Special Evening Lecture

57th Annual Convention of Chemists (ACC) - Indian Chemical Society (ICS)

Recent Trends in Chemical Sciences (RTCS 2020)

Fascinating Excursions into Entrepreneurial Chemistry: An Insider's Perspective

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We will discuss and exemplify some interesting contributions made by our groups to discovering new chemical entities. Process Chemistry / Route Selection are important activities in the path of a drug from mind to market. The medicinal chemistry routes for synthesis although amenable to analogue design are usually low yielding and are fraught with a plethora of intractable problems such as such as commercially unavailable reagents and intermediates, capricious and cryogenic reactions that preclude efficient scale up, tedious chromatography unfavorable atom economy and problems in waste disposal and management. Considerable research efforts have to be expended in developing novel, cost efficacious and scalable processes and seamlessly transferring these technologies to manufacturing operations. These principles will be demonstrated by our process development efforts on an anti-epileptic and an anti-asthma drug that have resulted in amelioration of many of these problems and removal of significant bottlenecks in the progress of a drug from conception to commercialization.

Several problems are currently associated with the use of biological systems in studying drug metabolism.

- In vitro studies produce very small quantities of the product. Primary metabolites are often hydrophilic and difficult to isolate.
- Animals studies necessitate the sacrifice of animals and are extremely expensive to conduct. Liver slice preparations are of variable potency; it is difficult to quantitate the precise stoichiometry of the oxidant.

- Many of the metabolites are not amenable to organic synthesis by conventional routes.

We present rare examples of porphyrin-mediated oxidations of sophisticated pharmaceutical entities. The reactions (mimics of cytochrome P-450) are generally applicable and have been used in our laboratories to achieve hydroxylation and N-demethylation on numerous other substrates. This approach affords and efficient method for the systematic preparation and identification of the entire spectrum of metabolites from a chosen drug.

We aim to reconfigure products into chemical hybrid "Molecular Legos" and to screen the deck of diverse compounds against targets. A significant disadvantage of natural products is the draconian organic synthesis/medicinal chemistry effort required for commercialization. In many cases, the availability of the natural-product compound is not sufficient for various biological assays, thereby limiting their exploration. We offer unique and elegant solutions to these twin challenges by bringing together structure guided drug design and hybrid molecule synthesis.

References and Notes:

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Bio-Sketch of Speaker

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Dr. Mukund Chorghade is President of Chorghade Enterprises and Chief Scientific Officer, THINQ Pharma/ THINQ Discovery, AGN Biofuels and Empiriko. He is also an adjunct research professor at Northeastern University and has appointments at Harvard and MIT. He provides synthetic chemistry and development expertise to pharmaceutical and biopharmaceutical companies. He also provides consultations on collaborations with academic, government and industrial laboratories. He advises technology-based companies on process re-engineering and project management of technology transfer; establishes strategic partnerships and conducts GLP/cGMP compliance training and implementation in chemical laboratories. He oversees projects in medicinal chemistry, chemical route selection, manufacturing and formulation of bulk actives to finished dosage forms.

Dr. Mukund Chorghade's fascination with both chemistry and the US started with an India-China border argument, a famine, a chemist, his father and a book. As Chorghade recalls, when he was nine years old, his father was stationed at Calcutta Airport as a Meteorologist working for the Government of India during a 1962 border conflict between India and China. American pilots flew in with arms deliveries to aid India's side of the border skirmish, and a young Chorghade sometimes accompanied his father to the airport at night. He got to talk to a few American pilots, who would give him candy and other small tokens, including books and a small chemistry set.

Dr. Chorghade earned his B. Sc. and M. Sc. degrees from the University of Poona, and a Ph. D. in organic chemistry at Georgetown University. He completed postdoctoral appointments at the University of Virginia and Harvard University, visiting scientist appointments at University of British Columbia, College de France / Universite' Louis Pasteur, Cambridge and Caltech and directed research groups at Dow Chemicals, Abbott Laboratories, CytoMed and Genzyme. A recipient of three "Scientist of the Year Awards", he is an elected Fellow of the ACS, AAAS and RSC and has been a featured speaker in several national and international symposia. He is active in ACS, AAAS, RSC, was NESACS and Princeton Section Chair and serves on numerous professional Scientific Advisory Boards and Committees.