ECMC 2023

Abstract

The comparative study of antimicrobial activity for 4-methylthieno[2,3-*d*]pyrimidine and their 4-oxo analogues †

Sergiy Vlasov [1,*], Hanna Severina [1], Olena Vlasova [1], Oleksandr Borysov [2,3], Pavlo Shynkarenko [3] and Victoriya Georgiyants [1]

[1] Department of Pharmaceutical Chemistry, National University of Pharmacy, 53 Pushkinska str., 61002 Kharkiv, Ukraine; sergiy.vlasov@gmail.com (S.V.); severina.ai@ukr.net (H.S.); olenavlasova94@gmail.com (O.V.); vgeor@ukr.net (V.G.);
[2] Institute of Organic Chemistry of the NASU, 5 Academician Kukhar str., 02660 Kyiv, Ukraine; boav.79@gmail.com (O.B.)
[3] Enamine Ltd., 78 Chervonotkatska str., 02094 Kyiv, Ukraine; shpe@ukr.net (P.Sh.)
* Correspondence: sergiy.vlasov@gmail.com; Tel.: +38(0572) 67-91-97
† Presented at the title, place, and date.

Abstract: The most effective small molecular inhibitors of TrmD with confirmed *in vivo* antibacterial activity contain either 3-indolyl of thieno[2,3-*d*]pyrimidine moiety. Recently we have reported the antimicrobial activity of the synthetically available 4-methylthieno[2,3-*d*]pyrimidine-6-carboxamides with benzyl substituents at the primary amide fragment as effective antimicrobials with the predicted affinity to TrmD isolated from *P. aeruginosa*. It was also reported that 4-oxothieno[2,3-*d*]pyrimidine derivatives were more effective TrmD inhibitors rather than their 4-alkoxy analogues with aromatic pyrimidine fragment. Therefore we have prepared *N*-(benzyl)-5-methyl-4-oxo-3,4-dihydrothieno[2,3-*d*]pyrimidine-6-carboxamides as the close analogues, which turned out to be active *in vitro* against the strains of *S. aureus* and *B. subtilis* and only moderately active against *P. aeruginosa* strain. Docking studies showed that despite the good values of the scoring functions, the conformational analysis of the ligands' poses in the active site revealed their ability for only partial inhibition of TrmD of *P. aeruginosa*. The study revealed better activity for *N*-benzyl-4,5-dimethylthieno[2,3-*d*]pyrimidine-6-carboxamide against *P. aeruginosa* in comparison to their 4-oxo analogues.

Keywords: thiophene, pyrimidine, TrmD, antibacterials

Citation: Vlasov, S.; Severina, H., Vlasova, O.; [1], Borysov, O.; Shynkarenko, P.; Georgiyants, V. The comparative study of antimicrobial activity for 4-methylthieno[2,3-*d*]pyrimidine and their 4-oxo analogues. *Med. Sci. Forum* **2023**, *2*, x. https://doi.org/10.3390/xxxxx

Academic Editor: Firstname Lastname

Published: date

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Copyright: © 2023 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

Supplementary Materials:

Author Contributions: For research articles with several authors, a short paragraph specifying their individual contributions must be provided. The following statements should be used "Con-ceptualization, S.V., O.V. and H.S., V.G., O.B.; methodology, O.V., S.V., H.S., V.G.; software, H.S.; validation, O.V., P.Sh., S.V. and H.S.; formal analysis, V.G.; investigation, O.V., H.S.; resources, V.G., S.V., O.B., H.S., P.Sh.; data curation, X.X.; writing—original draft preparation, O.V., S.V.; writing—review and editing, S.V., H.S.; visualization, O.V., H.S.; supervision, V.G., O.B.; project administration, H.S.; funding acquisition, H.S., O.B. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by by the Ministry of Health Care of Ukraine at the expense of the State Budget in the framework # 2301020 "Scientific and scientific-technical activity in the field of health protection" on the topic "Synthesis and study of new thienopyrimidines for the detection

of antimicrobial and related types of pharmacological activity" (State registration number: 0121U109472. Order of the Ministry of Health of Ukraine of November 17, 2020 № 2651.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: The data presented in this study are available within the article or in https://doi.org/10.7324/JAPS.2023.102631.

Acknowledgments: The authors acknowledge Enamine Ltd. for the measurement of ^{1}H, ^{13}C NMR and LCMS spectra of the obtained substances and Dr. T. P. Osolodchenko the Head of the Laboratory of Biochemistry of Microorganisms and Nutrient Media of the Mechnikov Institute of Microbiology for microbiological screening experiment.

Conflicts of Interest: The authors declare no conflict of interest.