

CURRENT RESEARCH TOPICS IN PHARMACY: *In silico* Approaches for Drug Design and Discovery

January 25th, 2023 13.00 PM
ISTANBUL

FOR REGISTRATION:



First Session- Moderator: Esra TATAR 13.00-14.30 PM

Welcome- Prof. Mesut SANCAR

In silico pharmacokinetics prediction of major coumarins present in *Aegle marmelos* L – Assist. Prof. Sneha Agrawal
Bharati Vidyapeeth's College of Pharmacy, Maharashtra, India

Pharmacokinetics evaluation with SimCYP program - Assoc.Prof.Enkelejda Goci
Aldent University, Tirana, Albania

A new approach in drug discovery: Network pharmacology - Dr. Yağmur Diker
Hacettepe University, Ankara, Turkey

Second Session- Moderator: Esra TATAR 15.00-16.30 PM

Computational identification of novel targets for drug candidate compounds - Assoc.Prof.Ceren Sucularlı
Hacettepe University, Ankara, Turkey

Designing novel mitochondrial fission inhibitors targeting Drp1-GTPase interaction using computational methods - Dr.Sefer Baday
Istanbul Technical University, Istanbul, Turkey

Artificial Intelligence: A member of drug discovery team – Assoc.Prof.Somaieh Soltani
Tabriz University of Medical Sciences, Tabriz, Iran

Discovery of novel Hepatitis C NS5B polymerase Inhibitors by *in silico* approaches - Dr. Berin Karaman Mayack
University of California Davis, Davis, USA

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COMPUTATIONAL IDENTIFICATION OF NOVEL TARGETS FOR DRUG CANDIDATE COMPOUNDS

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Computational applications have been used in several steps in research of identifying new drug candidates, such as target discovery and prediction of drug-target interactions, and facilitate drug discovery and development [1, 2]. Interaction of proteins with drug-like molecules, due to folding and physical properties of protein and structure of drug-like molecules, with high affinity is named as druggability. Computational methods have also been used in prediction of druggability [3]. Molecular docking has been used to model the interaction of drug-like molecules and protein, therefore, this tool become an important method in drug discovery [4]. The druglikeness of compounds can be assessed by Lipinski's rule of five (RO5), that poor absorption is more probable when a compound has more than 5 H-bond donors, 10 H-bond acceptors, molecular weight higher than 500 and the calculated Log P is greater than 5 [5]. In a previous study, some new triazolothiadiazine derivatives have been synthesized, characterized and their anti-proliferative effects on liver cancer cells have been investigated [6]. Three triazolothiadiazine derivatives 1h, 3c and 3h have been selected in our study to identify potential action mechanisms and targets and to evaluate their likeliness as new drug candidates. Druglikeness of these compounds were assessed according to Lipinski's rule of five by using SwissADME [7]. According to our results, 1h, 3c and 3h, had molecular weight ranged in 406-449, H-bond donors 0, H-bond acceptors between 4-5 and therefore fulfilled the required criteria. Among three compounds, 1h had consensus Log P at 4.85, 3c had 5.87 and 3h had 5.25 [8]. Biological activity prediction of compounds was performed by using PASS online version 2.0 [9]. According to our results, three compounds might have various biological activities, such as being inhibitors of several phosphodiesterases (PDEs) and Dual specificity phosphatase 1 (DUSP1) inhibitor activity. Potential targets of 1h, 3c and 3h have been investigated using Swiss Target Prediction and BindingDB databases [10, 11]. According to Swiss Target Prediction

results, muscleblind-like proteins, FAD-linked sulfhydryl oxidase ALR, and several phosphodiesterases might be targets [8]. BindingDB predicted targets for 1h and 3h. Cholinesterases were predicted to be target for 1h and 3h while PDE4A, Carbonic anhydrases and Steroidogenic factor-1 were predicted as targets for only 1h [8]. In order to further investigate the interaction of these compounds with predicted targets, we selected three targets, PDE4A, ALR and DUSP1, which were emerged in both or either in activity and target prediction results, and performed molecular docking analysis using SwissDock [12, 13]. According to our results, 1h, 3c and 3h might interact with selected proteins [8]. Our results anticipated new activities and targets for the 1h, 3c and 3h. PDE4A, DUSP1 and ALR could be important targets for these compounds, since PDE4A has been suggested as a therapeutic target for anxiety and central nervous system disorders [14]. DUSP1, as an oncogene, involves in several cellular processes, such as cell proliferation, differentiation, cell cycle arrest and apoptosis, by its involvement in MAPK signaling [15]. ALR is another important target, inhibition of ALR caused apoptosis in rat hepatocytes and human derived glioma cells [16, 17].

Keywords: Target prediction, activity prediction, molecular docking

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