Details of Research Work for which Sun Pharma Research Award Based

The research work done by Dr. Reddy in PHARMACEUTICAL CHEMISTRY is a perfect blend of academic excellence and industrial relevance. The art of organic synthesis is well exploited in making new processes for both generic and innovative drugs. The chemistry developed is not only environmentally benign but also made the products more affordable. His research group is also engaged in the synthesis of New Chemical Entities (NCEs) including natural product analogues as potential therapeutic agents towards drug discovery.

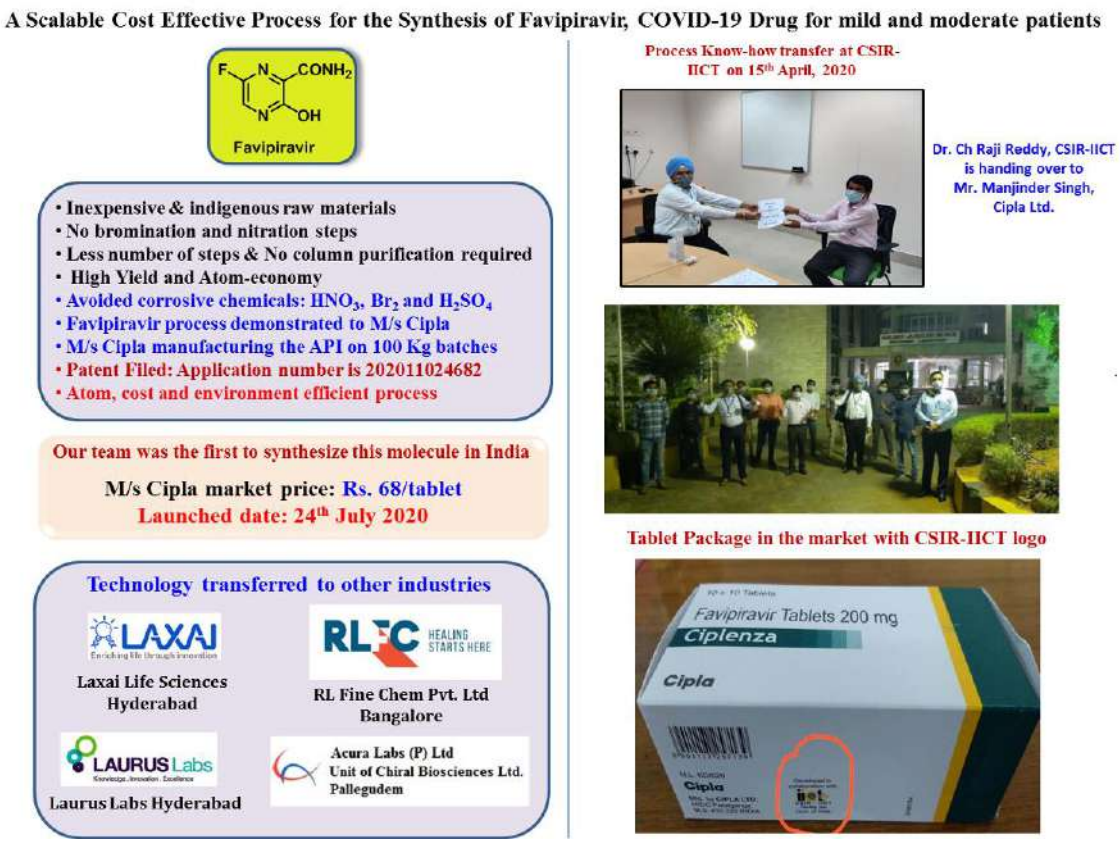
TOWARDS APPLIED PHARMACEITICAL CHEMISTRY:

The major works have been carried out essentially on two themes. ***1) Route of Synthesis and Process development for APIs*** *[Cipla Ltd, Bharat Biotech Int Ltd, Mylan Laboratories, Laxai Life sciences, Aurobindo pharma, Aisin Cosmos and Evolva Biotech and others]*. ***2) Synthesis of new Chemical Entities*** (Sai Life Sciences, Sun Pharma, Alfa Biosciences, Evolva and Bharat Biotech are the clients).

(i) ***Developed a novel process for FAVIPIRAVIR towards COVID-19 under repurposing drugs programme of CSIR (patent filed: Application No. 202011024682) with in short span of four weeks' time from procuring the raw materials to transferring the technology to Cipla Ltd for production. Cipla has done scale-up the compound using our process and launched the drug into market and commercialized in the name of Ciplenza. On the marketed pack, CSIR-IICT logo has also been printed*** **- [TECHNOLOGY COMMERCIALIZED]**

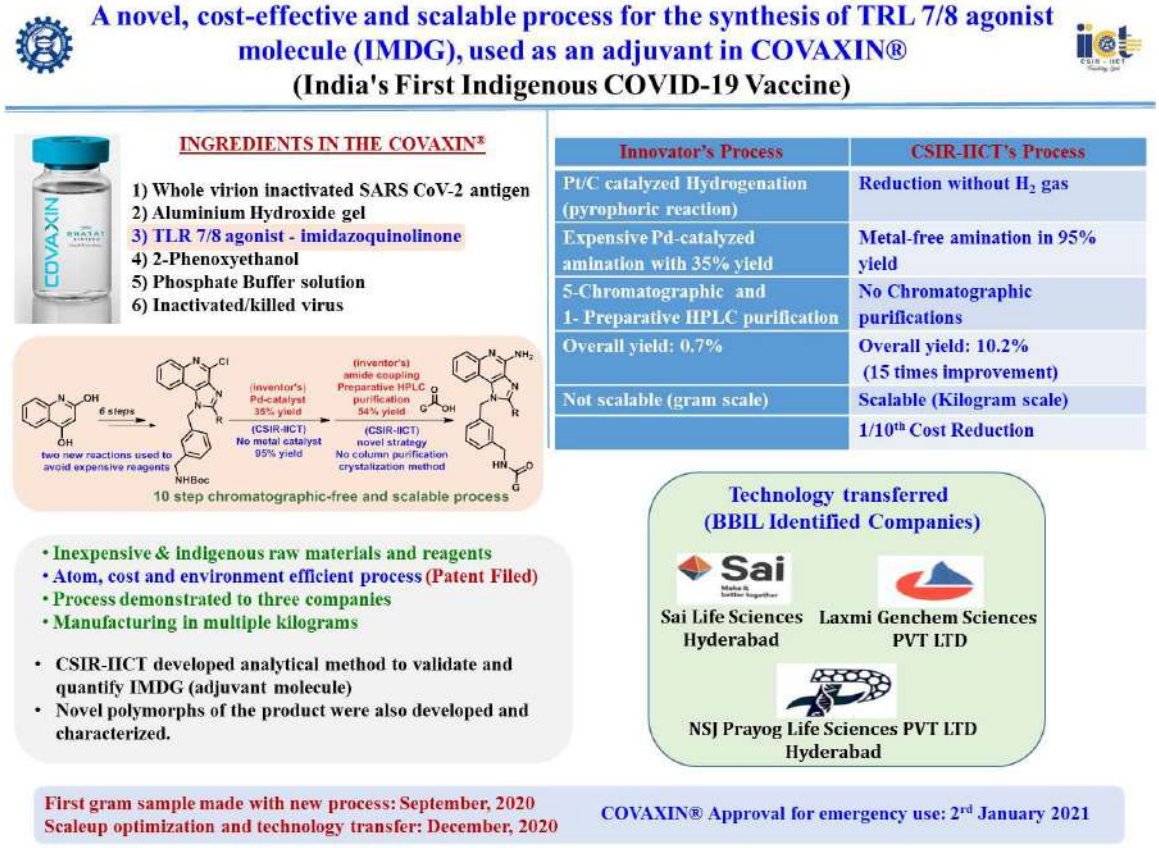
– Letter from Cipla Ltd enclosed.

- The process has also been transferred to four other API manufacturing companies. (mail enclosed)



(ii) **Developed a novel and efficient scalable process (patent filed-2021) for the synthesis of TLR 7/8 agonist molecule (IMDG), used as an adjuvant in COVAXIN® (COVID-19 vaccine) and transferred to Bharat Biotech Int. Ltd. and being produced in kilograms scale. BBIL has launched the vaccine, in COVAXIN® in the market and supplying to several countries. This demanding task was achieved within 4-months of record time. Based on the readiness of this process, BBIL approached three companies, viz., NSJ Prayog Life Sciences, LaxmiGenChem (for n-2 intermediate) and SaiLIfe Sciences Ltd (for TLR 7/8 agonist molecule) for further scaleup and the process has been transferred and demonstrated to these companies. - [TECHNOLOGY COMMERCIALIZED]**

- **[Letters from BBIL and other companies enclosed].**



(iii) Actively involved in the **process optimization of Remdesivir, which was approved for the emergency usage for the treatment of COVID-19**. As this was first time approved, there was no optimized process in India. Optimized process by our team at CSIR-IICT has been transferred to different companies, who got license from Gilead Sciences.

