



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

МАТЕРІАЛИ

**ВСЕУКРАЇНСЬКОЇ НАУКОВО- ПРАКТИЧНОЇ
КОНФЕРЕНЦІЇ З МІЖНАРОДНОЮ УЧАСТЮ
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HIF-1 α /p300). Hence, by assessing how strongly different substances bind to these proteins, it's possible to identify the potential drug candidates, anticipate side effects, and gain insights into the molecular mechanisms of various diseases and biological processes.

So, Matthews correlation coefficients and inhibitory potency predictions (IC₅₀, 0.11-8.65 μ M) were calculated for 43 derivatives of triazolo[1,5-*c*]quinazoline: carboxylic acids and esters (Fig. 1).

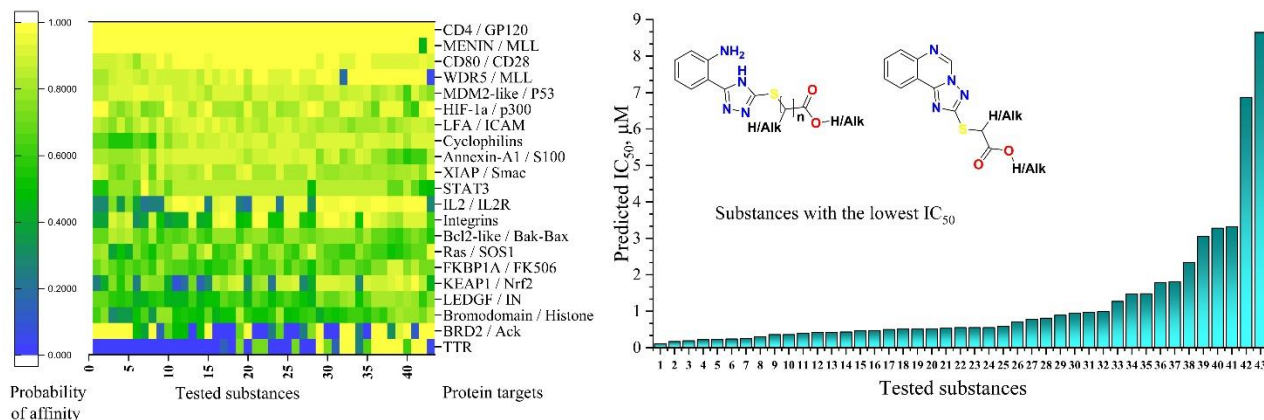


Fig. 1. Calculated Matthews correlation coefficients and average IC₅₀ (μ M) via pdCSM-PPI.

For some proteins, such as MENIN/MLL (involved in transcriptional regulation and leukemogenesis) and CD4/GP120 (their interaction is critical for HIV entry into cells), all tested substances consistently showed high affinity (MCC \geq 0.9), while to TTR (transport thyroid hormones and retinol) had the lowest values. Besides, variable affinity patterns were observed for proteins like IL2/IL2R (cytokine signaling important for T cell proliferation and immune response), KEAP1/Nrf2 (cellular response to oxidative stress), and BRD2/Ack (transcriptional regulation), indicating that certain substances may have selectivity towards them.

Thus, these findings highlight the importance of a broad affinity profile early in drug development to predict both expected and the possibility of off-target effects. The data also offer a strong foundation for further research into the molecular mechanisms of leading substance-protein interactions and their potential therapeutic applications.

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PREDICTING CARDIOTOXICITY OF 6-(1-(R-PHENOXY)ETHYL)-3-METHYL/PHENYL-2H-[1,2,4]TRIAZINO[2,3-C]QUINAZOLIN-2-ONES

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Introduction. Nowadays, predicting cardiotoxicity of novel synthesized compounds is crucial, especially in light of COVID-19's cardiovascular impacts: ischemic heart disease, heart failure, arrhythmias, myocarditis, etc. [1]. That's why there is a need to avoid additional cardiac stress from any medications.

Aim. To identify the potentially cardiotoxic novel synthesized compounds early, in order to reduce late-stage drug development failures, and to make the drug development process cost-effective.

Materials and Methods. The cardioToxCSM tool of Biosig Lab [2] was used to predict six types of cardiac toxicity of methyl, methoxy, chloro, fluoro, and trifluoromethyl derivatives of 6-(1-(R-phenoxy)ethyl)-3-methyl/phenyl-2H-[1,2,4]triazino[2,3-*c*]quinazolin-2-ones (Fig. 1).

