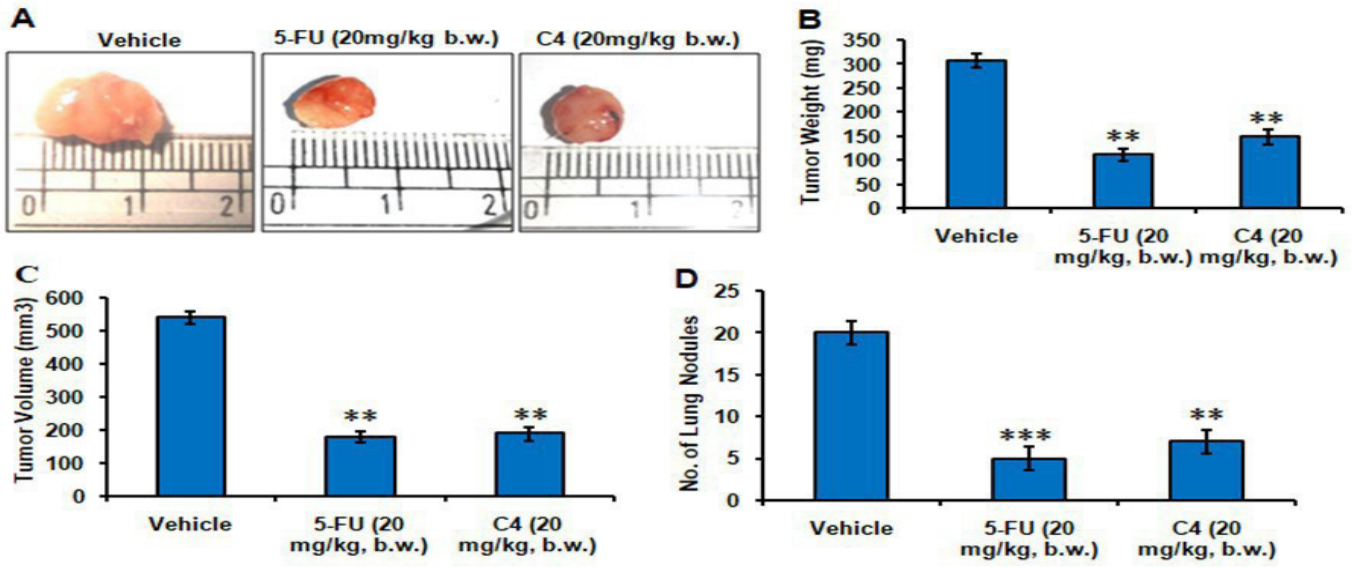


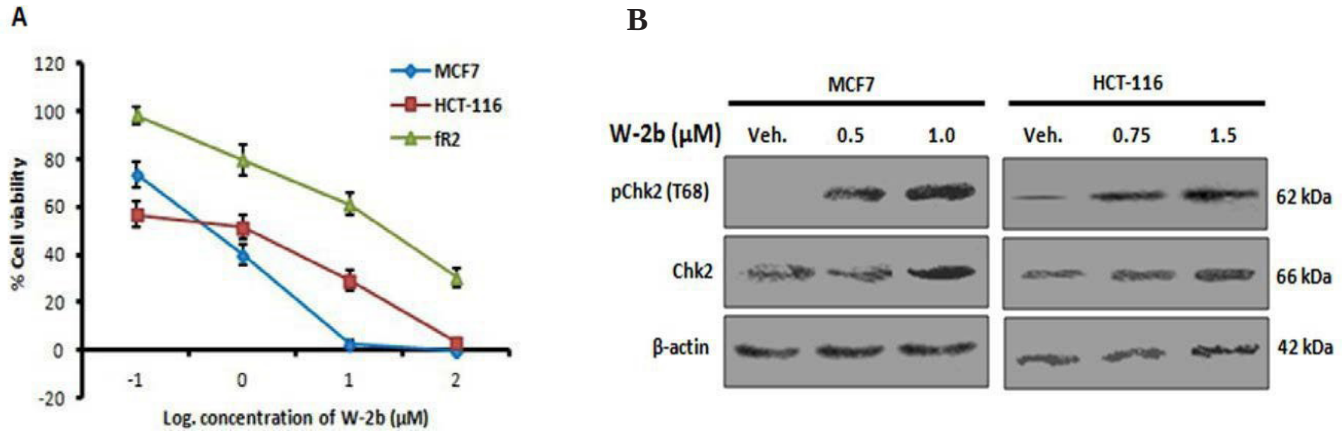
Figure 8.3.2. C4 inhibits primary tumor growth and prevents lung metastasis. (A) Mouse mammary carcinoma (4T1) cells were allowed to form the tumor subcutaneously beneath the second mammary pad of Balb/c mice and subsequently treated with 20mg/kg b.wt. of C4 for two weeks.5-FU (20mg/kg b.wt.) was used as a positive control. Animals were sacrificed thereafter and tumor growth was measured. (B and C) represent the tumor weight (mg) and tumor volume (mm3), respectively. (D) Lungs of the animals were then dissected carefully and observed under an inverted microscope for the formation of metastatic lung nodules. The number of lung nodules is given in the form of a bar graph. Data is representative of three independent experiments performed prior to the statistical analysis. * *P<0.05***P<0.01, ***P<0.001.*

8.4 Regiospecific Synthesis of Ring A Fused Withaferin A Isoxazoline Analogues: Induction of Premature Senescence by W-2b in Proliferating Cancer Cells.

Faheem Rasool, Debasis Nayak, Archana Katoch, Mir Mohd Faheem, Nazar Hussain, Syed Khalid Yousuf, Chetan Belawal, N. K. Satti, Anindya Goswami and Debaraj Mukherjee.

Withaferin A(WA) is a naturally occurring steroidal lactone, derived from the medicinal plant *Withania Somnifera*, commonly known as Ashwagandha. Its tremendous potential to modulate various oncogenes and tumor-suppressor genes with appreciable *in vivo* activities has been explored recently. Among the five- membered heterocyclic compounds, 2-isoxazolines have gained tremendous attention from the medicinal chemists as structural building blocks of biologically active molecules and versatile intermediates in organic synthesis. In this endeavour, we sought to examine the potential of fused 2- isoxazoline derivatives of WA to induce cytotoxicity in human cancer cells by abrogating cell proliferation through the induction of premature senescence. Our recent approach towards the development of ring. A modified derivatives of withaferin A successfully generated a 3-azido analogue with strong anticancer activities. In this regard, our medicinal chemistry approach with the ring A modified WA isoxazolines found out a potential lead molecule, **W-2b**, with strong antiproliferative and antitumor activities (**Fig. 8.4.1**). **W-2b** phosphorylates Chk2 (T68) and induces its expression in two rapidly proliferating cancer cells from diverse tissue origin (MCF7 and HCT-116) (**Fig. 8.4.1**). Evidence suggests that sub- lethal level of intracellular ROS generation could initiate premature senescence by inducing p21 expression through G1 arrest. Being a key regulator of the cell cycle machinery, p21 control cell proliferation and DNA replication through regulation of cyclin-dependent kinases (CDKs). Though, p53 is a major transcription factor that regulates p21, studies alsofound that Chk2 can induce senescence in cancer cells via p21 irrespective of the p53 status of the cell. Indeed, **W-2b** causes G2/M cell cycle arrest and induction of p21 in a dose dependent manner (**Fig. 8.4.2**) as well as modulates the expression of CDK-2 and CDK- 4. In conclusion, our study reports a potential lead from Withaferin A isoxazoline derivatives

(**W-2b**) that induces premature senescence as an antitumor safeguard mechanism against proliferating cancer cells through activation of tumor suppressor Chk2. It's (**W-2b**) strong *in vivo* efficacy (**Fig. 8.4.3**) and tolerability claim for its further development as a therapeutically relevant anticancer candidate.



8.4.1 W-2b is cytotoxic and induces premature senescence in cancer cells. (A) Graph showing the percent cell viability of MCF7, HCT-116 and fR2 cells in response to logarithmic concentrations of W-2b for 24 h, 48 h, and 72 h. (**B**) MCF7 and HCT-116 cells were treated with vehicle and increasing concentrations of **W-2b** for 48 h; whole cell lysates were prepared and subjected to western blotanalysis for the expression of pChk2 (T68), Chk2 and β-actin Data are representatives of three independent experiments

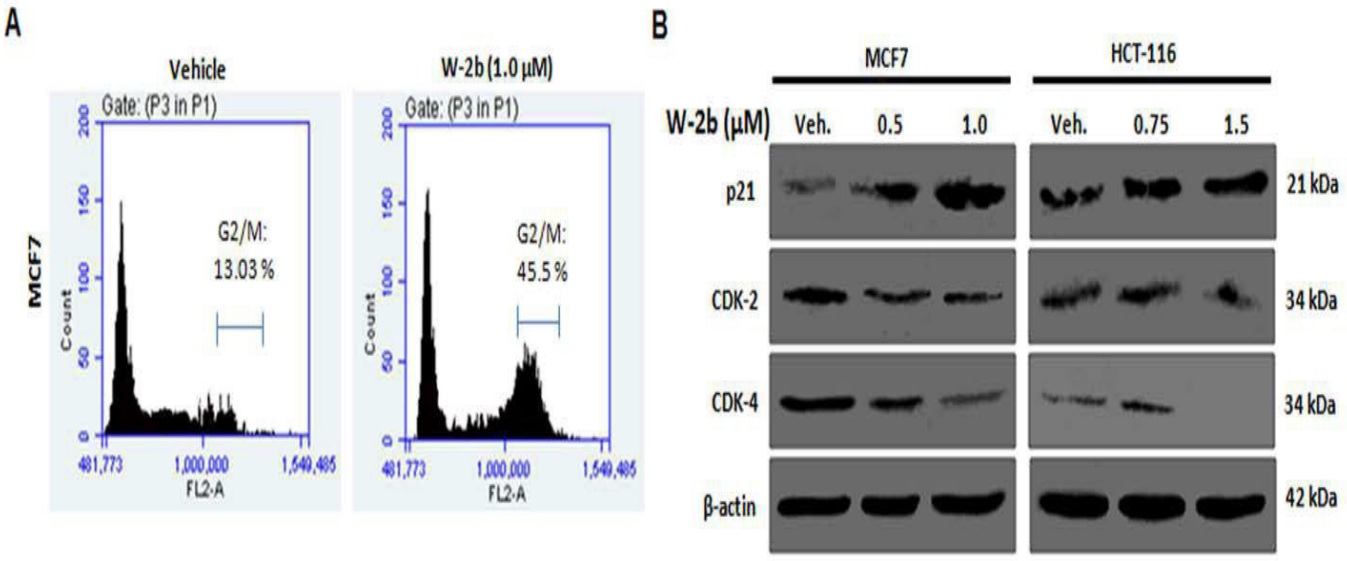
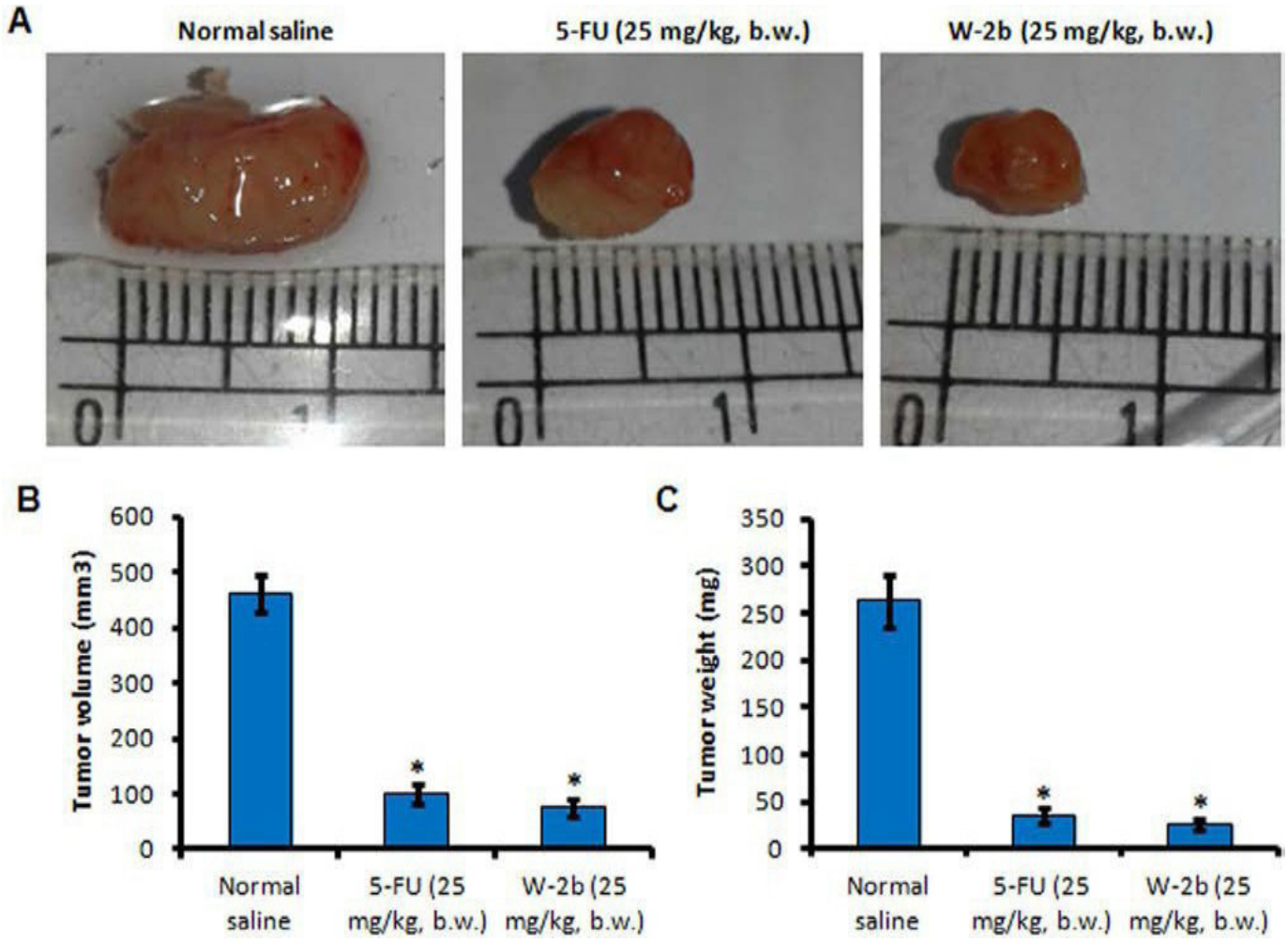


Figure 8.4.2 W-2b confers cell-cycle rrest and p21 induction in proliferating cancer cells. (A) Flow cytometriccell cycle analysis in MCF7 cells treated with vehicle and W-2b (1.0 μM) for 48 h. (B) MCF7 and HCT-116 cells were treated with vehicle and increasing concentrations of W-2b for 48 h; whole cell lysates were prepared and subjected to western blot analysis for the expression of p21, p16, p53, CDK-2, CDK-4 and β-actin. Bar graphs: mean s.d. of three independent experiments.*P<0.05.



8.5 AKT is indispensable for coordinating Par-4/JNK cross talk in p21 down modulation during ER stress

RU Rasool, D Nayak, S Chakraborty, MM Faheem, B Rah, P Mahajan, V Gopinath, A Katoch, Z Iqra, SK Yousuf, D Mukherjee, LD Kumar, A Nargotra and A Goswami.

2-Azido withaferin A (3-AWA), a derivative of the α-β-unsaturated functionality of ring A of withaferin A, has been well documented for its antiproliferative potential and is superior to its parent compound, withaferin A, in stalling cancer progression. Although, 3-AWA exerts strong antiproliferative activity in various cancer types, until now the detailed ER stress mediated mechanism of its apoptosis induction function has not been studied. In the current study, we demonstrate that pharmacological induction of ER stress by 3-AWA attenuates p21 levels, an effect that coincides with the activation of JNK (**Fig. 8.5.1**). We have also provided evidence that Par-4, a major player contributing to cancer cell apoptosis, may be involved in the regulation of the cell cycle regulator p21 during ER stress facilitating the commitment of cells to a proapoptotic program. However, a higher concentration of 3-AWA promotes p-JNK-dependent abrogation of p21 expression levels leading to Par-4- mediated proapoptotic effects of ER stress. Based on our previous studies, we found that, we have shown that initially, up to a certain concentration of 3- AWA, p21 expression elevated gradually, but as soon as ER stress reached to its UPR level, p21 sharply attenuated along with JNK phosphorylation. Recent report implied that during ER stress the expression of p21 is abolished through CHOP-dependent

suppression of its promoter-activity and CHOP- mediated apoptosis is associated with the suppression of antiapoptotic protein, p21. Compelling evidences suggest that p21 may be downmodulated by a mechanism, which operates through ER stress/JNK/casp-3 axis,but how this cascade is toggled is not clear. Here, for the first time, we distinctly prove that phosphorylation status of AKT is a key factor in favoring an association between Par-4 and JNK to ER stress condition (Figure 8.5.1). Indeed, stress inflicted activation of JNK, AKT inhibition, and Par-4induction are equally crucial to p21 downmodulation by 3-AWA in aggressive cancer cells. However, keeping in view that 3-AWA is a strong Par-4 inducer as well as a negative regulator of antiapoptotic p21, we investigated the physiologically relevant effects of 3-AWA on orthotopic tumor growth and we found that 3- AWA inhibits colorectal tumor growth and formation of colorectal polyps at a tolerable dose of 10 mg/kg, which was similar to the first-line drug for colorectal cancer-5- fluorouracil (**Fig. 8.5.2**). In conclusion, our findings unveil a novel mechanism of p21 regulation involving AKT/Par-4/JNK axis in the most aggressive type of cancers. Elucidation of this axis might lead to improvement of existing therapeutic regimens, which are mainly operating through DNA-damaging response or the ones targeting cell cycle regulation.

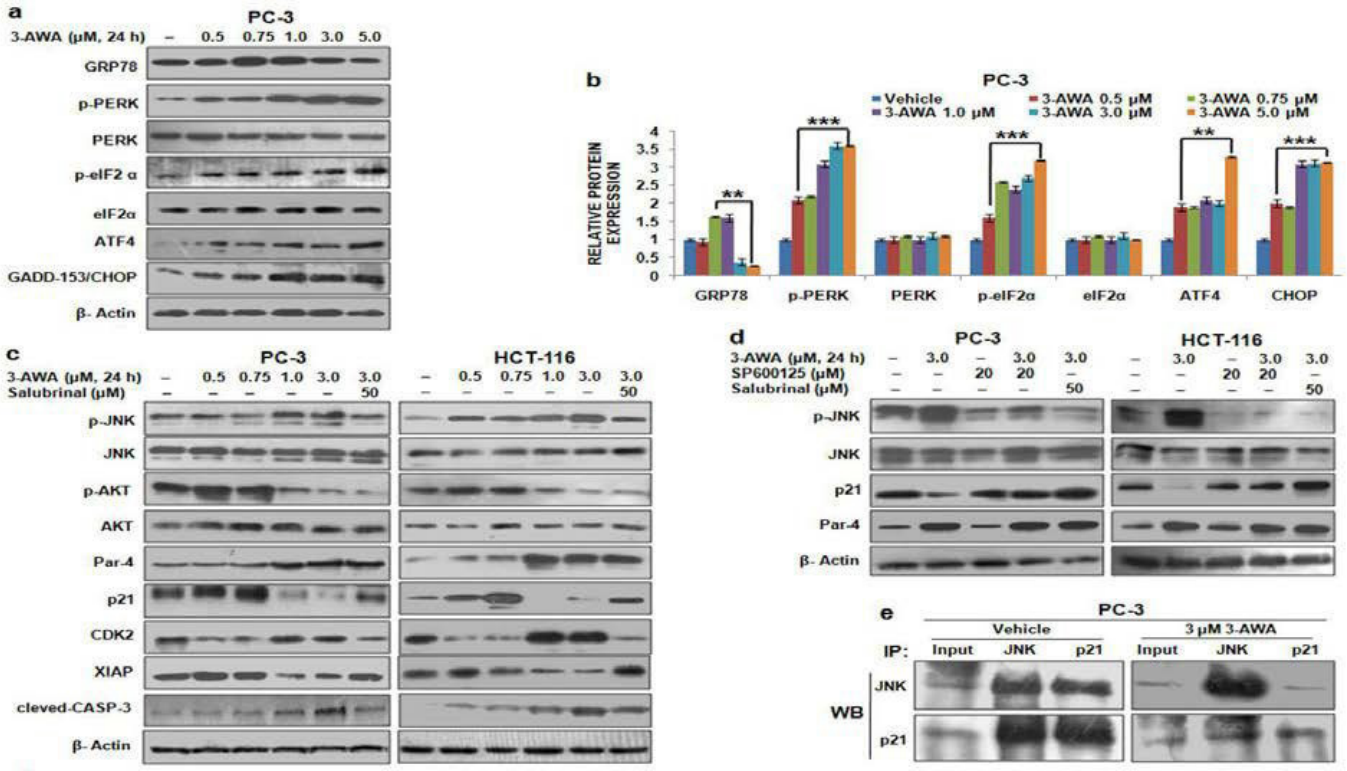


Figure 8.5.1 JNK activation and p21Cip1/WAF1 (p21) downregulation by 3-AWA. (a, b) PC-3 cells were exposed to given concentrations of3-AWA for 24 h. Lysates were prepared and immunoprobed for the indicated proteins through western blotting. The densitometry analysis of western blot results was based on ImageJ software version 1.44p (NIH, USA). (c) PC-3 and HCT-116 p53+/+ cells were treated with 3-AWAand/or salubrinal for the indicated time point. The protein-specific antibodies were used to analyze the expression of the given proteins through immunoblotting. (d) PC-3 and HCT-116 p53+/+ cells were treated with different concentrations of 3-AWA and/or SP600125 or salubrinal for the set time point and analyzed for the indicated proteins through western blotting. (e) Co-immunoprecipitation (co-IP) assay showing disruption of JNK and p21 interaction by 3-AWA

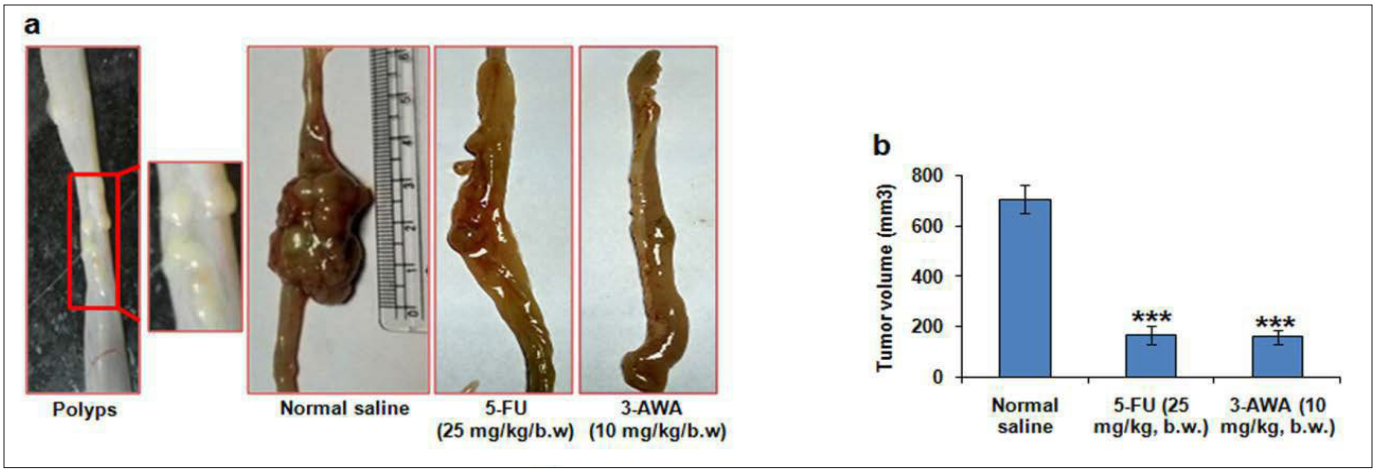


Figure 8.5.2 Efficacy of 3-AWA in orthotopic carcinogen-induced rat colorectal carcinoma model. (a) Colorectal polyps were induced in maleWistar rats as described in the 'Materials and methods' section; after sufficient tumor growth, the animals received 10 mg/kg b.w. of 3-AWA,the positive control group received 25 mg/kg b.w. of 5-FU and the negative control group animals were given 0.9% normal saline solution inalternate days for 3 weeks. The animals were then killed and tumor growth was measured. (b) Bar graphs showing tumor volume in eachgroup of animals (n =7 animals per group). In vitro as well as in vivo data are the means of three independent experiments. ***P ⩽0.001; **P⩽0.01.

