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Матеріали X науково-практичної конференції з міжнародною участю

НАУКОВО-ТЕХНІЧНИЙ ПРОГРЕС І ОПТИМІЗАЦІЯ ТЕХНОЛОГІЧНИХ ПРОЦЕСІВ СТВОРЕННЯ ЛІКАРСЬКИХ ПРЕПАРАТІВ

присвячена пам'яті завідувача кафедри управління та економіки фармації з технологією ліків, доктора фармацевтичних наук, професора Тараса Андрійовича Грошового

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Conclusions. The computational predictions and analyzes presented in the Poster presentation provide a comprehensive evaluation of paclobutrazol-derived compounds by combining rational design, computational predictions, synthesis, structural analysis, and pharmacokinetic evaluations. Notably, compound **26** emerges as an outstanding lead candidate, demonstrating a low toxicity profile, high binding affinity to therapeutically relevant protein targets, desirable pharmacokinetic properties, and compliance with drug-likeness criteria. The predicted activity suggests its potential application in the treatment of fungal and parasitic infections, migraine, inflammation or other GPCR-related disorders with further experimental validation and optimization.

References.

1. CropCSM: identifying safe and potent herbicides. https://biosig.lab.uq.edu.au/crop_csm.

2. pdCSM-GPCR: *In silico* prediction of GPCR ligands. https://biosig.lab.uq.edu.au/pdcsm_gpcr/.

3. MolPredictX. https://www.molpredictx.ufpb.br/home/.

4. CB-Dock2. Cavity detection guided blind docking. https://cadd.labshare.cn/cb-dock2/index.php.

5. pkCSM: predicting small-molecule pharmacokinetic properties using graph-based signatures. https://biosig.lab.uq.edu.au/pkcsm/.

DRUG-LIKENESS OF NOVEL HETARYL/CYCLOALKYL/SPIRO [1,2,4]TRIAZOLO[1,5-c]QUINAZOLINE CARBOXYLIC ACIDS' SALTS

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Introduction. There are known various websites, that offer tools for predicting properties, analyzing structures, and evaluating the potential biological activity of small molecules, like SwissADME [1], OCHEM [2], tox21 [3], etc. They're commonly used in drug discovery, toxicology research, and other fields of chemistry and biology. Among these, ADMETlab 3.0 [4] is a notable comprehensive platform for predicting ADMET (Absorption, Distribution, Metabolism, Excretion, Toxicity) properties. It features improved training data, robust model frameworks, specific functionalities, and uncertainty assessments, significantly aiding in accelerating drug development.

The aim of the work. To predict drug-likeness properties of novel compounds.

Materials and Methods. ADMETLab3 [4] was used for predicting ADMET properties of 2-(hetaryl/cycloalkyl)-[1,2,4]triazolo[1,5-*c*]quinazolin-5-yl carboxylic acids' salts and sodium 7-oxo-2-(pyridin-(2/3/4)-yl/cyclohexyl)-6,7-dihydro-pyrrolo[1,2-*a*][1,2,4]triazolo[1,5-*c*]quinazoline-4a(5*H*)-carboxylates (Fig.).

Results: All substances fall within the specified bounds for most parameters (Fig.), neither clustering at the extremes nor exceeding the limits: all have favorable values for criteria like TPSA and number of rotatable bonds; have reasonable numbers of rings, heteroatoms, and rigid bonds, which are additional factors often considered in drug-likeness assessments. For LogD, some substances are slightly below the lower bound of 1, but this is not necessarily problematic. Also, it's worth noting that all substances have a formal charge of -1, which may affect their behavior in biological systems, but isn't uncommon for drug molecules, and above the lower bound of -4.

Conclusions. Based on these physicochemical properties, all of these substances exhibit favorable drug-like properties and can be considered as promising candidates for further drug

development research. However, it is important to note that although these properties are satisfactory, they do not guarantee efficacy or safety, which must be determined through further toxicological and biological studies.