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 CF₃ as R, when R¹ = Me, while its analogue **148** with R¹ = Ph was predicted to cause myocardial infarction (Fig. 1).

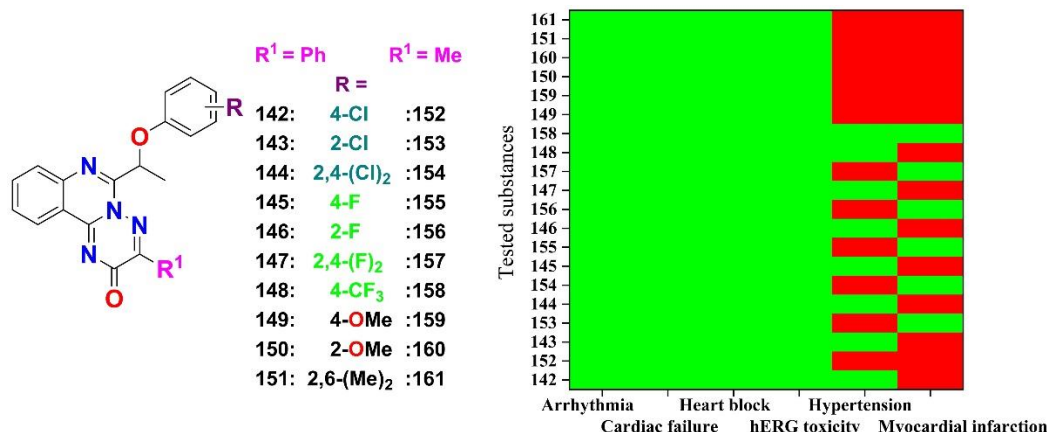


Fig. 1. The structural formulas of novel compounds and their predicted cardiotoxicity, where green indicates safe compounds and red indicates toxic ones.

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 R¹ and R² 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.

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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-