(iv) Involved in the **Development of a process for the synthesis of 2-deoxy glucose (2-DG, which was approved for the emergency usage for the treatment of COVID-19**. The developed process by our team at CSIR-IICT has been transferred to the following pharmaceutical companies.

- Suven Pharmaceuticals Ltd, Hyderabad
- Nosch Labs Private Limited
- Emmennar Pharma Pvt Ltd., Hyderabad

- Anthem Biosciences Pvt. Ltd., Bangalore,
- PI industries, Udaipur
- Aurabindo Pharma, Hyderabad
- Lee Pharma Limited, Hyderabad
- Krishna Pharma, Hyderbad
- Sarvotham Care Ltd, Hyderabad

(v) **Developed a cost-effective process for (*S*)-pregabalin (IN202011006475 and Patent filing date: February, 2020), used to treat epilepsy, neuropathic pain, fibromyalgia, and generalized anxiety disorder, required in ton scale**. This work was successfully completed in 10 weeks of time, wherein we met the objectives of cost, quality and process efficiency. Currently, we are in the process of transferring this process to pharmaceutical companies for commercialization and negotiations going on.

(vi) **Developed non-infringing route for the largest man made and most challenging drug, Eribulin mesylate (involved 65 steps), which will be helpful for an affordable treatment of breast cancer patients and there is no process available in India till date (Patent Filed: No. 0019NF2019). This process has been transferred to Cipla Ltd. and the product is under process for commercialization**. This molecule was made for the first time in India – (Mail from Cipla Ltd. Enclosed).

(vii) Accomplished a scalable process for the synthesis of Nicergoline from Lysergol, used for the treatment of dementia. ***A new photochemical reaction in flow chemistry has been developed in this process as a convenient approach*** – Discussions are on with KV Naturals for scaleup and commercialization. – (Correspondence enclosed).

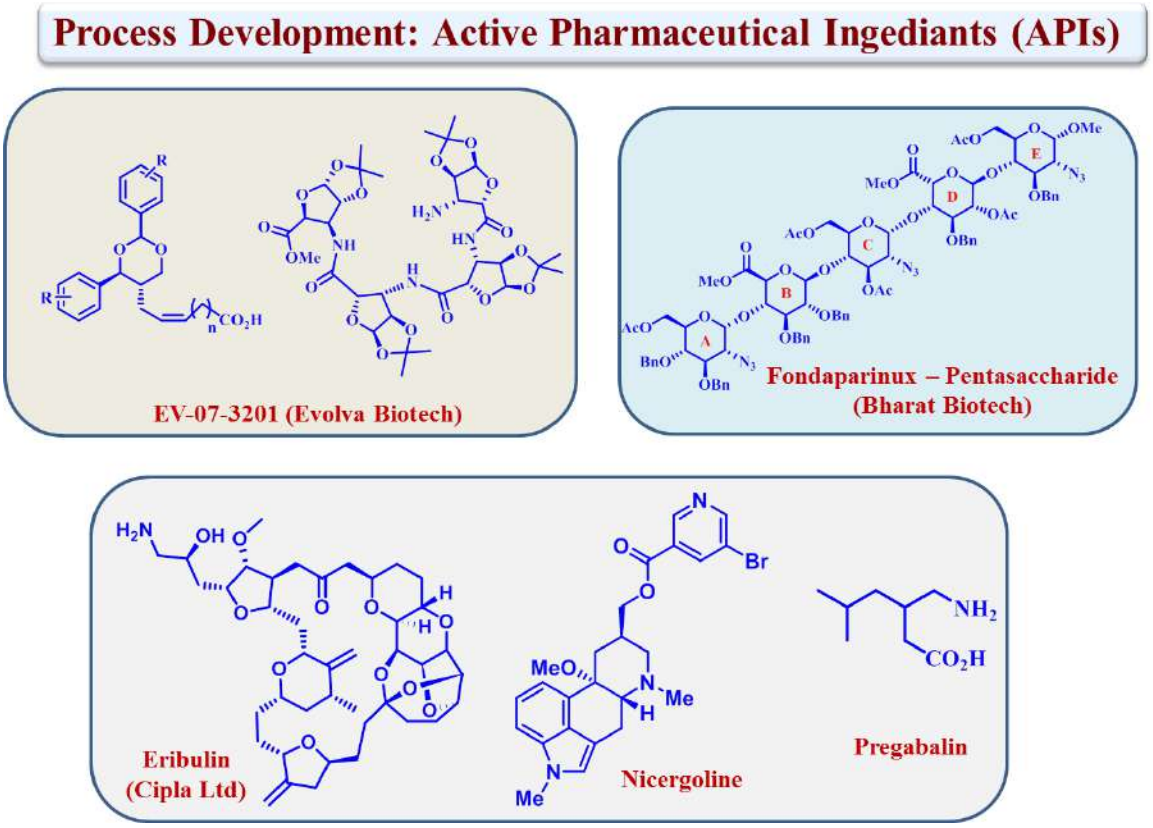
(viii) Successfully developed a facile process for Evolva-Biotech, EV-077-3201 (anti-fungal compound, made in kilogram scale) is presently under phase-III clinical trials. (as an Industry-Sponsored project).

Other Research work relevance to Pharmaceutical Chemistry Companies:

(a) The accomplishment of **chemo-selective tritylation** using activated alcohols under Lewis acid (***Tetrahedron Letters*** 2008, 49, 970-973) has been found to be extremely useful to avoid the pyridine as base in combination with trityl chloride. The method has been widely used by several pharmaceutical companies in nucleoside synthesis.
(b) Developed a process for Nonane fragment, a key subunit for Moxifloxacin.
(c) ***Development of new processes to commercially potential API's and key intermediates: (Industry sponsored projects):*** Various industry sponsored challenging projects were taken and completed successfully, which are relevant to pharmaceutical research.
(d) Betrixaban: New scalable route to synthesize the factor Xa (FXa) inhibitor betrixaban is obtained in a seven-step reaction sequence. Effective isolation of intermediates, use of cost-

effective amide formation and 2- methyltetrahydrofuran as an effective reaction solvent as well as for extraction in three of the stages, are key features. The strategy provides the desired product in 38% overall yield with high purity.
(***SynOpen*** 2020, 4, 62-65).

Technology/Process for compound	**Company/industry**
Favipiravir **(for the treatment of COVID 19)**	**Cipla Ltd – commercialized** Laxai Life Sciences, Hyderabad RL Fine Chem Ltd., Bangalore Laurus Labs, Hyderabad Acura Labs, Hyderabad
TLR 7/8 Agonist molecule used as an adjuvant in COVAXIN® **(COVID 19 Vaccine)**	**Bharat Biotech Int Ltd – commercialized** Laxai Life Sciences, Hyderabad RL Fine Chem Ltd., Bangalore Laurus Labs, Hyderabad Acura Labs, Hyderabad
2-Deoxy Glucose [2-DG] **(for the treatment of COVID 19)**	Suven Pharma Ltd, Hyderabad Anthem Biosci. Pvt. Ltd., Bangalore, PI industries, Udaipur Aurabindo Pharma, Hyderabad Lee Pharma Limited, Hyderabad Nosch Labs Private Limited Emmennar Pharma Pvt Ltd., Hyderabad Krishna Pharma, Hyderbad Sarvotham Care Ltd, Hyderabad
Remdesivir (for the treatment of COVID 19)	Anthem Biosciences Pvt. Ltd., Bangalore, India PI industries, Udaipur Aurabindo Pharma, Hyderabad
Eribulin Mesylate (anti-cancer)	Cipla Ltd
Fondaparinux (anti-thrombotic agent) and Low molecular weight Heparin analogues	Bharat Biotech
Key Intermediate for Vaccine Project	Bharat Biotech
16 New Chemical entities	Sai Life, Hyderabad
Butolic acid	IINRG, Ranchi
40 New Chemical Entities	Evolva Biotech, Switzerland
Process for EV-77-3201 (Clinical Trial Phase III)	Evolva Biotech, Switzerland
(*S*)-pregabalin	Neuland laboratories Ltd (under negotiation)
Nicergoline	LifeCare Laboratories (under negotiation)



