

Abstract

Non-steroidal anti-inflammatory drugs (NSAIDs) constitute one of the most widely used classes of pharmaceuticals. Due to their analgesic, anti-inflammatory, and antipyretic properties, they play a crucial role in the management of various pathological conditions. Globally, approximately 30 million individuals administer these agents daily, whereas in Poland an estimated 2 billion packages of analgesics are consumed annually, a substantial proportion of which are NSAIDs. Epidemiological studies demonstrate that approximately 40% of primary healthcare patients have used or currently use NSAIDs, while in the population over 60 years of age, regular administration of these drugs concerns more than 30%. In 2024, the global NSAID market exceeded 100 billion USD in value, with forecasts projecting further expansion to approximately 300 billion USD within the next decade. The ubiquity of NSAID underscores their remarkable therapeutic versatility and importance in contemporary pharmacotherapy; however, their misuse and overuse give rise to a broad spectrum of adverse effects, which constitute a significant challenge both for patients and for healthcare systems.

Within the NSAID class, particular attention is directed toward nimesulide. This compound belongs to the second generation of selective cyclooxygenase-2 (COX-2) inhibitors. It is distinguished by a relatively rapid onset of analgesic action, a favorable anti-inflammatory profile, and a reduced risk of gastrointestinal complications compared with traditional NSAIDs. Although its use has been subject to controversy in certain countries due to potential hepatotoxicity, when administered appropriately over short durations and under controlled conditions nimesulide remains a valuable therapeutic agent, particularly in the management of acute pain syndromes such as musculoskeletal pain, dental pain, dysmenorrhea, or soft tissue injuries.

The objective of the present doctoral dissertation was the synthesis, structural characterization, and *in silico* evaluation of the pharmacokinetic properties of novel nimesulide salts. A total of 13 salts were obtained, including alkylammonium salts (3 compounds), salts of group 1 and group 2 metals of the periodic table (7 compounds), and acridinium salts (3 compounds). These

compounds were subjected to single-crystal X-ray diffraction analysis, and their selected physicochemical and spectroscopic properties were determined. Furthermore, ADMET in silico analyses were conducted, enabling a preliminary assessment of their biopharmaceutical characteristics, potential metabolic interactions, and the risk of adverse effects.

The results obtained provide a foundation for further investigations into novel nimesulide derivatives with improved pharmacokinetic and safety profiles and may contribute to the rational design of innovative anti-inflammatory agents. This, in turn, opens perspectives for their potential application in the treatment of additional pathological conditions.