8.6 Identification of allosteric inhibitor binding pocket in IGF1R

Gayatri Jamwal, Gurjinder Singh, Mohd Saleem Dar, Nasima Bano, Mohd Jamal Dar

IGFIR and IR, two closely related members of tyrosine kinase receptor super family, signal through multiple pathways that include PI3K and MAPK pathways. IR is required for glucose homeostasis, where as IGF1R regulates cell growth and development. The IGFIR also plays crucial roles in the normal development of many tissues and its deregulation has been reported in many cancers. Furthermore, signaling mediated via the IGF1R is believed to be important for the maintenance of tissue resident adult stem cells and for embryonic stem cell self-renewal, therefore, suggesting an important role for the receptor in stem cell biology. We have identified role of individual domains of IGF1R in its subcellular localization, cytoplasmic and nuclear activities. We generated a library of IGF1R deletion and point mutants to examine various activities IGF1R. Moreover, we identified a cross talk between IGF1R and Wnt/beta-catenin signaling pathways and showed that the nuclear localization of IGF1R is defined by its cytoplasmic domain. Furthermore, we identified a unique inhibitor binding pocket in the C- terminal domain of IGF-1R which is different than the substrate and ATP binding pocket. We showed by in- silico analysis that this unique pocket falls in the vicinity of activation loop. Upon mutating lysine at 1055 position to arginine, autophosphorylation activity of IGF-1R and its subsequent downstream signaling activity is drastically reduced. This unique binding pocket is suited for designing allosteric small molecule inhibitors of IGF1R to block its various activities. Some of the experiments those we performmed to examine various activities of IGF1R include:

1. Analyzing expression, activity and sub-cellular localization of IGF1R in HEK-293 cells: We analyzed the subcellular localization of IGF1R by tagging GFP at its C- terminal end. Confocal microscopy analysis showed that IGF1R-GFP (wildtype) was present at the membrane, in the cytoplasm as well as in the nucleus. By contrast, GFP alone was diffused in the nucleus and cytoplasm as expected. EGFR-GFP used as controls for membranous localization showed predominant membraneous localization while as and S45Y-GFP (β- catenin mutant) was seen predominantly in the nucleus as expected. (Figure 8.6.1(A). Recombinant protein expression checked by immunoblot analysis showed that the phosphorylated IGF1R-GFP(WT) is expressed as a protein of nearly 200 kDa (pro-IGF1R) and 130 kDa (β-domain-GFP) (Figure 8.6.1B lane 2 upper panel) and a fully active protein detected by using phosphor-

IGF1R antibodies (Figure 8.6.1(B) lane 2 lower panel). Moreover, sub cellular fractionation analysis confirmed the nuclear translocation of IGF1R (Figure8.6.1).

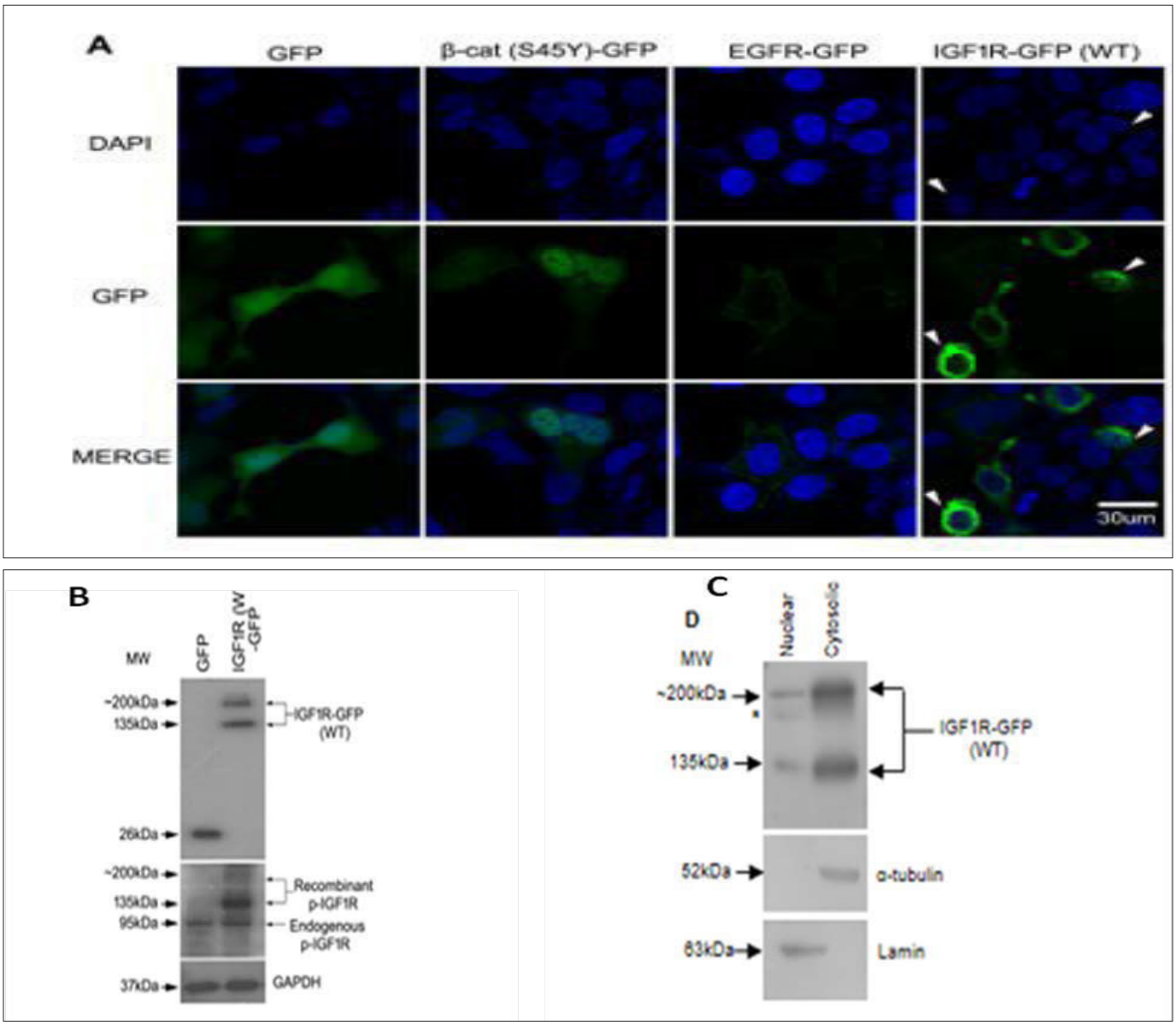


Figure 8.6.1 A. Subcellular localization of IGF1R in HEK-293 cells. B. Expression analysis by western blotting. C. Fractionation analysis by western blotting

2. Cytoplasmic domain defines the nuclear localization of IGF1R: To investigate whether the intact receptor or its individual domains localize to the nucleus, we generated deletion mutants of IGF1R as shown in Fig. 8.6.2 A Upon analyzing sub-cellular localization, GFP tagged α-subunit was predominantly seen at the membrane whereas β- subunit-GFP was seen at the membrane as well as in the nucleus and cytoplasm (Figure 8.6.2 B). Since, β- subunit possesses a transmembrane region; we assumed it may not translocate to nucleus, however, it showed prominent nuclear and cytoplasmic localization. Unlike β-subunit, CTD domain, which lacks transmembrane region, showed predominant nuclear localization (Figure 8.6.2 C)

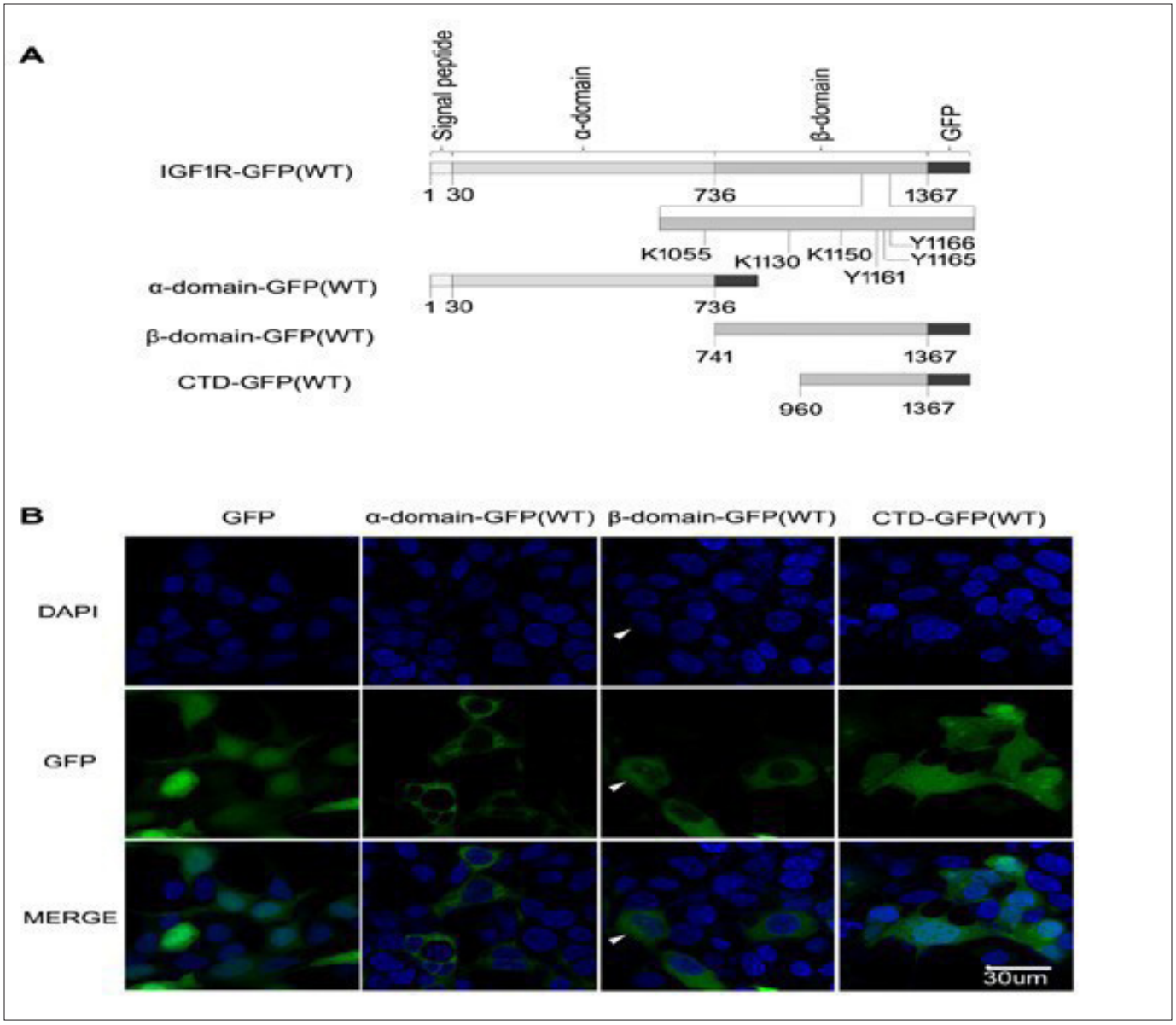


Figure 8.6.2 A. Schematics of IGF1R deletion mutants used in this study. B. Subcellular localization of deletion mutants in HEK-293 cells.

3. Impact of K1055R mutation on activity of IGF1R and its deletion mutants: We have identified the role played by K1055 mutation on various activities of wildtype IGF1R and various deletion mutants. Mutation of lysine residues at 1055, 1130 and 1055 failed to impeded the nuclear localization of IGF1R and its deletion mutants. However, the autophosphorylation activity and downstream signalling activity of IGF1R was drastically reduced upon mutating lysine 1055 to arginine (Fig. 8.6.3A). We also incorporated similar mutations in the β-subunit and CTD and observed that their autophosphorylation activity was completely abolished as well (Fig. 8.6.3B). Furthermore, we performed insilico analysis to examine the mechanism how K1055R mutation is abrogating activity of wildtype IGF1R and observed that this residue is sitting in a pocket separate than the ATP and substrate binding pocket. This new binding pocket is suited for designing small molecule allosteric inhibitors of IGF1R.

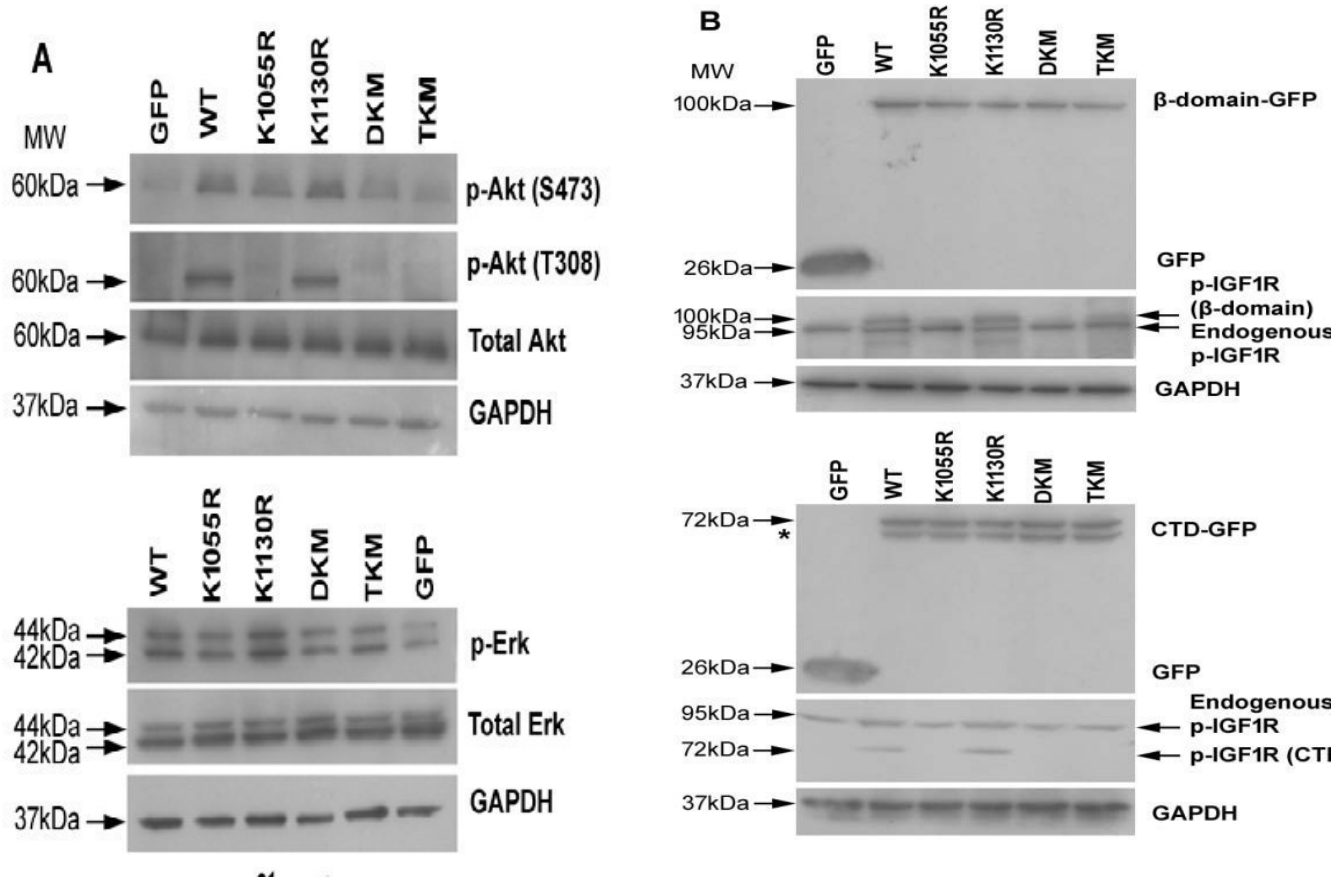


Figure 8.6.3 A. Downstream pathway analysis of wildtype IGF1R and its point mutants. B. Autophosphorylation and downstream pathway analysis of beta-domain, cytoplasmic domain and their point mutants

9.0 CHEMICAL ENGINEERING AND cGMP

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

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

Nurturing a new pan-CSIR drug pipe line: high intensity preclinical, clinical studies on lead candidates" (CSIR-DPL) Under BSC0205 project Several botanical leads and drug candidates have been identified at IIIM Jammu (RJM0862, ICB014, BC A002, DC A002, RJM0001, RJM0010, RJM0024, RJM0035 and RJM1195) for their Clinical trial batch production for the IND candidate leads. As objective of the BSC0205 project, to make available high quality innovative products in Indian, CSIR- IIIM Jammu collaboration with M/s. Cadila Pharmaceuticals Limited-Contract Research Organisation to conduct Phase I Clinical Trial titled "A Phase-I, Dose escalation study to evaluate safety, tolerability and Pharmacokinetic studies of ICB014-A002, IIIM160, A002 & RJM0862 A001 on desired formulations in healthy adult volunteers". In this review, attempts have been made to know about some medicinal plants which may be used in ayurvedic as well as modern science for the treatment or prevention of peptic ulcer, Arthritis & Hepato-protective activity of the ICB014-A002, IIIM160 A002 & IIIM0862 A001 respectively.

9.2 Anti-Ulcer activity:

CSIR-IIIM, Jammu has been developed a standardized drug product i.e., ICB014-A002 Capsule, the manufacturing procedure has been scaled up in cGMP facility and all the manufacturing process has been optimized. Analytical method for drug substance and drug product has been developed and validated at QC/QA section. Drug product was found to be stable when stored at 30°C±2°C/65%±5%RH for 01 year in PVC bottle pack. The present invention comprising an effective amount of an extract or lyophilized extract at least one bioactive fraction obtained from ICB014 A002 (*Woodfordia fructicosa*) along with one or more pharmaceutically acceptable additives/carriers. This invention envisages the potential of an extract obtained from the flower of ICB014 A002 (*Woodfordia fructicosa*) to act an effective therapy against peptic ulcer disease.With this background data, CSIR- IIIM, Jammu compile a dossier (IND) to the AYUSH department to conduct the Phase-I Clinical trial on Healthy volunteer on 18/12/2017 through CRO with following study related documents viz.,

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

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

Woodfordia fructicosa (flowers)

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

9.3 New Facility Creation for Stability Studies: Walk-In-Stability Chambers

IIIM Jammu as an emerging entrepreneur in the field of AYUSH drugs manufacturing. This institution set up a National cGMP facility for extraction, formulation and packing Traditional ISM herbal medicine formulation dosage forms (Tablets, capsule, Liquid oral dosage forms and churna). In this connection, IIIM Jammu created a new facility at cGMP facility, to conduct the stability studies at three different conditions like Accelerated (40±2°C, 75%±5%RH) and Long term condition ((30±2°C, 65%±5%RH) and intermediate condition (25±2°C, 60%±5%RH). The capacity of each chambers are 12000 Litres, to determine the Shelf life/Retest period and Expiry date of products.

Walk in stability chambers (Capacity: 12000 L)

The facility is to cater to the needs of IIIM in terms of preparation of extracts, their formulation in the form of a tablet/capsule and liquid orals for pre clinical and clinical trials of the NCE's derived from botanicals and being pursued for Investigational New Drug application IND filing to different regulatory authorities like CDSCO, Dept. of AYUSH etc., under PAN CSIR project BSC 0205 and also other NCEs that are being evaluated for IND potential. It may also prove a boon for small scale industry (SSI) (Commercialization) to take advantages of this facility which may not be accessible to them due to high cost and maintenance requirements. In the above all contexts, Stability chambers are mandatory for Regulator market to determine the **shelf life/Retest period and Expiry date of the formulations** (As per ICH Q1A) of the products which are manufactured in the cGMP facility.

9.4 Service to Industry:

Sl. No	Title of the project	Project Type/ Category	Amount received with your initiative	Govt./ Industry	Lab Reserve generation
1	Development of extract of *Pterocarpus santalinus* (Red Sanders)	Consultancy project	1,40,000/-	M/s. Andhra Fogaku (P) Ltd. Hyderabad	1,40,000/-

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

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

Secondary IDs if Any

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

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

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

Details Contact Person (Scientific Query)

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

Details Contact Person (Public Query)

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

Source of Monetary or Material Support

Source of Monetary or Material Support
> Indian Institute of Integrative Medicine, (Council of Scientific & Industrial Research) Canal Road, Jammu-180001 (J&K) India.

Primary Sponsor

Primary Sponsor Details	
Name	Indian Institute of Integrative Medicine Council of Scientific Industrial Research
Address	Canal Road, Jammu-180001 (J&K) India.
Type of Sponsor	Government funding agency

Details of Secondary Sponsor

Name	Address
NIL	NIL

Countries of Recruitment

List of Countries
India

Sites of Study

Name of Principal Investigator	Name of Site	Site Address	Phone/Fax/Email
Dr Dushyant Balat	Apollo Hospitals International Limited	Health Check Department Plot no. 1A, Bhat, GIDC Estate, Gandhinagar – 382428. Gandhinagar GUJARAT	9825015055 drdushyant.balat@gmail.com

Details of Ethics Committee

Name of Committee	Approval Status	Date of Approval	Is Independent Ethics Committee?
Institutional ethics Committee Clinical Studies	Approved	22/09/2017	No

Regulatory Clearance Status from DCGI

Status	Date
Not Applicable	No Date Specified

Health Condition / Problems Studied

Health Type	Condition
Healthy Human Volunteers	Adult Healthy Human Volunteers

Intervention / Comparator Agent

Type	Name	Details
Intervention	ICB-014-A002 Oral Capsule Formulation	For Single dose escalation study: Route of administration: Oral. Total 5 dose level of ICB-014-A002. ? Dose-level – I : ICB-014-A002 300 mg. ? Dose-level – II : ICB-014-A002 600 mg. ? Dose-level – III : ICB-014-A002 900 mg. ? Dose-level – IV : ICB-014-A002 1200 mg. ? Dose-level – V : ICB-014-A002 1500 mg. Single day Oral administration after at least 10 hours of fasting. For Multiple dose: Dose: Based on the results of single dose study, Maximum Tolerated Dose (MTD) and two immediate lower doses to the MTD will be administered. 14 days oral

9.5 Anti-Inflammatory & Rheumatoid arthritis:

CSIR-IIIM, Jammu has been developed a standardized drug substance (Extract) i.e., IIIM 160 A002, the manufacturing procedure has been scaled up in cGMP facility and all the manufacturing process has been optimized. Analytical method for drug substance and drug product has been developed and validated at QC/QA section. Drug product was found to be stable when stored at 30°C±2°C/65%±5%RH for 02 year in LDPE bags. IIIM Jammu, developed a prototype Novel drug delivery formulation (Gastro Retentive sustained release) on the standardised extract and has been filed a patent, bearing CSIR Ref. # 0120NF2017, Dated: 25-MAY-2017). The present invention comprising an effective amount of an extract or lyophilized extract at least one bioactive fraction obtained from IIIM 160 A002 (*Bergenia ciliata*) along with one or more pharmaceutically acceptable additives/carriers. This invention envisages the potential of an extract obtained from the whole plant of IIIM 160 A002 (*Bergenia ciliata*) to act an effective therapy against Anti-inflammatory & rheumatoid arthritis. With this background data, CSIR-IIIM, Jammu has to be compiling a dossier (IND) to the AYUSH department to conduct the Phase-I Clinical trial on Healthy volunteer through CRO.