TOWARDS Synthesis of New Chemical Entities-Development of Novel Methods:

(a). Development of alkyne- and enyne-assisted approaches towards new chemical entities (NCEs)

Dr. Reddy's research group at CSIR-IICT focuses mainly on the synthesis of new molecular entities towards medicinal chemistry with an eventual purpose of drug discovery. In this direction, Dr. Reddy has designed and developed a novel Morita-Baylis-Hillman adduct from acetylenic aldehydes for the first time in 2011 (Org. Biomol. Chem, 2011, 6027) towards the synthesis of pyrrole. Later, these MBH-adducts have been successfully utilized by him as handy substrates for the synthesis of various heterocycles such as thiophenes, furans, pyridines, indoles, benzothiophenes, carbazoles etc and carbocycles such as cyclopentenes, cyclopentenones as well as polyaromatichydrocarbons, naphthalenes, anthracenes, phenanthrenes, through the enyne-assisted cycloisomerization reactions (resulted in 21-publications). Representative accomplishments were shown in **Figure 1**. One of the noteworthy contributions from MBH-chemistry is the development of novel [4+2]-benzannulation reaction of MBH-acetates of acetylenic aldehydes with aryl/heteroaryl/styryl boronic acids for the synthesis of benzenes, naphthalenes, polycyclic aromatic and benzne-fused heteroaromatic compounds. In addition, he has also successfully demonstrated the synthesis of niconitic acid derivatives (pyridines) through aza-annulation of enynyl azides, generated from these MBH-acetates (Org. Lett. 2015, *17*, 896,

Org. Lett. 2018, *20*, 3128, Org. Lett. 2019, *21*, 623, Org. Lett. 2020, 22, 689 and Org. Lett. 2021, *23*, 4749). A new protocol has been developed for the synthesis of substituted thiophenes under mild and metal-free reaction conditions via the base-promoted thioannulation of Morita–Baylis–Hillman acetates of acetylenic aldehydes with potassium thioacetate (J. Org. Chem. 2013, 78, 6495).

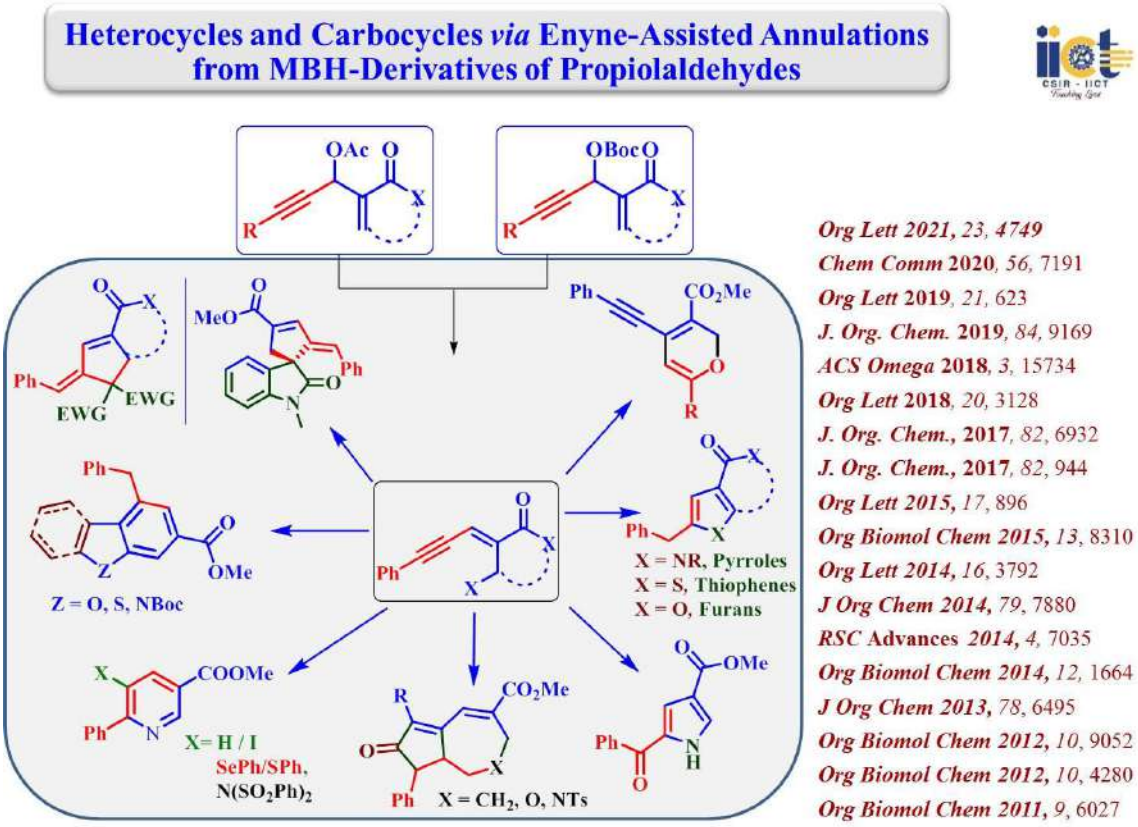


Figure 1: Synthesis of new chemical entities from enyne-assisted annulations

Apart from the development of novel methods, he is also enthusiastic in using those methods to generate the library of new chemical entities (NCEs) and to submit the National MolBank at CSIR-IICT towards find out their biological activity. In this direction, various pyrrole derivatives have been synthesized. Noteworthy to mention that, one of the derivatives (from pyrrole series, see **Figure 2**) showed potential activity as neuroprotective as well as neurotrophic agents. Further, this compound has been subjected to in vivo test using Zebrafish model for anti-anxiety properties and the results are promising (Patent filed). At present, pharmacokinetic studies are under progress for this molecule.

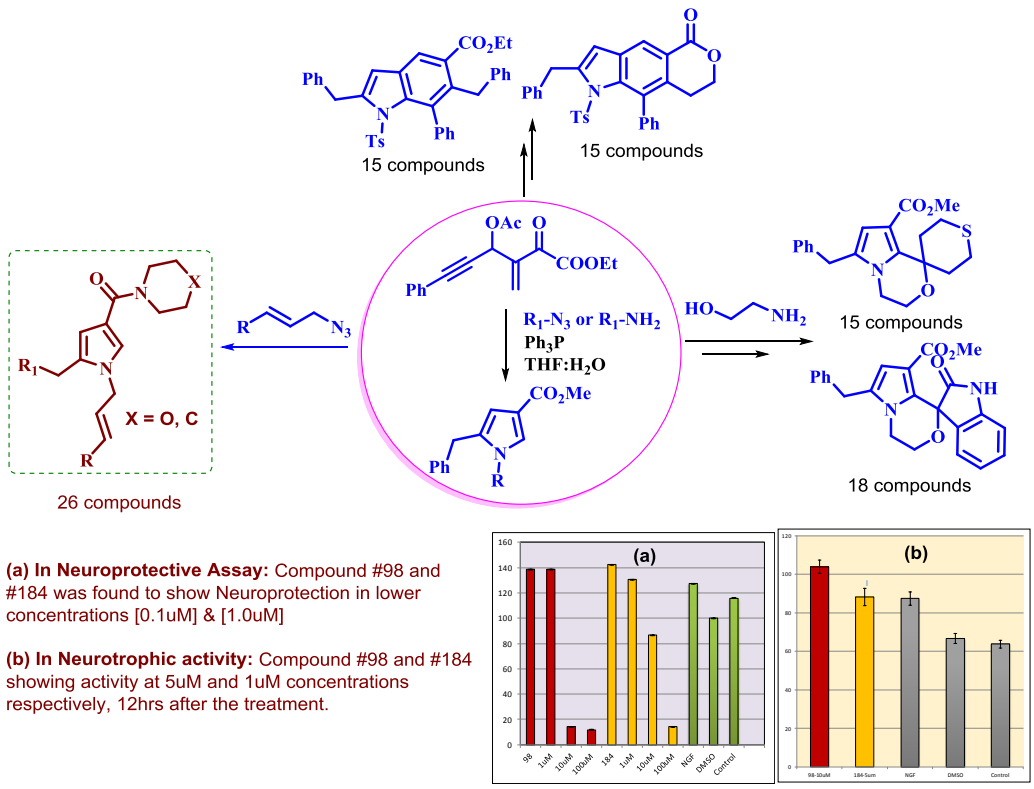


Figure 2: Synthesis of Novel Pyrrole derivatives and their biological evaluation

A significant contribution from Dr. Reddy includes the exploitation of 1-aryl propargylic alcohols as useful synthons for the synthesis of various heterocycles. Importantly, majority of these reactions are metal-free, atom-economical, one-pot reactions giving water as only the by-product. 1-Aryl propargylic alcohols have been successfully used as electrophiles and subsequent cyclization reactions provided the number of heretocycles such as furans, pyrazoles, benzofurans, benzothiophenes, indoles, carbazoles, furano-coumarins, oxazoles, and isoxazoles (resulted in 18-publications). Representative accomplishments were shown in Figure 3. Synthesis of polyaromatichydrocarbons (naphthalenes, anthracenes, chrysenes, picenes and benzopicene etc. through [4+2]-benzannulation is one of the remarkable contributions. Recently, a novel strategy for the synthesis of 3-hydroxycarbazoles has been developed installing the hydroxyl group externally at the third position on the carbazole during the annulation (hydroxylative benzannulation) for the first time.

