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Design and synthesis of gyrase and topoisomerase IV inhibitors

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Bacterial resistance to antibiotics has long been recognized, and it is today considered to be a serious worldwide health problem. As a result of resistance, some bacterial infections are either difficult to treat with antibiotics or even untreatable. This problem has become especially serious with the recent development of multiple drug resistance in certain strains of bacteria, such as *Streptococcus pneumoniae* (sp), mycobacterium tuberculosis, and enterococcus. As a result of the need to combat drug-resistant bacteria and the increasing failure of the available drugs, there has been a resurgent interest in discovering new antibiotics. One attractive strategy for developing new antibiotics is to inhibit DNA gyrase and topoisomerase IV, bacterial enzymes necessary for DNA replication, and therefore, necessary for bacterial cell growth and division. Type II topoisomerases catalyse the inter-conversion of DNA topoisomers by transporting one DNA segment through another bacteria encode two type II topoisomerase enzymes, DNA gyrase and DNA topoisomerase IV. DNA gyrase controls DNA supercoiling and relieves topological stress. Topoisomerase IV decatenates daughter chromosomes following replication and can also relax supercoiled DNA. Bacterial type II topoisomerases form a heterotetrameric complex composed of two subunits. DNA gyrase forms an A2B2 complex comprised of GyrA and GyrB, whereas topoisomerase IV forms a C2E2 complex comprised of ParC and ParE. As bacterial resistance to antibiotics has become an important public health problem, there is a continuing need to develop newer and more potent antibiotics. More particularly, there is a need for antibiotics that represent a new class of compounds not previously used to treat bacterial infection. Compounds that target the ATP binding sites in both the GyrB (gyrase) and parE (topoisomerase IV) subunits would be useful for treating various bacterial infections.

Biography

Janarthanan Thathan is doing his PhD in J S S College of Pharmacy, Ooty (a Constituent of J S S University, Mysore). He has 5 years of experience in pharmaceutical industry as a Quality Control Executive. He has a few publications in national and international journals. He has attended various industrial and academic training and workshop programs.

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