9.6 Sickle cell Anaemia Mission Project (HCP0008)

Hydroxycarbamide/Hydroxy Urea, is a generic medicine for the long treatment of Myeloproliferative disease (primarily polycythemia vera and essential thrombocythemia). It has been found to be superior to anagrelide for the control of ET. Later on, this product, "Droxia" (New Drug Application NDA) was approved for the Management/ treatment of Sickle cell anemia in favor M/s. Bristol Mayer Squibb, Princeton, NJ, USA by USFDA on 04/04/2001 which was Reference listed drug (RLD) in the Orange book of USFDA. Currently, M/s. Bristol Mayer Squibb is supplying the Hydroxyurea capsules with the brand name "Droxia" in three different strengths i.e., 200 mg, 300mg & 400mg for the treatment of Sickle cell anemia to the US population. As on day, there is no any clinical studies were conducted on Indian population for the indication of Sickle cell anemia. **So, IIIM Jammu is seeking permission to conduct interventional bioavailable and bioequivalence (BA/BE) studies on the Indian population with a comparator of reference listed drug (RLD) i.e, Droxia, 400 mg, to make available to the Indian patients.** In this connection, IIIM Jammu has been applied for the License for import of Droxia, 400 mg (RLD) to make Equivalent formulation and same has been got, bearing license number: **TL/NZ/18/000289, dated: 27/03/2018** in favour of IIIM Jammu from the Govt. of India, CDSCO, Ministry of Health and family welfare, New Delhi. Licence copy in preceding page.

Form 11
[See Rule 33]
LICENCE TO IMPORT DRUGS FOR THE PURPOSES OF EXAMINATION,TEST OR ANALYSIS

Number of Licence: TL/NZ/18/000289

I, Mr. Durga Prasad Mindala (Technical Assistant), of Indian Institute Of Integrative Medicine CSIR, Canal Road, Jammu Tawi, Jammu tawi, Jammu And Kashmir - 180001 is hereby licensed to import from M/s. Bristol Myers Squibb , Princeton, New Jersey 08543, Princeton, New Jersey - 08543 United States the drugs specified below for the purposes of examination, test or analysis at M/s. CSIR-Indian Institute of Integrative Medicine, Canal Road, Jammu Tawi, Jammu Tawi, Jammu And Kashmir - 180001 or in such other places as the licensing authority may from time to time authorize.

2. This licence is subject to the conditions prescribed in the Rules under the Drugs and Cosmetics Act, 1940.

3. This licence shall, unless previously suspended or revoked, be in force for a period of three year from the date specified below:

S.No.	Name of drugs and Brand Name	Class of Drug	Quantity which may be imported
1	Hydroxyurea 400 milligram (mg) (Droxia)	Anti metabolite	180 Capsules (60 capsules per bottle)

Item(s) One (1) only
Not for any commercial purpose and to be used for clinical studies/trials i.e. BA/BE for Export purpose & related testing only

AJAY SACHAN
Digitally signed by AJAY SACHAN
Date: 2018.03.27 10:41:34 +05'30'

Date 27-MAR-2018

LICENSING AUTHORITY
Seal/Stamp

Conditions of Licence

1. The licensee shall use the substances imported under the licence exclusively for purpose of examination, test or analysis and shall carry on such examination, test or analysis in the place specified in the licence, or in such other places as the licensing authority may from time to time authorise.
2. The licensee shall allow any inspector authorized by the licensing authority in this behalf to enter, with or without prior notice, the premises where the substances are kept, and to inspect the premises, and investigate the manner in which the substances are being used to take samples thereof;
3. The licensee shall keep a record of, and shall report to the licensing authority, the substances imported under the licence, together with the quantities imported, the date of importation and the name of the manufacturer.
4. The licensee shall comply with such further requirements, if any, applicable to the holders of licences for examination, test or analysis as may be specified in any rules subsequently made under Chapter III of the Act and of which the licensing authority has given to him not less than one month's notice.
5. The drugs imported under this licence shall not be directed to or for Commercial Marketing including export purposes.
6. The firm shall obtain No Objection Certificate from the Narcotics Commissioner of India, 19, The Mall Morar, Gwalior for the import of drugs under Narcotic Drugs and Psychotropic Substances Act and Rules, 1985.

9.7 TBI-Skill Development Program

cGMP Unit, CSIR-IIIM Jammu, provide opportunity to new entrepreneurs/SMEs engaged in manufacture of standardised extracts and botanical drug formulations, natural products etc., to evaluate their research leads and eventually graduate as entrepreneurs so that more number of industries can be setup and employment can be generated. This facility will also be used as the Technology Business Incubator (TBI), for which Department of Science and Technology has already approved a project.

Biotech Industrial Training Programme under BCIL, have been selected for dissertation training programme in Technology Business Incubator of Indian Institute of Integrative Medicine (TBI-IIIM), Jammu, for the batch commencing in DECEMBER, 2017 Training was imparted through lectures by the experts and through Practical in the area of extraction, formulation, QA/QC, and Utilitiesetc.

IIIM TBI

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

STUDENTS SELECTED FOR TRAINING PROGRAMME UNDER BITP (2017-18

This is to notify that the following applicants have been selected for dissertation trainin programme in Technology Business Incubator of Indian Institute of Integrative Medicin (TBI-IIIM), Jammu, for the batch commencing in DECEMBER, 2017.

List of students selected for training programme under BITP 2017-18

S.No.	Name	Date of Joining	Programme
1.	Ms. Apoorva Choudhary	18th Dec. 2017	BITP 2017
2.	Ms. Jyoti	18th Dec. 2017	BITP 2017
3.	Ms. Somya Agarwal	1st Jan. 2018	BITP 2017
4.	Ms. Ruby Chauhan	18th Dec. 2017	BITP 2017
5.	Ms. Pooja Patwal	1st Jan. 2018	BITP 2017
6.	Mr. Ashvani Yadav	13th Dec. 2017	BITP 2017
7.	Mr. Anuj Kumar	13th Dec. 2017	BITP 2017
8.	Mr. Gaurav Yadev	18th Dec. 2017	BITP 2017
9.	Mr. Harshit Tiwari	18th Dec. 2017	BITP 2017
10.	Mr. Ambikesh Tiwari	18th Dec. 2017	BITP 2017

The main objective of CSIR- IIIM is conducting One/three month certificate course to create a stream of highly trained manpower by enhancing practical and regulatory skills of science, pharmacy and medicine graduates in the area of extraction and formulation of phyto-pharmaceutical drugs.

Course structure: The course will be a right mix of lectures by experts drawn from CSIR, academia and Industry and intensive hands on training on good agriculture and collection practices (GACP), current Good Manufacturing Practices (cGMP), good documentation practices (GDP), QC/QA-CMC and regulatory aspects related to production of botanical/herbal formulations. Separate modules for practical training on analytical instruments, GMP based preparation of extracts and formulations, will be the integral part of this course.

10.0 QUALITY CONTROL AND QUALITY ASSURANCE

Quality Control and Quality assurance Division, a National Accreditation Board for Testing and Calibration Laboratories (NABL) accredited laboratory for chemical testing a has undergone NABL audit on 09-10 Dec 2017 for renewal of certificate. The QCQA division successfully completed the audit and got accredited in accordance with standard ISO/IEC 17025: 2005 bearing certificate no TC-6948 from 01 Mar 2018 till 29 Feb 2020.

National Accreditation Board for Testing and Calibration Laboratories
(A Constituent Board of Quality Council of India)

CERTIFICATE OF ACCREDITATION

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

has been assessed and accredited in accordance with the standard

ISO/IEC 17025:2005

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

for its facilities at

Canal Road, Jammu-Tawi, Jammu & Kashmir

in the field of

TESTING

Certificate Number TC-6948 *(in lieu of 1021)*
Issue Date 01/03/2018 Valid Until 29/02/2020

This certificate remains valid for the Scope of Accreditation as specified in the annexure subject to continued satisfactory compliance to the above standard & the relevant requirements of NABL.
(To see the scope of accreditation of this laboratory, you may also visit NABL website www.nabl-india.org)

Signed for and on behalf of NABL

N. Venkateswaran
Program Director

8907697010003000889

Anil Relia
Chief Executive Officer

QCQA division has also been notified as NRL (National Referral Lab) for analysis of aflatoxins, pesticide residues, heavy metals in nuts, honey and nutraceuticals by FSSAI, approved by GOI, Ministry of Health & Family Welfare under Food Safety Standard Act 2006.

fssai
Referral lab for
Nuts, Honey & Nutraceuticals

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

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

Scope of Accreditation

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

AYUSH Products
- Ayurvedic Drugs
- Unani drugs
- Herbal Formulations

Cosmetic & Essential Oils
- Qualitative analysis

Animal Food & feeds

Nutraceuticals

Competencies

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

It is dedicatedly involved in Chemistry Manufacturing & Control (CMC) of medicinal plants, herbal extracts and formulations. Generation of CMC data on the following high value medicinal plants has been undertaken as given below.

➢ *Woodfordia fruticosa*
- ➢WF/CMC/B-10 (DEXTD 0027) (I-2089)
- ➢WF/CMC/B-11 (DEXTD 0028) (I-2089)
- ➢WF/CMC/B-12 (I-2040)
- ➢WF/CMC/B-13 (I-2056)
- ➢WF/CMC/B-14 (I-2056)
- ➢WF/CMC/B-15 (I-2043)
- ➢WF/CMC/B-16 (EEXTD003) (I-2090)

➢ Red Sandal wood
- ➢01/Plant Material/CMC (1-2024)

➢ *Withania somnifera*
- ➢WS/CMC/B-02 Hydroalcoholic Extract (I-1949)
- ➢WS/CMC/B-01/Capsules (DEXTD0003) (I-2008)

➢ Nutraceuticals
- ✓Phalsa Juice/Oct/2017/01 (I-1983)
- ✓Phalsa Juice/Nov/2017/02 (I-1995)
- ✓Phalsa Juice/Dec/2017/03 (I-2013)
- ✓Phalsa Juice/Jan/2018/04 (I- 2036)
- ✓Sea buckthorn Juice/Oct/2017/01 (I-1984)
- ✓ Sea buckthorn pulp/LAS/Oct/2017 (I-1988)
- ✓Sea buckthorn Juice/ Nov/2017/02 (I-1994)
- ✓ Sea buckthorn /Tab/11/2017/CMC (I-1996)
- ✓Sea buckthorn Juice/Dec/2017/03 (I-2012)
- ✓Sea buckthorn Juice /Jan/2018/04 (I-2036)

➢ *Colebrookea oppositifolia*
- ➢CO-04 (DEXTD 009)/CMC Alcoholic Ext (I-1970)
- ➢CO-04 (2015) Alcoholic ext, Quant Study (I-1959)
- ➢CO-05/CMC (DEXTD 0013) (I-1971) Alcoholic ext
- ➢CO-07 (B-07) (Plant Leaves) (I-2023)

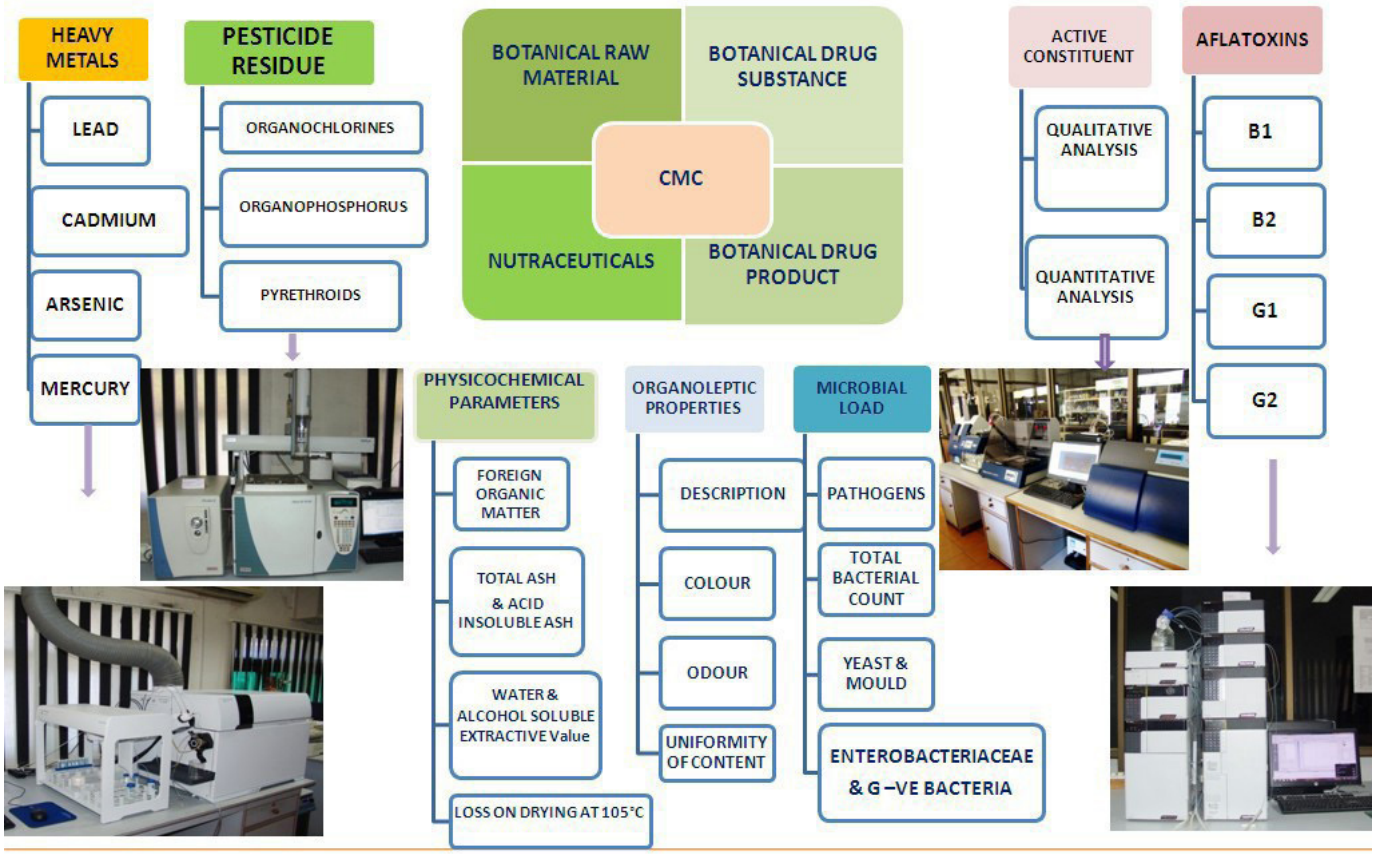
➢ *Glycyrrhiza glabra*
- ➢GG/CMC/B-01 (DEXTD0008) Hydro alcoholic Ext (I-1952)
- ➢GG/CMC/B-01/Capsules-Liquorice-P (DEXTD0008) (I-2008)

➢ *Tinospora cordifolia*
- ➢TC/CMC/B-01/Capsules- Diacord-P (CEXTD006) (I-2008)

➢ *Boswellia serrata*
- ➢BS-03/CMC (DEXTD0014) (I-1970) Alcoholic Extract
- ➢BS/04/CMC (DEXTD0020) (I-1985) Alcoholic Extract

Analysis carried out
- Vitamins (Fat & water soluble)
- Crude fat
- Microbial Load
- pH
- Proteins
- Carbohydrates
- Viscosity
- Specific Gravity
- Total Sugar

The above CMC data was generated by carrying out following analysis using analytical instruments.



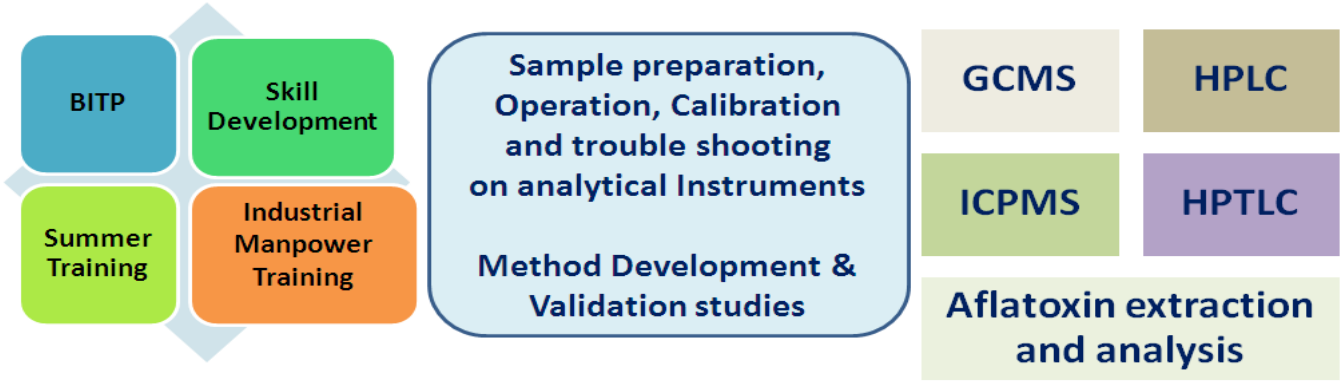
10.2 QCQA division has accrued many benefits to Society and industry as follows:

Food industry, Alcoholic drinks and beverages industry, Animal feeds and of Spices and condiments. Analysis of heavy metals, pesticides, aflatoxins, various physicochemical parameters like total ash, acid insoluble ash, crude fiber, peroxide value, free fatty acids etc has being carried out. Physiochemical testing and microbial load of water from various public and private schools, universities, hospitals, small and large scale industries across whole J&K and from all parts of India. As a part of Skill Development Program (SDP) for manpower trainings are also organized on analytical instruments for postgraduate students giving them hands on experience on modern high end analytical instruments.

Biotech Industrial Training Programme (BITP)

Industrial Manpower Training Programme

Skill Devlopment Training Programme



S.No.	NAME	University	Division	Duration
1	Jubin J Kurichiyil	Mar Athanasios College For Advanced Studies Tiruvalla (MACFAST)	QA & QC	02 months
2	Nikhil A.N	Mar Athanasios College For Advanced Studies Tiruvalla (MACFAST)	QA & QC	02 months
3	Sujay Basak	Jiwaji University, M.P	QA & QC	04 months
4	Mahendar	Jaipur National University	QA & QC	06 months
5	Ishita Bhattacharya	Baba Faird Institute of Technology (BFIT), Uttrakhand	QA & QC	06 months

College/University	No. of Trainees
Beant College of Engg & tech , Gurdaspur	4
Suresh Gyan Vihar University, Rajasthan	4
Shoolini Universities Solan, HP	3
SMVDU, Katra	6
M Anthanasios College (MACFAST), Tiruvalla, Kerala	2
Jiwaji University, Gwalior	1
Baba F Institute of Technology (BFIT), Uttrakhand	1
Drug Inspectors	3
Food and Safety Officer (FSO)	3
Drug analyst	1

The QCQA division is proudly moving ahead for being designated as Drug Testing Laboratory (DTL Ayurveda). As the testing of AYUSH drugs is now covered under the provision of Drug and Cosmetic Act 1940, this requires application to be submitted to licensing authority as well as AYUSH department, New Delhi. Application is under process for approval on Form 48 as private AYUSH drug testing laboratory under Rule 160 A -J to the Drugs & CosmeticRules.

11.0 ANIMAL HOUSE

11.1 Standardization and Establishment of Mouse Model for testing of compounds / drugs for infection and inflammation of mammary gland

Rakesh Nagar, Amit Kumar and Narendra Chouhan , Govind Yadav and Satheesh Kumar P

Aim to develop pharmaceutical product for bovine mastitis and to study other inflammatory conditions of mammary gland. For that 5 days post partum nursing females (C57BL/ iiim mice) were anesthetised with *Ketamine* and *Xylazine* combination and inflammation induced by LPS (lipo-polysaccharide). The characteristic of inflammation in induced group as evident by infiltration of inflammatory cells in mammary gland (fig 11.1.2b) compare to vehicle control group (fig 11.1.2a). The clearance of inflammatory cells in dexamethazone treated group showing in (Fig 11.1.2c). So, this model tested for all three conditions (Negative control (a), inflammation (b) and treatment (c). It indicates the mouse model suitable for testing and screening anti-inflammatory compounds for inflammatory conditions of mammary gland (i.e. bovine mastitis.). This also suitable to test the anti-infective compounds against localized mammary gland infection and inflammatory condition due to infection.

Effect of compound/ extract oral treatment in LPS induced Mammary gland of mouse model of mastitis – Macroscopic pathology (Fig.11.1.1), Histopathology 10X and 40X (Fig.11.1.2a & 2b) (from A to H). A. *Vehicle control,* B. Treated with 50 µl of 20% *LPS,* C. Treated with dose of 0.5 mg/kg *Dexamethasone,*

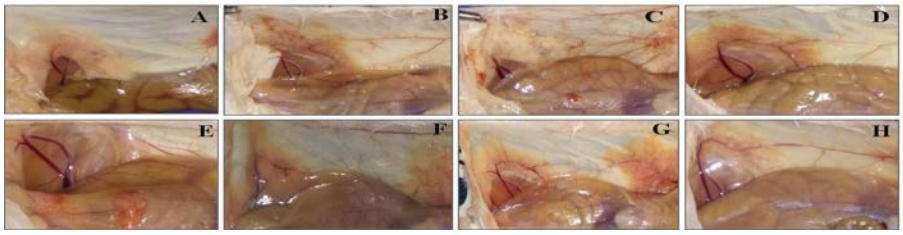


Fig.11.1.1. LPS induced Mammary gland of mouse model of mastitis (Macroscopic pathology A-C).

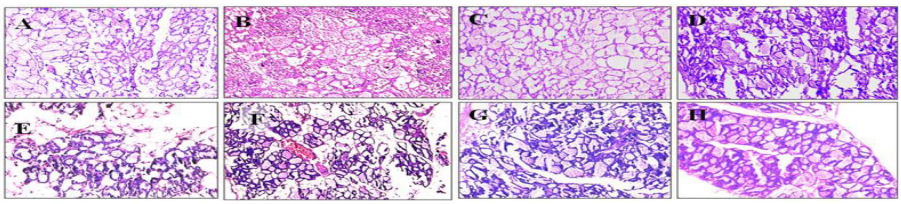


Fig.11.1.2a. Dose dependent inhibition of infiltration of inflammatory cells in 5th day postpartum LPS induced (intra-mammary) mouse modal of mastitis (**10X, H&E Staining**).

