Research Projects in Progress

Enediyne chemistry has captured the imagination of the chemist and biologist throughout the world since the discovery of natural product enediynes such as calicheamicin, esperamicin, maduroptin, dynamicin and more recently uncialamycin. Some of the natural product enediynes are three orders of magnitude more potent than other anti-cancer drugs. The anti-cancer activity of these compounds is due to the presence of highly unsaturated 1,5-diyne-3-ene unit that undergoes cycloaromatization and generates benzene-1,4-diradical, which cleaves the DNA. In order to improve the biological activity of the enediynes, efforts are being made to synthesize analogous compounds with better efficacy. We have made a significant contribution in this area, and have shown first time that enediyne reactivity can be modulated by the judicious choice of the metals. Also first time we have shown that enediynes can have potential in the antimicrobial infections as well [***Bioorg. Med. Chem. Lett***. *17*, 3226-3230 (**2007**)]. Another area we worked during the last five years in the Ftase inhibitors, as a tool for the cancer treatment. Following project are underway at the moment at University of Delhi.

- **Synthesis and biological evaluation of tetraoxane based antimalarials**: Malarial has remained one of the deadly diseases which affects more than 300 million people worldwide. The problem is more acute as most of the drugs have developed resistance against Plasmodium falciparum, which is becomes lethal if not treated in time. Only artimisinin derivatives can be used for such the treatment of such infection. Low bioavailability and poor pharmacokinetic properties are limiting factor of these compounds. We are exploring possibility to synthesize tetraoxane based antimalarials, and have made significant progress in this direction [***Bioorg. Med. Chem. Lett***. *18*, 1446-1449 (**2008**)].

- **Enediyne synthesis and biological evaluations:** Enediynes are known for their DNA cleavage activity, but recently it has been observed that these compounds also exhibit topoisomerase inhibitory activity, and cytotoxicity against various cell lines.

- **Synthesis of phidolopin (a marine natural product):** Phidolopin is a marine natural product isolated in 1984. Over 70% of the marine natural product studied so far are known for their anticancer activity, but biological importance of phidolopin has not been explored, so we have started a project which deals with the synthesis and biological evaluation of of phidolopin analouges.

- **Synthesis and biological activity study of sintenin analogues:** Sintenin is a natural product exhibit potent cytotoxicity, and we are exploring the biological activity of sintenin analouges.

- **Synthesis of antimicrobial agents:** It is estimated that nosocomial infections leads to 90,000 deaths per year in the US, and 70% of these infections are caused by bacterial pathogens that have become resistant to one or more antibiotics. Drug

resistance of existing antimicrobial and particularly antibacterial agents is a worldwide problem and majority of such hospital-acquired infections are caused by Gram-positive pathogens. We have started a project that deals with the synthesis of antimicrobial agents, and have made significant progress [**Patent Application No: 1462/DEL/2008**] in this direction [IC_{50} = 0.03 to 52 ng/mL].

- **Synthetic methodology:** We are also developing synthetic methodologies of novel organic compounds which have biomedical applications [***J. Heterocylic Chem****. 45***, 737-739 **(2008)]**.