

Effect of Single and Combined Permeation Enhancers on the Skin Permeation of Ketoprofen Transdermal Drug Delivery Systems

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ABSTRACT

There are two main approaches to improve the efficacy of transdermal drug delivery systems (TDDSs): chemical and physical enhancements. Chemical substances, known as permeation enhancers, can be incorporated into the formulation and promote the skin permeation of several drugs. In this study, ketoprofen (KP) TDDS was prepared as the monolithic drug-in-adhesive. Eudragit[®]NE30D and Eudragit[®]E100 were used as acrylate pressure sensitive adhesives. The effects of several permeation enhancers on the skin permeation of KP across excised abdominal rat skin were investigated. Modified Franz[®] diffusion cells were used. KP transdermal patch was placed on the epidermal side of the rat skin and mounted between donor and receptor compartments of the diffusion cell. Isotonic phosphate buffer, pH 7.4, was added into the receptor compartment and stirred constantly at 32±1°C. Sample solution was withdrawn at specific time interval up to 30 hr. Permeated KP was analyzed by high pressure liquid chromatographic method. Single and combined permeation enhancers, selected from fatty acids and/or pyrrolidone derivatives, were incorporated into the formulation. It was shown that among four types of fatty acids; lauric acid, capric acid, caprylic acid and oleic acid, oleic acid was the most effective enhancer. In the meantime, among four types of pyrrolidone derivatives; N-methyl-2-pyrrolidone, 2-pyrrolidone, 1-(2-hydroxyethyl)-2-pyrrolidone and 1-ethyl-2-pyrrolidone, N-methyl-2-pyrrolidone and 2-pyrrolidone had a trend to act as more powerful enhancers than the others. Furthermore, oleic acid combined with 2-pyrrolidone was the excellent paired-enhancer when compared with the other combinations. In conclusion, monolithic drug-in-adhesive TDDS of KP containing oleic acid and 2-pyrrolidone as the combined permeation enhancer was the most effective formulation.

Key words: Ketoprofen, Transdermal drug delivery system, Skin permeation, Permeation enhancers