МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
ЗАПОРІЗЬКИЙ ДЕРЖАВНИЙ МЕДИКО-ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ

МАТЕРІАЛИ

ВСЕУКРАЇНСЬКОЇ НАУКОВО- ПРАКТИЧНОЇ КОНФЕРЕНЦІЇ З МІЖНАРОДНОЮ УЧАСТЮ

«ЗАПОРІЗЬКИЙ ФАРМАЦЕВТИЧНИЙ ФОРУМ - 2024»

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Results. All substances were found to be safe for arrhythmia, cardiac failure, heart block, and hERG toxicity. Interesting, that the only substance without any cardiotoxicity appeared to be **158**, bearing CF_3 as R, when R^1 = Me, while its analogue **148** with R^1 = Ph was predicted to cause myocardial infarction (Fig. 1).

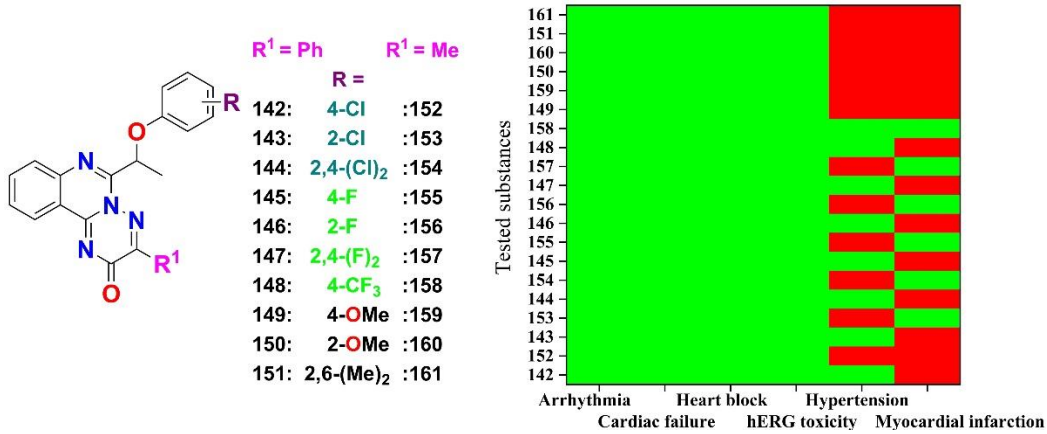

Fig. 1. The structural formulas of novel compounds and their predicted cardiotoxicity, where green indicates safe compounds and red indicates toxic ones.

Furthermore, it was found that all phenyl substituted series **142-151** would result in myocardial infarction, but their methylated series **152-161** would produce hypertension. Additionally, it appears that **152** and all methyl and methoxy derivatives (**149**–**151**, **159**–**161**) are the least tolerated, resulting in both forms of toxicity.

Conclusions. The results suggest that modifications to the R^1 and R^2 substituents can have a significant impact on the cardiotoxicity profile of these compounds. Substances might influence hypertension or myocardial infarction, so have several significant implications, and the following measures should be taken into consideration: further safety research, additional structure modifications, evaluation of drug delivery methods, dose adjustments, and individual risk assessment.

References:

1. Cardiac Manifestations of Coronavirus (COVID-19) - StatPearls - NCBI Bookshelf. *National Center for Biotechnology Information*. URL: https://www.ncbi.nlm.nih.gov/books/NBK556152 (date of access: 05.11.2024).

2. cardioToxCSM | Home. *Biosig | Home*. URL: https://biosig.lab.uq.edu.au/cardiotoxcsm (date of access: 05.11.2024).

PREDICTING CARDIOTOXICITY OF HETARYL/CYCLOALKYL/SPIRO [1,2,4]TRIAZOLO[1,5-*C*]QUINAZOLINE CARBOXYLIC ACIDS' SALTS BY MACHINE LEARNING

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Introduction. Machine learning (ML) to predict cardiotoxicity can be effectively used for the prediction, diagnosis, and treatment of cardiotoxicity [1]. ML models can integrate different types of data to provide a more comprehensive assessment of toxicity, than traditional methods.

Aim. To use ML tools to identify potentially cardiotoxic compounds among novel synthesized ones in the early stages of development, saving time and resources.

