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Editor
Komarytskyy M.L.
Ph.D. in Economics, Associate Professor

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SEARCH FOR POTENTIAL AFI IN A SERIES OF DERIVATIVES OF 1-4-METHYL-5,7-DICHLORO-9-HYDRAZINOACRIDINES USING IN SILICO TECHNOLOGIES

Yaremenko Vitaliy Dmytrovich,
Kobzar Nataliia Petrivna
PhD in Pharmacy, Associate Professor
Perekhoda Lina Oleksiivna
Doctor of Pharmacy, Professor
Kononenko Vladyslava Oleksandrivna
Student
National University of Pharmacy
Kharkiv, Ukraine

Abstract. The synthesis of new potentially active pharmaceutical ingredients by modification of methyl halogen hydrazinoacridines was carried out experimentally in laboratory conditions. In order to optimise the experimental study of various types of biological activity and the level of their predicted toxicity, in silico computer modelling methods were used with the help of "Way2Drug pharmaexpert online" and "Molinspiration Cheminformatics Software".

Keywords. 9-hydrazinoacridines, in silico methods, APIs, active pharmaceutical ingredients, QSAR, SAR, computer modelling, Way2Drug, pharmaexpert online, Molinspiration Cheminformatics Software.

Acridine derivatives are widely used in both experimental and practical medicine. A large number of applications for these derivatives have been identified in the current literature.

Acridines have been used as potential antimicrobial [1, p. 1], cytostatic

[2, p. 1], antimalarial [3, p. 1], antiphlogistic [4, p. 1] agents, DNA intercalators [5, p. 1], in analytical chemistry (lucigenin is an indicator for determining water in non-aqueous media), in biological chemistry (acridine orange is used for vital staining), in analytical chemistry (lucigenin is an indicator for determining water in non-aqueous media), in biological chemistry (acridine orange - used for lifetime staining of nuclei and lysosomes in the analysis of biological membranes), in construction (Rikka acriflavin - a mould remover for aquariums, swimming pools and wooden products), dyes for dyeing linen, silk and cotton.

The aim of our study was to identify potential pharmacological activities and toxicity levels for synthetically prepared 9-hydrazinoacridine substituents using in silico methods with the help of Way2Drug pharmaexpert online and Molinspiration Cheminformatics Software.

We synthesised 18 compounds derived from 1-4-methyl-5,7-dichloro-9-hydrazinoacridine.

The obtained compounds are readily soluble in acids and organic solvents, such as ethanol, dioxane and dimethylformamide.

The main criteria for evaluating the pharmacological activity of the compounds studied by the pharmaexpert online software product are Pa (probability of the compound having the specified activity) and Pi (probability that the compound will not exhibit this activity). It is believed that the greater the interval between Pa and Pi (Pa>>Pi), the higher the probability of the tested compound exhibiting the specified pharmacological activity.

In the case when Pa=Pi, the probability of the specified pharmacological activity is minimal (close to zero).

Based on the test results, the most probable types of pharmacological activity characteristic of substituted 1-4-methyl-5,7-dichloro-9-hydrazinoacridines were identified: antiviral, diuretic, antituberculosis, antidiarrhoea, muscle relaxant, and antimicrobial.

For our estimation, we adopted the restriction for the probability variable (Pa): $0,5<Pa\leq0,8$. This correlation is sufficient to obtain a critical estimate of the biological

probability for the described compounds.

The toxicological assessment of potential APIs was performed using the Way2Drug software product of the pharmaexpert online software package (https://www.way2drug.com/gusar /acutoxpredict.html).

Prediction of in silico LD50 values for rats at four routes of administration (oral, intravenous, intraperitoneal, intraperitoneal, subcutaneous) was performed using the Way2Drug software. The training sets were created based on data from the SYMYX MDL toxicity database. They include information on ~10,000 chemical structures with acute toxicity data for rats.

As a result of the study, the acute toxicity LD50 for the investigated compounds was found to be from 66.9 to 1260.0 mg/kg for unsubstituted 1-4-methyl-5,7-dichloro-9-hydrazinoacridines, which places the investigated APIs in the toxicity classes 4 and 5. For substituted 1-4-methyl-5,7-dichloro-9-[β-benzylidenehydrazino] acridines, the LD50 ranges from 77.4 to 1401.0 mg/kg in the experiment, which is class 4 to 5 toxicity.

To predict the possible bioavailability, it made sense to evaluate the compounds for their compliance with the Lipinski rules. The study was conducted using Molinspiration Cheminformatics Software (https://www.molinspiration.com/ services/properties.html).

This free property calculation service, Molinspiration, is a well-proven resource for the online chemical community (at least judging by the number of users, which currently reaches about 200,000 calculations per month!!!).

The results of the mathematical evaluation of the studied compounds allowed us to reveal the full compliance of the obtained compounds with Lipinski's rules. Namely: the distribution coefficient (Log P) averaged 4.20 - 4.63 (optimal for Lipinski ≤ 5), molecular weight (MW) - 278.14 - 379.27 (Lipinski ≤ 500), number of hydrogen bond acceptors (Ha) - 3 (Lipinski ≤ 10), number of hydrogen bond donors (Hd) - 3 (Lipinski ≤ 5), number of nonterminal bonds (Rot B) - 4 (Lipinski ≤ 10).

As a generalisation, the following conclusions can be drawn: all the obtained compounds based on 1-4-methylsubstituted 5,7-dichloro-9-hydrazinoacridines satisfy

the five Lipinski rules, have low toxicity, i.e. they are promising for experimental study of the most probable types of pharmacological activity - antiviral, diuretic, antituberculosis, antidiarrhoea, muscle relaxant, antimicrobial; the described compounds are not very promising as antimicrobial agents against general hospital microflora, but it makes sense to conduct studies on specific types of microorganisms that were identified in in silico testing.

REFERENCES

1. A new 1-nitro-9-aminoacridine derivative targeting yeast topoisomerase II able to overcome fluconazole-resistance / Kamila Rząd, Ewa Paluszkiewicz, Iwona Gabriel // Bioorg Med Chem Lett. 021 Mar 1:35:127815. doi: 10.1016/j.bmcl.2021.127815. Epub 2021 Jan 21.

2. Can Zeolite-Supporting Acridines Boost Their Anticancer Performance? / Maja Ranković, Anka Jevremović, Aleksandra Janošević Ležaić et all. // J. Funct. Biomater. 2023 Mar 22; 14 (3) : 173. doi: 10.3390/jfb14030173.

3. New 4-(N-cinnamoylbutyl)aminoacridines as potential multi-stage antiplasmodial leads / Mélanie Fonte, Diana Fontinha, Diana Moita et all. // J. Med. Chem. 2023. Oct 5:258:115575. doi:10.1016/j.ejmech.2023.115575.

4. Caffeic Acid Modified Nanomicelles Inhibit Articular Cartilage Deterioration and Reduce Disease Severity in Experimental Inflammatory Arthritis / Akshay Vyawahare, Ravi Prakash, Chandrashekhar Jori et all. // ACS Nano. 2022 Nov 22;16(11):18579-18591. doi:10.1021/acsnano.2c07027.

5. Preparation and Preliminary Evaluation of 68Ga-Acridine: An Attempt to Study the Potential of Radiolabeled DNA Intercalator as a PET Radiotracer for Tumor Imaging / Subhajit Ghosh, Tapas Das, Shishu K Suman et all. // Anticancer Agents Med. Chem. 2020; 20 (13) : 1538-1547. doi:10.2174/1871520620666200502002609.