These methodologies have also been utilized by him to synthesize the library of new chemical entities. C5-Alkylation of oxindole is one of the significant accomplishment (Org. Biomol. Chem., 2011, 3940), which further provided an opportunity to make new molecules, furano-oxindoles and 5,6-disubstituted oxindoles and subsequently converted to arylidene-derivatives.

Couple of these compounds have shown very good cytotoxicity in leukemic and breast-cancer cell lines through tyrosine-kinase inhibition **(patent filed: IN201611037409; US2018/0127365 A1)**. At present, pharmacokinetic and pharmacodynamic studies are under progress for these two molecules.

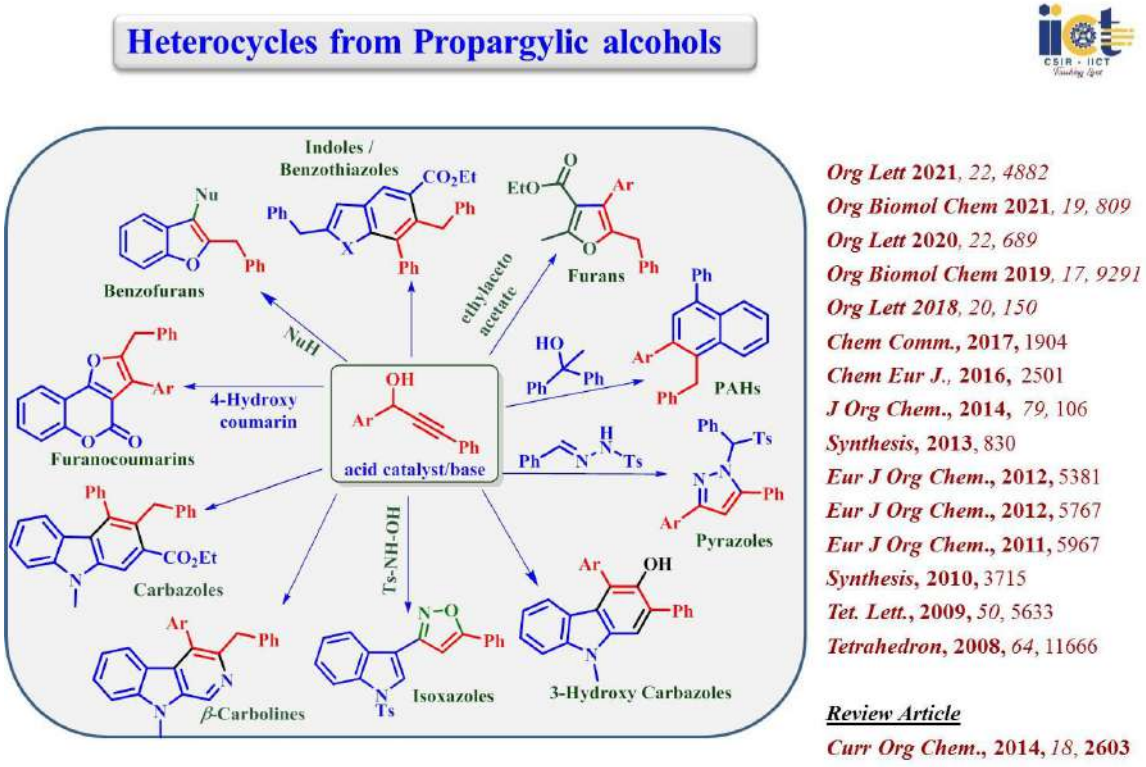
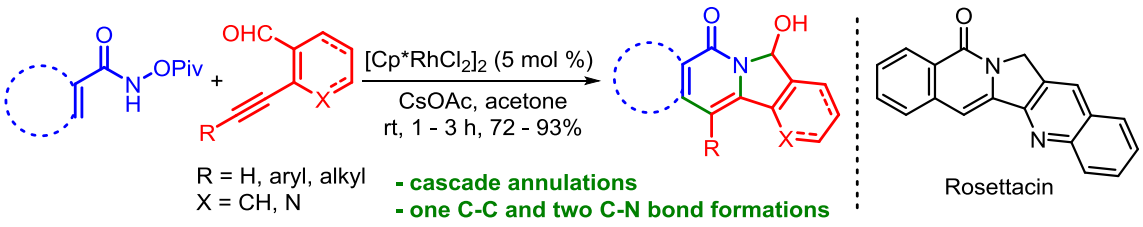


Figure 3: Synthesis of heterocycles from propargylic alcohols

A recent significant contribution from Dr. Reddy is the synthesis of diversely substituted 7-hydroxy-isoindolo[2,1-b]isoquinolin-5(7*H*)-ones from the reaction of *N*-(pivaloyloxy)benzamides with 2-alkynyl aldehydes has been developed, which proceeds through sequential alkyne insertion followed by addition of the amide nitrogen on to the aldehyde (**Figure 4**). The synthetic utility of this strategy was successfully illustrated by
the concise, two-step synthesis of an alkaloid, rosettacin, and a topoisomerase I inhibitor.



Organic Letters **2018,** ***20,*** **150**

Figure 4: Rh(III)-Catalyzed Cascade Annulations to Access Isoindolo[2,1-b]isoquinolin-5(7H)-ones *via* C−H Activation: Synthesis of Rosettacin

(b). Total Synthesis of Bio-active Natural Products and their analogues.

Natural products are one of the main sources for drug discovery program to identify the lead molecules and many natural products or their derivatives have become drugs for various therapeutics. Therefore, total synthesis of natural products from commercially available resources is an important research activity in the pharmaceutical field. In addition, verification of the structure and stereochemistry can also be verified through the synthesis.

Dr. Raji Reddy is working in this challenging research area of total synthesis of bio-active natural products. He has designed and accomplished an efficient synthesis of several natural products which helps to access in sufficient quantities for further derivatization to make more analogues. During the last 14-years, his research group has achieved the total synthesis of more than 40-Natural Products, which includes tetrahydropyranyl (THP) compounds, macrolides and alkaloids (**Figure 5 & 6**). Among these, the synthesis towards complex macrolides such as (-)-exiguolide (*RSC Adv.* **2012**, *2*, 7724) and iriomoteolide 3a (*Org. Lett*. **2009**, *11*, 5730) are remarkable achievements.

During the synthesis to bio-active molecules, he has successfully revised the absolute configuration of few natural products like Seimatopolides A and B (*Org. Biomol. Chem*. **2013**, *11*, 3355) and proved the ambiguity in stereochemistry of Ieodoglucomides (*J. Org. Chem.* **2013**, *78*, 4251).