Materials and Methods. CardioToxCSM tool of Biosig Lab [2] was used to predict six types of cardiac toxicity outcomes, including arrhythmia, cardiac failure, heart block, hERG toxicity, hypertension, and myocardial infarction 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-4*a*(5*H*)-carboxylates (Fig. 1) It is a free web-based tool designed specifically for predicting cardiotoxicity of small molecules using machine learning approaches, which provides binary classification (cardiotoxic or non-cardiotoxic), and uses a centering support machine algorithm. The models presented robust performances with area under the receiver operating characteristic curves of up to 0.79 on 10-fold cross validation, consistent with metrics on blind tests.

Results. It was shown, that the majority of studies compounds are safe, except partially two, which have cycloalkyl substituents: adamantyl (488) and cyclohexyl (483), respectively (Fig. 1).

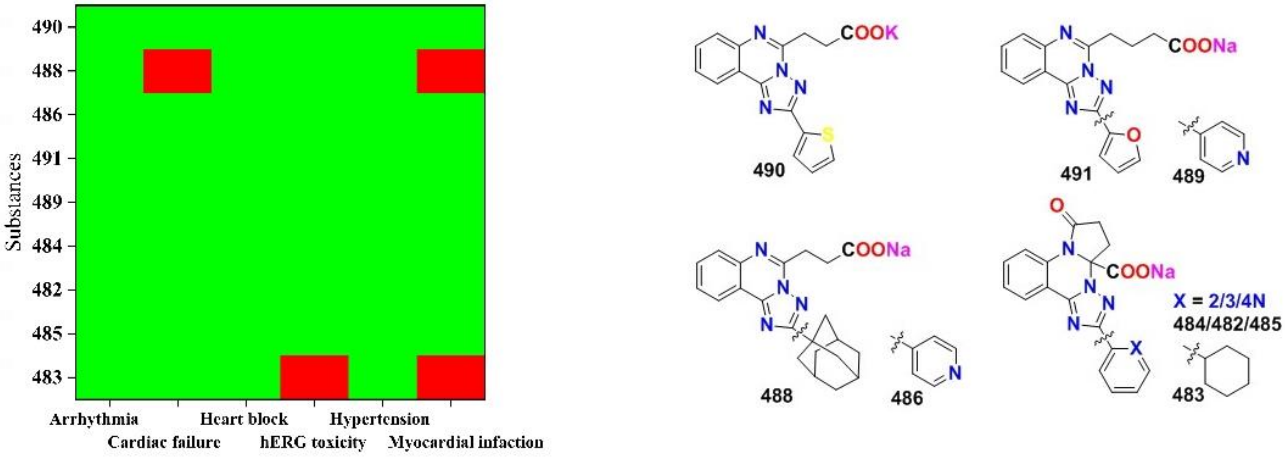

Fig. 1. Predicted tested substances' cardiotoxicity and their structural formulas.

Conclusions. CardioToxCSM is a useful tool for predicting cardiotoxicity, even considering its limitations of not taking into account the metabolic transformations of compounds, etc. The obtained results should be used in conjunction with other toxicity prediction tools as part of a larger evaluation approach, particularly for novel chemical compounds. Nevertheless, the shown safe cardiotoxic profile could lead to the development of safer drugs among the mentioned series of compounds.

References:

1. Zheng Y., Chen Z., Huang S., et al. Machine learning in cardio-oncology: new insights from an emerging discipline. *Rev Cardiovasc Med.* **2023**. Vol. 24, no.10, P. 296.

2. CardioToxCSM | Home [Electronic resource] // Biosig | Home. – Mode of access: https://biosig.lab.uq.edu.au/cardiotoxcsm/ (date of access: 01.11.2024).

MEDICAL, SOCIAL AND PHARMACEUTICAL ASPECTS OF THE MORBIDITY OF ALLERGIC RHINITIS

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A comprehensive analysis of domestic and foreign scientific literature on the problem under study has revealed a significant level of allergic diseases. According to WHO, currently about 5% of the adult population and 15% of children suffer from allergic diseases. Allergic rhinitis occupies one of the leading places in the structure of these diseases. Official statistics on the prevalence of allergic rhinitis, based on the rate of patients' applications, is dozens of times lower than the actual values and does not fully reflect the depth of the problem. The main method of conservative therapy of allergic rhinitis is drug therapy.

The growth of the medicines nomenclature significantly increases the possibility of choosing medicines taking into account the ability to pay and individual characteristics of each patient.