Міжнародний
науково-практичний симпозіум

«100 РОКІВ УСПІХУ ТА ЯКОСТІ»,

присвячений 100-річчю кафедри
фармацевтичної хімії
Національного фармацевтичного
університету

MINISTRY OF HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY
PHARMACEUTICAL CHEMISTRY DEPARTMENT

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
НАЦІОНАЛЬНИЙ ФАРМАЦЕВТИЧНИЙ УНІВЕРСИТЕТ
КАФЕДРА ФАРМАЦЕВТИЧНОЇ ХІМІЇ

100 РОКІВ УСПІХУ ТА ЯКОСТІ

Матеріали міжнародного науково-практичного симпозіуму,
присвяченого 100-річчю кафедри фармацевтичної хімії
Національного фармацевтичного університету

100 YEARS OF SUCCESS AND QUALITY

Materials of the international scientific and practical symposium,
dedicated to the 100th anniversary of pharmaceutical chemistry
department of National University of Pharmacy

18 жовтня 2021 р.
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Електронне видання мережне

Реєстраційне посвідчення УКРІНТЕІ № 756 від 20.09.2021 р.

100 років успіху та якості : матеріали міжнар. наук.-практ.
С 81 симпозіуму, присвяченого 100-річчю кафедри фармацевтичної хімії Національного фармацевтичного університету (18 жовтня 2021 р., м. Харків) = 100 years of success and quality: materials of the international scientific and practical symposium, dedicated to the 100th anniversary of pharmaceutical chemistry department of National University of Pharmacy (October, 18, 2021, Kharkiv). – Електрон. дані. – Х.: НФаУ, 2021. – 89 с.

Збірка містить матеріали Міжнародного науково-практичного симпозіуму «100 років успіху та якості», присвяченого 100-річчю кафедри фармацевтичної хімії Національного фармацевтичного університету, які згруповано за напрямками, представленими науковцями в ході роботи симпозіуму. Розглянуто теоретичні та практичні аспекти цілеспрямованого конструювання та синтезу біологічно активних сполук; створення на лікарських субстанцій; стандартизації ліків, фармацевтичного аналізу субстанцій, фітопрепаратів та екстемпоральної рецептури.

Для широкого кола наукових і практичних працівників фармації та медицини.

The collection contains materials of the International Scientific and Practical Symposium «100 years of success and quality», dedicated to the 100th anniversary of Pharmaceutical Chemistry Department of National University of Pharmacy, which are grouped by the topics of the scientific reports presented during the symposium. It contains the theoretical and practical aspects of targeted design and synthesis of biologically active compounds, development on medicinal substances, standardization of drugs, pharmaceutical analysis of substances as well as plant drugs and individually prepared formulations.

The book is published for a wide number of scientific and practical workers in pharmacy and medicine.

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Search for antimicrobial agents with DHFR-inhibitory activity among diacylthiosemicarbazides

Olena Kholodniak, Sergiy Kovalenko

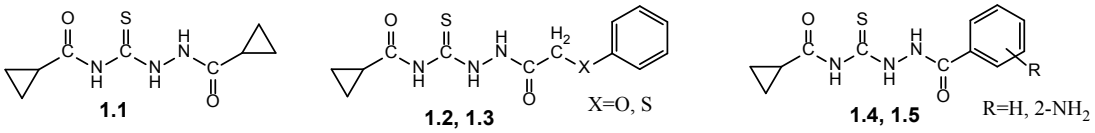
[1]*Department of Organic and Bioorganic Chemistry, Zaporizhzhia State Medical University, Mayakovsky Av. 26, 69035, Zaporizhzhia, Ukraine*

**Corresponding author e-mail: alena.holodniak@gmail.com*

Introduction. Antibacterial drugs (ABD) play an important role in the treatment of infectious diseases, but in the last decade growth in the number of dangerous and resistant to ABP microorganisms was observed. Causes of ABD resistance include irresponsible or excessive use of drugs in areas such as medicine, veterinary and agriculture. Moreover, the range of new antimicrobial drugs is constantly depleted, while the resistance of microorganisms to them increases. Thus, the topical issue of modern medical chemistry is the synthesis of new compounds with high antibacterial activity, different mechanisms of activity and low levels of toxicity. Of interest in this regard are the unknown disubstituted thiosemicarbazides, which inhibit dihydrofolate reductase (DHFR) and, as a result, have a diverse chemotherapeutic effect.

Materials and methods. Unknown diacylthiosemicarbazides (**1.1-1.5**, Fig. 1) were selected for the study, for which the ability to inhibit DHFR was evaluated and antimicrobial activity was studied according to the methods described in the literature [1, 2].

Results and discussion. Primary *in vitro* screening for the ability to inhibit DHFR showed that compounds (**1.1-1.5**) at a concentration of 100 μM inhibit the enzyme by 45.77-82.57%. In this case, higher rates of DHFR inhibition (82.57%) were characteristic of compound **1.1**, which competed in activity with methotrexate (82.57%).



It is important, that diacylthiosemicarbazides **1.1-1.5** have antibacterial activity against *St. aureus* (MIC 6.25-50.0 μg/ml, MBC 12.5-200.0 μg/ml), *E. coli* (MIC 3.125-12.5 μg/ml, MBC 6.25-50.0 μg/ml), *P. aeruginosa* significantly lower (MIC 50.0-100.00 μg/ml, MBC 100.0-200.0 μg/ml) and fungicidal action against *C. albicans* (MIC 25.0-100.00 μg/ml, MFC 25.0-100.0 μg/ml). It is necessary to highlight compound **1.1**, which in terms of antibacterial and fungicidal activity competes with nitrofural and ketoconazole. Therefore, it can be argued that the antibacterial activity of compounds **1.1-1.5** is probably related to their ability to inhibit DHFR. Inhibition of the catalytic activity of DHFR leads to disruption of dTMP biosynthesis in bacteria, which prevents genomic DNA replication and cell division. It is through this mechanism that the delay in cell division is realized and it is this mechanism that underlies the strategy of finding chemotherapeutic agents.

Conclusions. It was found that *N*-(2-R-hydrazine-1-carbonothioyl)cycloalkanecarboxamides are highly active antibacterial agents with DHFR-inhibitory activity, which justifies the continuation of systemic studies in this direction.

References

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ЗМІСТ
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