

Preparation and *In vitro*- *In vivo* Evaluation of Different Transdermal Formulations of Betahistine Dihydrochloride

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Objective: Betahistine has been used in the treatment of diseases accompanied by impaired peripheral circulation (e.g. Ménière's syndrome) to reduce the frequency of episodes of vertigo and tinnitus. The drug has a short half-life and should be taken three times daily due to the rapid elimination. Its contraindication in patients with peptic ulcer history and the difficulty of frequently dosing requires administration ways other than the oral route. The aim of this study is to prepare and evaluate the transdermal formulations of betahistine.

Methods: Transdermal formulations were prepared with FDA approved polymers, Eudragit RL 100 and Eudragit RS 100, by using solvent evaporation technique. *In vitro* drug release tests were carried out using dissolution apparatus and the drug was assayed spectrophotometrically. Ex-vivo studies were carried out with Franz diffusion cells using excised human skin and the drug was assayed using HPLC method. In the next step, *in vivo* studies were carried out in three groups (2 transdermal and 1 i.v., total of 12 rats) with Wistar rats and blood concentrations were assayed using a different HPLC method modified for this purpose.

Results: Physically acceptable matrix type transdermal formulations of betahistine were prepared successfully. Compared with i.v., transdermal application maintained blood levels for more than 24 hours. Intravenous application was effective only for 6 hours.

Conclusion: Our results confirm the feasibility of developing matrix type transdermal patches containing betahistine. However, further *in vivo* pharmacokinetic studies should be performed in humans in order to determine the blood levels of the drug.

Key Words: Betahistine, eudragit, transdermal therapeutic system, HPLC assay method, human skin, Franz diffusion cell, rat, *in vivo* percutaneous absorption