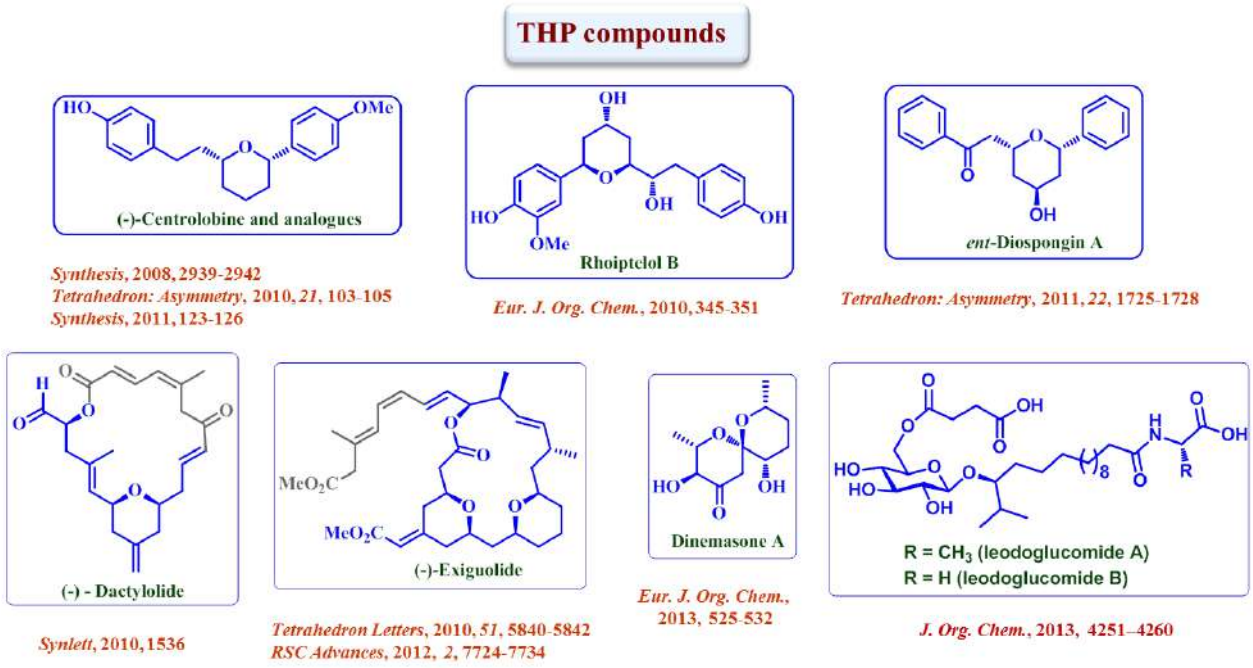


Figure 5: Representative structures of Tetrahydropyranyl natural products

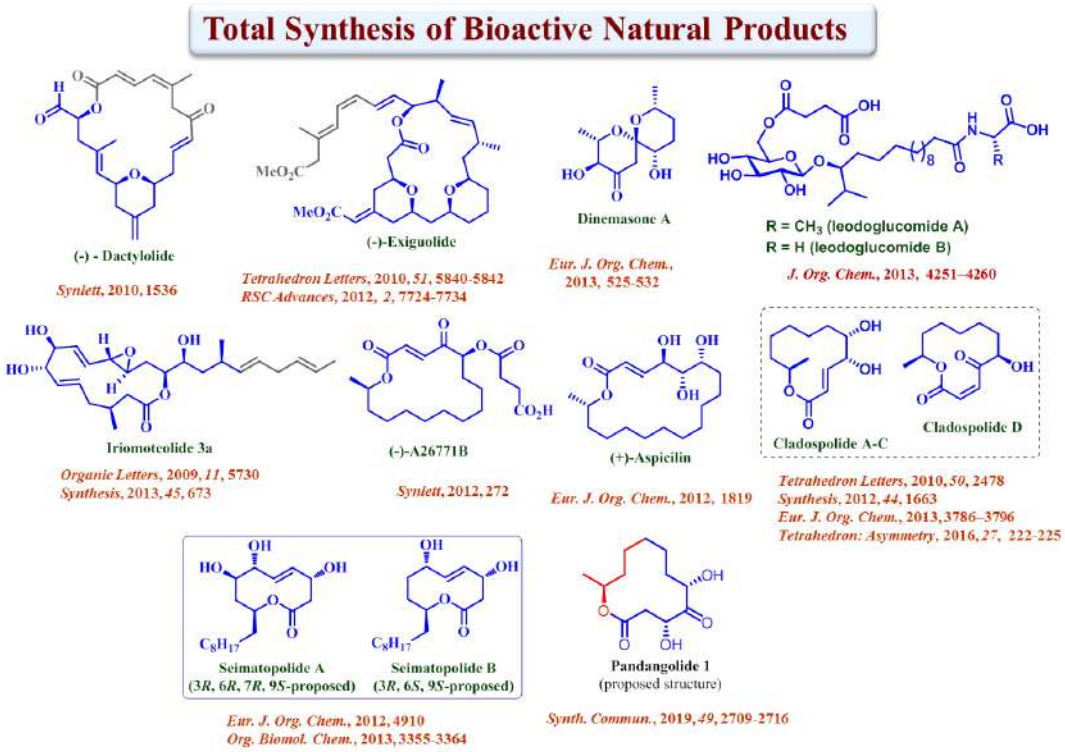
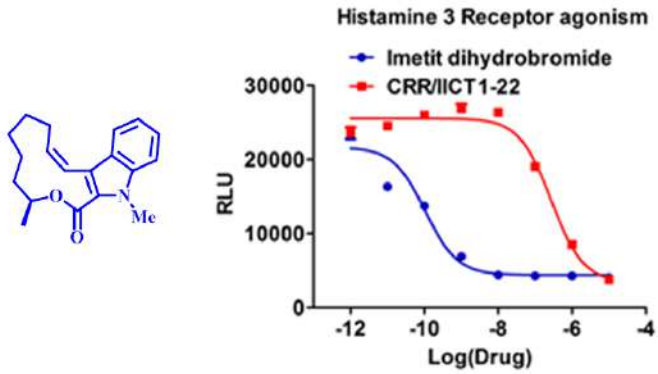


Figure 6: Representative structures of THP and macrolide bio-active natural products

While working on total synthesis of cladospolide D, he has also made a wide variety of its analogues as part of "Drugs from the Sea" project by Ministry of Earth Sciences. Out of 35-analogues made by him (screening at CSIR-CDRI), five compounds were found to be active against human Histamine 3 receptor (hH3R) agonistic activity. One of the molecules activity data is shown in **Figure 7**.



	Imetit dihydrobromide	CRR/IICT1-22
LogIC50	-9.975	-6.561
IC50	1.060e-010	2.745e-007

Possible Applications:

- **H3R agonists block the release of certain neurotransmitters like monoamine which is involved in progression of mental disorders. They may also improve cognitive functions and work as anti-psychotics.**

Figure 7: Human Histamine 3 Receptor agonistic activity of cladospolide analogue-22

Dr. Reddy has developed one novel stable chiral synthon in his lab for the first time (*Tetrahedron: Asymmetry* 2011, *22*, 1849) and used for the synthesis of various bioactive piperidine and indolizidine alkaloid molecules (Figure 8). In addition to the above molecules, few more pyrrole-based alkaloids are also synthesized for the first time in gram quantities towards the synthesis of their analogues.

