PhD thesis abstract

Amino acid ionic liquids as carrier systems for non-steroidal anti-inflammatory drugs

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This thesis concerns the synthesis of salts of non-steroidal anti-inflammatory drugs (ibuprofen, ketoprofen, naproxen and salicylic acid) based on alkyl esters of L-amino acids. The main objective of this work was to obtain derivatives of the selected active substances, which belong to the group of ionic liquids, with an increased bioavailability and skin permeability compared with the parent drug.

The theoretical part focuses on the presentation of problems related to traditional forms of non-steroidal anti-inflammatory drugs (NSAIDs) and methods of counteracting them, with particular emphasis on transdermal and topical drug delivery and the transformation of the drug substance into an ionic liquid with pharmaceutical activity. The experimental part presents the synthesis and characterisation of the physico-chemical and biological properties of selected acids from the group of NSAIDs. The identification and the determination of the purity of the compounds obtained were mainly based on the analysis of the proton and carbon nuclear magnetic resonance spectra, the analysis of the FT-IR spectra and the elemental analysis.

Physical and chemical properties important for transdermal and systemic application were determined, such as: solubility in water, selected buffer solutions and organic solvents, lipophilicity, thermal stability, phase transition temperatures, and optical activity. The influence of the amino acid structure and the length of the alkyl chain in the ester part on the determined properties of the obtained derivatives and the possibility of their potential design depending on the selection of the starting cation were demonstrated.

In addition, the work focused on the determination of the biological properties, with particular emphasis on skin permeation tests and the ability to accumulate in the skin, which were carried out in collaboration with the Pomeranian Medical University in Szczecin. The biodegradability of the obtained derivatives, the antibacterial activity against selected strains of bacteria and the antioxidant activity have also been determined. A correlation between the biological properties and the drug counterion structure was also demonstrated.

It has been shown that modifying an acid from the NSAID group by combining it with an L-amino acid alkyl ester significantly increases the solubility of the drug substance

in body fluids and its permeability through biological membranes. This can contribute to reducing the dose of the drug substance after its subsequent application and minimizing the occurrence of side effects. Furthermore, based on the research carried out, the structure of the cation has also been selected to obtain salts with the most favourable parameters for further application and permeability through the skin.

Keywords: amino acid-based ionic liquids with pharmaceutical activity, non-steroidal anti-inflammatory drugs, transdermal and topical drug delivery

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