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## Molecular modeling studies on DNA topoisomerase I inhibitors

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DNA topoisomerases, which catalyze the interconversion of various topological states of DNA, were originally discovered to change the superhelical structure of closed circular DNAs. Depending on the nature of the reactants and reaction conditions, topoisomerases can catalyze DNA relaxation/supercoiling, catenation/decatenation and knotting/unknotting reactions. Based on their functional mechanisms, DNA topoisomerases have been classified into two types. Type I DNA topoisomerase breaks and rejoins only one of the two strands during catalysis, while type II DNA topoisomerase acts on both strands for each DNA strand-passing reaction and it requires ATP for full activity. The mechanisms of intereference with Topoisomerase activity are quite different and can be divided into two classes; Topoisomerase poisons and Topoisomerase catalytic inhibitors. Investigation of the inhibitory activity of eukaryotic Topoisomerases is widely used in anticancer drug development. In this study, molecular modeling studies such as pharmacophore analysis and molecular docking were realised using software Discovery Studio 3.5, because of the lead optimisation and generation of DNA Topoisomerase I inhibitory active heterocyclic compounds and the results were discussed.

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## Branched peptide/DOTAP hybrid systems are efficient antisense oligonucleotide transfection reagents in bacteria

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Antisense technology has been a promising strategy for combating infectious diseases caused by multi-drug resistant bacterial strains, but the poor cellular uptake and transfection efficiency of these "antisense antibiotics" is strangling the development of antisense RNA therapeutics. This study was aimed at evaluating the cellular uptake characteristics and transfection efficiency of antisense phosphorothioate oligodeoxyribonucleotides (PS-ODN) in bacterial cells mediated by branched peptide/DOTAP hybrid system. The size and surface morphology of peptide/DOTAP/ODN nanoparticle were determined by dynamic light scattering and transmission electron microscope. Then the characteristics of cellular uptake were studied by flow cytometry analysis, and antibacterial efficacy of peptide/DOTAP/ODN nanoparticle targeting *rpoD*, an RNA polymerase primary $\sigma^{70}$, was tested by analyzing the growth inhibition of targeted bacteria and by RT-PCR analysis of the target genes. And the results indicated that the size of the spherical nanoparticle obtained was about 120 nm with a zeta potential about -10 mV, and the encapsulation efficiency of PS-ODN was about 95%. The peptide/DOTAP/ODN nanoparticle could be efficiently uptaked by both Gram-positive bacteria and Gram-negative bacteria, and both drug-sensitive bacteria and drug-resistant bacteria, such as extended-spectrum β-lactamase-producing *Escherichia coli* (ESBLs-*E. coli*) and methicillin resistant *Staphylococcus aureus* (MRSA) in a time-independent manner. Interestingly, the uptake process was not altered by the incubation temperature. After being incubated with peptide/DOTAP/ODN, the growth of tested bacteria was significantly retarded and the transcription of *rpoD* was inhibited. Our research not only provided a basis for further studies on delivery systems for antisense antibiotics.

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