



Міністерство охорони здоров'я України
Міністерство освіти і науки України
Національний фармацевтичний університет
Кафедра фармацевтичної хімії
Кафедра загальної хімії

Міжнародна internet-конференція

Modern chemistry of medicines

25 вересня 2024 р.
м. Харків, Україна

Посвідчення Державної наукової
установи «Український інститут
науково-технічної експертизи та
інформації» № 263 від 16.04.2024 р.

Міністерство охорони здоров'я України
Міністерство освіти і науки України
Національний фармацевтичний університет
Кафедра фармацевтичної хімії
Кафедра загальної хімії

Ministry of health of Ukraine
Ministry of education and science of Ukraine
National university of pharmacy
Pharmaceutical chemistry department
General chemistry department

MODERN CHEMISTRY OF MEDICINES

Матеріали

**Міжнародної Internet-конференції «Modern chemistry of medicines»,
до 85-річчя з дня народження професора Петра Овксентійовича Безуглого
25 вересня 2024 року**

Materials

**of the International Internet Conference 'Modern chemistry of medicines',
dedicated to the 85th Anniversary of Professor Petro O. Bezuglyi
September 25, 2024**

**ХАРКІВ
KHARKIV
2024**



Molecular hybrids based on 2-(3-R-1,2,4-triazol-5-yl)anilines as potential chemotherapeutic agents

Kostiantyn Shabelnyk, Oleksii Antypenko¹, Oleksii Vosokoboinik², Serhiy Kovalenko³

¹ Zaporizhzhia State Medical and Pharmaceutical University, Zaporizhzhia, Ukraine

² National University «Zaporizhzhia Polytechnic», Zaporizhzhia, Ukraine

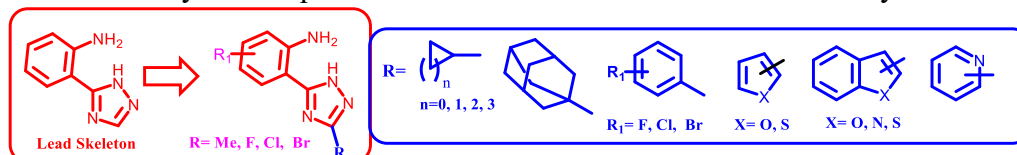
³ Oles Honchar Dnipro National University, Dnipro, Ukraine

*kovalenkoserhiy@gmail.com

Introduction. The complexity and diversity of antibiotic resistance mechanisms remains the main factor that encourages scientists to further search for the new chemotherapeutic agents. In most of cases, the design is aimed at modifying known drugs, new “small” molecules synthesis, hybrid molecules composing, polypeptides developing, preparation of complexes with transition metals, etc [1-3]. Thus, the development of synthesis methods and evaluation of the chemotherapeutic effect of hybrid molecules created by combining of 2-(3-R-1,2,4-triazol-5-yl)anilines with molecular fragments is an urgent problem of medical chemistry.

Materials and methods. Organic synthesis, spectral methods (HPLC-MS, ¹H and ¹³C NMR spectra, X-ray analysis), *in vitro* (microbiological screening, anticancer screening on 60 cancer cell lines according to NCI methodology) and *in silico* (ProTox-II, ADME analysis, SAR-, QSAR-, molecular docking) methods.

Results and discussion. The molecular docking study was performed for the combinatorial library of 2-(3-R-1,2,4-triazol-5-yl)anilines (Fig. 1) to estimate their affinity to the some enzymes (DNA gyrase (PDB ID; 2XCT); transmembrane receptor (PDB ID; 2IVU); epidermal growth factor receptor (PDB ID - 2ITY); ras-related protein Rab-9A (PDB ID: 1WMS), 50S ribosomal protein L19 (PDB ID: 6WQN), sterol 14-alpha demethylase (PDB ID: 5TZ1), etc.). The obtained satisfactory results served as a prerequisite for their synthesis. In this case, the target products were obtained by a "one-pot three-step" synthesis from 4-hydrazinoquinazoline or 2-aminobenzonitrile and carboxylic acid derivatives.



