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SYNTHESIS, PREDICTION AND EXPERIMENTAL CONFIRMATION OF PHARMAKOLOGICAL ACTIVITY OF 2-((4-AMINO-5-(FURAN-2-YL)-4H-1,2,4-TRIAZOLE-3-YL)SULFANYL)-N-ACETAMIDE DERIVATIVES

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Introduction. Despite the rapid progress in medicine and pharmacology observed in recent years, a treatment of inflammation remains a topical problem. Researchers devote a great care to this problem, especially the study of various heterocyclic compounds such as 3-thio-2,4-triazoles and their condensed derivatives as potential non-steroidal anti-inflammatory drugs (NSAIDs). The prospective of these compounds is based on their high reactivity, low toxicity, availability of reagents for synthesis, solubility in most solvents and broad spectrum of biological activity.
The aim. The targeted synthesis, prediction and experimental confirmation of the pharmacological activity of 2-((4-amino-5-(furan-2-yl)-4H-1,2,4-triazole-3-yl) sulfanyl)-N-acetamide as potential NSAIDs.
Materials and methods. 10 novel compounds of 2-((4-amino-5- (furan-2-yl)-4H-1,2,4-triazole-3-yl) sulfanyl)-N-acetamide with following radicals R1 = 4-OMe; R2 = H; R3 = 4-Bu; R4 = 4-OEt; R5 = 2-COOEt; R6 = 4-Et; R7 = 4-COOEt; R8 = 3-COMe; R9 = 4-NO2; R10 = 3-OMe were received during the alkylation reaction of aryl substituted N-α-chloroacetamides of 2-((4-amino-5-(furan-2-yl)-2,4-dihydro-3H-1,2,4-triazoles-3-thiones. Prediction of pharmacological activity was conducted using the program «PASS-online». The predicted anti-exudative action was studied on the white male rats using experimental models of formalin-induced edema, which was modeled using subplantar introduction of 0,1 ml of 2% formalin solution in hind paw of rat. Paw volume was measured with the digital plethysmometer (IITC Life Science (USA)) before the introduction of newly synthesized compounds and after 4 hours followed the formalin injection (maximum swelling). The investigated substances were administered orally in a form of suspension and 3% starch mucus 1 hour before the maximum development of edema at a dose of 10 mg/kg.
Results of research. 10 new compounds of 2-((4-amino-5- (furan-2-yl)-4H-1,2,4-triazole-3-yl)sulfanyl)-N-acetamide was synthesized for the first time. PASS prediction of synthesized compounds indicates the presence of the anti-exudative activity (AA) of compounds with radicals R1; R2; R6; R7; R8; R9; R10 (37,0 - 81,5%). Among the studied derivatives AA of five leaders' compounds exceeds AA of the reference drug Diclofenac sodium (44,0%). According to the value of AA, new synthesized leaders' compounds are arranged as follows R8 – 53,0%, R6 – 61,1%, R9 – 62,9%, R1 – 70,3%, R2 – 81,5%.
Conclusions. For the first time we have synthesized 10 derivatives of 2-((4-amino-5-(furan-2-yl)-4H-1,2,4-triazole-3-yl)sulfanyl)-N-acetamide. 7 of 10 compounds demonstrate moderate or high AA (37,0 - 81,5%). Among the synthesized derivatives the following five leaders' compounds were selected: R8 (3-COMe) – 53,0%, R6 (4-Et)– 61,1%, R9 (4-NO2)– 62,9%, R1 (4-O-Me) – 70,3%, R2 (H) – 81,5%, which indicates their prospects for further in-depth study as potential NSAIDs.