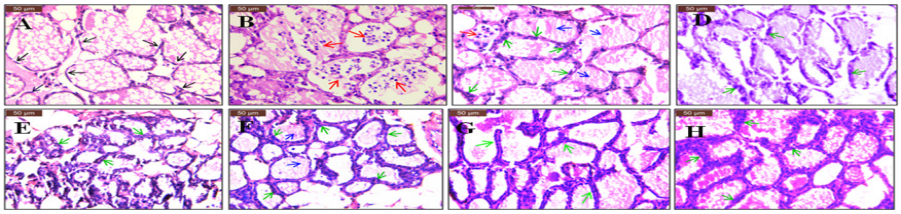


Fig.11.1.2b. Dose dependent inhibition of infiltration of inflammatory cells in 5th day postpartum LPS induced (intra-mammary) mouse modal of mastitis **(40X, H&E Staining).** (**Black arrow** – indicates thin epithelial cell layers; **Red arrow** – denote leukocyte infiltration; **Green arrow** – indicates thick active epithelial cell layers; **Blue arrow** – indicates the regenerated alveoli cells were replaced)

11.2 Establishment of Pedigree and its evaluation in different pharmacological studies

Govind Yadav, Satheesh Kumar P, Rakesh Nagar, Amit Kumar and Narendra Chouhan

1. IIIM Animal House Facilitated R&D activities for proof of concept studies by providing Laboratory Animals of four different species viz., Mice, Rat, Guinea Pig, and Rabbit (Fig11.2.1a & 11.2.1b:). Currently available strains are being maintained by as per the ethical guidelines (Health Monitoring and Genetic Monitoring) and accreditation with CPCSEA.Since last five years our animal house facility systematically programmed to establish pedigree from available stock of strains. Now pedigrees were established by standard selection procedures, systematic mating methods and strict record keeping. Our continuous efforts results in establishment of pure breed line and sub-lines. These pedigreed rodent lines being evaluated for their suitability in different pharmacological procedures in the area of drug discovery and development (Fig 11.2.2:). In our facility each line's upcoming filial generations were genetically improved by minimizing the traits variances within the line through scientific selections. Similarly, for outbred stocks were genetically improved by maximize the variance by avoiding inbreeding through maintains effective population size.

2. Breeding performance upto 31, March 2018:

S.No	Strain	No of sub-lines developed	Matting Group Total Nos.	Filial generation No.	Developed by
1	C57BL/iiim Mice	3	MG-121	F-32	Full Sub-Mating
2	DBA2/iiim Mice	3	MG-151	F-31	Full Sub-Mating
3	BALBc/iiim Mice	3	MG-419	F-22	Full Sub-Mating
4	SWISS/iiim Mice	2*	MG-25	F-2	Selective Mating
5	Wister Rat	2*	MG-172	F25	Selective Mating

* From Out breeding based on growth pattern two new sub populations developed.

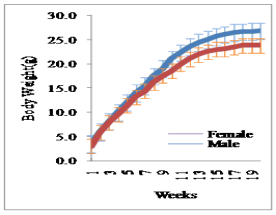
Fig11.2.1a: IIIM Strains (Apr2017-Mar2018)

DBA2/iiim

Used in Research (2017-18): Murine Tumor Model

Produced no. 842
litter size 8-10
Wean: Birth Ratio 0.91
Male: Female Ratio 0.91
Mating syatem - **Inbred**

Growth Pattern



CDF1/iiim

Used in Research (2017-18): Anti-Cancer Efficacy study

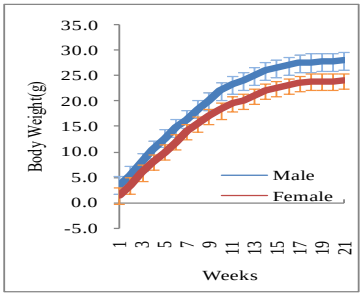
Produced no. 35
litter size
Wean: Birth Ratio 0.98
Male: Female Ratio 1.33
Mating syatem - **Hybrid (Cross Breed)**

Swiss Mice/iiim

Used in Research (2017-18):
- Anti-inflamatory
- Acute Toxicity
- Pharmacokinetic

Produced no. 1605
litter size 10-12
Wean: Birth Ratio 0.94
Male: Female Ration 0.95
Mating syatem Outbred

Growth Pattern



BALB/c/iiim

Used in Research (2017-18): ADME (Absorption, Digestion, Metabolism and Excretion) study, in vivo Anti-TB, Intestinal Motility, Drug Safety & Efficacy study, Drug Analgesic study, Animal Model, Metastatic, Mutagenesis, Drug Pharmacokinetic, Anti-inflamatory, Tumor Inhibition, Murine Tumor Model, NCRP3 Activity.

Produced no. 2559
litter size 9-11
Wean: Birth Ratio 0.92
Male: Female Ratio 1.26
Mating syatem - **Inbred** (Full-Sib Mating)

Growth Pattern

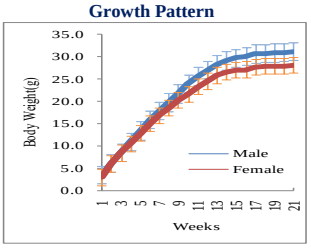
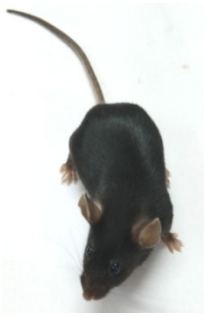


Fig 11.2.1b: IIIM Strains (Apr2017-Mar2018)

C57BL/iiim

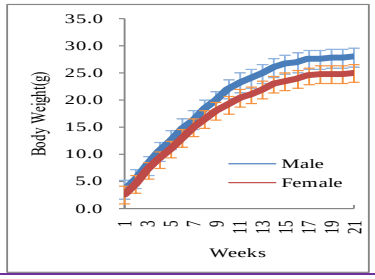
Used in Research (2017-18):

- Anti-cancer study
- Primary glial culture
- Melonogenesis
- Skin Biology Study (UV-Induced Skin Modal)
- Antibody detection
- Mitochondrial Biogenesis
- *in vivo* Drug validation
- NLRP3 Activity



Produced no. 1198
litter size 8-10
Wean: Birth Ratio 0.85
Male: Female Ratio 0.57
Mating syatem **Inbred** (Full-Sib Mating)

Growth Pattern



WISTAR RAT/iiim

Used in Research (2017-18):

- Anti-Arthritis
- Anti-inflamatory
- Cytokine analysis G.I.Transit
- GIT Activity
- *In sito* Perfusion
- *in vivo* perfusion
- Intestinal transit
- Mutagenesis
- Pharmacokinetic
- Mutagenesis
- Acute Toxicity
- Sub-acute Toxicity

Produced no. 2445
litter size 8-13
Wean: Birth Ratio 0.95
Male: Female Ratio 1.05
Mating syatem **Outbred**

Albino/iiim Guinea Pig

Used in Research

- Bovine Mastitis Model

Population size -
litter size -
Wean: Birth Ratio 0.96
Male: Female Ratio 1.16
Mating syatem **Outbred**

NZW Rabbit/iiim

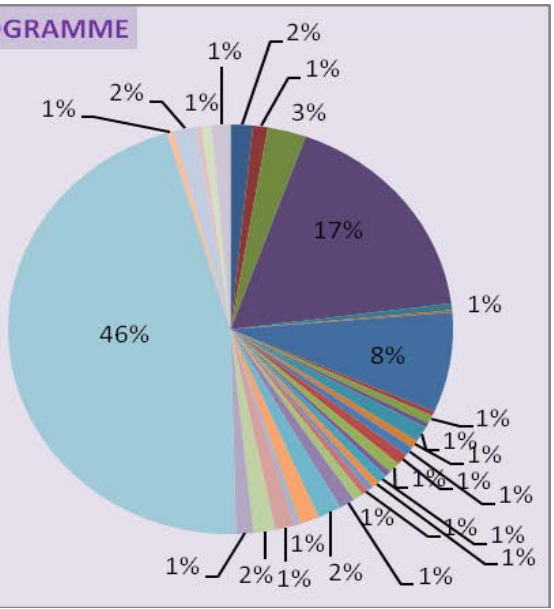
Used in Research

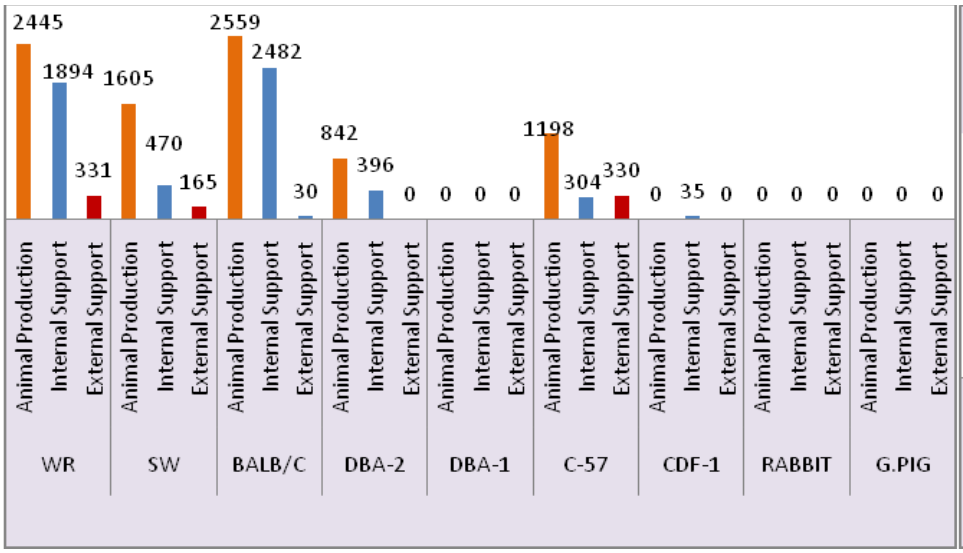
- PD-E5 Inhibition
- Antibody production
- Skin irritation study
- Coagulase test study

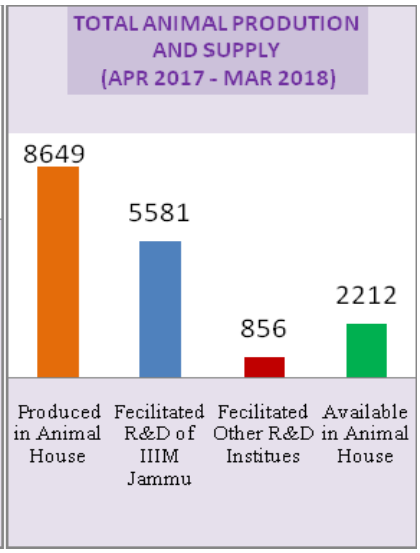
Produced no. -
litter size -
Wean: Birth Ratio 0.90
Male: Female Ratio 0.75
Mating syatem **Outbred**

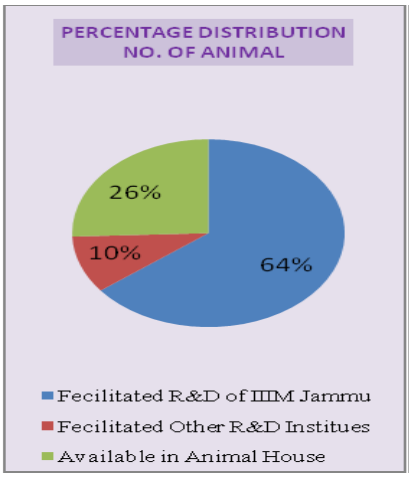
Fig2: PERCENT DISTRIBUTION OF RODENTS TO IIIM R&D PROGRAMME

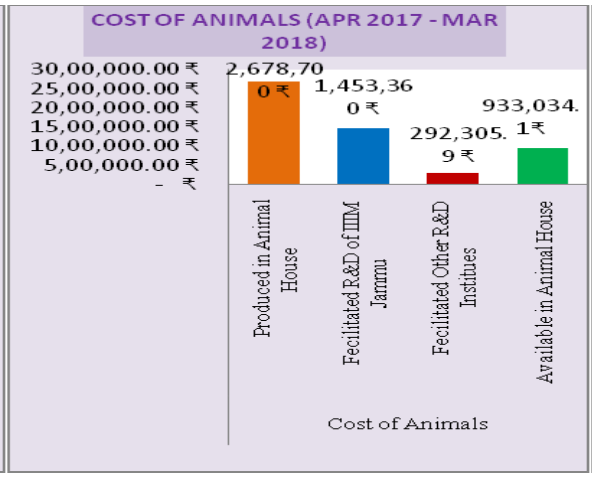
- Acute Toxicity
- Analgesic
- Anti-Arthritis
- Anti-inflamatory
- G.I.Transit
- In sito Perfusion
- Anti-Tuberculosis
- in vivo Efficiency
- Inflamatory
- Intestinal transit
- LPS Induced Aseptic check
- Metastatic
- Mutagenesis
- NLRP3 Activity
- Pharmacokinetic
- Sub-acute Toxicity
- UVB+HFT
- ADME
- Animal/Tumor Modal
- Antibody detection
- Cytokine analysis
- GIT Activity
- Anti-Cancer
- in vivo Drug validation
- in vivo perfusion
- Intestinal Motility
- LPS Induced
- Melonogenesis
- Mitochondrial Biogenesis
- NCRP3 Activity
- Phagocytosis
- Safety & Efficacy
- Tumor Inhibition
- UV-Induced skin modal

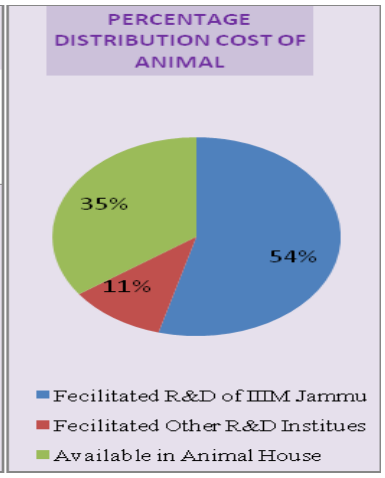












11.3 Other Scientific Outcomes (Animal House Division)

Projects:

Development of phyto-pharmaceutical product for bovine mastitis: To provide the solution for treatment of mastitis (related to farmers keeping dairy animals for livelihood)

- **Animal model:** Mouse model of Mastitis standrised and used for in *in vivo* proof of concept study.
- Anti-inflammatory and anti-infective ***phyto-pharmaceutical product*** is in process of development
- ***IND-Enabling studies (Mutagenecity):*** 7 compound/extracts evaluated for mutagencity.

Science and Technology Services: IIIM AH supported total of 48 IAEC project proposals which covers total of 211 no. of *in vivo* studies (fig 11.2.2 & fig 11.3.1), supplied total of 5581 laboratory animals.

Table 11.3.1: No. of in vivo studies and animal issued to IIIM R&D Program (Apr 2017 to Mar 2018)

Year (Apr17-Mar18)	*No. of in vivo Studies*	*No. of Animal*	*Equalent Cost*
Total	211	5581	Rs.14,53,360/-

Funds generated (Figure 11.3.1**)**

S.No	Cost of animals provided to inhouse R&D:	Rs. 14,53,360/-
1	Cost of animals sold :	Rs. 2,92,305/-
2	From training:	Rs. 30,000/-
3	External Funded Project: DBT	Rs. 28,25,400/-
4	Total funds	Rs. 46,01,065/-

No of Clients: 11 clients added from Scientific Institutions.

Awards and honors: First price in poster presentation for work in mutagencity at 36th Annual Convention of Indian Society for Veterinary Medicine

New initiative for revenue generation: took initiative to get CPCSEA permission/ Registration for

i. Animal research for commercial uses.
ii. Animal breeding for trade

12.0 KNOWLEDGE RESOURCE CENTRE (LIBRARY)

IIIM Knowledge Resource Centre (Library) is playing an important supportive role in the research & development activities of the Institute. It offers services and support to the Scientists, Research Scholars and other S&T users to abreast them of significant developments and even evolving knowledge in their respective spheres of R&D activities. It caters to the information requirements of not only internal users but also of external users, like - postgraduate students, faculty members of colleges & universities; and corporate members. However, the membership for external users is on nominal payment basis.

Resources:

12.1.1 Print:

Over the years, it has grown into one of the most valuable research libraries in the country. It has a rich collection of books, periodicals, databases and other intellectual material. Broadly speaking, its collection covers subject areas like Biotechnology, Botany, Medicinal Chemistry, Natural Products Chemistry (NPC), Pharmacology, Quality Control and Agro- technology & Cultivation of Medicinal and Aromatic plants. During financial year 2017-18, a total of 69 numbers of books and reference resource, including books in Hindi language, were added in its collection.

The present holding status is as under:

No. of purchased documents: 27767
No. of Periodicals Bound Volumes: 17187 Doctoral Thesis: 70
Standards: 1093

List of latest additions have been uploaded on KRC (Library) website.

12.1.2Online/e-Resources:

IIIM is an important member of 'National Knowledge Resource Consortium (NKRC)'. Through this consortium, KRC provides access to thousands of journals published by various publication groups - like American Chemical Society, Emerald, IEEE, JCCC, Nature Publishing Group, Oxford University Press, Royal Society of Chemistry, Taylor and Francis, Wiley, etc. It also subscribes other e- resources which are not available through NKRC. Presently, a total of 15 online e-Journals and six online databases are being subscribed. IIIM KRC (Library) has co m p u t er i z ed all its in-house activities which are being maintained and updated on a regular basis in KOHA (an open source software). 'Online Public Access Catalogue (OPAC)' available at url: http://library.iiim.res.in is a very useful tool for searching offline (print)resources.

Services:

Presently, IIIM (KRC) is offering the following services to its users:

- ✓ Online access to e-journals anddatabases;
- ✓ Electronic Document Delivery Service(EDDS);
- ✓ Information search and retrievalfacility;
- ✓ Reprographic & printfacility;
- ✓ Web OPAC

Other initiatives:

During the period 2017-18, the following worth mentioning initiatives were taken and successfully completed:

a) Procurement & installation of LED Panel (55") for presentation purposes duringofficial meetings;

b) Four desktop computers were procured and installed for providing access to Internet facility, Library services;

e-Resources; Web-OPAC, etc to the research scholars and other users / members of theLibrary;

c) On 1st December, 2017, on the occasion of CSIR-IIIM Foundation day, Library (KRC) was included in the list of divisions to be covered by visiting students. On this occasion, an online presentation of the available resources, & services was demonstrated to various groups of students;

The total budget allocation during the financial year 2017-18 was Rs.1.05 crore. URL for IIIM KRC (Library): www.library.iiim.res.in/.

13.0 ACADEMY OF SCIENTIFIC AND INNOVATIVE RESEARCH (AcSIR)

Activities

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

13.1.1 Biological Sciences;
13.1.2 Chemical Sciences.

The admission takes place twice in a year i.e., for the January & July/ August sessions. In July/August, 2017 session a total of twenty six (26) PhD Students were registered at IIIM, Jammu. Similarly, in January, 2018 session seven (07) Students were selected for admission to PhD programme.

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

A total of twenty three (23) Comprehensive Examination Meetings were conducted during the period. Also, twenty two (22) AcSIR students successfully defended their PhD viva voice (OEB) examination. The list of successful candidates is as under:

S. No.	Name & Enrollment No. of Scholar	Supervisor/ Co-Supervisor	Month & Year
1.	Mr. Ramesh Deshidi (10CC12A37035)	Dr. Bhahwal Ali Shah	April, 2017
2.	Mr. Shekaraiah Devari (10CC12A37034)	Dr. Bhahwal Ali Shah	April, 2017
3.	Mr. Umed Singh (10CC11A37011)	Dr. Parvinder Pal Singh	May, 2017
4.	Mr. Rasheed Shaikh (10CC11A37013)	Dr. Parthasarathi Das	May, 2017
5.	Mr. Varma Saikam (10CC11J37043)	Dr. Ram A. Vishwakarma	June, 2017
6.	Mr. Sunil Kumar (10CC11J37041)	Dr. Asif Ali	July. 17
7.	Mr. Hariprasad Aruri (10CC11J37025)	Dr. Parvinder Pal Singh	Sept., 2017
8.	Mr. Suresh Kumar (10BB11J37004)	Dr. Fayaz malik	Oct., 2017
9.	Mr. Rohit Sharma (10CC12A37029)	Dr. Sandip Bharate	Nov., 2017
10.	Ms. Harvinder Kour Khera (10BB11A37008)	Dr. Subhash Singh	Nov., 2017
11.	Ms. Richa Sharma (10BB12A37018)	Dr. Asha Chaubey	Nov., 2017
12.	Mr. Srinivas Ambala (10CC11J37038)	Dr. Parvinder Pal Singh	Dec., 2017

S. No.	Name & Enrollment No. of Scholar	Supervisor/ Co-Supervisor	Month & Year
13.	Ms. Ankita Magotra (10BB12A37022)	Dr. Asha Chaubey	Dec., 2017
14.	Mr. Prakash Kannaboina (10CC12A37033)	Dr. Parthasarathi Das	Dec., 2017
15.	Mr. Kusuma Ranjith Kumar (10CC12A37038)	Dr. Parthasarathi Das	Dec., 2017
16.	Mr. Venkateswarlu Vunnam (10CC11J37044)	Dr. S. D. Sawant	Dec., 2017
17.	Mr. Nawab John Dar	Dr. Muzamil / Dr. Abid Dar	Dec., 2017
18.	Mr. Ankit Saneja	Dr. P. N. Gupta	Jan., 2018
19.	Mr. Reyaz Ur Rasool (10BB13J37002)	Mr. Reyaz Ur Rasool	Jan., 2018
20.	Mr. Zahoor Ahmd Wani (10BB12A37003)	Dr. Nasheeman Ashraf / Dr. Syed Riyaz Ul Hassan	Feb., 2018
21.	Mr. Shoib Ahmad Baba (10BB12A37017)	Dr. Nasheeman Ashraf	Feb., 2018
22.	Mr. Abid Manzoor Shah (10BB12J37005)	Dr. Qazi Parvaiz Hassan	Feb., 2018

LIST OF PUBLICATIONS
(Calendar Year 2017)

