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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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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Azolo-(azino-)[c]quinazolines – a promising class of biologically active compounds

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Introduction. Despite the significant level of studies in the fields of quinazolines and their condensed derivatives chemistry and their biological properties evaluation, as well as successful promotion of quinazoline-containing active pharmaceutical ingredients as basis of anticancer medications aforementioned classes of compounds remain promising objects of studies that aimed to the search of novel bioactive agents. Moreover, substantiated design of research process and application of modern «drug-design» instruments in most of cases results the identification of «lead-compound» with determined type of biological activity.

Materials and methods. Reactions of [4+1]-, [4+2]- та [5+1]- cyclocondensation were used for synthesis of target compounds, purity and structure verification were conducted by appropriate physicochemical methods (UV-, IR-, ^{1}H, ^{13}C NMR-spectroscopy, elemental analysis, X-ray diffraction study, LC-MS). *In silico* studies included usage of such software as AutoDock Vina, AutoDockTools1.5.6, BIOVIADraw 2017R2, Chem3D, HyperChem 7.5, Discovery Studio Visualizer 2017/R2,. SwissADME. Appropriate methods of *in vitro* and *in vivo* studies were used for screening of biological activity of obtained compounds. ANOVA was used for statistical processing of obtained data.

Results and discussion. Azolo-(azino-)[*c*]quinazolines are original tricyclic heterocyclic compounds that in spite of rigid planar structure have wide possibilities of structural modification. The synthesis of abovementioned compounds in most of cases based on [4+1]-and [4+2]-cyclocondensations of substituted 4-hydrazinoquinazolines with bielectrophiles. On this stage the various substituents may be introduced as to the azole(azine) ring (depend on bielectrophile nature), so to the benzene ring (depend on of substituted 4-hydrazinoquinazoline nature). Further consequent hydrolytic cleavage of pyrimidine ring and [5+1]- cyclocondensation allow to conduct as partial saturation of the heterocyclic system so introducing of additional substituents to the reconstructed pyrimidine ring. Obtained by listed above synthetic procedures compounds were screened by *in silico* methods for substantiation of directions of following *in vitro* and *in vivo* studies. *In vitro* studies comprise the study of antiradical, antioxidant, DHFR-inhibiting and LOX-inhibiting activity. DHFR-inhibiting activity was studied for promising anticancer and antimicrobial agents, antiradical and antioxidant for promising anti-convulsant and anti-inflammatory agents, LOX-inhibiting activity for promising compounds with anti-inflammatory activity [1]. *In vivo* studies were aimed to identification of pharmacologically valuable compounds and evaluation of their toxicity. Compounds with anti-inflammatory, anti-convulsant, anti-cancer activity were developed and proposed for profound studies.

Conclusions. The problem of purposeful search of biologically active compounds among azolo-(azino-)[c]quinazolines was solved by substantiation and elaboration of strategy that combines usage of original synthetic procedures, preliminary selection of promising bioactive molecules by *in silico* and *in vitro* methods and *in vivo* studies of biological activity. Developed strategy allowed identification promising bioactive agents with various biological activity.

References

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Молекулярний дизайн, спрямований синтез та біологічна активність
Molecular design, directed synthesis and biological activity