The *in vitro* studies confirmed the results of the docking and allowed us to identify highly active antitumor (GI₅₀ 3.8-7.0 μM), antimicrobial (MIC 5.2-62.4 μM) and antifungal (MIC 30.6-200 μM) agents. The ADME analysis and the created SAR and QSAR models showed the direction of further enhancement of the chemotherapeutic effect.

Conclusions. A strategy for the search for new hybrid molecules, namely insufficiently known [2-(3-R-1H-[1,2,4]-triazol-5-yl)]anilines, which provided the purposeful introduction of certain structural motifs into the desired target products to enhance chemotherapeutic action, has been developed and successfully implemented. Among the obtained compounds, high active antibacterial, antifungal and antitumor agents were identified, which confirms the reasonableness of further structural modification of this class of compounds.

References

1. Soltan O. M., Shoman M. E., Abdel-Aziz S. A., Narumi A., Konno H., Abdel-Aziz M. (2021). Molecular hybrids: A five-year survey on structures of multiple targeted hybrids of protein kinase inhibitors for cancer therapy. *European Journal of Medicinal Chemistry*, 225, 113768. <https://doi.org/10.1016/j.ejmech.2021.113768>.
2. Li Jie, Zhang Junwei (2022). The Antibacterial Activity of 1,2,3-triazole- and 1,2,4-Triazole-containing Hybrids against *Staphylococcus aureus*: An Updated Review (2020–Present). *Current Topics in Medicinal Chemistry*, 22(1): 41-63. <https://doi.org/10.2174/156802662166621111160332>.



Molecular hybrids based on 2-(3-R-1,2,4-triazol-5-yl)anilines as potential chemotherapeutic agents	42
Kostiantyn Shabelnyk, Oleksii Antypenko, Oleksii Vosokoboinik, Serhiy Kovalenko	
Preformulation studies on the development of a transdermal therapeutic system with Captopril.....	43
Tatyana Shyteyeva, Elena Bezchasnyuk, Oleg Kryskiv	
Assessment of total phenolic content and antioxidant activity of Staghorn sumac (<i>Rhus typhina</i> L.).....	44
Asta Špadienė	
New flavonoid glycoside from <i>Oxytropis Rosea</i>.....	45
Sh.A. Sulaymonov, B.J. Komilov, K.A. Eshbakova, Sh.V. Abdullayev	
Design of prototypes of nootropic drugs based on racetams and ampakines	46
Rustam Suleiman, Nataliia Kobzar, Vitaliy Yaremenko, Lina Perekhoda	
Synthesis of glutaric acid divinyl ester by the transvinylation method	47
Tursunov Sh.Sh., Parmanov A.B., Nurmanov S.E.	
High performance thin layer chromatography (HPTLC) assessment of <i>Epilobii herba</i>	48
Kateryna Uminska, Michal Korinek, Liudas Ivanauskas, Mohamed El-Shazly, Victoriya Georgiyants, Zigmantas Gudžinskas, Olha Mykhailenko	
Selection of optimal extraction conditions and phytochemical analysis of <i>Sorbus aucuparia</i> L. aqueous extracts.....	49
Augustė Morta Vaitkutė, Agnė Mazurkevičiūtė, Kristina Zymonė	
Electrospun fibres for drug delivery: Some recent advances	50
Gareth R. Williams	
Electrospun Nanofibers with Natural or Synthetic Compounds	51
G.R. Williams, O. Mykhailenko	
An alternative to chemical preparations containing salicylic acid made from natural products	52
Madinabonu Dilmurod Qizi Hamdamova	
Electrospun Nanofibres Loaded with <i>Lavandula angustifolia</i> Mill. Extract for Potential Use in Cutaneous Wound Healing	54
Nan Yang, G.R. Williams, and O. Mykhailenko	
The total phenolic content and antioxidant activity <i>in vitro</i> in linden honey from Lithuania.....	55
E. Zaksaitė, M. Liaudanskas, S. Trumbeckaitė	