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Hybridization strategies in the development of anti tubercular agents

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Molecular hybridization is a strategy of rational design of new ligands or prototypes based on the recognition of pharmacophoric sub-units in the molecular structure of two or more known bioactive derivatives. The adequate fusion of these sub-units, lead to the design of new hybrid architecture that maintain pre-selected characteristics of the original template. The natural product bioactives are essential sources for rational design and for hybridization. They offer promising and amazing chemical diversity thereby inspiring the development of, structurally diverse new molecules to play a major role in drug discovery. The promising natural anti-mycobacterials include carbazole alkaloids such as Clausine and Micromeline, isolated independently from several sources and dibenzofuran based on secondary metabolite of lichen Usnic acid isolated from *Cladonia substellata*, were shown to have moderate antitubercular activity. Modified natural product like synthetic analogues of dibenzofuran and carbazole exhibited significantly improved *in vitro* as well as *in vivo* antitubercular activity against *M.tuberculosis* H_{37}Rv. Structure activity relationship (SAR) studies direct that the presence of dibenzo*[b,d]*furan or carbazole moiety play a vital role on their pharmacological properties. On the other hand, 1,2,3-triazoles conjugated with a wide range of heterocyclic moieties exhibited potent antitubercular activity. We present here natural product integrated molecular hybrids and their *in vitro* antimycobacterial activity against *Mycobacterium tuberculosis* H37Rv.

Biography

KANTEVARI SRINIVAS obtained his Ph.D. degree (1996) from Department of Chemistry, Indian Institute of Technology (IIT), New Delhi. He was research associate (1996-97) at National Institute of Immunology (NII) New Delhi. Later he was a post-doctoral Fellow (2001-2003) with Prof. Graham Ellis-Davies at Department of Pharmacology and physiology, Drexel University College of Medicine, Philadelphia, USA and Research Associate (2006-2008) at Department of Neuroscience Mt Sinai School of Medicine, New York, USA. He has been associated with Indian Institute of Chemical Technology (IICT), Hyderabad since 1997 and presently he is Sr. scientist. His research interests are in the area of Fragment based, receptor targeted approaches for drug design and discovery and the development of new photolabile compounds to control cellular chemistry. Presently 7 students are working for Ph.D. and 4 students for Master's dissertation work. He has 56 Publications and 5 patents for his credit. He is an editorial board member for open Journal of catalysis, member, and editorial board of reviewers for ARKIVOC, and expert reviewer for various journals international reputation. He was also developed several processes for APIs and drug molecules of interest and involved in transferring the technologies.

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Stereoselective synthesis of biologically active azacyclic compounds

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Azacyclic ring system is a common structural feature present in many naturally occurring and biologically active molecules such as immunosuppressant FR901483, anticancer agent lepadiformine and antidiabetic agents polyhydroxy indolizidine & pyrrolizidine alkaloids. Alkyl substituted indolizidine and pyrrolizidine alkaloids (gephyrotoxins), isolated from skin secretion of poison dart frogs, are known to function as sodium channel activators, noncompetitive blockers of nicotinic channels and positive modulators of sodium channels. Recently, we have developed a novel and general method for the stereoselective construction of azacyclic ring systems based on epoxide-initiated cationic cyclization of azides. This methodology has been elegantly applied in the stereo- and enantioselective total synthesis of indolizidine and pyrrolizidine alkaloids. Moreover, the stereoselective construction of azapolycyclic ring systems bearing aza-quaternary center has been developed based on *domino* semipinacol-Schmidt reaction.

Biography

Baskaran received a Ph.D. degree in Chemistry from IIT Kanpur in 1991 and performed PDF studies at the University of Duesseldorf, Germany (AvH Fellow, 1991-93) and Harvard University, USA (1993-95). After a brief stint in Dr. Reddy's Research Foundation-Hyderabad as a Sr. Scientist, he started his academic carrier at IIT Madras in 1999 and promoted to Professor in 2006. He is a recipient of several awards, honours and Fellowships, notable among them are: AvH fellowship, CRSI Bronze Medal and National Representative for IUPAC. He has published more than fifty five papers in international journals and filed five patents in Indian and Abroad.

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