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5+1-Heterocyclization as preparative approach for carboxy-containing triazolo[1,5-c]quinazolines with anti-inflammatory activity

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Abstract

Present article is devoted to the purposeful search of novel anti-inflammatory agents among carboxylcontaining partially hydrogenated [1,2,4]triazolo[1,5-c]quinazolines and products of their tandem cyclization. It has been shown that target compound's could be obtained via interaction between [2-(3-R-1H-1,2,4-triazol-5-yl)phenyl]amines and oxo-containing carboxylic acids and their esters of various structure. The structures of synthesized compounds were verified by appropriate methods, the features of NMR-spectra patterns were discussed as well. The low predicted toxicity of obtained compounds has been estimated using in silico methods. In vivo study on the model of acute aseptic inflammation (carrageenan test) have been revealed that synthesized compounds expose antiinflammatory activity in the range of 0.94-52.66%. 4-(2-(Ethoxycarbonyl)-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolin-5-yl)benzoic acid has been identified as most active compound. Additionally, the effects of some (2-R-5,6-dihydro[1,2,4]triazolo[1,5-c]quinazolin-5-yl)benzoic acids (compounds 3) on the levels of key inflammatory markers have been estimated. It has been shown that studied compounds decrease the level of neutrophils, COX-2, nitrotyrosine, IL-1b, C-reactive protein and increase level of eNOS. 4-(2-(Ethoxycarbonyl)-5,6-dihydro-[1,2,4]triazolo[1,5-c]quinazolin-5yl)benzoic acid (3.2) has been identified as compound with most expressed anti-inflammatory activity and significant effect on the levels of marker of inflammatory processes. Molecular docking study towards COX-1 and COX-2 has been conducted to substantiate possible mechanism of obtained compounds anti-inflammatory activity. It has been found that fixation of 4-(2-(ethoxycarbonyl)-5,6dihydro-[1,2,4]triazolo[1,5-c]quinazolin-5-yl)benzoic acid (3.2) molecule in active site of enzyme is outstandingly similar to the reference ligands. The essential value of carboxylic group for presence of anti-inflammatory activity has been estimated as result of SAR-analysis. It has been found that studied class of compounds is perspective for further structural modification aimed to the creation of novel anti-inflammatory agents.

Keywords: 5+1-heterocyclization; Anti-inflammatory activity; Carboxy-containing triazolo[1,5c]quinazolines; Inflammation markers; Molecular docking; Predicted toxicity; SAR-analysis; [2-(3-R-1H-1,2,4-triazol-5-yl)phenyl]amines.

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Declaration of competing interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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 Antiinflamm Antiallergy Agents Med Chem. 2020;19(1):61-73. doi: 10.2174/1871523018666190115092215.

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Stavytskyi V, Antypenko O, Nosulenko I, Berest G, Voskoboinik O, Kovalenko S. Antiinflamm Antiallergy Agents Med Chem. 2021;20(1):75-88. doi: 10.2174/1871523019666200505073232. PMID: 32368980

Design, Synthesis and Anti-inflammatory Activity of Derivatives 10-R-3-Aryl-6,7-dihydro-2H-[1,2,4] triazino[2,3-c]quinazolin-2-ones of Spiro-fused Cyclic Frameworks.

Kolomoets O, Voskoboynik O, Antypenko O, Berest G, Nosulenko I, Palchikov V, Karpenko O, Kovalenko S. Acta Chim Slov. 2017 Dec;64(4):902-910. doi: 10.17344/acsi.2017.3575. PMID: 29318300

Design, synthesis, anti-inflammatory activity, and molecular docking studies of perimidine derivatives containing triazole.

Zhang HJ, Wang XZ, Cao Q, Gong GH, Quan ZS. Bioorg Med Chem Lett. 2017 Sep 15;27(18):4409-4414. doi: 10.1016/j.bmcl.2017.08.014. Epub 2017 Aug 9. PMID: 28823493

Quinazoline-containing Hydrazydes of Dicarboxylic Acids and Products of Their Structural Modification: A Novel Class of Anti-inflammatory Agents.

Krasovska N, Stavytskyi V, Nosulenko I, Karpenko O, Voskoboinik O, Kovalenko S. Acta Chim Slov. 2021 Jun;68(2):395-403. PMID: 34738126

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