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

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

S.No.	Title	Author	Impact Factor
21	New Semi-Synthetic Rosmarinic Acid-Based Amide Derivatives as Effective Antioxidants. *CHEMISTRYSELECT* **(2017),** 2(31), 10153-10156	Ayoob, I; Lone, SH; Masood-ur-Rahman; Zargar, OA; Bashir, R; Shakeel-u-Rehman; Khuroo, MA; Bhat, KA	YET TO COME
22	Regiospecific Synthesis of Ring A Fused Withaferin A Isoxazoline Analogues: Induction of Premature Senescence by W-2b in Proliferating Cancer Cells. *Scientific reports* **(2017)**, 7(1), 13749	Rasool Faheem; Nayak Debasis; Katoch Archana; Faheem Mir Mohd; Yousuf Syed Khalid; Hussain Nazar; Goswami Anindya; Mukherjee Debaraj; Rasool Faheem; Hussain Nazar; et al	4.259
23	Anti-inflammatory chromone alkaloids and glycoside from Dysoxylum binectariferum. *Tetrahedron Letters* **(2017)**, 58(42), 3974-3978. DOI:10.1016/j.tetlet.2017.09.005	Kumar, Vikas; Gupta, Mehak; Gandhi, Sumit G.; Bharate, Sonali S.; Kumar, Ajay; Vishwakarma, Ram A.; Bharate, Sandip B.	2.193
24	Synthesis, pH dependent, plasma and enzymatic stability of bergenin prodrugs for potential use against rheumatoid arthritis. *Bioorganic & Medicinal Chemistry* **(2017),** 25(20), 5513-5521, DOI:10.1016/j.bmc.2017.08.011	Singh, Rohit; Kumar, Vikas; Bharate, Sonali S.; Vishwakarma, Ram A.	2.93
25	Development and evaluation of long- circulating nanoparticles loaded with betulinic acid for improved anti-tumor efficacy. *International Journal of Pharmaceutics* (Amsterdam, Netherlands) **(2017),** 531(1), 153-166, DOI:10.1016/j.ijpharm.2017.08.076	Saneja, Ankit; Kumar, Robin; Singh, Amarinder; Dhar Dubey, Ravindra; Mintoo, Mubashir J.; Singh, Gurdarshan; Mondhe, Dilip M.; Panda, Amulya K.; Gupta, Prem N	3.649
26	Boeravinone B, A Novel Dual Inhibitor of NorA Bacterial Efflux Pump of Staphylococcus aureus and Human P- Glycoprotein, Reduces the Biofilm Formation and Intracellular Invasion of Bacteria. *Frontiers in microbiology* **(2017)**, 81868.	Singh Samsher; Kalia Nitin P; Khan Inshad A; Singh Samsher; Joshi Prashant; Sharma Parduman R; Kumar Ashok; Bharate Sandip B; Khan Inshad A; Joshi Prashant; et al	4.076
27	Synthesis of pleurolactone and related mono- and sesquiterpenoids: Bioactive constituents of edible mushrooms. *Tetrahedron Letters* **(2017)**, 58(40), 3800-3802, DOI:10.1016/j.tetlet.2017.08.026	Rashid, Showkat; Bhat, Bilal A.; Mehta, Goverdhan	2.193
28	Metal-Free Ionic-Liquid-Mediated Synthesis of Benzimidazoles and Quinazolin-4(3H)-ones from Benzylamines. *Asian Journal of Organic Chemistry* **(2017**), 6(10), 1370-1374, DOI:10.1002/ajoc.201700214	Sharma, Rohit; Abdullaha, Mohd.; Bharate, Sandip B.	2.788
29	Chemoprofile and functional diversity of fungal and bacterial endophytes and role of ecofactors - A review. *Journal of basic microbiology* **(2017)**, 57(10), 814-826.	Shah Aiyatullah; Hassan Qazi Parvaiz; Mushtaq Saleem; Shah Aabid Manzoor; Hussain Aehtesham; Shah Aiyatullah; Hassan Qazi Parvaiz; Shah Aabid Manzoor; Hussain Aehtesham	1.438
30	Isolation of isoxanthanol and synthesis of novel derivatives as potential cytotoxic agents. *Medicinal Chemistry Research* **(2017)**, 26(10), 2499-2513, DOI:10.1007/s00044-017-1949-z	Chinthakindi, Praveen K.; Rath, Santosh K.; Singh, Jasvinder; Singh, Shashank; Koul, Surrinder; Sangwan, Payare L.	1.277

S.No.	Title	Author	Impact Factor
31	Mining and characterization of EST-SSR markers for Zingiber officinale Roscoe with transferability to other species of Zingiberaceae. *Physiology and Molecular Biology of Plants* **(2017)**, 23(4), 925-931, DOI:10.1007/s12298-017-0472-5	Awasthi, Praveen; Singh, Ashish; Sheikh, Gulfam; Mahajan, Vidushi; Gupta, Ajai Prakash; Gupta, Suphla; Bedi, Yashbir S.; Gandhi, Sumit G.	0.883
32	Natural alkaloids as P-gp inhibitors for multidrug resistance reversal in cancer. *European Journal of Medicinal Chemistry* **(2017),** 138, 273-292, DOI:10.1016/j.ejmech.2017.06.047	Joshi, Prashant; Vishwakarma, Ram A.; Bharate, Sandip B.	4.519
33	Perspective Insights of Exosomes in Neurodegenerative Diseases: A Critical Appraisal. *Frontiers in aging neuroscience* **(2017)**, 9317	Jan Arif Tasleem; Rahman Safikur; Yeo Hye R; Lee Eun J; Choi Inho; Malik Mudasir A; Abdullah Tasduq S	4.504
34	A marine sponge alkaloid derivative 4-chloro fascaplysin inhibits tumor growth and VEGF mediated angiogenesis by disrupting PI3K/Akt/mTOR signaling cascade. *Chemico-biological interactions* **(2017)**, 27547-60	Sharma Sonia; Kumar Ashok; Mintoo Mubashir J; Mondhe Dilip M; Guru Santosh Kumar; Manda Sudhakar; Bharate Sandip B; Prasad Venna Deva; Sharma Parduman R; Bhushan Shashi	3.143
35	Oxidant-Controlled C-sp2/sp3-H Cross- Dehydrogenative Coupling of N-Heterocycles with Benzylamines. *Journal of Organic Chemistry* **(2017)**, 82(18), 9786-9793, DOI:10.1021/acs.joc.7b00856	Sharma, Rohit; Abdullaha, Mohd; Bharate, Sandip B.	4.849
36	Base-Controlled Reactions through an Aldol Intermediate Formed between 2-Oxoaldehydes and Malonate Half Esters. *Organic Letters* **(2017)**, 19(18), 4730-473, DOI:10.1021/acs.orglett.7b02016	Kumar, Atul; Khan, Shahnawaz; Ahmed, Qazi Naveed	6.579
37	Pd-Catalyzed Regio- and Stereoselective C- Nucleoside Synthesis from Un-activated Uracils and Pyranoid Glycals. *Organic Letters* **(2017)**, 19(18), 4936-4939, DOI:10.1021/acs.orglett.7b02402	Rasool, Faheem; Mukherjee, Debaraj	6.579
38	Triazole tethered isatin-coumarin based molecular hybrids as novel antitubulin agents: Design, synthesis, biological investigation and docking studies. *Bioorganic & medicinal chemistry letters* **(2017)**, 27(17), 3974-3979.	Singh Harbinder; Singh Jatinder V; Nepali Kunal; Bedi Preet Mohinder S; Gupta Manish K; Saxena Ajit K; Sharma Sahil	2.454
39	Antimicrobial investigation of selected soil actinomycetes isolated from unexplored regions of Kashmir Himalayas, India. *Microbial Pathogenesis* **(2017)**, 110, 93-99, DOI:10.1016/j.micpath.2017.06.017	Shah, Aabid Manzoor; Shakeel-u-Rehman; Hussain, Aehtesham; Mushtaq, Saleem; Rather, Muzafar Ahmad; Shah, Aiyatullah; Ahmad, Zahoor; Ali Khan, Inshad; Bhat, Khursheed Ahmad; Hassan, Qazi Parvaiz	2.009
40	Chemical chaperone 4-phenyl butyric acid (4- PBA) reduces hepatocellular lipid accumulation and lipotoxicity through induction of autophagy. *Journal of Lipid Research* **(2017)**, 58(9), 1855-186, DOI:10.1194/jlr.M077537	Nissar, Ashraf U.; Sharma, Love; Mudasir, Malik A.; Nazir, Lone A.; Umar, Sheikh A.; Sharma, Parduman R.; Vishwakarma, Ram A.; Tasduq, Sheikh A.	4.81

S.No.	Title	Author	Impact Factor
41	Production dynamics in relation to ontogenetic development and induction of genetic instability through in vitro approaches in Pelargonium graveolens: A potential essential oil crop of commercial significance. *Flavour and Fragrance Journal* **(2017)**, 32(5), 376- 387, DOI:10.1002/ffj.3390	Pandith, Shahzad A.; Dhar, Niha; Wani, Tareq A.; Razdan, Sumeer; Bhat, Wajid Waheed; Rana, Satiander; Khan, Shabnam; Verma, Mahendra K.; Lattoo, Surrinder K.	1.644
42	Antituberculotic activity of actinobacteria isolated from the rare habitats. *Letters in Applied Microbiology* **(2017)**, 65(3), 256-264, DOI:10.1111/lam.12773	Hussain, A.; Rather, M. A.; Shah, A. M.; Bhat, Z. S.; Shah, A.; Ahmad, Z.; Parvaiz Hassan, Q.	1.575
43	Isolation and characterization of Streptomyces tauricus from Thajiwas glacier-a new source of actinomycin-D. *Medicinal Chemistry Research* **(2017)**, 26(9), 1897-1902, DOI:10.1007/s00044-017-1842-9	Rather, Shabir Ahmad; Shah, Aabid Manzoor; Ali, Sheikh Abid; Dar, Refaz Ahmad; Rah, Bilal; Ali, Asif; Hassan, Qazi Parvaiz	1.277
44	Withanone, an Active Constituent from Withania somnifera, Affords Protection Against NMDA-Induced Excitotoxicity in Neuron-Like Cells. *Molecular Neurobiology* **(2017)**, 54(7), 5061-5073, DOI:10.1007/s12035-016-0044-7	Dar, Nawab John; Bhat, Javeed Ahmad; Satti, Naresh Kumar; Sharma, Parduman Raj; Hamid, Abid; Ahmad, Muzamil	6.19
45	Biotransformation of Chrysin to Baicalein: Selective C6-Hydroxylation of 5,7- Dihydroxyflavone Using Whole Yeast Cells Stably Expressing Human CYP1A1 Enzyme. *Journal of agricultural and food chemistry* **(2017),** 65(34), 7440-7446	Williams Ibidapo S; Gatchie Linda; Chaudhuri Bhabatosh; Williams Ibidapo S; Gatchie Linda; Chaudhuri Bhabatosh; Chib Shifali; Saran Saurabh; Nuthakki Vijay K; Joshi Prashant; et al	3.154
46	Biopharmaceutic parameters, pharmacokinetics, transport and CYP- mediated drug interactions of IIIM-017: A novel nitroimidazooxazole analogue with anti- tuberculosis activity. *European Journal of Pharmaceutical Sciences* **(2017)**, 106, 71-78, DOI:10.1016/j.ejps.2017.05.053	Kour, Gurleen; Singh, Parvinder Pal; Bhagat, Asha; Ahmed, Zabeer	3.756
47	Arginase purified from endophytic Pseudomonas aeruginosa IH2: Induce apoptosis through both cell cycle arrest and MMP loss in human leukemic HL-60 cells. *Chemico-biological interactions* **(2017)**, 27435-49	Husain Islam; Bala Kiran; Wani Abubakar; Makhdoomi Ubaid; Malik Fayaz; Sharma Anjana	3.143
48	Mortierella alpina CS10E4, an oleaginous fungal endophyte of Crocus sativus L. enhances apocarotenoid biosynthesis and stress tolerance in the host plant. *Scientific reports* **(2017)**, 7(1), 8598	Wani Zahoor Ahmed; Sultan Phalisteen; Ashraf Nasheeman; Wani Zahoor Ahmed; Riyaz-Ul-Hassan Syed; Ashraf Nasheeman; Kumar Amit; Bindu Kushal; Riyaz-Ul-Hassan Syed	4.259
49	Development and validation of a highly sensitive LC-ESI-MS/MS method for estimation of IIIM-MCD-211, a novel nitrofuranyl methyl piperazine derivative with potential activity against tuberculosis: Application to drug development. *Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences* **(2017)**, 1060, 200-206, DOI:10.1016/j.jchromb.2017.06.015	Magotra, Asmita; Sharma, Anjna; Gupta, Ajai Prakash; Wazir, Priya; Sharma, Shweta; Singh, Parvinder Pal; Tikoo, Manoj Kumar; Vishwakarma, Ram A.; Singh, Gurdarshan; Nandi, Utpal	2.603

S.No.	Title	Author	Impact Factor
50	Synthesis and biological evaluation of pyrrole- based chalcones as CYP1 enzyme inhibitors, for possible prevention of cancer and overcoming cisplatin resistance. *Bioorganic & medicinal chemistry letters* **(2017),** 27(16), 3683-3687.	Williams Ibidapo S; Gatchie Linda; Joshi Prashant; Vishwakarma Ram A; Sharma Mohit; Satti Naresh K; Chaudhuri Bhabatosh; Bharate Sandip B	2.454
51	Dendrimer encapsulated and conjugated delivery of berberine: A novel approach mitigating toxicity and improving in vivo pharmacokinetics. *International journal of pharmaceutics* **(2017)**, 528(1-2), 88-99	Gupta Lokesh; Sharma Ashok Kumar; Gothwal Avinash; Khan Mohammed Shahid; Khinchi Mahaveer Prasad; Qayum Arem; Singh Shashank Kumar; Gupta Umesh	3.649
52	3,4-Dimethyl diphenyldithiophosphate of mononuclear cobalt(II) with N-donor ligands: Synthesis, structural characterization, DFT and antibacterial studies. *Journal of Molecular Structure* **(2017),** 1141, 23-30	Kumar, S; Kour, G; Schreckenbach, G; Andotra, S; Hundal, G; Sharma, V; Jaglan, S; Pandey, SK	1.753
53	Cladosporol A triggers apoptosis sensitivity by ROS-mediated autophagic flux in human breast cancer cells. *BMC cell biology* **(2017)**, 18(1), 26.	Koul Mytre; Kumar Ashok; Singh Jasvinder; Sharma Parduman Raj; Singh Shashank; Koul Mytre; Kumar Ashok; Deshidi Ramesh; Sharma Vishal; Singh Jasvinder; et al	2.96
54	Fungal endophytes associated with Viola odorata Linn. as bioresource for pancreatic lipase inhibitors. *BMC complementary and alternative medicine* **(2017),** 17(1), 385	Katoch M; Singh G; Paul A; Sridhar S N C	2.94
55	Fusion of Structure and Ligand Based Methods for Identification of Novel CDK2 Inhibitors. *Journal of Chemical Information and Modeling* **(2017)**, 57(8), 1957-1969, DOI:10.1021/acs.jcim.7b00293	Mahajan, Priya; Chashoo, Gousia; Gupta, Monika; Kumar, Amit; Singh, Parvinder Pal; Nargotra, Amit	3.76
56	Anti-inflammatory potential of hentriacontane in LPS stimulated RAW 264.7 cells and mice model. *Biomedicine & Pharmacotherapy* **(2017)**, 92, 175-186, DOI:10.1016/j.biopha.2017.05.063	Khajuria, Vidushi; Gupta, Shilpa; Sharma, Neha; Kumar, Ashok; Lone, Nazir A.; Khullar, Mowkshi; Dutt, Prabhu; Sharma, Parduman Raj; Bhagat, Asha; Ahmed, Zabeer	2.759
57	Crocus sativus Extract Tightens the Blood- Brain Barrier, Reduces Amyloid β Load and Related Toxicity in 5XFAD Mice. *ACS chemical neuroscience* **(2017)**, 8(8), 1756-1766	Batarseh Yazan S; Kaddoumi Amal; Bharate Sonali S; Kumar Vikas; Kumar Ajay; Vishwakarma Ram A; Bharate Sandip B	3.883
58	Phylogeny, antimicrobial, antioxidant and enzyme-producing potential of fungal endophytes found in Viola odorata. *Annals of Microbiology* (Heidelberg, Germany) **(2017)**, 67(8), 529-540, DOI:10.1007/s13213-017- 1283-1	Katoch, Meenu; Singh, Arshia; Singh, Gurpreet; Wazir, Priya; Kumar, Rajinder	1.122
59	Synthesis of novel benzylidene analogues of betulinic acid as potent cytotoxic agents. *European Journal of Medicinal Chemistry* **(2017)**, 135, 517-530, DOI:10.1016/j.ejmech.2017.04.062	Gupta, Nidhi; Rath, Santosh K.; Singh, Jasvinder; Qayum, Arem; Singh, Shashank; Sangwan, Payare L	4.519

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60	β-CD/CuI catalyzed regioselective synthesis of iodo substituted 1,2,3-triazoles, imidazo[1,2- a]-pyridines and benzoimidazo[2,1-b]thiazoles in water and their functionalization. *Tetrahedron* **(2017)**, 73(30), 4295-4306, DOI:10.1016/j.tet.2017.05.081	Dheer, Divya; Rawal, Ravindra K.; Singh, Virender; Sangwan, P. L.; Das, Parthasarathi; Shankar, Ravi	2.651
61	Synthesis of Novel Mannich Derivatives of Bakuchiol as Apoptotic Inducer through Caspase Activation and PARP-1 Cleavage in A549 Cells. *ChemistrySelect* **(2017)**, 2(18), 5196-5201, DOI:10.1002/slct.201700504	Gupta, Nidhi; Sharma, Sonia; Raina, Arun; Bhushan, Shashi; Malik, Fayaz A.; Sangwan, Payare L.	YET TO COME
62	Cobalt-catalyzed regioselective ortho C(sp2)-H bond nitration of aromatics through proton- coupled electron transfer assistance. *Journal of Organic Chemistry* **(2017),** 82(14), 7234-7244, DOI:10.1021/acs.joc.7b00808	Nageswar Rao, Desaboini; Rasheed, Sk.; Raina, Gaurav; Ahmed, Qazi Naveed; Jaladanki, Chaitanya Kumar; Bharatam, Prasad V.; Das, Parthasarathi	4.849
63	Ruthenium-catalyzed site-selective C-H arylation of 2-pyridones and 1- isoquinolinones. *Organic & Biomolecular Chemistry* **(2017),** 15(26), 5457-5461, DOI:10.1039/C7OB01277B	Anil Kumar, K.; Kannaboina, Prakash; Das, Parthasarathi	3.564
64	Revelation and cloning of valinomycin synthetase genes in Streptomyces lavendulae ACR-DA1 and their expression analysis under different fermentation and elicitation conditions. *Journal of Biotechnology* **(2017)**, 253, 40-47, DOI:10.1016/j.jbiotec.2017.05.008	Sharma, Richa; Jamwal, Vijaylakshmi; Singh, Varun P.; Wazir, Priya; Awasthi, Praveen; Singh, Deepika; Vishwakarma, Ram A.; Gandhi, Sumit G.; Chaubey, Asha	2.599
65	Beta-catenin N-terminal domain: An enigmatic region prone to cancer causing mutations. *Mutation research* **(2017)**, 773122-133	Dar Mohd Saleem; Singh Paramjeet; Mir Riyaz A; Dar Mohd Jamal	2.133
66	α-pyrones: Small molecules with versatile structural diversity reflected in multiple pharmacological activities-an update. *Biomedicine & Pharmacotherapy* **(2017)**, 91, 265-277, DOI:10.1016/j.biopha.2017.04.012	Bhat, Zubair Shanib; Rather, Muzafar Ahmad; Maqbool, Mubashir; Lah, Hafiz U. L.; Yousuf, Syed Khalid; Ahmad, Zahoor	2.932
67	Immunostimulatory activity of plumieride an iridoid in augmenting immune system by targeting Th-1 pathway in balb/c mice. *International Immunopharmacology* **(2017),** 48, 203-210. Language: English, Database: CAPLUS, DOI:10.1016/j.intimp.2017.05.009	Singh, Jasvinder; Qayum, Arem; Singh, Rachna D.; Koul, Mytre; Kaul, Anpurna; Satti, N. K.; Dutt, Prabhu; Hamid, Abid; Singh, Shashank	2.956
68	Inhibition of Twist1-mediated invasion by Chk2 promotes premature senescence in p53- defective cancer cells. *Cell Death & Differentiation* **(2017)**, 24(7), 1275-1287, DOI:10.1038/cdd.2017.70	Nayak, Debasis; Kumar, Anmol; Chakraborty, Souneek; Rasool, Reyaz ur; Amin, Hina; Katoch, Archana; Gopinath, Veena; Mahajan, Vidushi; Zilla, Mahesh K.; Rah, Bilal; et al	8.339
69	A convergent synthesis of novel alkyne-azide cycloaddition congeners of betulinic acid as potent cytotoxic agent. *Steroids* **(2017)**, 123, 1- 12, DOI:10.1016/j.steroids.2017.04.002	Dangroo, Nisar A.; Singh, Jasvinder; Rath, Santosh K.; Gupta, Nidhi; Qayum, Arem; Singh, Shashank; Sangwan, Payare L.	2.282

S.No.	Title	Author	Impact Factor
70	Design, synthesis and biological evaluation of hydrazone derivatives as anti-proliferative agents. *Medicinal Chemistry Letters* **(2017),** 26(7), 1459-1468.	Design, synthesis and biological evaluation of hydrazone derivatives as anti-proliferative agents	3.746
71	Protein kinase B: emerging mechanisms of isoform-specific regulation of cellular signaling in cancer. *Anti-cancer drugs* **(2017)**, 28(6), 569-580.	Wadhwa Bhumika; Makhdoomi Ubaid; Vishwakarma Ram; Malik Fayaz	2.32
72	An Unprecedented Pseudo-[3+2] Annulation between N-(4-Methoxyphenyl)aldimines and Aqueous Glutaraldehyde: Direct Synthesis of Pyrrole-2,4-dialdehydes. *European Journal of Organic Chemistry***(2017),** (24), 3461-3465	Ramaraju, P; Mir, NA; Singh, D; Sharma, P; Kant, R; Kumar, I	2.834
73	Molecular and functional characterization of two isoforms of chalcone synthase and their expression analysis in relation to flavonoid constituents in Grewia asiatica L. *PLoS One* **(2017)**, 12(6), e0179155/1-e0179155/24, DOI:10.1371/journal.pone.0179155	Wani, Tareq A.; Pandith, Shahzad A.; Gupta, Ajai P.; Chandra, Suresh; Sharma, Namrata; Lattoo, Surrinder K.	2.806
74	Graphene oxide: A carbocatalyst for the one- pot multicomponent synthesis of highly functionalized tetrahydropyridines. *Tetrahedron Letters***(2017),** 58(26), 2583-2587	Gupta, A; Kaur, R; Singh, D; Kapoor, KK	2.193
75	POCl3-mediated cyclization of (+)-S- mahanimbine led to the divergent synthesis of natural product derivatives with antiplasmodial activity. *New Journal of Chemistry* **(2017)**, 41(12), 4923-4930, DOI:10.1039/C7NJ00487G	Nalli, Yedukondalu; Thakur, Vandana; Mohmmed, Asif; Kumar Gupta, Vivek; Ali, Asif	3.269
76	Anti-tubercular drug discovery: in silico implications and challenges. *European Journal of Pharmaceutical Sciences* **(2017)**, 104, 1-15, DOI:10.1016/j.ejps.2017.03.028	Mehra, Rukmankesh; Khan, Inshad Ali; Nargotra, Amit	3.756
77	Transition Metal-free Single Step Approach for Arylated Pyrazolopyrimidinones and Quinazolinones Using Benzylamines/Benzylalcohols/Benzaldehydes. *ChemistrySelect* **(2017**), 2(17), 4963-4968, DOI:10.1002/slct.201700896	Hudwekar, Abhinandan D.; Reddy, G. Lakshma; Verma, Praveen K.; Gupta, Sorav; Vishwakarma, Ram A.; Sawant, Sanghapal D.	YET TO COME
78	Synthesis, spectroscopic, DFT and in vitro biological studies of vanadium(III) complexes of aryldithiocarbonates. *Spectrochimica acta. Part A, Molecular and biomolecular spectroscopy* **(2017)**, 180127-137	Andotra Savit; Kumar Sandeep; Kour Mandeep; Vikas; Chayawan; Sharma Vishal; Jaglan Sundeep; Pandey Sushil K	2.536
79	Antioxidant and oxidative DNA damage protective properties of leaf, bark and fruit extracts of Terminalia chebula. *Indian Journal of Biochemistry & Biophysics***(2017)**, 54(4), 127-134.	Guleria, S; Singh, G; Gupta, S; Vyas, D	0.579
80	An endophytic Fusarium sp isolated from Monarda citriodora produces the industrially important plant-like volatile organic compound hexanal. *Microbiology* (London, United Kingdom) **(2017),** 163(6), 840-847, DOI:10.1099/mic.0.000479	Katoch, Meenu; Bindu, Kushal; Phull, Shipra; Verma, M. K.	0.856

