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Platform: Nano/Energy

RCMS Research Center for Materials Science, Nagoya University

Theoretical Chemistry Colloquium

October 28, 2013 (Mon), 16:00-17:00

RCMS, 2nd floor, Chemistry Gallery

Computer aided drug design

of anti-tubercular agents and anti-cancer agents

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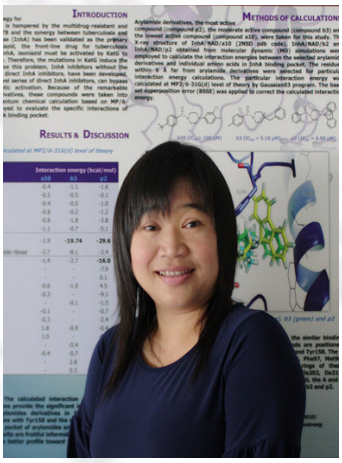

Abstract: Molecular modeling and computer aided drug design approaches have been employed to elucidate the beneficial information at molecular level for developing new and more potent anti-TB agents and anti-cancer agents. The Enoyl-ACP reductase (InhA) of *Mycobacterium* tuberculosis has been shown to be the primary target of the frontline drug isoniazid (INH). However, INH must be first activated by katG gene, mutations in which have mediated resistance to INH. Arylamides have been identified as potentially direct InhA inhibitors which overcome the drug-resistance problem of isoniazid. However, arylamide properties are not yet optimal against *M. tuberculosis*. To achieve the structural basis to improve antimycobacterial activity, QSAR and molecular dynamics (MD) simulations were applied. In an attempt to develop more effective anti-cancer agents with showing lower organ toxicity, azanaphthoquinone annelated pyrrole core structures have been developed. With the remarkable antiproliferative activities of the novel azanaphthoquinone annelated pyrrole derivatives, a structurally novel scaffold of these compounds is appropriated for further development of the cancer chemotherapy. Therefore, QSAR studies were applied on azanaphthoquinone derivatives to evaluate their key structural features. To model the binding mode of these compounds in the DNA duplex, MD simulations were carried out. Consequently, the integrated results from structure-based, ligand-based design approaches provide the useful structural information which is powerful guideline for designing and discovering novel and more potentially effective antitubercular agents and anti-cancer compunds.

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