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The system of tolfenamic acid with cyclodextrins and their identification

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Introduction & Objective: Tolfenamic acid is a Non-Steroidal Anti-Inflammatory Drug (NSAID) with antipyretic, analgesic and anti-inflammatory effects. Its action is mainly based on the inhibition of COX-1 and COX-2. It is effecative in treating the pain associated with the acute attack of migraines in adults. The drug is absorbed slowly by oral administration. The oral absorption is delayed and it gives a mean lag-time to absorption of 32 minutes. Tolfenamic acid is slightly soluble in water, buffer pH=6.8 and 0.1 M hydrochloric acid.

Method: To increase the solubility, tolfenamic acid was connected with magnesium stearate in a ratio of 1:1. An alkaline environment was created that allowed the tolfenamic acid to be dissolved in the buffer pH=6.8. Inclusion cyclodextrin systems (methyl-β-cyclodextrin and 2-hydroxypropyl-β-cyclodextrin) were prepared in solid phase using co-precipitation method. Technique involves stirring together equimolar methanol solution of mixture of tolfenamic acid and magnesium stearate and water cyclodextrin solution. Identification of cyclodextrin tolfenamic acid complex was based on changes FT-IR (Fourier Transform-Infrared Spectroscopy), XRPD (X-ray Powder Diffraction) and DSC (Differential Scanning Calorimetry). The system of tolfenamic acid and cyclodextrin was dissolved in a buffer pH=6.8 imitating the digestive environment in intestines. The studies of apparent solubility were conducted by using Paddle Drug Dissolution Apparatus.

Results: Apparent solubility study showed that tolfenamic acid in system with methyl-β-CD after 190 minutes was solvated in 86%, while system with 2-hydroxypropylo-beta-cyclodextrin after 190 minutes was solvated in 91%. The tolfenamic acid in free form was dissolved in 62.5%. The results were evaluated significantly.

Conclusion: These studies showed that the combination of the tolfenamic acid with cyclodextrin alters its dissolution rate. The tolfenamic acid-cyclodextrin systems showed better solubility in compared to the free form. The type of cyclodextrin used to obtain the tolfenamic acid was a significant importance.

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References:

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Biography

Karina Grzanka is a student of the fifth year of Pharmacy at the Poznań University of Medical Sciences. 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 complex. She has also 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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