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ABSTRACT BOOK

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Purposeful search of novel anti-inflammatory agents among substituted pyrrolo[1,2-*a*][1,2,4]azolo-(azino-)[*c*]quinazolines

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Introduction: For several decades, quinazoline derivatives have been in the focus of researchers developing innovative medicines. This is due to the wide range and high level of biological action of above-mentioned substances, as well as significant opportunities for their chemical modification. Thus, antifungal (Albacanazole), antihypertensive (Doxazosin, Prazosin), sedative (Etaqualon) and anti-inflammatory (Proquazone) drugs were developed and introduced in medical practice. [1]. Despite the fact, that in modern medicinal chemistry quinazoline derivatives mostly considered as promising anticancer agents, the recent studies proved their potential as compounds with high anti-inflammatory activity [2-4].

Materials and methods: Implementation of the concept of searching for innovative anti-inflammatory agents included the design of a combinatorial library of compounds, its formation by organic synthesis methods, *in silico* screening, determination of free radical scavenging activity, evaluation of enzyme-inhibitory activity (soybean type I-B and human lipoxygenase, COX-2). For the most promising candidates the anti-inflammatory activity *in vivo* was established.

Result and discussion: Considering the results of previous studies [2-4], the strategy of novel anti-inflammatory compounds searching was elaborated and realized. The target compounds were obtained *via* tandem heterocyclization of substituted 2-triazolo-(triazino-)anilines with 2-ketoglutaric or 4-ketopimelinic acids. The abovementioned transformation allowed to annulate pyrrole cycle to triazolo(triazino)[c]quinazoline system, as well, as to introduce pharmacophore carboxylic group. Obtained compounds were studied for anti-inflammatory activity. The *in silico* and *in vitro* methods were used to select promising objects for *in vivo* studies. It was shown, that a number of the obtained compounds exhibited a pronounced anti-inflammatory effect that was comparable with activity of reference -compound sodium diclofenac [5-7]. It was established that the presence of a triazine cycle and carboxyethyl fragment was essential for the anti-inflammatory effect appearance.

Conclusions: The concept of directed search for anti-inflammatory agents among condensed quinazoline derivatives was developed. The implementation of this concept revealed a number of promising anti-inflammatory agents among the named class of compounds.

References

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