Seminar

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Institute for Plasma Research

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Title: Study of Drug-DNA interaction using Quantum Mechanics Tools

Speaker: Dr. Ruchi Mishra
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Date: 4th May 2023 (Thursday)

Time: 03:30 PM

Venue: Join the talk online:
https://meet.ipr.res.in/join/2874658798?be_auth=MTE3MTgz
(Conference ID: 2874658798; Password: 117183)

Abstract

Deoxyribonucleic acid (DNA) has a great biological significance. Transcription and replication are the vital processes essential for the survival of the living system. To design effective chemotherapeutic agents and better anticancer drugs, there is a need to have the detailed mechanistic insight on how they interact with DNA. Molecular docking and other molecular modelling techniques are well parameterized for protein-ligand and for the protein-protein interaction; but there is a lack of systematic parameterization involving nucleic acid ligand binding.

In the present study the mechanism of molecular interaction of different types of DNA binding small molecules (intercalators and minor groove binders) and stability of the complexes using available molecular modelling methods such as Molecular Docking, Molecular Dynamics Simulation, Quantum-mechanics/molecular-mechanics (QM/MM) etc. has been investigated. Molecular Docking predicts the mode of binding of drug molecule to the DNA. On the other hand, Molecular Dynamics simulations assure the stability of the drug-DNA complex. QM/MM approach is used for the modelling of reaction mechanism in biomolecular systems which are not understood so far. This study confirms that the intercalators and minor groove binders bind to DNA through different types of non-covalent interactions. Intercalators are stabilized by π-π stacking between the drug and DNA bases while, DNA minor groove binders form hydrogen bonds between the drug and DNA bases end terminal. DNA recognition by drug molecules does not directly depend on the bases sequence but also depends on the sequence dependent conformation or DNA modifications and distortions. This study provides full understanding of drug-DNA interactions, sequence selectivity and sequence specificity. The array of available computational approaches and molecular modelling methods are being used for complementing the experimental efforts to improve the existing drugs and in designing novel drug candidates which can act as good DNA inhibitors.