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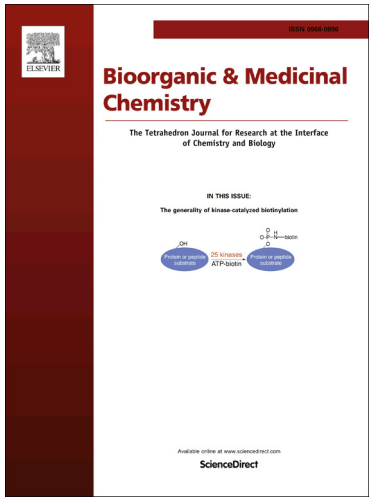

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Polyfluorinated salicylic acid derivatives as analogs of known drugs: synthesis, molecular docking and biological evaluation

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Abstract. We have developed the convenient methods for synthesis of polyfluorosalicylic acids and their derivatives. For the first time the biological properties of polyfluorosalicylates were investigated *in vitro* (permeability through the biological membranes, COX-1 inhibitory action) and *in vivo* (anti-inflammatory, analgesic activities, acute toxicity). Molecular docking of polyfluorinated salicylates confirmed *in vitro* and *in vivo* experiments.

Keywords: Polyfluoronated salicylates, Nucleophilic substitution, *ortho*-Methoxylation, Molecular docking, Anti-inflammatory and analgesic activities, COX-1 inhibition, Toxicity, Permeability.

1. Introduction

Salicylic acid (SA), its derivatives (salicylates), and particularly acetylsalicylic acid (aspirin, ASA), are among the most successful drug classes ever: it has been serving on the drug market since the end of 19th century and is still broadly used current days to treat a variety of pain, fever, inflammation and other diseases.

The successful chemical modifications of initially quite toxic and ineffective SA allowed obtaining a number of salicylates such as sodium salicylate, methyl salicylate, trolamine salicylate, salsalate, ASA etc. Due to triad of anti-inflammatory, antipyretic and analgesic effects, salicylates take place in the registry of clinically used non-steroidal anti-inflammatory drugs (NSAIDs).[1] Another equally important property of ASA is antiplatelet action and it is successfully used in the treatment of cardiovascular diseases.[2] Recent studies show that ASA reduces blood sugar levels,[3] has anti-cancer effect,[4] and reduces the activity of the brain during migraine attacks[5] and so on.

However, the salicylate drugs retain some strong side effects. The main side effects of salicylates including ASA are gastrointestinal ulcers, stomach bleeding, and ringing in the ears.

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