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81	(Z)-2-(3-Chlorobenzylidene)-3,4-dihydro-N-(2-methoxyethyl)-3-oxo-2H- benzo[b][1,4]oxazine-6-carboxamide as GSK- 3β inhibitor: Identification by virtual screening and its validation in enzyme- and cell-based assay. *Chemical Biology & Drug Design* **(2017),** 89(6), 964-971, DOI:10.1111/cbdd.12913	Joshi, Prashant; Gupta, Mehak; Vishwakarma, Ram A.; Kumar, Ajay; Bharate, Sandip B.	2.396
82	A longitudinal study of whole body, tissue, and cellular physiology in a mouse model of fibrosing NASH with high fidelity to the human condition. American journal of physiology. *Gastrointestinal and liver physiology* **(2017)**, 312(6), G666-G680	Krishnan, A; Abdullah, TS; Mounajjed, T; Hartono, S; McConico, A; White, T; LeBrasseur, N; Lanza, I; Nair, S; Gores, G; Charlton, M	NOT KNOWN
83	Identification of Potent and Selective CYP1A1 Inhibitors via Combined Ligand and Structure- Based Virtual Screening and Their in Vitro Validation in Sacchrosomes and Live Human Cells. *Journal of Chemical Information and Modeling* **(2017),** 57(6), 1309-1320, DOI:10.1021/acs.jcim.7b00095	Joshi, Prashant; McCann, Glen J. P.; Sonawane, Vinay R.; Vishwakarma, Ram A.; Chaudhuri, Bhabatosh;	3.76
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85	Transcriptome wide identification, phylogenetic analysis, and expression profiling of zinc-finger transcription factors from Crocus sativus L. *Molecular Genetics and Genomics* **(2017)**, 292(3), 619-633, DOI:10.1007/s00438-017-1295-3	Malik, Aubid Hussain; Ashraf, Nasheeman	2.979
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88	Comprehensive GC-FID, GC-MS and FT-IR spectroscopic analysis of the volatile aroma constituents of Artemisia indica and Artemisia vestita essential oils. *Arabian Journal of Chemistry***(2017),** 10, S3798-S3803	Rather, MA; Dar, BA; Shah, WA; Prabhakar, A; Bindu, K; Banday, JA; Qurishi, MA	4.553
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94	Exploring Derivatives of Quinazoline Alkaloid L-Vasicine as Cap Groups in the Design and Biological Mechanistic Evaluation of Novel Antitumor Histone Deacetylase Inhibitors. *Journal of Medicinal Chemistry* **(2017),** 60(8), 3484-3497, DOI:10.1021/acs.jmedchem.7b00322	Ahmad, Mudassier; Aga, Mushtaq A.; Bhat, Javeed Ahmad; Kumar, Brijesh; Rouf, Abdul; Capalash, Neena; Mintoo, Mubashir Javeed; Kumar, Ashok; Mahajan, Priya; Mondhe, Dilip Manikrao; et al	6.259
95	Quinazoline derivatives as selective CYP1B1 inhibitors. *European journal of medicinal chemistry* **(2017)**, 130320-327	Mohd Siddique Mohd Usman; Jayaprakash Venkatesan; Sinha Barij N; McCann Glen J P; Sonawane Vinay R; Horley Neill; Gatchie Linda; Joshi Prashant; Bharate Sandip B; Chaudhuri Bhabatosh	4.519
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101	Synthesis, characterization and augmented anticancer potential of PEG-betulinic acid conjugate. Materials science & engineering. C, Materials for biological applications (2017), 73616-626	Saneja Ankit; Sharma Love; Singh Amrinder; Dubey Ravindra Dhar; Mintoo Mubashir Javed; Kumar Amit; Sangwan Payare Lal; Tasaduq Sheikh Abdullah; Singh Gurdarshan; Mondhe Dilip M; et al	4.164
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118	Arylsulfatase K is the Lysosomal 2- Sulfoglucuronate Sulfatase. *ACS Chemical Biology***(2017),** 12(2), 367-373.	Dhamale, OP; Lawrence, R; Wiegmann, EM; Shah, BA; Al-Mafraji, K; Lamanna, WC; Lubke, T; Dierks, T; Boons, GJ; Esko, JD	4.995
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121	Diapolic acid A-B from an endophytic fungus, Diaporthe terebinthifolii depicting antimicrobial and cytotoxic activity. *Journal of Antibiotics* **(2017)**, 70(2), 212-215, DOI:10.1038/ja.2016.109	Yedukondalu, Nalli; Arora, Palak; Wadhwa, Bhumika; Malik, Fayaz Ahmad; Vishwakarma, Ram A.; Gupta, Vivek K.; Riyaz-Ul- Hassan, Syed; Ali, Asif	2.237
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129	Development and mechanistic insight into enhanced cytotoxic potential of hyaluronic acid conjugated nanoparticles in CD44 overexpressing cancer cells. *European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences* **(2017),** 9779-91	Saneja Ankit; Nayak Debasis; Srinivas M; Kumar Amit; Khare Vaibhav; Katoch Archana; Goswami Anindya; Vishwakarma Ram A; Sawant Sanghapal D; Gupta Prem N	3.756
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136	TNF-α and IL-6 inhibitory effects of cyclic dipeptides isolated from marine bacteria Streptomyces sp. *Medicinal Chemistry Research* **(2017)**, 26(1), 93-100, DOI:10.1007/s00044-016-1730-8	Nalli, Yedukondalu; Gupta, Shilpa; Khajuria, Vidushi; Singh, Varun P.; Sajgotra, Mehak; Ahmed, Zabeer; Thakur, Narsinh L.; Ali, Asif	1.277
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139	Endophytic fungi associated with Monarda citriodora, an aromatic and medicinal plant and their biocontrol potential. *Pharmaceutical biology* **(2017)**, 55(1), 1528-1535	Katoch Meenu; Pull Shipra	1.241
140 correction	Synthesis and characterization of TPGS- gemcitabine prodrug micelles for pancreatic cancer therapy. *RSC Advances***(2017),** 7(28), 17367-17367	Khare, V; Al Sakarchi, W; Gupta, PN; Curtis, ADM; Hoskins, C	3.108
141	Thiazolidinone Constraint Combretastatin Analogs as Novel Antitubulin Agents: Design, Synthesis, Biological Evaluation and Docking Studies. *Anti-Cancer Agents in Medicinal Chemistry* **(2017),** 17(2), 230-240	Sharma, S; Gupta, MK; Saxena, AK; Bedi, PMS	2.598
142	Therapeutic Potential, Challenges and Future Perspective of Cancer Stem Cells in Translational Oncology: A Critical Review. *Current stem cell research & therapy* **(2017)**, 12(3), 207-224	Shukla Gaurav; Khare Piush; Patidar Rahul; Saxena Rajiv; Khera Harvinder Kour; Srivastava Amit Kumar	2.684

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144	Bioactivity-guided isolation, antimicrobial and cytotoxic evaluation of secondary metabolites from Cladosporium tenuissimum associated with Pinus wallichiana. *ChemistrySelect* **(2017)**, 2(3), 1311-1314, DOI:10.1002/slct.201601942	Naseer, Syed; Bhat, Khursheed A.; Qadri, Masroor; Riyaz-Ul-Hassan, Syed; Malik, Fayaz A.; Khuroo, Mohammad A.	YET TO COME
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146	T- and B-cell immunosuppressive activity of novel alpha-santonin analogs with humoral and cellular immune response in Balb/c mice. *Medchemcomm***(2017),** 8(1), 211-219.	Dangroo, NA; Singh, J; Gupta, N; Singh, S; Kaul, A; Khuroo, MA; Sangwan, P	2.608
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150	Discovery of novel small molecule EGFR inhibitory leads by structure and ligand-based virtual screening. *Medicinal Chemistry Research* **(2017)**, 26(1), 74-92, DOI:10.1007/s00044-016-1728-2	Mahajan, Priya; Suri, Nitasha; Mehra, Rukmankesh; Gupta, Monika; Kumar, Amit; Singh, Shashank Kr.; Nargotra, Amit	1.277
151	Breaking the resistance of Escherichia coli: Antimicrobial activity of Berberis lycium Royle. *Microbial pathogenesis* **(2017)**, 10212-20,	Malik Tauseef Ahmad; Kamili Azra N; Chishti M Z; Tantry Mudasir A; Ahad Shazia; Hussain P R; Johri R K	2.009
152	Penicillium spp.: prolific producer for harnessing cytotoxic secondary metabolites. *Anti-Cancer Drugs* **(2017)**, 28(1), 11-30, DOI:10.1097/CAD.0000000000000423	Koul, Mytre; Singh, Shashank	2.32
153	Toxicogenetic evaluation of dichlorophene in peripheral blood and in the cells of the immune system using molecular and flow cytometric approaches. *Chemosphere* **(2017)**, 167520-529	Lone Mohammad Iqbal; Nabi Arisa; Dar Nawab John; Hussain Aashiq; Nazam Nazia; Ahmad Waseem; Hamid Abid	4.208

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154	De novo transcriptome analyses reveals putative pathway genes involved in biosynthesis and regulation of camptothecin in Nothapodytes nimmoniana (Graham) Mabb. *Plant Molecular Biology* **(2017)**, DOI:10.1007/s11103-017-0690- 9	Rather, Gulzar A.; Sharma, Arti; Pandith, Shahzad A.; Kaul, Veenu; Nandi, Utpal; Misra, Prashant; Lattoo, Surrinder K.	3.356
155	The amino analogue of β-boswellic acid efficiently attenuates the release of pro- inflammatory mediators than its parent compound through the suppression of NF- κB/IκBα signalling axis. *Cytokine* **(2017)**, DOI:10.1016/j.cyto.2017.12.004	Gupta, Shilpa; Ul Ahsan, Aitizaz; Wani, Abubakar; Khajuria, Vidushi; Nazir, Lone A.; Sharma, Simmi; Bhagat, Asha; Raj Sharma, Parduman; Bhardwaj, Subhash; Peerzada, Kaiser J.; et al	3.488
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157	Synthesis and in vitro evaluation of substituted 3-cinnamoyl-4-hydroxy-pyran-2-one (CHP) in pursuit of new potential antituberculosis agents. *MedChemComm* **(2017),** DOI:10.1039/c7md00366h	Bhat, Zubair Shanib; Ul Lah, Hafiz; Rather, Muzafar Ahmad; Maqbool, Mubashir; Ara, Tabassum; Ahmad, Zahoor; Yousuf, Syed Khalid	2.608
158	Multifunctional neuroprotective effect of Withanone, a compound from Withania somnifera roots in alleviating cognitive dysfunction. *Cytokine* **(2017),** DOI:10.1016/j.cyto.2017.10.019	Pandey, Anjali; Bani, Sarang; Dutt, Prabhu; Kumar Satti, Naresh; Avtar Suri, Krishan; Nabi Qazi, Ghulam	3.488
159	Auxin response factor (GaARF) cloning and expression in relation to reproductive maturation in Grewia asiatica L. *Plant Gene* **(2017)**, 12, 123-130, DOI:10.1016/j.plgene.2017.10.001	Wani, Tareq A.; Lattoo, Surrinder K.	2.1
160	Photoredox-Catalyzed Isatin Reactions: Access to Dibenzo-1,7-Naphthyridine Carboxylate and Tryptanthrin. *ChemPhotoChem* **(2017)**, 1(4), 120-124, DOI:10.1002/cptc.201700028	Sultan, Shaista; Gupta, Vivek; Shah, Bhahwal Ali	NOT KNOWN
161	Therapeutic applications of resveratrol nanoformulations. *Environmental Chemistry Letters* (2017), DOI:10.1007/s10311-017-0660-0	Arora, Divya; Jaglan, Sundeep	3.594
162	In-vitro and in-vivo pharmacokinetics of IS01957, p-coumaric acid derivative using a validated LC-ESI-MS/MS method in mice plasma. *Journal of Pharmaceutical Investigation* **(2017)**, DOI:10.1007/s40005- 017-0350-8	Sharma, Anjna; Magotra, Asmita; Rath, Santosh Kumar; Wazir, Priya; Nandi, Utpal; Koul, Surrinder; Sangwan, Payare Lal; Gupta, Ajai Prakash; Singh, Gurdarshan	NOT KNOWN
163	C11/C9 Helical folding in αβ hybrid peptides containing 1-amino-cyclohexane acetic acid (β3, 3-Ac6c). *Chemistry - A European Journal* **(2017)**, 23(35), 8364-8370, DOI:10.1002/chem.201700265	Wani, Naiem Ahmad; Raghothama, Srinivasarao; Singh, Umesh Prasad; Rai, Rajkishor	5.317

S.No.	Title	Author	Impact Factor
164	Attenuation of Glutamate-Induced Excitotoxicity by Withanolide-A in Neuron- Like Cells: Role for PI3K/ Akt/MAPK Signaling Pathway. *Molecular Neurobiology* **(2017)**, DOI:10.1007/s12035-017-0515-5	Dar, Nawab John; Satti, Naresh Kumar; Dutt, Prabhu; Hamid, Abid; Ahmad, Muzamil	6.19
165	Editorial: Medicinal Chemistry Research in India. *ACS Medicinal Chemistry Letters* **(2017)**, 8(3), 270-272, DOI:10.1021/acsmedchemlett.7b00064	Vishwakarma, Ram	3.746
166	Synthesis of Gallic-Acid-1-Phenyl-1H- [1,2,3]Triazol-4-yl Methyl Esters as Effective Antioxidants. *Drug Research* (Stuttgart, Germany) **(2017)**, 67(2), 111-118, DOI:10.1055/s-0042-118860	Lone, S. H.; Rehman, Shakeel U.; Bhat, K. A.	0.7
167	Bacillus amyloliquefaciens induces production of a novel blennolide k in co-culture of Setophoma terrestris. *Journal of applied microbiology* **(2017).**	Arora Divya; Sharma Nisha; Jaglan Sundeep; Arora Divya; Sharma Nisha; Chashoo Gousia; Singamaneni Venugopal; Gupta Prasoon	2.099
168	Tacrolimus: An updated review on delivering strategies for multifarious diseases. *European journal of pharmaceutical sciences : official journal of the European Federation for Pharmaceutical Sciences* **(2017),** 114217-227	Dheer Divya; Jyoti; Gupta Prem N; Shankar Ravi	3.756
169	Bovine mastitis: An appraisal of its alternative herbal cure. *Microbial pathogenesis* **(2017)**, 114357-361	Mushtaq Saleem; Shah Aabid Manzoor; Shah Aiyatullah; Lone Sajad Ahmad; Hussain Aehtesham; Hassan Qazi Parvaiz; Ali Md Niamat	2.009
170	Modulation of dietary folate with age confers selective hepatocellular epigenetic imprints through DNA methylation. *The Journal of nutritional biochemistry* **(2017)**, 53121-132	Najar Rauf Ahmad; Bhat Javeed Ahmad; Dar Nawab John; Wani Nissar Ahmad; Rahat Beenish; Kaur Jyotdeep; Gupta Ajai Prakash; Kaur Jaspreet; Hamid Abid	4.518
171	In silico evaluation of the resistance of the T790M variant of epidermal growth factor receptor kinase to cancer drug Erlotinib. *Journal of biomolecular structure & dynamics* **(2017)**, 1-11	Singh Inderpal; Verma Vijeshwar; Chandra Ratna; Singh Inderpal; Verma Vijeshwar; Singh Shashank; Uversky Vladimir N; Uversky Vladimir N	2.15
172	Physicochemical, pharmacokinetic, efficacy and toxicity profiling of a potential nitrofuranyl methyl piperazine derivativeIIIM- MCD-211 for oral tuberculosis therapy via in- silico-in-vitro-in-vivo approach. *Pulmonary pharmacology & therapeutics* (2017)	Magotra Asmita; Sharma Anjna; Singh Samsher; Kumar Sunil; Ojha Probir Kumar; Bokolia Naveen; Khan Inshad Ali; Wazir Priya; Sharma Shweta; Singh Parvinder Pal; et al	2.525
173	Camphor sulphonic acid mediated quantitative 1,3-diol protection of major Labdane diterpenes isolated from Andrographis paniculata. *Natural product research* **(2017)**, 1-9	Sharma Venu; Dhar Manoj K; Kaul Sanjana; Kapoor Kamal K; Mukherjee Debaraj; Gupta Vivek K	1.828

S.No.	Title	Author	Impact Factor
174	In Silico Evaluation of Variable pH on the Binding of Epidermal Growth Factor Receptor Ectodomain to its Ligand Through Molecular Dynamics Simulation in Tumors. *Interdisciplinary sciences, computational life sciences* **(2017)**	Singh Inderpal; Singh Gurvinder; Verma Vijeshwar; Chandra Ratna; Singh Inderpal; Verma Vijeshwar; Singh Gurvinder; Singh Shashank	0.64
175	Novel Hyaluronic Acid Conjugates for Dual Nuclear Imaging and Therapy in CD44- Expressing Tumors in Mice In Vivo. *Nanotheranostics* **(2017)**, 1(1), 59-79	Dubey Ravindra Dhar; Gupta Prem N; Klippstein Rebecca; Wang Julie Tzu-Wen; Hodgins Naomi; Mei Kuo-Ching; Hider Robert C; Abbate Vincenzo; Al-Jamal Khuloud T; Sosabowski Jane	8.766
176	4-aryl/heteroaryl-4H-fused pyrans as Anti- proliferative Agents: Design, Synthesis and Biological Evaluation. *Anti-cancer agents in medicinal chemistry* **(2017).**	Kumar Dinesh; Singh Gurpreet; Bedi Pms; Jain Subheet K; Sharma Pooja; Qayum Arem; Mahajan Girish; Mintoo M J; Singh Shashank Kumar; Mondhe Dilip Manikrao; et al	2.598
177	Identification, isolation, and synthesis of seven novel impurities of anti-diabetic drug Repaglinide. *Drug testing and analysis* **(2017).**	Kancherla Prasad; Alegete Pallavi; Khagga Mukkanti; Kancherla Prasad; Keesari Srinivas; Alegete Pallavi; Das Parthasarathi	3.469

Other Publications

(a) S Kumar, A Singh, V Bajpai, **Bikarma Singh** and B Kumar (2017). Development of a UHPLC- MS/MS method for the quantification of bioactive compounds in *Phyllanthus* species and its herbal formulations. *Journal of Separation Science* 40(17): 3422–3429 [ISSN: 1615-9306; NAAS Rating: 8.56 in 2018; Impact factor: 2.557 in 2018]. (Publisher: Wileypublication)

(b) **Bikarma Singh** and YS Bedi (2017). Eating from raw wild plants in Himalaya: traditional knowledge documentary on Sheena tribes along LoC border in Kashmir. *Indian Journal of Natural Products and Resources* 8(3): 269-275. [Print ISSN: 0976-0512; Online ISSN: 0976- 0504; NAAS Rating: 4.08 in 2018; Impact factor: yet to come]. (Publisher: NISCAIR publication).

LIST OF PATENTS (2017-2018)

a) Patents Filed in India

S. NO.	NF NO.	Title	Inventors	Priority Date	Application No.
1	0180NF2016/IN	Indolylkojyl Methane Analogues, Process Of Preparation Thereof And Use As Inhibitor Of Cancer Cell Invasion AndMetastasis	Debaraj Mukherjee, Anindya Goswami, Deepak Sharma, Debasis Nayak, Shreyans Kumar Jain	27-Jun-17	201711022402
2	0120NF2017/IN	Gastroretentive Sustained Release Formulations Of Bergenia Ciliata	Bharate Sonali Sandip, Singh Rohit, Gupta Mehak, Singh Bikarma, Katare Anil Kumar, Kumar Ajay, Bharate Sandip Bibishan, Vishwakarma Ram	16-Oct-17	201711036683
3	0092NF2017/IN	Sustained Release Formulations Of Crocus Sativus	Bharate Sonali Sandip, Kumar Vikas, Singh Rohit, Rani Sarita, Gupta Mehak, Kumar Ajay, Bharate Sandip Bibishan, Vishwakarma Ram	16-Oct-17	201711036084
4	0074NF2017/IN	A Novel Isolated Strain Of Mortierella Alpina And Its Use For Plant Growth Promotion And Inhibition Of Corm Rot In Crocus Sativus	Zahoor Ahmed Wani, Amit Kumar, Phalisteen Sultan, Nasheeman Ashraf, Syed Riyaz-Ul-Hassan, Ram A. Vishwakarma	16-10-2017	201711036682
5	0210NF2017/IN	A Process For The Preparation Of Natural Crystallized Thymol From Monarda Citriodora (Jammu Monarda) Oil	Shankar Ravi, Chandra Suresh, Meena Siya Ram, Verma Mahendra Kumar, Bindu Kushal, Vij Bhavna, Dheer Divya, Jyoti, Vishwakarma Ram Asrey	03-01-2018	201811000289

b) Patents Filed in Foreign

SNO	NFNO	Title	Inventors	Priority Date	Application No.
1	0060NF2014/EP	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	06-Apr-17	15774722.1
2	0059NF2014/CA	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	12-Apr-17	2964437

SNO	NFNO	Title	Inventors	Priority Date	Application No.
3	0059NF2014/US	10-Substituted Colchicinoids As Potent Anticancer Agents	Vishwakarma Ram, Bharate Sandip Bibishan, Kumar Ajay, Singh Baljinder, Kumar Ashok, Bhushan Shashi, Hamid Abid, Joshi Prashant, Guru Santosh Kumar, Kumar Suresh, Hussain Aashiq, Qazi Asif Khurshid, Bharate Sonali Sandip, Sharma Parduman, Saxena Ajit Kumar, Mondhe Dilip Manikrao, Mahajan Girish, Wani Zahoor	13-Apr-17	15/519,054
4	0059NF2014/EP	10-Substituted Colchicinoids As Potent Anticancer Agents	Vishwakarma Ram, Bharate Sandip Bibishan, Kumar Ajay, Singh Baljinder, Kumar Ashok, Bhushan Shashi, Hamid Abid, Joshi Prashant, Guru Santosh Kumar, Kumar Suresh, Hussain Aashiq, Qazi Asif Khurshid, Bharate Sonali Sandip, Sharma Parduman, Saxena Ajit Kumar, Mondhe Dilip Manikrao, Mahajan Girish, Wani Zahoor	13-Apr-17	15805323.1
5	0060NF2014/US	Polyalkylated Acyl And Benzoyl-Phloroglucinols As Potent P-Glycoprotein Inducers	Bharate Sandip, Kumar Ajay, Bharate Jaideep, Joshi Prashant, Wani Abubakar, Mudududdla Ramesh, Sharma Rohit, Vishwakarma Ram	18-Apr-17	15/520063
6	0176NF2014/US	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	20-Apr-17	15/520799
7	0176NF2014/JP	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	21-Apr-17	2017-521997
8	0302NF2013/US	N-Substituted Beta-Carbolinium Compounds As Potent P-Glycoprotein Inducers	Bharate Sandip, Kumar Ajay, Manda Sudhakar, Joshi Prashant, Bharate Sonali, Vishwakarma Ram	21-Apr-17	15/521170