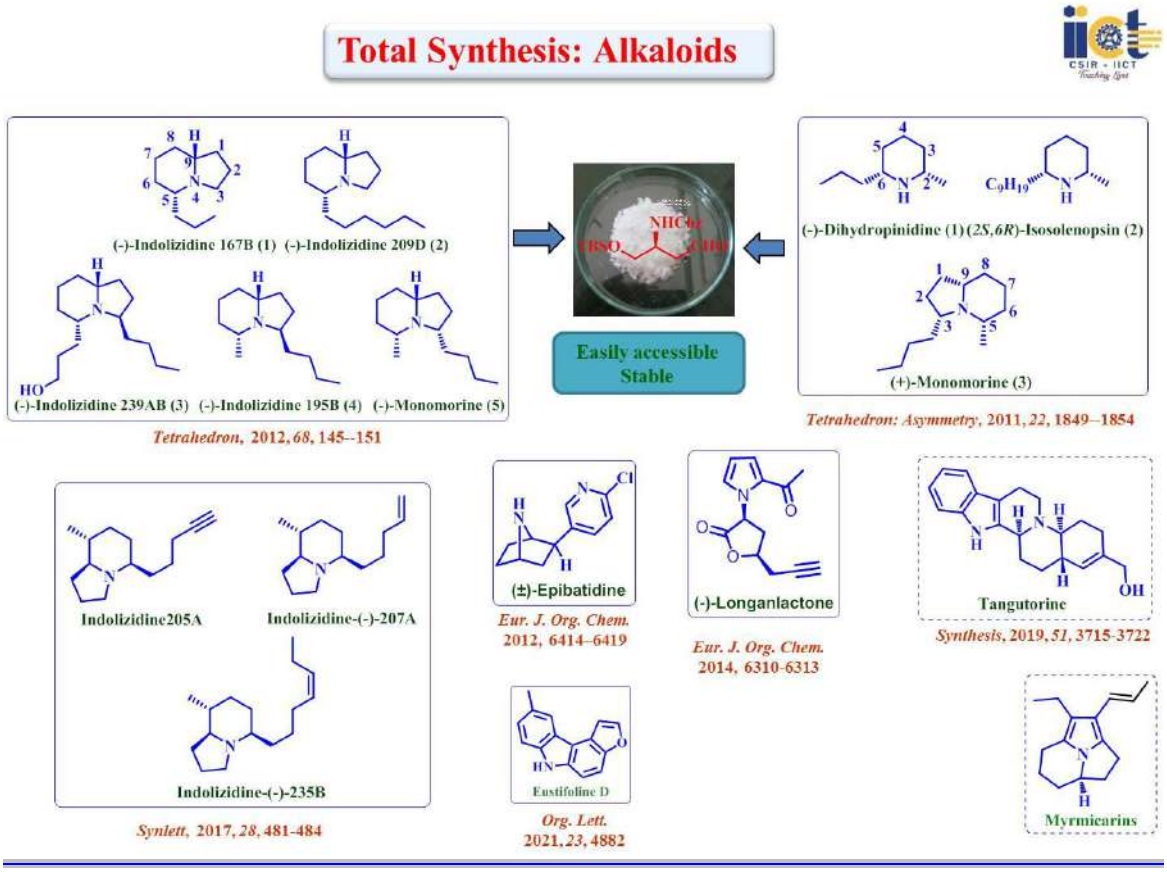


Figure 8: Representative structures of alkaloid bio-active natural products

TOWARDS MEDICINAL CHEMISTRY:

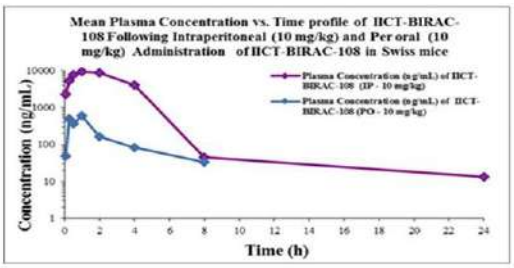
The above mentioned basic research work of Dr. Reddy has been converted to medicinal chemistry research projects. The new molecular entities obtained from the developed methodologies were screened for their biological activity and found some of the molecules are active. From these results, new derivatives of the active molecules have been designed and synthesized for further screening to identify the lead/hit molecule. The methodologies developed by Dr. Reddy have found to be significant in generating the new molecular entities in the following therapeutic areas.

(a) **Anti-cancer agents**: C5-Alkylation of oxindoles method (*Org. Biomol. Chem.*, **2011,** 3940)) lead to synthesize novel C5, C6-Substituted Fused Oxindoles which showed the potent activity against various leukemic and breast cancer cell lines through tyrose kinase inhibition.

At present, pharmacokinetic and pharmacodynamic studies are under progress for these two molecules. **(patent filed: Application Number: 201611037409; US 2018/0127365 A1**)

(b) **HDAC-Inhibitors:** The methodology developed in our laboratory for the synthesis of oxindole derivatives provided an opportunity to find excellent selective HDAC-inhibitors (HDAC-6 & 8). Based on these results, a new project has been built as a team member in collaboration with GVK Bio Pvt. Ltd under BIRAC-CRS research scheme. Dr. Reddy has developed the key process to synthesize the library of molecules. This resulted in identification of one indole-sulphonamide and studied ADME and PK studies as well the efficacy on tumor model with positive results (**Figure 9).** Presently, this project is being continued as CSIR-Fast Track Translational Project (FTT) and he has successfully developed the novel compound with pico-molar activity (**IN201711042426, 2017**). Negotiations are in progress to our-license the molecule.

Profile of Lead compound IICT-108	
Scaffold	Sulfonamide
Mol_Wt	456
Clog P	4.413
HDAC_6_IC50_nM	539
HDAC_8_IC50_nM	27
Hela_IC50_uM	3.3
MCF-7_IC50_uM	3.1
DU-145_IC50_uM	1.3
SK-o-V3_uM	1.8
HLM_ % Rem @ 60 min	93.44
MLM_ % Rem @ 60 min	65.41
pION Solubility (µg/mL)	0.79
Thermodynamic Solubility (ug/mL)	0.18
PAMPA (P(10-6cm/s))	8.70 (Good)
%unbound_human PPB	1.18%



	IP	PO
Dose (mg/kg)	10.00	10.00
Cmax (ng/mL)	9476.55	609.96
Tmax (h)	1.00	1.00
t1/2 (h)	2.45	2.64
Vd_F (L/kg)	1.10	28.83
Cl_F (mL/min/kg)	5.17	125.98
AUC0-last (ng·h/mL)	32200.74	1197.41
AUC0-inf (ng·h/mL)	32248.20	1322.98
AUCExtra(%)	0.15	9.49
MRT0-last (h)	2.38	2.22
Rsq	0.9952	0.9918

Cytochrome P450 Inhibition using human liver microsomes

Compound	IC50 (µM)				
	1A2	2C9	2C19	2D6	3A4
IICT-108	>30	>30	>30	>30	2.88

HDAC selectivity

	HDAC1	HDAC2	HDAC3	HDAC10	HDAC11	HDAC6	HDAC8
	IC50, nM	IC50, nM	IC50, nM	IC50, nM	IC50, nM	IC50, nM	IC50, nM
BIRAC-108	177	822	2230	463	512	539	27

Figure 9: Biological profile of the lead compound (IICT-108)

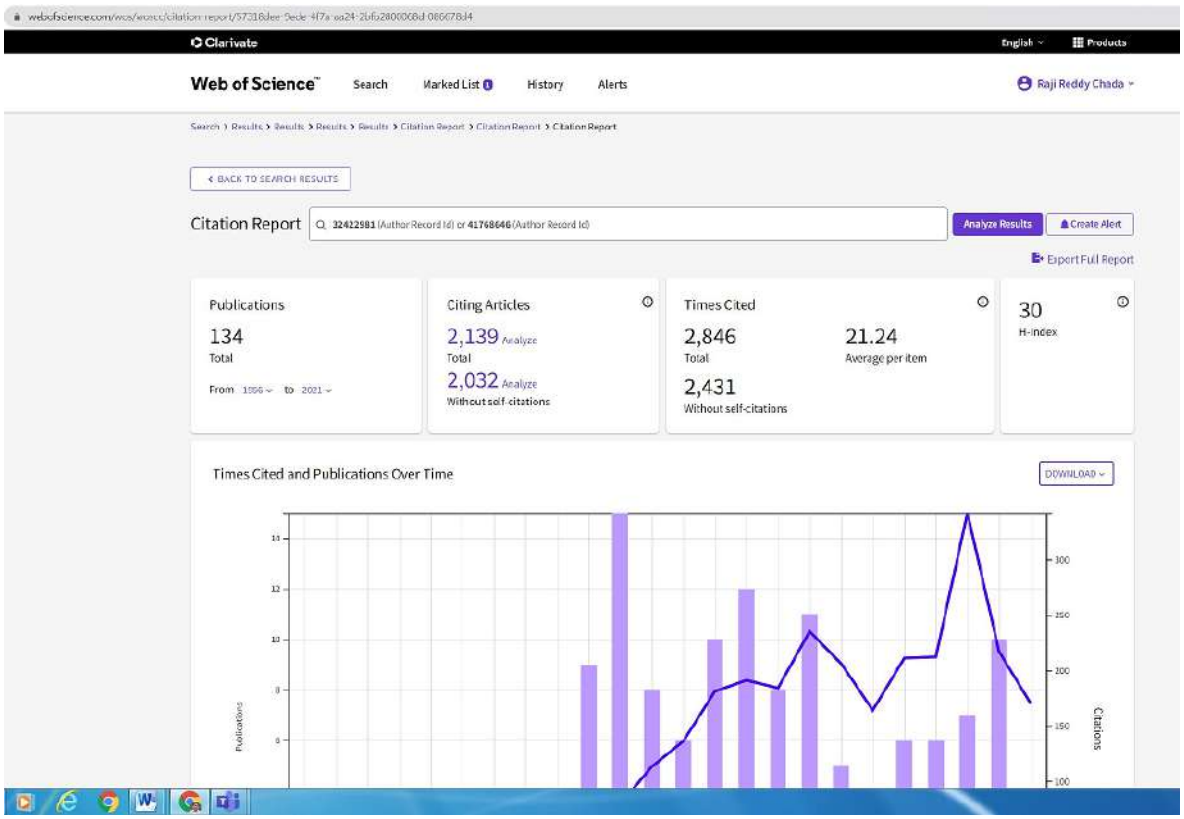
Further, these HDAC compounds are found be useful for Idiopathic pulmonary fibrosis. (Patent Application number as: **202011038497).** The generation of further data towards IND filing is in progress.

