

Title: Studies of the effect of selected oligosaccharides on tolfenamic acid permeability through the biological membrane system in the gastrointestinal model

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Tolfenamic acid belongs to non-steroidal anti-inflammatory drugs (NSAIDs). It's mechanism is based on the inhibition of COX-1 and COX-2 pathways to inhibit prostaglandin secretion and action and thus, to exert its anti-inflammatory and pain-blocking action. Tolfenamic acid is effective in treating the pain associated with the acute attack of migraines in adults, treatment of progressive supranuclear palsy and behavioural variant frontotemporal dementia. The most important limitations of the use of tolfenamic acid include its poor solubility in the range of pH <8.0 and in effect the low degree of penetration through the blood-brain barrier. As one of the possibilities to improve solubility, it can consider combining tolfenamic acid with cyclodextrins. Identification of cyclodextrin tolfenamic acid complex was based on changes FT-IR, XRPD and DSC.

In the view of the limitations in the solubility of the tolfenamic, its systems were obtained with the excipients increasing the pH (magnesium stearate) and the solubilizing substances - methyl-β and 2-hydroxypropyl-β cyclodextrins. In the first part of studies, the tolfenamic acid systems were prepared with magnesium stearate (1:1) by kneading, to which cyclodextrins were added. Cyclodextrins systems of tolfenamic acid were obtained by co-precipitation. Identification of cyclodextrin-tolfenamic acid systems was based on analysis of changes on: FT-IR spectra, XRPD diffractograms and DSC thermograms. In the second part, the permeability of tolfenamic acid after its introduction into cavity of cyclodextrin systems was investigated. As a model for permeability testing, the PAMPA GIT as well as the BBB model were used, simulating respectively penetration through the gastrointestinal epithelium and the blood-brain barrier. Identification of cyclodextrin-tolfenamic acid systems was based on analysis of changes on: FT-IR spectra, XRPD diffractograms and DSC thermograms. The PAMPA is a technique developed to predict passive permeability through numerous different biological membranes. Changes in permeability of tolfenamic acid after introduce into cyclodextrin cavity were measured by using UV spectroscopy. Apparent coefficient of permeability of tolfenamic acid through gastrointestinal barrier was $1{,}61*10^{-5}$, which allows him to characterize as highly permeable. While system of tolfenamic acid with 2-hydroxypropyl-β-cyclodextrine has apparent coefficient of permeability $1{,}027*10^{-4}$ and with methyl-β-cyclodextrin $1{,}75*10^{-5}$ $cm*s^{-1}$ through gastrointestinal barrier. Apparent coefficient of permability for highly permeating was $> 1*10^{-6}$ $cm*s^{-1}$.

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Biography

Karina Grzanka is a student of the fifth year of pharmacy at the Poznań University of Medical Sciences. For 2 years, she has been actively working in the Herba student research group in the area of searching for possibilities of using cyclodextrin inclusion complexes. In particular with regard to the possibility of modifying the release of the active substance from the prepared complexes. She has the skills and experience necessary to work on the study of permeability through the system of biological membranes and the rate of dissolution.

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