СИНТЕЗ ТА ДОСЛІДЖЕННЯ БІОЛОГІЧНИХ ВЛАСТИВОСТЕЙ 5-(2-БРОМ-5-МЕТОКСИФЕНІЛ)-4- <i>R</i> -1,2,4-ТРИАЗОЛ-3-ІОЛІВ, КИСЛОТ ТА ЇХ ЕСТЕРІВ.....	112
<i>М.П. Скорий, Р.О. Щербина</i>	
ДОСЛІДЖЕННЯ КОНСИСТЕНТНИХ ВЛАСТИВОСТЕЙ МАЗЕЙ З ЦИМІНАЛЕМ ДЛЯ ДЕРМАТОЛОГІЧНОЇ ПРАКТИКИ.....	113
<i>І.М. Скупий, В.В. Гладішев, Г.П. Лисянська, С.А. Гладішева</i>	
МАРКЕТИНГОВЕ ДОСЛІДЖЕННЯ УКРАЇНСЬКОГО РИНКУ АНТИГЕМОРАГІЧНИХ ЗАСОБІВ	114
<i>Г. П. Смойловська, Т. В. Хортецька</i>	
ЕЛЕКТРОННИЙ ДОКУМЕНТООБІГ У ФАРМАЦІЇ НА БАЗІ ХМАРНИХ СЕРВІСІВ	115
<i>Н.І. Строїтелева</i>	
РІВЕНЬ ПОІНФОРМОВАНОСТІ НАСЕЛЕННЯ ЩОДО НЕБЕЗПЕКИ КУРІННЯ	116
<i>Тежжіні Шаїма, П. Пономаренко, О. Кілеєва</i>	
ПЕРЕДУМОВИ УДОСКОНАЛЕННЯ ФАРМАЦЕВТИЧНОЇ ДОПОМОГИ ПРИ ТЕРАПІЇ НАБРЯКІВ СЕРЦЕВО-СУДИННОЇ ЕТІОЛОГІЇ У КОНТЕКСТІ БЕЗПЕКИ ПАЦІЄНТІВ.....	118
<i>Н.О. Ткаченко, М.О. Хоменчук</i>	
РОЗРОБКА ТА ОПТИМІЗАЦІЯ УМОВ ВЕРХ-МС ДЕТЕКТУВАННЯ НАТРІЙ 2-((4-АМІНО-5-(ТІОФЕН-2-ІЛМЕТИЛ)-4 <i>H</i> -1,2,4-ТРИАЗОЛ-3-ІЛ)ТІО)АЦЕТАТУ В КОМПЛЕКСІ З СУПУТНИМИ ДОМІШКАМИ	119
<i>Д.Л. Усенко, А.Г. Каплаушенко</i>	
ПОХІДНІ 5-(3-МЕТИЛКСАНТИН-7-ІЛ)-4-ФЕНІЛ-1,2,4-ТРИАЗОЛ-3-ІОЛУ ЯК ПЕРСПЕКТИВНЕ ДЖЕРЕЛО БІОЛОГІЧНО АКТИВНИХ РЕЧОВИН.....	120
<i>А.С. Фоцан, А.С. Гоцуля</i>	
ПРЕДСТАВНИКИ РОДУ ЛОФАНТ ПЕРСПЕКТИВНІ ДЖЕРЕЛА ЛІКАРСЬКОЇ РОСЛИННОЇ СИРОВИНИ	121
<i>О.П. Хворост, К.С. Скребцова, Т.В. Опрошанська</i>	
ВЛАСНА ТОРГОВЕЛЬНА МАРКА ЯК ЧИННИК КОНКУРЕНТНОЇ ПЕРЕВАГИ АПТЕЧНОЇ МЕРЕЖІ.....	122
<i>О.О. Чемерис, О.Ю. Рогуля</i>	
МАРКЕТИНГОВІ ДОСЛІДЖЕННЯ ФАРМАЦЕВТИЧНОГО РИНКУ УКРАЇНИ НА НАЯВНІСТЬ ПРЕПАРАТІВ У ФОРМІ СУПОЗИТОРІЇВ ДЛЯ ЛІКУВАННЯ ПРОКТОЛОГІЧНИХ ЗАХВОРЮВАНЬ	123
<i>О. Шматенко, П. Сирота, А. Луцька, В. Томчук</i>	
ВСТАНОВЛЕННЯ СУЧАСНИХ ВИМОГ ЩОДО ЯКОСТІ ГОТОВОГО ЛІКАРСЬКОГО ЗАСОБУ З ДІЮЧОЮ РЕЧОВИНОЮ, ЯКА Є ОПТИЧНИМ ІЗОМЕРОМ КЕТОПРОФЕНУ	124
<i>Н. Шпиця, К. Виноградова</i>	
AFFINITY OF [1,2,4]TRIAZOLO[1,5- <i>c</i>]QUINAZOLINE'S CARBOXYLIC ACIDS AND ESTERS TO KEY REGULATORY PROTEINS INVOLVED IN CELLULAR SIGNALING, IMMUNE RESPONSE, AND GENE EXPRESSION	125
<i>L.M. Antypenko, O.M. Antypenko, T.S. Brytanova</i>	
PREDICTING CARDIOTOXICITY OF 6-(1-(<i>R</i> -PHENOXY)ETHYL)-3-METHYL/PHENYL-2 <i>H</i> - [1,2,4]TRIAZINO[2,3- <i>c</i>]QUINAZOLIN-2-ONES	126
<i>L.M. Antypenko, O.A. Hrytsak, K.P. Shabelnyk</i>	
PREDICTING CARDIOTOXICITY OF HETARYL/CYCLOALKYL/SPIRO [1,2,4]TRIAZOLO[1,5- <i>c</i>]QUINAZOLINE CARBOXYLIC ACIDS' SALTS BY MACHINE LEARNING	127
<i>L.M. Antypenko, K.P. Shabelnyk, O.A. Hrytsak</i>	
MEDICAL, SOCIAL AND PHARMACEUTICAL ASPECTS OF THE MORBIDITY OF ALLERGIC RHINITIS..	128
<i>S.O. Baryshpolets, T.S. Nehoda, Zh.M. Polova</i>	
WAYS TO OPTIMISE THE LIKELY COST OF THERAPY FOR PATIENTS WITH RHEUMATOID ARTHRITIS....	129
<i>K.Y. Berezniuk, T.S. Nehoda, Zh.M. Polova</i>	
SYNTHESIS AND MOLECULAR SCREENING OF <i>N</i> -((5-PHENYL-6,11-DIHYDRO-5 <i>H</i> - [1,2,4]TRIAZOLO[1',5':1,6]PYRIDO[3,4- <i>b</i>]INDOL-2-YL)METHYL)- <i>R</i> -AMIDE	130
<i>S.O. Fedotov, A.S. Gotsulia</i>	
INVESTIGATION ANTI-INFLAMMATORY ACTIVITY OF RED RASPBERRY LEAF EXTRACT ON CARRAGEENAN EDEMA MODEL.....	131
<i>D. Horopashna, L. Derymedvid, M. Komisarenko, O. Maslov</i>	