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Synteza i aktywność biologiczna nowych pochodnych pirolo[3,4-*d*]pirydazynonu

ABSTRACT

Introduction:

Effective and safe treatment of various pain and inflammatory diseases is a significant and challenging clinical problem for modern medicine and pharmacy. The commonly used NSAIDs have limited efficiency, and their chronic use carries a considerable risk of dangerous gastrointestinal side effects, which notably limits their long-term usage. For this reason, it is necessary and justified to search for new compounds that possess potent analgesic and anti-inflammatory activity, but at the same time, are safe and free of severe side effects.

The objective of study:

The aims of the conducted research were the design and synthesis of new 1,3,4-oxadiazole and 1,2,4-triazole derivatives of pyrrolo[3,4-*d*]pyridazinone with the expected good analgesic and anti-inflammatory activity and the lack of harmful impact on the gastric mucosa. Subsequently, the evaluation of the new compounds' toxicity and the pharmacological activity profile in *in vitro* and *in vivo* experiments has been carried out.

Materials and methods:

Commercially available solvents, reagents and catalysts were used in the synthesis, analysis and purification of the newly received compounds. Their structure was confirmed using different spectroscopic techniques such as NMR, MS, FT-IR and elemental analysis. Toxicity and biological activity of novel derivatives were assessed using appropriate enzyme tests, cell lines and animals. Molecular docking and various types of spectral studies, such as FT-IR, CD, were also performed.

Results and conclusions:

The new 1,3,4-oxadiazole and 1,2,4-triazole derivatives of pyrrolo[3,4-*d*]pyridazinone turned out to be devoid of cytotoxic activity and most of them show good anti-inflammatory activity *in vitro*. These compounds preferentially or selectively block the induced COX-2 enzyme. Their potency is comparable to that of meloxicam. Moreover, the tested compounds show anti-radical activity and protect chromatin against damage caused by oxidative stress. Their promising biological activity was confirmed by experiments performed in an animal model. The tested compounds effectively inhibit the pain and inflammatory reaction *in vivo*, reduce the concentration of inflammatory mediators in the plasma and, what is very important, do not cause damage to the gastric mucosa. Therefore, the obtained results indicate that the pyrrolo[3,4-*d*]pyridazinone derivatives being the subject of this dissertation, are interesting and promising candidates for new, effective and safe drugs with potential application in the treatment of various types of inflammatory diseases.