The Role of Computational Chemistry in Drug Discovery

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ABSTRACT

Natural products are secondary metabolites produced and utilized by organisms for defending or adapting purposes. These molecules undergo evolutionary constraint, hence incur a great degree of selectivity, based on the origin, habitat, and the particular challenges faced the specie. Despite recent advancements in synthetic medicinal chemistry, these natural products remain a significant source of drug-like compounds or the leads thereof. The natural products present a huge potential for the development of leads against a number of therapeutic targets, the data suggest only a fraction of their potential has been explored and consequently documented. Herein, we aim to utilize a comprehensive database of the Natural products and to explore their therapeutic potential against the Neglected tropical diseases, by utilizing advance Computational Chemistry techniques. In silico drug design efforts exploring the therapeutic potential of natural products will be discussed along with some successful example from our ongoing projects.

One of the examples is from the tradition of Natural product uses that has been deep-rooted in all over the world, the work we are presenting here are the natural product examples from African and Arabian Peninsula for centuries. Its and amphetamine-like psycho-stimulant or euphoric effect, Catha edulis, a narcotic drug has been used by millions in Somalia, Ethiopia, Saudi Arabia and Yemen. The long-term use of this and other kind of these plants can induce many major health outcomes, which may be serious and irreversible.

Objective: Prolongeduse of Catha edulis constituents has been associated with different types of cancers such as prostatic, breast and ovarian cancer. However, it has been very difficult to identify the molecular targets involved in Catha edulis,and its constituents by in vitro/in vivo experimental tools.

Method: In silico toolswere usedto predict potential targets involved in the carcinogenesis. Pass on-line prediction server was used for the prediction of a potential molecular target against Catha edulis constituents. Molecular Dynamics simulation and MM-GBSA calculation of the predicted target were carried out.

Results: The results ofMolecular Dynamics simulation and MM-GBSA calculationrevealed that among Catha edulis constituents, β-Sitosterol showed a high binding affinity towards 17β-HSD5. On the other hand, this study highlights for the first time some new interactions, which were observed in the case of cathine, cathinone and nerol during the simulation.

Conclusion: In silicomolecular dynamic simulation tools were used for the first time to investigate the molecular mechanism of widely used leaves of psychoactive (Catha edulis) constituent, extensively used all over the world. The present study provides deep insight to understand the effect of its constituents involved in the impairment of the reproductive system and its binding to 17β-HSD5. ADMET profiling also suggested that few constituents do not fulfill the requirements of the Lipinski rule of five i.e. poor absorption and blood-brain barrier impermeability

Keywords: Catha edulis, computational chemistry, *Insilico*, natural products

REFERENCES

1. Saeed, Maria, et al. "Exploring the Molecular Mechanisms of 17β-HSD5-induced Carcinogenicity of Cathaedulis via Molecular Modeling Approach." Medicinal Chemistry 17.4 (2021): 418-428.