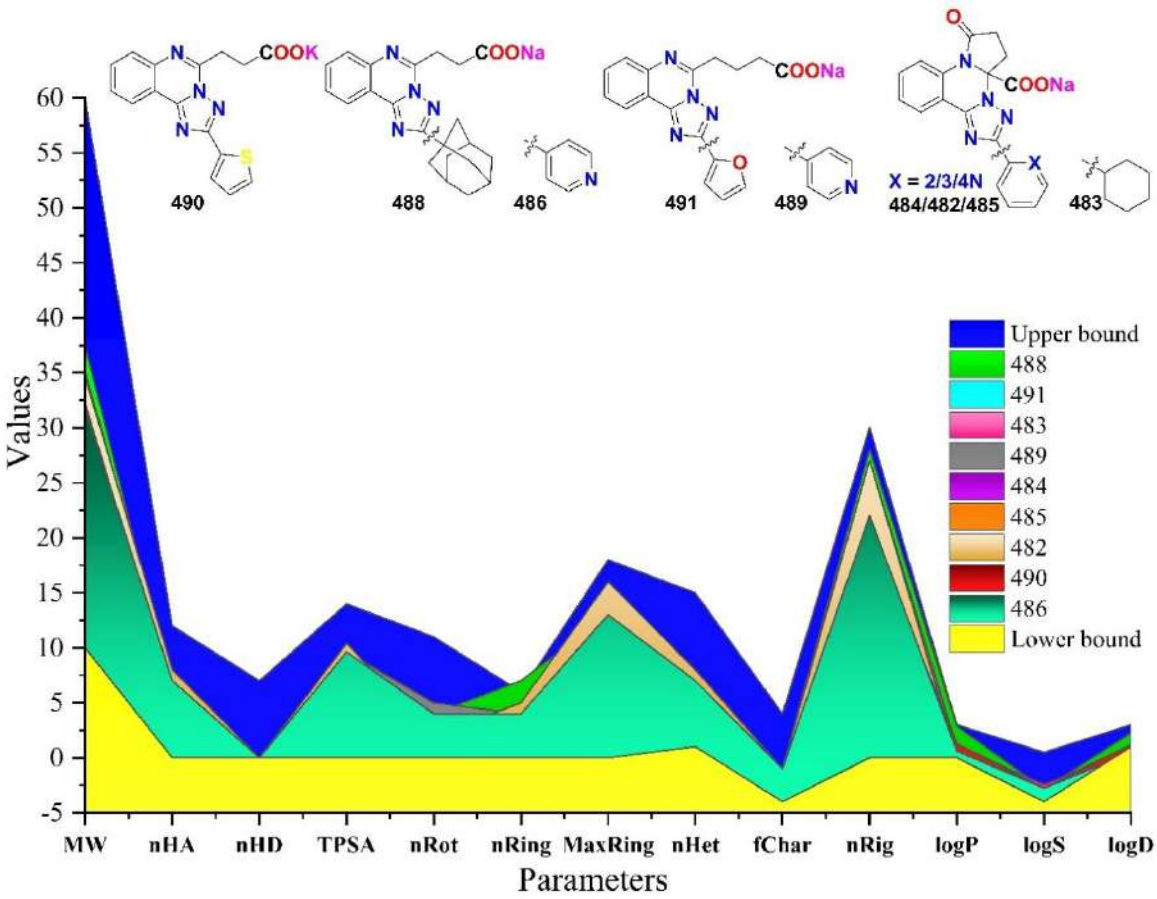

Figure. Molecular structures, and ADMETLab3 predictions of tested substances to be drug-like, where MW: molecular weight; nHA: number of hydrogen bond acceptors; nHD: number of hydrogen bond donors; TPSA: topological polar surface; nRot: number of rotatable bonds; nRing: number of rings; MaxRing: maximum ring size; nHet: number of heteroatoms; fChar: formal charge; nRig: number of rigid bonds; logP: partition coefficient; logS: aqueous solubility; and logD: distribution coefficient. MW and TPSA values were divided in 10 to fit into the figure.

References:

1. SwissADME. SwissADME. URL: http://www.swissadme.ch/ (date of access: 19.09.2024).

2. Online Chemical Modeling Environment. URL: https://ochem.eu/home/show.do (date of access: 19.09.2024).

3. DeepTox: Deep Learning for Toxicity Prediction. Institute of Bioinformatics. URL: http://bioinf.jku.at/research/DeepTox/tox21.html (date of access: 19.09.2024).

4. ADMETlab 3.0 https://admetlab3.scbdd.com/server/evaluationCal (date of access: 18.09.2024).