Prediction of the biological activity of naphthoquinone N-derivatives on the basis of virtual screening and drug-like characteristics

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Abstract – *The predicted screening of the biological activity of aminopyrazole derivatives dichloronaphthoquinone with the use of the PASS program was carried out and their acute-looking characteristics were determined. On the basis of virtual screening data, perspective directions of experimental biological research of heterocyclic N-derivatives of 1,4-dichloronaphthoquinone were revealed.*

Key words - naphthoquinone, amines, pyrazole, drug-like characteristics, Lipinski's parameters, PASS Online.

Introduction

The work on the implementation of new drugs is extremely diligent and costly. Therefore, at the initial stage for the search of pharmacologically active compounds, it is advisable to use pre-experimental methods of the virtual screening *in silico* that precede experimental methods *in vitro* and *in vivo*. Such areas of virtual screening in the search of new potential candidates for a drug substance are the use of drug-like characteristics and the prediction of compounds biological activity using the computer program PASS.

For modern pharmacology, the relationship between biological activity and the structure of chemical substances, as well as on their basis the search of new highly active drug compounds has the fundamental importance. It is known that naphthoquinone N-derivatives are potential biologically active compounds with a wide spectrum of action [1]. Therefore, we chose them for experimental purposes.

Discussion of results

As subjects of research, we chose such aminopyrazole derivatives of naphthoquinone:

For planning the directions of experimental research on the biological activity of aminopyrazole derivatives of naphthoquinone, we used the previous computer prediction by the program PASS (Prestance of Activity Spectra for Substances) [2, 3].

After analyzing the results on the screening of the biological activity of aminopyrazoles with the quinone fragment, obtained by the PASS program, the perspective directions of their experimental biological researches were determined, namely: antitumor activity, analgesic,

antiparkinsonian, anti-neurodegenerative activity, activity against diabetic neuropathy, as well as the possibility of their use as inhibitors of many enzymes.

Also, an important informative method of prediction is the drug-like characteristics. Using the Internet service [4], which offers a software package for processing introduced structures and property calculations, the Lipinski's criteria have been calculated, and it has been determined that heterocyclic naphthoquinone derivatives (1a-1d) have no deviations from the Lipinski's rules. And, consequently, it is advisable to carry out further experimental biological studies of synthesized compounds (1a-1d).

Table 1.

The value of the drug-likeness criteria for 1,4-naphthoquinone N-heterocyclic derivatives

Number of compound	Log P	Molecular polar surface, Å ²	Number of non-hydrogen atoms	Molecular weight	Number of hydrogen bond acceptors (O and N atoms)	Number of hydrogen bond donors (NH and OH groups)	Number of rotating bonds	Molecular volume, Å ³
1a	2.57	63.99	20	287.71	5	1	2	233.70
1b	2.77	63.99	20	287.71	5	1	2	233.70
1c	4.82	74,85	26	363.80	5	2	3	304.73
1d	4.49	90.30	30	421.84	7	1	6	349.88

Conclusions

The calculation of drug-likeness criteria and predictive screening of biological activity using the PASS program for synthesized compounds have been carried out and the promising N-derivatives of naphthoquinone as potential drug substances have been identified.

References

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