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

Pharmakokinetics 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 identificaion 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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ONLINE SYMPOSIUM

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DISCOVERY OF NOVEL HCV NS5B POLYMERASE INHIBITORS BY IN SILICO APPROACHES

Berin KARAMAN MAYACK[1,2,]

[1]Department of Pharmacology, School of Medicine, University of California Davis, Davis, CA 95616, USA
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Istanbul University, Istanbul, Türkiye

bkaramanmayack@ucdavis.edu, karaman.berin@gmail.com

Hepatitis C Virus (HCV) is a blood-borne RNA virus that causes inflammation of the liver that can lead to liver cirrhosis and hepatocellular carcinoma [1]. Non-structural protein 5B (NS5B) is an essential component of HCV for viral transcription and genome replication [2]. As there is no close mammalian analog for this enzyme, it has been the focus of many drug discovery projects [3]. In the present work, a combination of different computer-aided drug design approaches such as ensemble docking, binding free energy calculations, and quantitative structure-activity relationship (QSAR) model generation was applied to identify novel inhibitors of NS5B.

In the first step, all available protein structures in Protein Data Bank in a complex with thumb site 2 inhibitors were collected. Then, an automated KNIME [4] workflow was generated to select a few representative structures of the conformational changes in the binding pocket upon ligand binding. In total eight NS5B-inhibitor complexes were selected for further *in silico* work. Next, a virtual combinatorial library was obtained using the privileged substructures of known NS5B inhibitors. Different congeneric series of compounds including phenylalanine derivatives, thiophene-2-carboxylic acid derivatives, and anthranilic acid derivatives were used for the database formation. Upon ligand preparation, over 182.000 molecules were built. Consequently, known thumb site 2 inhibitors were docked with GLIDE-SP [5-7] and rescored with Prime MM-GBSA [8,9] protocol implemented in Schrödinger software to estimate the docking and binding free energy scores that will be used as a threshold for filtering the newly produced combinatorial library. In addition, categorical and numerical QSAR models were generated based on the known thumb site 2 inhibitors and used in the post-filtering step. Compounds that were predicted as actives will be visually analyzed and selected further for synthesis and biological evaluation.

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Keywords: HCV, NS5B, ensemble docking, MM-GBSA, QSAR

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