(c) **Neuroprotective and Neurotrophic agents:** The method developed by him, for the synthesis of pyrroles from MBH-Acetates of acetylenic aldehydes has provided a tool to generate various novel pyrrole structural motifs, which were found to show neuroprotective as well as neurotropic activity **(see Figure 3)**. One of the molecules in this series has been subjected to in vivo test using Zebrafish model for anti-anxiety properties.

(d) Dr. Reddy has accomplished the total synthesis of (-)-Longanlactone (traditionally used in Chinese medicines) in six steps and 31% overall yield from commercially available L-aspartic acid (from 375 mg, 200 mg of natural product). This gave an opportunity to study the biological activity profile of this natural product (not studied by isolation group), which shown excellent activity as Neurotrophic agent. Having good quantity in hand, several (-)-longanlactone analogues have been made and found to show neuroprotective and neurotropic activity.

ORIGINAL PUBLICATION:

Total Number of Papers published	**:**	**140 (List enclosed)**
Total Number of Patents	**:**	**10 (6-granted and 4-filed)**
Total Number of Citations	**:**	**2,846**
H-Index	**:**	**30**



CH. RAJI REDDY

Mail from Dr. V. Krishna Mohan, Vice President, Bharat Biotech Ltd - Process Adjuvant Molecule – COVAXIN®

BHARAT BIOTECH
Lead Innovation

To,
Sun Pharma Science Foundation
New Delhi, INDIA

Dear Sir,

Bharat Biotech India Ltd. (BBIL) is very happy to share with you the achievements of CSIR-IICT, particularly by Dr Ch Raji Reddy. BBIL has approached CSIR-IICT with a task to develop an efficient process for the synthesis of novel TLR7/8 agonist, which is the key molecule in COVAXIN, the vaccine manufactured by Bharat Biotech. A novel TLR7/8 against molecule has a complex structure and was acquired by BBIL from a US company (ViroVax, LLC, Lawrence, KS). The process shared by the BBIL was very tedious and had multiple steps requiring chromatographic purifications, including the final step purification by preparative HPLC. These limitations were acting as deterrents in large scale manufacture of the vaccine.

The project has been assigned to Dr. Raji Reddy, who played a key role in simplifying the manufacturing process, at every step of the process. The use of expensive reagents and catalysts was avoided in the new process and resulted in improved yield at each step, which made the process economically efficient. Importantly the process is chromatographic-free in all the stages and the final compound are now being carried out by crystallization.

The process developed has been transferred to three companies, *viz*., NSJ Prayog Life Sciences, LaxmiGenChem and SaiLife Sciences Ltd. Successful demonstration of the process has been carried out by him and these companies are producing the TLR7/8 agonist molecule in multiple kilogram scale on a regular basis. The TLR7/8 agonist molecule manufactured based on CSIR-IICT technology has become part of a few crores number of vaccine vials.

We congratulate the team of CSIR-IICT ably led by Dr S Chandrasekhar, in particular Dr. Raji Reddy as the project coordinator who has taken up the challenge to develop an efficient and affordable synthetic route for the manufacture of the TLR7/8 agonist molecule. We strongly recommend Dr. Raji Reddy for the ***SUN PHARMA Science Foundation Research Award***, as the process developed by his team helped in scaling up of vaccine production and played in important role in vaccination of millions of people across the globe.

We wish Dr. Ch. Raji Reddy all the best for his future endeavors.

With Regards

Dr. V. Krishna Mohan

Whole-Time Director

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T:+91 40 2348 0567 / 4645 4545 M:+91 99480 80567 F:+91 40 2348 0560
email: info@bharatbiotech.com www.bharatbiotech.com
CIN: U24230TG1996PLC023232

Letter from NSJ Prayog Life Sciences – Demonstration of Process Adjuvant Molecule – COVAXIN®

NSJ PRAYOG LIFE SCIENCES PVT. LTD.

CIN No. : U73200TG2018PTC123113

Date: 16th April, 2021

To Whomsoever It May Concern

NSJ Prayog Life Sciences, a company based in Hyderabad, has been working on the scale-up of the adjuvant molecule, based the request from Bharat Biotech International Ltd., using the process developed by CSIR-IICT. Dr. Ch. Raji Reddy, Project Leader has demonstrated this efficient process for manufacture of N-2 stage of the molecule and our company has successfully supplied 5 Kg and presently 7.5 Kg of the intermediate for further processing. The process could be scaled up from laboratory to pilot plant without any issues.

We sincerely thank Dr. Ch. Raji Reddy and his team at CSIR-IICT for developing a very simple, scalable and cost-effective process.

We wish him all the best for their future endeavors.

With Regards

Jaya Prakash Samala
Director
NSJ Prayog Life Sciences Pvt Ltd

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Process Transfer and Demonstration by Dr. Ch. Raji Reddy to NSJ Prayog Life Sciences

Letter from Laxmi GenChem Sciences Pvt Ltd – Demonstration of Process Adjuvant Molecule – COVAXIN®

LAXMI GENCHEM SCIENCES PVT LTD

Solutions for Healthier Life

Date: March 10, 2021

To Whomsoever It May Concern

I am very happy to share with you that, the initial request by Bharat Biotech to make 1 Kg of n-2 intermediate of agonist molecule has been fulfilled and delivered the compound with the required purity in the given timelines. This was successfully accomplished using process know-how developed by Dr. Ch. Raji Reddy and his team at CSIR-IICT. Our technical team could follow the given process easily to make the compound. The team has expressed their satisfaction on the process and they are ready to take up on multiple kilograms. With this success, Bharat Biotech gave another order to make 8 Kgs of this key intermediate and presently is being made at our facility. We are very much pleased to be connected with Dr. Ch. Raji Reddy at CSIR-IICT in this project, through Bharat Biotech.

We sincerely thank Dr. Ch. Raji Reddy for the support with an effective process and wish his team for success in future projects.

With Regards

(Jaganmohan)
CEO
Laxmi Genchem Sciences Pvt.Ltd.

Plot No. 90, 1st Floor, Aleap Industrial Estate, Pragathi Nagar, Kukatpally, Hyderabad - 500090. T.S. India.
Email : info@laxmigenchem.com, Phone : +91 9440 124136, +91 40 2988 8172, www.laxmigenchem.com

Letter from Cipla Ltd. for Favipiravir Process Transfer

Cipla

To

Dr S Chandrasekhar

Director

CSIR-Indian Institute of Chemical Technology

Hyderabad

Dear Dr Chandrasekhar,

I am happy to inform you that, the process know how developed by your team on Favipiravir, the important drug to treat the current pandemic(covid-19) is well received by our technical team. Also the demonstration batches product made by your team has matched all the requirements of purity. Our production team has expressed their utmost satisfaction on the process know -how which is currently produced in our manufacturing facility. As informed by our Chairman, Dr Y K Hamied, we are delighted to be associated with you on this important product to make it available to the needy.

Wishing your team all the best,

Purandare

Dr. S. Purandare

Senior Vice President

This work is fully Co-ordinated by Dr Raji Reddy as PI. This is the best technology done for Favipiravir.