SNO	NFNO	Title	Inventors	Priority Date	Application No.
9	0176NF2014/EP	Substituted 1,2,3-Triazol-1-Yl-Methyl-2,3-Dihydro-2-Methyl-6-Nitroimidazo[2,1-B]Oxazoles As Anti-Mycobacterial Agents And A Process For The Preparation Thereof	Yempalla Kushalava Reddy, Munagala Gurunadham, Singh Samsher, Sharma Sumit, Khan Inshad Ali, Vishwakarma Ram Asrey, Singh Parvinder Pal	24-Apr-17	15787313.4
10	0127NF2014/US	Novel 1,3,5 -Triazine Based Pi3k Inhibitors As Anticancer Agents And A Process For The Preparation Thereof	Thatikonda Thanusha, Kumar Suresh, Singh Umed, Mahajan Priya, Mahajan Girish, Nargotra Amit, Malik Fayaz, Mondhe Dilip Manikrao, Vishwakarma Ram Asrey, Singh Parvinder Pal	19-May-17	15/528435
11	0127NF2014/EP	Novel 1,3,5 -Triazine Based Pi3k Inhibitors As Anticancer Agents And A Process For The Preparation Thereof	Thatikonda Thanusha, Kumar Suresh, Singh Umed, Mahajan Priya, Mahajan Girish, Nargotra Amit, Malik Fayaz, Mondhe Dilip Manikrao, Vishwakarma Ram Asrey, Singh Parvinder Pal	19-May-17	15820891.8
12	0127NF2014/JP	Novel 1,3,5 -Triazine Based Pi3k Inhibitors As Anticancer Agents And A Process For The Preparation Thereof	Thatikonda Thanusha, Kumar Suresh, Singh Umed, Mahajan Priya, Mahajan Girish, Nargotra Amit, Malik Fayaz, Mondhe Dilip Manikrao, Vishwakarma Ram Asrey, Singh Parvinder Pal	19-May-17	2017-527241
13	0176NF2014/CN	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	16-Jun-17	2.0158e+12
14	0127NF2014/CN	Novel 1,3,5 -Triazine Based Pi3k Inhibitors As Anticancer Agents And A Process For The Preparation Thereof	Thatikonda Thanusha, Kumar Suresh, Singh Umed, Mahajan Priya, Mahajan Girish, Nargotra Amit, Malik Fayaz, Mondhe Dilip Manikrao, Vishwakarma Ram Asrey, Singh Parvinder Pal	19-Jul-17	20158007386.X
15	0294NF2015/WO	Furanochalcones As Inhibitors Of Cyp1a1, Cyp1a2 And Cyp1b1 For Cancer Chemoprevention	Bharate Sandip Bibishan, Sharma Rajni, Joshi Prashant, Vishwakarma Ram, Chaudhuri Bhabatosh	11-Aug-17	Pct/In2017/050340
16	0180NF2016/WO	Indolylkojyl Methane Analogues, Process Of Preparation Thereof And Use As Inhibitor Of Cancer Cell Invasion And Metastasis	Debaraj Mukherjee, Anindya Goswami, Deepak Sharma, Debasis Nayak, Shreyans Kumar Jain	05-Feb-18	Pct/In2018/050060

c) Patents Granted in India

SNO	NFNO	Title	Inventors	Priority Date	Applicati on No.	Grant Date	Patent No.
1	0126NF2007/I N	Novel-4-Beta-[(4-Substituted)-1,2,3-Triazol-1- Yl] Podophyllotoxins As Potential Anticancer Agents	Qazi Ghulam Nabi, Halmuthur Mahabalarao Sampath Kumar, Saxena Ajit Kumar, Reddy Pitta Bhaskar, Bhat Bilal Ahmad, Agrawal Satyam Kumar	05-Mar-08	0528del20 08	11-Jul-17	285048
2	0073NF2010/I N (IICT + IIIM)	A Process For The Synthesis Of New Quinolylpiperazino Substituted Congeners Of Thiolactomycin As Anti-Tubercular Antibiotics	Ahmed Kamal, Shaik Azeeza, Ahmed Ali Shaik, M Shaheer Malik, Inshad Ali Khan, Sheikh Tasduq Abdullah, Sandeep Sharma, Anshu Beulah Ram	06-May-10	1069del20 10	28-Jul-17	285763

d) Patents Granted in Foreign

SN O	NFNO	Title	Inventors	Priority Date	Applicatio n No.	Grant Date	Patent No.
1	0195NF2011 /TW	Boronic Acid Bearing Liphagane Compounds As Inhibitors Of Pi3k-A And/Or ß	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, NayanChanauria	19-Mar-13	102109708	11-Apr-17	I577687

2	0195NF2011 /JP	Design, Synthesis And Biological Evaluation Of Isoform Selective Analogs Of Liphagane Scaffold As Anticancer Agents: P13k- Alpha/ BetaInhibitors	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, NayanChanauria	19-Sep-14	2015-501053	14-Apr-17	6126197
3	0038NF2013 /US	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	24-Feb-16	14/914,094	18-Apr-17	9624266
4	0038NF2013 /EP	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	23-Feb-16	14790347	09-Aug-17	3039031
5	0038NF2013 /GB	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	23-Feb-16	14790347	09-Aug-17	3039031

6	0037NF2013 /US	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	12-Oct-15	14/783878	03-Oct-17	9776989
7	0063NF2012 /US	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 SandipBibishan	17-Nov-15	14/891,706	03-Oct-17	9777014
8	0219NF2012 /EP	Rohitukine Analogs As Cyclin-Dependent Kinase Inhibitors And A Process For The Preparation Thereof	Vishwakarma Ram Asrey, Bharate Sandip Bibishan, Bhushan Shashi, Mondhe Dilip Manikrao, Jain Shreyans Kumar, Meena Samdarshi, Guru Santosh Kumar, Pathania Anup Singh, Kumar Suresh, Behl Akanksha, Mintoo Mubashir Javed, Bharate Sonali Sandip, Joshi Prashant	14-Oct-15	14734915.3	15-Nov-17	2986605

9	0037NF2013 /EP	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	12-Oct-15	14724520.3	15-Nov-17	2984078
10	0219NF2012 /GB	Rohitukine Analogs As Cyclin-Dependent Kinase Inhibitors And A Process For The Preparation Thereof	Vishwakarma Ram Asrey, Bharate Sandip Bibishan, Bhushan Shashi, Mondhe Dilip Manikrao, Jain Shreyans Kumar, Meena Samdarshi, Guru Santosh Kumar, Pathania Anup Singh, Kumar Suresh, Behl Akanksha, Mintoo Mubashir Javed, Bharate Sonali Sandip, Joshi Prashant	14-Oct-15	14734915.3	15-Nov-17	2986605
11	0176NF2014 /US	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	20-Apr-17	15/520799	21-Nov-17	9822126

12	0225NF2012 /US	6-Notro-2,3-Dihydroimidazo [2,1-B] Oxazoles And A Process For The Preparation Thereof	Parvinder Pal Singh, Gurunadham Munagala, Kushalava Reddy Yempalla, Inshad Ali Khan, Nitin Pal Kalia, Vikrant Singh Rajput, Amit Nargotra, Sanghapal Damodhar Sawant, Ram Asrey Vishwakarma	04-Apr-16	15/027137	19-Dec-17	9845330
13	0059NF2014 /US	10-Substituted Colchicinoids As Potent Anticancer Agents	Vishwakarma Ram, Bharate Sandip Bibishan, Kumar Ajay, Singh Baljinder, Kumar Ashok, Bhushan Shashi, Hamid Abid, Joshi Prashant, Guru Santosh Kumar, Kumar Suresh, Hussain Aashiq, Qazi Asif Khurshid, Bharate Sonali Sandip, Sharma Parduman, Saxena Ajit Kumar, Mondhe Dilip Manikrao, Mahajan Girish, Wani Zahoor	13-Apr-17	15/519,054	16-Jan-18	9868695

BOOKS CHAPTERS

- Epimedium elatum (Morr & Decne): A Therapeutic Medicinal Plant from Northwestern Himalayas of India Sajad Ahmad Lone, Ajai Prakash Gupta, Malik Muzafar Manzoor, Pooja Goyal, Qazi Pervaiz Hassan, and Suphla Gupta. Plant and Human Health, Volume 1,Ethnobotany and Physiology. **Ozturk**, Munir, **Hakeem**, Khalid Rehman (Eds.) 2018. Accepted.
- Submitted five gene sequences and four barcode sequences in NCbIdatabase.
- **Bikarma Singh,** B Singh, S Singh, R Bhanwaria and S Chandra **(2017)** "Biological Spectrum and Floral Diversity of Western Himalaya-A Case Study of Nandini Wildlife Sanctuary In J&K State pp 589-605" in edited book by Priyanka Agnihotri & J.S. Khuraijam "Angiosperm systematics: Recent trends and emerging issues". Published by Bishen Singh Mahendra Pal Singh, Dehra Dun, India (ISBN: 978-81-211-0981-9.
- **Bikarma Singh (2017)** "Indian Folklore Medicinal Herbalism-contribution of pharmaceutically active Himalayan Orchids traditionally used as herbal medicine, pp.45-61" in edited book by P Medhi and H Roy "Compendium on Botanical Research in Eastern India-A Felicitation Volume of Prof SK Borthakur". Publisher: Eastern Book House, Guwahati, India, 448 pages (ISBN: 13- 9789386302236).

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

- Popular lecture to students of Class XI & XII UNDER Jigyasa programe. The visit was done to KV Hiranagar on Sept 27, 2017 *(Delivered by Dr. (Mrs) Suphla Gupta, Sr.Scientist).*
- Invited guest for 3 day International training programme at SKAUST-J on Recent trends in Bioinformatics and Biotechnology for sustainable development. Presented on Revelations and Restrictions: Plant DNA Barcoding *(Delivered by Dr. (Mrs) Suphla Gupta, Sr.Scientist).*
- Invited Lecture on Role of molecular markers in establishing genetic fidelity of *in vitro* regenerated clonal plants' in 10 days National Training Programme on **Plant Tissue Culture Techniques for Quality Planting Material Production and Crop Improvement** from 1-10 Sept. 2016 at School of Biotechnology, Sher-e-Kashmir University of Agricultural Sciences and Technology of Jammu, Jammu (J&K) *(Delivered by Dr. (Mrs) Suphla Gupta, Sr. Scientist).*
- Sajad Ahmad Lone, Saleem Mushtaq, Qazi Pervaiz Hassan and Suphla Gupta Multidisciplinary Studies on Epimedium elatum (Morren & Decne): A Rare Medicinal Herb in Berberidaceace Family from Kashmir Himalayas in India AT NATIONAL CONFERENCE ON INTERDISCIPLINARY ASPECTS OF PLANT SCIENCES (27TH APSI SCIENTIST MEET) 2 nd - 4 th November, 2017 BESTPRESENTATION
- Oral Presentation of Assessment of genetic diversity by DNA Fingerprinting in Epimedium elatum (Morr & Decne) – An important aphrodisiac medicinal plant of Northwestern Himalayas in India Sajad Ahmad Lone1,3* , Saleem Mushtaq1 , Qazi Parvaiz Hassan1,3, Suphla Gupta2,3 AT International Conference in SKAUST-Jammu in Nov2017:
- Phylogenetic utility of the Internal Transcribed Spacer2 rDNA secondary structure in *Zingiber*: Identification of species specific sequence motif. *Pankaj Pandotra,* [a] *Pooja Goyal*[a], *Malik Muzafar Manzoor*[a], *Ajai. P. Gupta*[b], Surrinder Kitchloo[c] *and Suphla Gupta*[a]*
- "Cloning and hetrologous expression of β- amyrin synthase, a key regulatory genes of glycyrrhizin biosynthetic pathway" by Malik Muzafar Manzoor, Pooja Goyal, Pankaj Pandotra, Ajai P Gupta and Suphla Gupta for Poster presentation n the International Conference on "Recent Trends in Bioinformatics and Biotechnology for Sustainable Development" w.e.f. 12- 13 October, 2017 at FVSc&AH,SKUAST-J, R.S. Pura,Jammu.
- "Analysis of a seed protein gene promoter" by Pooja Goyal, Malik Muzafar Manzoor, Pankaj Pandotra, Ajai P Gupta and Suphla Gupta for Poster presentation n the International Conference on "Recent Trends in Bioinformatics and Biotechnology for Sustainable Development" w.e.f. 12-13 October, 2017 at FVSc&AH,SKUAST-J, R.S. Pura,Jammu.
- *Dr. (Mrs) Suphla Gupta, Sr. Scientist* was the External reviewer of the evaluation of thesis of Ms Richa Sharma entitled, Characterization of pea germplasm using EST-SSR markers and biochemical traits at SKAUST-Jammu.
- *Dr. (Mrs) Suphla Gupta, Sr. Scientist* was the External expert for RA selection Panel at SKAUST-J, Chatha on 17th Jan,2018.
- Received best presentation award on abstract /paper entitled "Evaluation of actinomycetes and their bioactive metabolites for discovery of new for anti-tuberculosis drugs" at "National Seminar on Biodiversity and Climate Change: Challenges and Prospects" held at Govt. SAM Degree College Budgam on 26th October 2017 *(Delivered by Dr. Qazi Parvaiz Hassan, Sr. Scientist).*
- *Dr. Saurabh Saran, Sr. Scientist* was Judge in JIGYASA Programme 45th Regional Level Jawaharlal Nehru Science, Mathematics and Environment Exhibition on29.01.2018
- Talk on *"Biocatalytic synthesis of pharmaceutically important chiral intermediates"* in the National Conference on "Bioresources as a Key to Value Added Products" held on 29th & 30th April, 2016. *(Delivered by Dr. Vikash Babu, Scientist).*
- *Trichoderma velutinum* ACR-P1: a psychrotrophic fungus as a potential biocontrol agent, Richa Sharma, Ankita Magotra , Ravi S. Singh, Asha Chaubey, Presented in National Symposium on Ecologically Sustainable

Plant Diseases Management under Diversified Farming Situation & IPS Annual (North Zone) Meet during 13-14 November, 2017 at Sher-e-Kashmir University of Agricultural Sciences and Technology, Chatha, Jammu (J&K)

- *Penicillium halotolerans* ACR-D24: a psychrotroph with potential for PUFA production. Richa Sharma, Farnaz Yusuf, Ankita Magotra, and Asha Chaubey. Presented in 5th International conference on Science, Technology & Management (ICSTM-2017); The Institution of Engineers India, Visvesvaraya Bhavan, Hyderabad, Telangana, India; 3 Dec2017.
- Poster presented on "Screening of metagenomic fosmid genebank for industrially important enzymes" by Jasmine Kour Khosla, Priya Darshini, Verruchi Gupta, Asha Chaubey, Shafaq Rasool and V. Verma during International Conference on Drug Discovery: Biotechnology and Pharma, held on 15-17 Feb 2018 at Thapar University, Patiala, Punjab.
- Participated as Judge in the Sahodaya Science Exhibition under the theme Science and Technology for Nation Building, organized by Army Public School on 08 Sep 2017 (*Dr. Asha Chaubey, Sr. Scientist*).
- *Dr. (Mrs) Suphla Gupta, Sr. Scientist* was the External examiner for the Ph D thesis viva at School of Biotechnology on QTL Mappping inrice.
- Plaque of honour received for a talk during the Value Addition work shop of Aromatic plants *(Delivered by Dr. Qazi Parvaiz Hassan, Sr. Scientist).*
- *Dr. Saurabh Saran, Sr. Scientist,* Presented paper on "Development of Nano-cellulosic membranes for the synthesis of antibiotic based transdermal patches" published in conference "International conference on Nano-Technology, Nano-bio interface & Sustainable Environment (INTENSE 2017)" held on 19th – 21st August, 2017 at Amity University Rajasthan, Jaipur, India.
- Poster presented on "Screening of Metagenomic Fosmid Genebank for Selected Enzymes" by Jasmine Kour Khosla, Verruchi Gupta, Asha Chaubey and V. Verma during National Conference on Interdisciplinary aspects of plant sciences held on 2-4 November, 2017 at SMVDU, Katra (J&K)
- *Trichoderma velutinum* ACR-P1: a psychrotrophic fungus as a novel non-ribosomal peptide producer. Richa Sharma, Varun P. Singh, Ankita Magotra, Deepika Singh, Farnaz Yusuf, Ram A. Vishwakarma and Asha Chaubey, Presented in National conference on Fungal Biology during Present Trends & Future Prospects & 44th Annual Meeting of the Mycological Society of India 16- 18 November, 2017 at University of Jammu, Jammu
- Attended workshop on "Translational R&D grant funding & entrepreneurship" at New Conference Hall, CSIR-IIIM campus on 6th February, 2018 (*Dr. Asha Chaubey, Sr. Scientist*).
- Attended One day National Workshop on CSIR- Aroma Mission: Value Addition of High Value Aroma Ingredients for Socio-Economic Upliftment & Rural Prosperity being held in IIIM Jammu on 8th March 2018, (*Dr. Asha Chaubey, Sr. Scientist*).
- Attended and delivered talk during one day Workshop for Kendriya Vidyalaya Scienceteachers under JIGYASA programme on 26th September 2017 (*Dr. Asha Chaubey, Sr. Scientist*).
- Participated in Run for Unity during Rashtriya Ekta Diwas on 31 October 2017 (*Dr. Asha Chaubey, Sr. Scientist*).
- Delivered Invited talk on "Science: An integral part of our lives" to the School Children in Army Public School, Damana on 21 December 2017 (*Dr. Asha Chaubey, Sr. Scientist*).

THESIS /AWARDS

- Isolation and characterization of endophytes from *Grewia asiatica* L. for production of bioactive molecules (*Awarded to Ms.Ankita Magotra*)
- *Dr. Qazi Parvaiz Hassan, (Sr. Scientist)* received Certificate for Plant germplasm registration for NEW variety PG-IIIM-101 of Rose scented geranium developed byus.

- Isolation and Characterization of microorganisms for production of Non-Ribosomal Peptides *(Awarded to Ms. Richa Sharma)*

- *Dr. (Mrs) Nasheeman Ashraf, (Scientist)* granted EMBO short term fellowship(2017-18)

LAUNCH OF TISSUE CULTURE GROWN BANANA FRUIT AT CSIR-IIIM JAMMU

In order to bring commercial cultivation of banana in J&K, CSIR-IIIM has conceived a new biotechnology driven programme. This work was jointly done by CSIR-IIIM, Jammu and Cadila Pharmaceutical, Ahmedabad. After full trial and established tissue culture and agriculture practice, Dr Ram Vishwakarma, Director IIIM, Jammu launched the J&K grown banana fruit. Dr Vishwakarma, flanked by Desh Ratna, president Agro Divisional and Narendra Brahmbhatt, GM Finance & Costing, Cadila Pharmaceutical Limited, Ahmedabad, held a press conference in IIIM, Jammu and revealed that the samplings of this high quality tissue culture variety known as Bhim Grand Naine (G-9) banana were brought from Agro Division of Cadila Pharmaceutical Limited, Ahmedabad, Gujarat and the first trial of cultivation over 2 acres land of field experimental farm Chatha has been successfully completed.

RESEARCH COUNCIL COMPOSITION 2017-2018
(w.e.f 10th August, 2017)

1.	**Dr. Bipin Alreja**	Chairman	503, Marble Arch, 94, Pali Hill, Bandra, Mumbai
2.	**Dr. G.N. Qazi**	Member	(Former VC, Jamia Hamdard) Director General, Hamdard Institute of Medical Sciences & Research New Delhi
3.	**Dr. G.N. Singh**	Member	Drugs Controller General of India, CDSCO,ITO, Kotla Road, New Delhi
4.	**Prof. Gautam Desiraju**	Member	Professor, Solid State and Structural Chemistry Unit Indian Institute of Science Bangaluru-560 012
5.	**Dr. Rajesh Kotecha** (Special Secretary, Ministry of AYUSH)	Member	Special Secretary, Ministry of AYUSH, Ayush Bhavan, B Block, GPO Complex, INA, New Delhi
6.	**Dr. Altaf Lal**	Member	Senior Advisor, Global Health and Innovation, Sun Pharma, USA
7.	**Dr. D.B. Ramachary**	Member	School of Chemistry, University of Hyderabad, Hyderabad
8.	**Dr. D.Ramaiah**	Member	Director, CSIR- North East Institute of Science & Technology, Jorhat- 785006, Assam
9.	**Dr. S. Chandrasekhar**	Member	Director, CSIR- Indian Institute of Chemical Technology, Uppal Road, Tarnaka, Hyderabad - 500 007, Telangana State
10.	**Dr. Ram Vishwakarma** (Director, CSIR-IIIM)	Member	Director. CSIR- Indian Institute of Integrative Medicine, Canal Road, Jammu-180001
11.	DG CSIR or his nominee	Member	

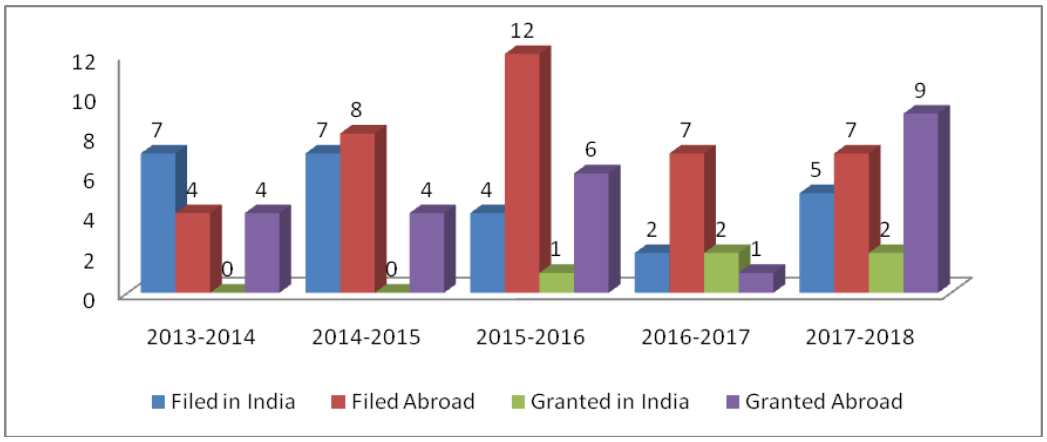
MANAGEMENT COUNCIL 2017 – 2018

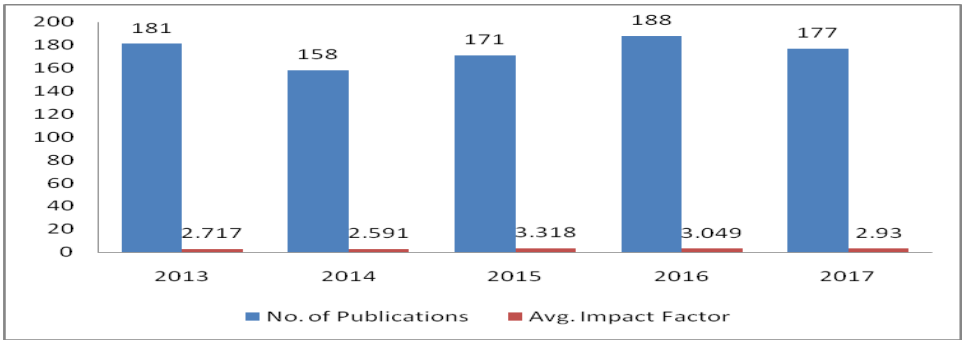
Dr. Ram Vishwakarma Director, Indian Institute of Integrative Medicine Canal Road, Jammu	**Chairman**
Dr. (Ms.) Madhu Dikshit, Director, Central Drug Research Laboratory, Lucknow	**Special Invitee** **Ex-officio Member**
Dr. Sanjay Kumar Director, Institute of Himalayan Bioresource Technology, Palampur, Himachal Pradesh	**Member**
Dr. Suresh Chandra Chief Scientist, Indian Institute of Integrative Medicine Canal Road, Jammu	**Member**

Dr. Inshad Ali Khan Principal Scientist Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Dr. (Smt.) Suphla Gupta Sr. Scientist Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Dr. Bhahwal Ali Shah Scientist Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Dr. N.K. Satti Principal Technical Officer Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Er. Abdul Rahim Sr. Principal Scientist /Head, PME Division Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Sh. K.C. Paliwal F&AO Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member**
Sh. Pankaj Bahadur, COA Indian Institute of Integrative Medicine, Canal Road, Jammu	**Member-Secretary**

PERFORMANCE PARAMETERS

Patents



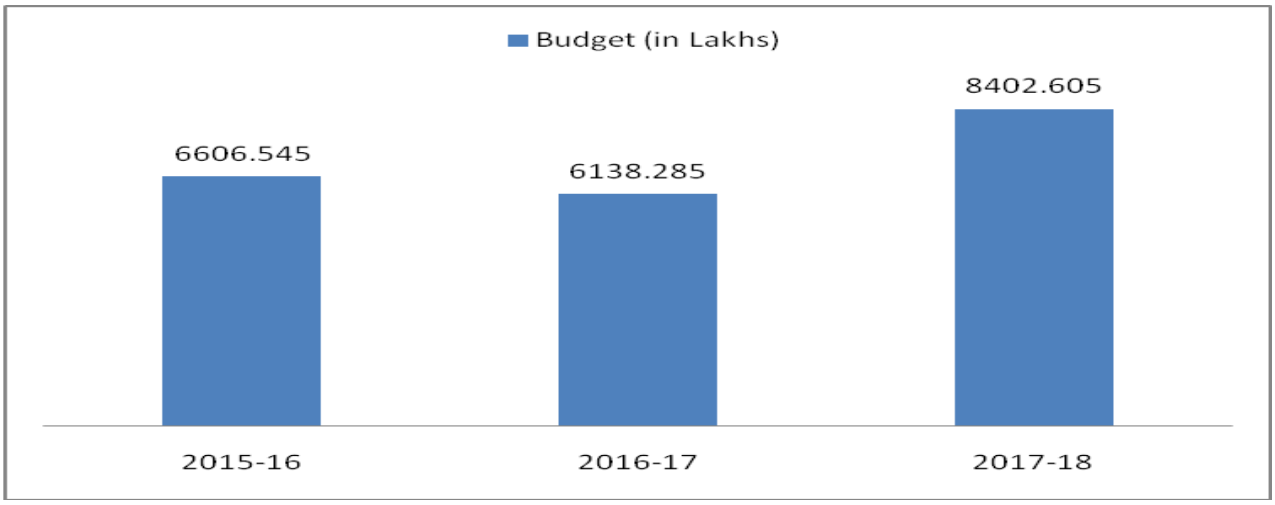


Publications [Calendar Year 2017]

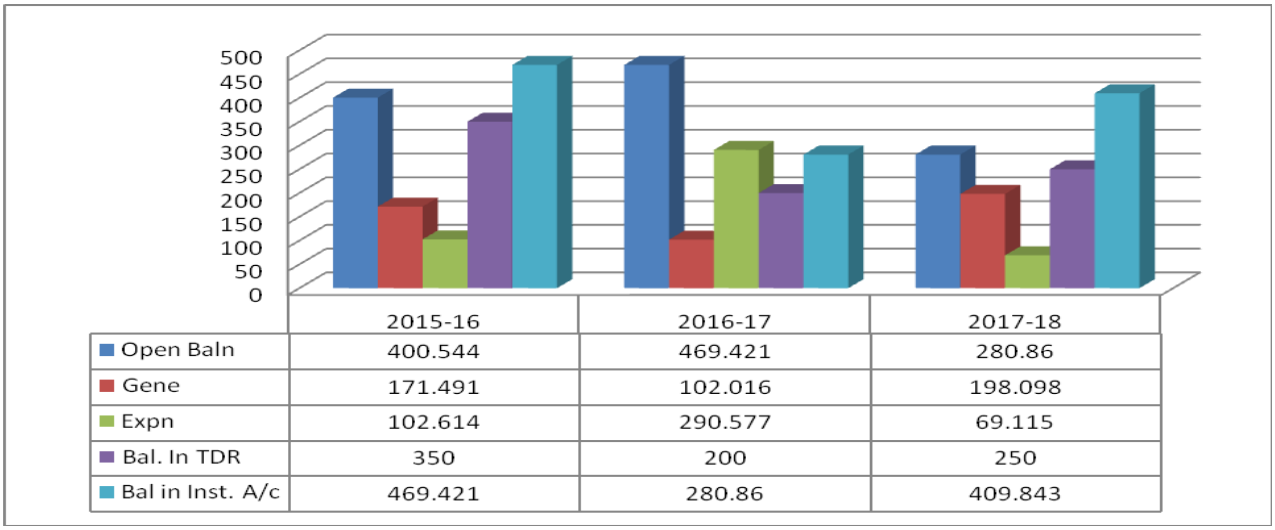
Fellows

Fellowship	No. of Students	Fellowship	No. of Students
SRF (CSIR) GATE	2	JRF (DBT)	1
SRF (CSIR) GPAT	2	SRF (DBT)	1
JRF (CSIR)	30	Women Scientist	4
SRF (CSIR)	21	Young Scientist	3
RA (CSIR)	1	Inspire Faculty	2
JRF (UGC)	25	Post Doctoral Fellowship	7
SRF (UGC)	15	N.P.D.F.	1
JRF (ICMR)	1	CSIR TWAS Fellowship	1
SRF (ICMR)	5	Project Fellows	133
RA (ICMR)	1	Senior Project Fellow	6
JRF (DST) INSPIRE	12	Research Associate	2
SRF (DST) INSPIRE	9		

Budget (Rs. In Lakhs)

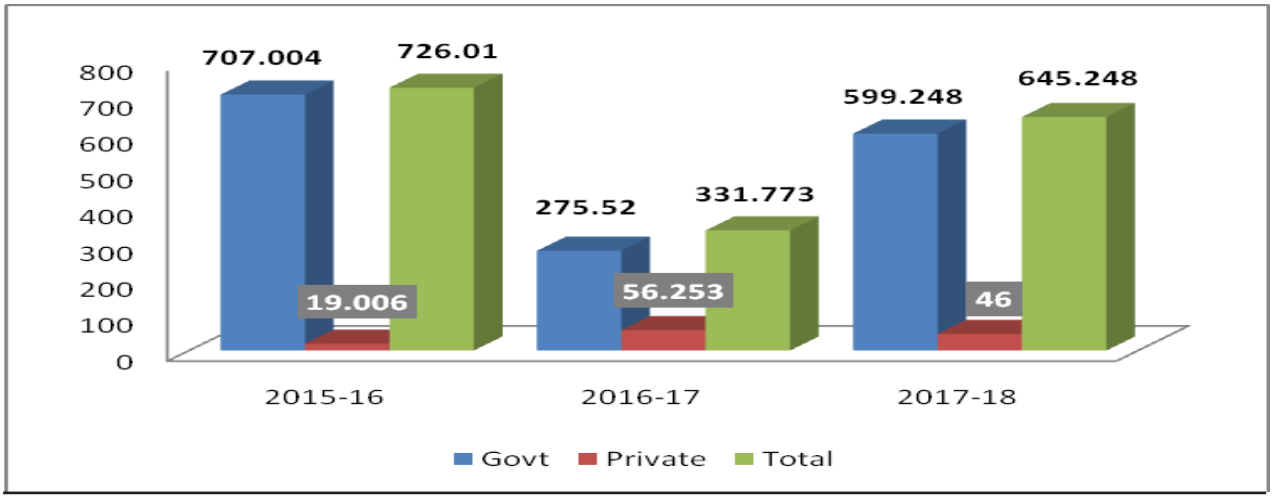


Institute's Reserve (Rs. In Lakhs)



	2015-16	2016-17	2017-18
Open Baln	400.544	469.421	280.86
Gene	171.491	102.016	198.098
Expn	102.614	290.577	69.115
Bal. In TDR	350	200	250
Bal in Inst. A/c	469.421	280.86	409.843

External Cash Flow



1. **Pilot scale optimization for standardization of processing & agro technologies of selected high value aromatic & medicinal plants including technology demonstration and extension for socio- economic upliftment.**
2. **Field demonstration of region specific Medicinal & Aromatic plants genotypes of CSIR for socio-economic upliftment of masses in J&K region (J&K AROMA AROGYA GRAM-JAAG)**
3. **Catalyzing Rural Empowerment through Cultivation, Processing, Value Addition and Marketing of Aromatic Plants. AromaMission)**

End to end technology development right from cultivation up to processing in case of Lavender, Rose, Rosemary, Salvia and Rose geranium which are the frontline aromatic crops of the state has been established. A new variety of Rose geranium was established and released by Honorable Prime Minister of India in 2017. Aroma Mission a network project raised large scale quality planting material of Lavender, Rose geranium, Salvia and Rosemary in our nurseries and supplied the same to local farmers, government departments and entrepreneurs of the different states of India. The extension activities of these and some other plants like Lemon grass, Rosagrass, Mentha, Lavender and Monarda has been extended at around more than 1500 acres of land in various states of India. Region specific crops have been extended up to Kishtawar, Bhaderwah, Patnitop, Ladakh, drass, Gurez and Nagaland.


Nursery
Lavender seedlings
I.I.I.M.


S.R.

CSIR Exhibition organized at CSIR-IIIM Jammu from August 25-27, 2017.

As part of CSIR Platinum Jubilee Celebrations, CSIR-Indian Institute of Integrative Medicine (IIIM) holds three days CSIR Capsule Exhibition from August 25 to 27, 2017, in its main campus at Jammu. Prof. Anju Bhasin, Vice Chancellor, Cluster University, Jammu, was the chief guest to inaugurate this scientific exhibition on 25 August. This scientific exhibition was first of its kind which was organised at Jammu, in which the students, researchers, faculty members, entrepreneurs and general public drawn across the length and breadth of State participated in this three days exhibition. In order to showcase the technologies from its 38 national laboratories of CSIR, the exhibitions and technofests are being organized. In Jammu & Kashmir State, the technologies of CSIR are exhibited at IIIM, Jammu.

SC/ST/OBC REPORT-I

ANNUAL STATEMENT SHOWING THE REPRESENTATION OF SCs, STs AND OBCs AS ON FIRST JANUARY OF THE YEAR AND NUMBER OF APPOINTMENTS MADE DURING THE PRECEDING CALENDER YEAR 2017

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH (DSIR)

O/o INDIAN INSTITUTE OF INTEGRATIVE MEDICINE, JAMMU

	Representation of SCs/STs/OBCs (As on 01.01.2018)				Number of appointments made during the calendar year 2017									
					By Direct Recruitment				By Promotion			By Deputation		
Groups	Total number of Employees	SCs	STs	OBCs	Total	SCs	STs	OBCs	Total	SCs	STs	Total	SCs	STS
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Group A	93	11	03	08	01	-	-	-	-	-	-	-	-	-
Group B	91	20	01	09	02	-	-	-	-	-	-	-	-	-
Group C	84	36	01	03	10	01	-	03	-	-	-	-	-	-
Group D (Excluding Sweepers)	*													
Group D (Sweepers)	*													
TOTAL	268	67	05	20	13	01		03						

*shown in group c column.

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

SC/ST/OBC REPORT-II

ANNUAL STATEMENT SHOWING THE REPRESENTATION OF SCs, STs AND OBCs IN VARIOUS GROUP'A' SERVICES AS ON FIRST JANUARY AND NUMBER OF APPOINTMENTS MADE IN THE SERVICE IN VARIOUS GRADES IN THE CALENDER YEAR 2017

DEPARTMENT OF SCIENTIFIC AND INDUSTRIAL RESEARCH (DSIR)

O/o INDIAN INSTITUTE OF INTEGRATIVE MEDICINE, JAMMU

	Representation of SCs/STs/OBCs (As on 01.01.2018)				Number of appointments made during the calendar year 2017									
					By Direct Recruitment				By Promotion			By Deputation		
Pay Band and Grade Pay	Total number of Employees	SCs	STs	OBCs	Total	SCs	STs	OBCs	Total	SCs	STs	Total	SCs	STS
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
PB-3 Rs.5400	10	03	01	-	01	01	-	-	01	01	-	-	-	-
PB-3 Rs.6600	21	04	-	05	-	-	-	-	-	-	-	-	-	-
PB-3 Rs.7600	38	04	-	03	01	-	-	-	-	-	-	-	-	-
PB-4 Rs.8700	24	01	01	-	-	-	-	-	-	-	-	-	-	-
PB-4 Rs.8900	02	-	01	-	-	-	-	-	-	-	-	-	-	-
PB-4 Rs.10,000	02	01	-	-	-	-	-	-	-	-	-	-	-	-
HAG+Above	01	-	-	-	-	-	-	-	-	-	-	-	-	-
TOTAL	98	13	03	08	02	01	-	-	01	01	-	-	-	-

SO (Estb)

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

PWD Report I

ANNUAL STATEMENT SHOWING THE REPRESENTATION OF THE PERSONS WITH DISABILITIES IN SERVICES (AS ON 1ST JANUARY 2018)

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

Group	Number of Employees				
	Total	In Identifiedposts	VH	HH	OH
1	2	3	4	5	6
Group A	02				02
Group B	01				01
Group C	01				01
Group D					
TOTAL	04				04

Note: (i) VH stands for Visually Handicapped (persons suffering from blinders or low vision).
(ii) HHstandsfor Hearing Handicapped(personssufferingfromhearing impairment).
(iii) OHstands forOrthopaedicallyHandicapped(personssufferingfromlocomotor disabilityor cerebralpalsy).

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

PWD REPORT II

STATEMENT SHOWING THE NUMBER OF PERSONS WITH DISABILITIES APPOINTED DURING THE YEAR (As on 1st. January 2018)

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

GROUP	DIRECT RECRUITMENT								PROMOTION							
	No. of vacancies reserved			No. of Appointments Made					No. of vacancies reserved			No. of Appointments Made				
	V H	HH	OH	Total	In Identified Posts	VH	HH	OH	VH	HH	OH	Total	In Identified Posts	VH	HH	OH
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Group A	-	01	02	03	03	-	-	02	-	-	-	-	-	-	-	-
Group B	01	01	01	03	03	-	-	02	-	-	-	-	-	-	-	-
Group C&D	-	01	02	03	03	-	-	01	-	-	-	-	-	-	-	-

Note: (i) VH stands for Visually Handicapped (persons suffering from blinders or low vision).
(ii) HH stands for Hearing Handicapped (persons suffering fromhearingimpairment).
(iii) OH stands for Orthopaedically Handicapped (persons suffering from locomotor disability orcerebralpalsy).
(iv) There is no reservation for persons with disabilities in case of promotion to Group A and B posts. However, persons with disabilities can be promoted to such posts, provided the concerned post is identified suitable for persons with disabilities.

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

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

वित्तीय वर्ष 2017–18 में हिन्दी अनुभाग द्वारा संस्थान में निम्नलिखित कार्यक्रम आयोजित किए गए:–.

1. भारत सरकार, गृह मंत्रालय, राजभाषा विभाग के निर्देशानुसार नगर राजभाषा कार्यान्वयन समिति, जम्मू की अर्द्धवार्षिक बैठकों का सफलतापूर्वक आयोजन किया गया। विवरण इस प्रकार से है:

(क) पहली अर्द्धवार्षिक बैठक दिनांक 28 जून, 2017 को सीएसआईआर–भारतीय समवेत औषध संस्थान, जम्मू के कान्फ्रेंस हॉल में सम्पन्न हुई। बैठक की अध्यक्षता संस्थान के निदेशक एवं नराकास, अध्यक्ष डॉ. राम विद्यकर्मा ने की। इस अवसर पर सुश्री अंजलि शर्मा, निदेशक, आकाशवाणी केन्द्र, जम्मू, श्री नवीन कुमार, डिवीजनल ट्रैफिक मैनेजर, उत्तरी रेलवे, जम्मू, श्री राकेश कुमार पाण्डेय, रक्षा लेखा अपर नियंत्रक, रक्षा लेखा नियंत्रक, उत्तरी कमान, जम्मू, श्री पवन कोहली, उपमंडल प्रमुख, पंजाब नेशनल बैंक, प्रशासनिक कार्यालय, जम्मू एवं नराकास के केन्द्रीय कार्यालयो बैंक उपक्रमों के सभी कार्यालयाध्यक्ष/नोडल अधिकारी/प्रशासनिक प्रमुख/राजभाषा अधिकारी/हिन्दी अधिकारी/ हिन्दी अनुवादक/प्रिन्ट व इलैक्ट्रॉनिक मीडिया के सभी संवाददाता तथा अन्य गणमान्य व्यक्ति उपस्थित थे।

(ख) नगर राजभाषा कार्यान्वयन समिति, जम्मू की वर्ष 2017 की दूसरी अर्द्धवार्षिक बैठक दिनांक 27 नवम्बर, 2017 (सोमवार) को सीएसआईआर–भारतीय समवेत औषध संस्थान, जम्मू के कॉन्फ्रेंस हॉल में आयोजित हुई। बैठक की अध्यक्षता संस्थान के निदेशक एवं नराकास अध्यक्ष डॉ. राम विद्यकर्मा ने की। इस अवसर पर श्री प्रमोद कुमार शर्मा, उपनिदेशक (कार्या.), भारत सरकार, गृह मंत्रालय, राजभाषा विभाग, क्षेत्रीय कार्यान्वयन कार्यालय, दिल्ली से उपस्थित हुए तथा श्री तिलक राज चौधरी, निदेशक, केन्द्रीय विद्यालय संगठन, गांधी नगर, जम्मू, श्री संजय धर, पंजाब नेशनल बैंक, क्षेत्रीय कार्यालय, जम्मू, डॉ. कृ८णा कुमारी, प्रभारी, क्षेत्रीय आयुर्वेदीय अनुसंधान संस्थान, जम्मू, प्रो. हरिनारायण तिवारी, प्रिंसीपल, रा८ट्रीय संस्कृत संस्थानम्, जम्मू, श्री पंकज बहादुर, नियंत्रक प्रशासन, भारतीय समवेत ओषध संस्थान, जम्मू एवं नराकास के केन्द्रीय कार्यालयों/बैंकों/उपक्रमों के सभी कार्यालयाध्यक्ष/नोडल अधिकारी/ प्रशासनिक प्रमुख/राजभाषा अधिकारी/हिन्दी अधिकारी/हिन्दी अनुवादक/ प्रिन्ट व इलैक्ट्रॉनिक मीडिया के संवाददाता तथा अन्य गणमान्य व्यक्ति उपस्थित थे।

2 सीएसआईआर–भारतीय समवेत औषध संस्थान, जम्मू में हिन्दी दिवस/पखवाड़ा, 2017 का आयोजन

राजभाषा हिन्दी के उत्तरोत्तर विकास और अधिकारियों/कर्मचारियों में हिन्दी प्रति जागरूकता उत्पन्न करने और रूचि जगाने के उद्देद्यय से प्रत्येक वर्ष सितम्बर माह में हिन्दी दिवस/पखवाड़ा, 2017 का आयोजन दिनांक 14 सितम्बर, 2017 से 25 सितम्बर, 2017 तक तत्संबंधी अनेक प्रतियोगिताएं हिन्दी कार्यशाला, निबन्ध लेखन, अनुवाद टिप्पण एवं प्रा रूपण, अन्तरविभागीय भाषण प्रतियोगिता, हिन्दी में मूलकार्य आदि कार्यक्रम आयोजित किए गए और सभी स्टॉफ सदस्यों, शोध छात्रों एवं नराकास सदस्यों ने भी भाग लिया।

3 संस्थान में दिनांक 14 सितम्बर, 2017 को हिन्दी पखवाड़ा एवं कार्यशाला का आयोजन।

संस्थान में दिनांक 14 सितम्बर, 2017 को एक दिवसीय हिन्दी कार्यशाला का आयोजन किया गया। जिसकी अध्यक्षता संस्थान के निदेशक एवं नराकास अध्यक्ष, डॉ. राम विद्यवकर्मा ने की और मुख्य वक्ता के रूप में प्रो. चंचल डोगरा, सेवानिवृत्त एम.ए.एम. कॉलेज, जम्मू ने 'राष्ट्रहित में राजभाषा हिन्दी और उसका महत्त्व' विषय पर व्याख्यान पस्तुत की। जिसमें संस्थान के श्री पंकज बहादुर, नियंत्रक प्रशासन, वित्त एवं लेखा अधिकारी, श्री के. सी.पालीवाल, भण्डार एवं क्रय अधिकारी, श्री प्रफुल्ल कुमार, वैज्ञानिकों/तकनीकी अधिकारियों एवं शोध छात्रों तथा अन्य स्टॉफ सदस्यों ने हिन्दी पखवाड़े के उपलक्ष्य में बढ़-चढ़कर भाग लिया।

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Sh. Sumit Kumar
Sh. Arvind K. Yadav
Sh. Yogesh Kumar
Sh. AmitKumar
Sh. Rajinder Gochar
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E. E. (Elect.)
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Sh. Bishan Kumar
Sh. Jasbir Singh
Sh. Sham Lal Bhagat
Sh. Abdul Hamid Dar
Sh. Neel Kamal
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Sh. Manoj Kumar
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Sh. Om Parkash
Sh. Girdhari Lal
Sh. Abdul Ahed Sheikh
Sh. Fayaz Ahmad Dar
Mrs. Darshana
Sh. Kuldeep kumar
Sh. Tarachand
Sh. Nagar Lal
Sh. Ashok Kumar

Controller of Administration
Sh. Pankaj Bhadur

Finance & Accounts Officer
Sh. K.C. Paliwal

Store & Purchase Officer
Sh. Praphul Kumar

Section Officer (G)
Sh. Rajesh Kumar Gupta

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Sh. Ramesh Kumar

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Sh. Parshotam Lal
Sh. Mohd. Farooq Bhat
Sh. Ram Lal
Sh. Ashok Kumar
Sh. Tarseem Kumar (Appointed as LDC)
Sh. Pawan Kumar
Sh. Rajesh K. Tandon
Sh. Moses Tegi
Sh. Girdhari Lal.
Sh. Rashpal

Sh. Prithvi Raj
Sh. Mangal Dass
Sh. Sham Lal
Sh. Subash Chander
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Sh. Tara Chand
Sh. Rattan Lal
Sh. Sukhdev Raj
Sh. Kala Ram
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Sh. Seva Ram
Sh. Ashok Kumar
Sh. Munna
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Sh. Surinder Kumar
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