डॉ. एस. चंद्रशेखर
Dr. S. Chandrasekhar
निदेशक / Director
सी.एस.आई.आर - भारतीय रासायनिक प्रौद्योगिकी संस्थान
CSIR-Indian Institute of Chemical Technology
हैदराबाद / Hyderabad-500 007, तेलंगाना / Telangana, भारत / India

Cipla Ltd. R & D Centre, LBS Marg, Vikhroli West, Mumbai - 400 083.
Phone (022) 2576 1800, 2575 6000

Cipla Ltd. Regd. Office Cipla House, Peninsula Business Park, Ganpatrao Kadam Marg, Lower Parel, Mumbai - 400 013
Phone +91 22 24826000 Fax +91 22 24826120 E-mail contactus@cipla.com Website www.cipla.com
Corporate Identity Number L24239MH1935PLC002380

Process Know-how transfer by Dr. Chada Raji Reddy to Dr. Manjinder Singh from Cipla Ltd at CSIR-IICT on 15th April, 2020

Photograph of the Tablet Cover with CSIR-IICT logo (Marketed by Cipla)

Mail from Cipla Ltd after the demonstration of process for Fragment of Eribulin on 26th June, 2018

Raji Reddy Ch <rajireddy@csiriict.in>

Reg - demonstration of process for compd 2B- Eribulin project

Dr. Srinivas V. Pullela/R&D/PTG <Srinivas.Pullela@cipla.com> Tue, Jun 26, 2018 at 9:31 AM
To: Raji Reddy Ch <rajireddy@csiriict.in>
Cc: "Dr. Vinod P Acharya/R&D/PTG" <Vinod.Acharya@cipla.com>, Subhash Ghosh <subhashbolorg3@gmail.com>, "Mayur C. Bhandari/R&D/PTG" <Mayur.Bhandari@cipla.com>, "Chandrasekhar Srivari (srivaric@iict.res.in)" <srivaric@iict.res.in>, M Singh/API-R&D/VKH R&D <MSingh@cipla.com>

Dear Dr. Reddy

Thank you very much for the successful demonstration on 5g. scale. Will be looking forward for the scale up.

Dear Vinod

Hope you are in receipt of the process write up for this stage. Please ask Mayur to go ahead and sign the required document

Regards

PV

Sent from my iPhone

On 26-Jun-2018, at 9:28 AM, Raji Reddy Ch <rajireddy@csiriict.in> wrote:

> Dear Vinod,
>
> Hope everything is fine at your end.
>
> Here, we have demonstrated the enzymatic resolution for compound 2B - Eribulin project to Mayur on 5 g scale successfully. As per our guidelines, both our scientist/chemist as well as Cipla chemist - Mayur have to sign on the lab note book as well as analytical data generated during the demonstration. I request you to inform Mayur accordingly to sign as desired.
>
> Next we are planning to repeat the same process on large scale.
>
> With Regards
> Raji Reddy
> ---
>
> On Fri, Jun 1, 2018 at 10:12 PM, Dr. Vinod P Acharya/R&D/PTG <Vinod.Acharya@cipla.com> wrote:
>> Dear Dr. Subhash,
>> There is a slight change. Mayur will be there on Monday for the enzyme trials
>> Regards
>> Vinod
>>
>> Sent from Samsung S8 plus
>> "Legally privileged confidential information and subject to "Disclaimer".

CSIR - Indian Institute of Chemical Technology
Tarnaka, Uppal Road, Hyderabad - 500 007
www.iictindia.org

Mail from Sr. General Manager, RLFC Ltd. Bangalore on Favipiravir Process Transfer

Email **rajireddy@iict.res.in**

RE: FAVIPIRAVIR API Tech transfer

From : bhaskar r <bhaskar.r@rlfinechem.com> Mon, Sep 28, 2020 02:20 PM

Subject : RE: FAVIPIRAVIR API Tech transfer 1 attachment

To : RajiReddy Chada <rajireddy@iict.res.in>, Shailaja D <sdonempudi@iict.res.in>

Cc : Director IICT <director@iict.res.in>, Mainkar Prathama S <prathama@iict.res.in>, Bathula BathulaSurendarReddy <bsreddy@iict.res.in>, Haridas Baburao Rode <haridas.rode@iict.res.in>, Rama Mohan S <rmohan@iict.res.in>, Shailaja D <sdonempudi@iict.res.in>

Dear Dr. RajiReddy,
We R L Fine Chem Pvt Ltd., would like to thank you and much appreciate you and your team for kind support and extended cooperation in transfer of "FAVIPIRAVIR" API technology. We are looking forward to receive many such tech transfer projects from IICT in future for mutual benefit of both the organizations.

Thank you Once again,

Warm Regards

Bhaskar R
Sr.GM - CQA
Tel : +91-80-42488999
Mobile: +91 7899945955
E-Mail : bhaskar.r@rlfinechem.com

R L Fine Chem Pvt. Ltd. | C-10, Ist Cross, KSSIDC Industrial Estate, Yelahanka New Town, Bangalore - 560 064, India
www.rlfinechem.com

Mail on process for Nicergoline from LifeCare Laboratories

Raji Reddy Ch <rajireddy@csiriict.in>

Nicergoline and Alpha Lipolic Acid

JS VARMA <varmajs@clavita.com> Mon, Sep 6, 2021 at 4:29 PM
To: rajireddy@csiriict.in
Cc: akhil A <akhil@lifecarelabs.com>

Dear Dr. Raji Reddy garu

Greetings !!!

It was a pleasure meeting on Saturday and we are happy to associate with you.

1) We will wait for your advice on Nicergoline information.

2) Please study to develop " LYSERGOL" either Synthetic or Fermentation process. Then only the product Nicergoline is feasible.

By the way, We are also interested in " Alpha LIPOIC ACID". Can you please share some data like Raw material list and we can
calculate costs. Please advise the number of steps.

Best Regards

J.S.Varma
Director
102, Doyen Chambers
Behind Saradhi Studio, Ameerpet,
Hyderabad - 500 073, T.S India
Phone No's : + 91 40 23750124/23750123
Fax No. : + 91 40 23746024
Email : varmajs@clavita.com
Web : www.clavita.com

CLAVITA
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Supporting Letter - from the Chairman, Research Council of CSIR-IICT

Sun Pharmaceutical Industries Ltd.
Tandalja, Vadodara - 390 020, INDIA.
Tel. : 91-265-6615500/6615600/6615700
Fax : 91-265-2354897
CIN : L24230GJ1993PLC019050

Date: 16th September, 2021

To Whomsoever It May Concern

I am writing this letter of recommendation about Dr. Chada Raji Reddy, in support of his nomination for OPPI Scientist Award in Pharmaceutical Sciences. I have known Dr. Chada Raji Reddy since last four years as a senior principal scientist in CSIR-IICT, participating in the institute Research Council meetings. Wherein, I am one of the Research Council Chair/member of the institute. Dr. Reddy was actively presenting his research work in the meetings having clarity of the institutes objectives and goals. I am monitoring the contributions of his team in the project "Innovative Processes & Technologies [INPROTICS-Pharma] for Indian Pharmaceutical Sector Industries are commendable, which are helpful to the pharmaceutical Industries. The research/technologies emerged out of his team was with high quality and keeping with customer necessities, cost, simplified process and environmental benign strategies.

Last year, I had an opportunity as a Research Council Chair of CSRIR-IICT to mentor one of project towards COVID 19 treatment, wherein Dr. Reddy showed excellent commitment to complete the development of a cost-effective process for Favipiravir (Patent: 202011024682) within short period of four weeks and also transferred to Cipla Ltd and presently it is commercialized in the name of Ciplenza in to the market.

In addition, he has played a key role in development of a novel and scalable process for TLR 7/8 agonist molecule (IMDG), used as an adjuvant in COVAXIN® (COVID-19 vaccine) and transferred to Bharat Biotech Int. Ltd. and being produced in kilograms scale. BBIL has launched the vaccine, in COVAXIN® in the market.

Recently, Dr. Raji Reddy took guidance on the process development of 2-deoxy glucose (2-DG), which he has executed in short period and transferred to multiple companies. In 2019, another process development project for (*S*)-Pregabalin, which he executed in about 10 weeks at a laboratory scale, wherein the objective of cost, quality and process efficiency was met with a very good process yielding high productivity (Patent: IN 202011006475).

He is also excelling in fundamental research work, wherein he developed innovative approaches to access novel heterocycles including natural products, which is very much essential for drug discovery. His group has made a library of compounds, from which one of the motif, Indole sulphonamide–Selective HDAC Inhibitor (WO 2019/102488 A1), having potential for pulmonary fibrosis treatment with differentiation from the approved medicines. Presently various biological studies are ongoing for this molecule.

Apart from being very creative organic chemist, he is also good leader with lot of motivation, tenacity and enthusiasm to translate ideas on paper to successful results in the lab. His research work resulted in 140 publications and 10 patents, which is creditable in his age group of scientists. I strongly recommend his candidature without any reservation for the prestigious **SUN PHARMA Research Award**. He deserves all the encouragement.

Please feel free to contact me for additional information, if required.

Yours sincerely

T. Rajamannar