

Topical Permeation Characteristics of Ibuprofen from Poloxamer Gels with Chemical Promoters

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Non-steroidal anti-inflammatory drugs (NSAIDs) have three main actions: anti-inflammatory, analgesic and antipyretic. Oral therapy of NSAIDs can be effective, but the clinical use is often limited because of their potential to cause adverse effects such as gastroduodenal irritation and ulceration. Administration of these agents via the dermal route can bypass such disadvantages. Utilizing standard excipients, often irritating substances, many topical creams and gels have been prepared; yet, penetration beyond a few superficial layers of corneal cells has not been demonstrated and it is unlikely, at best. Ideally, the success of all transdermal systems depends on the ability of the drug to diffuse into deeper layer of the skin, and even to internal structures such as joints and muscles. The stratum corneum has been recognized as the predominant diffusion-barrier of the skin. It has been proposed that, in order to surpass this obstacle, the so-called “chemical penetration enhancers” (QPE) may be included in a given transdermal formulations, thus achieving a real percutaneous diffusion of a given drug. Many studies have evaluated if such enhancers can indeed facilitate drug diffusion.

Poloxamer 407 is a triblock copolymer with a central hydrophobic chain of polyoxypropylene (PPO) and two lateral hydrophilic chains of polyoxyethylene (PEO). The polymer solution is a highly viscous gel at room temperature but becomes a liquid at refrigerator temperatures. The gel has thermoreversible gelification ability. To obtain a poloxamer-based solution with low gelling tendency, ibuprofen was first dissolved in ethanol followed by rapid incorporation of the required amounts of propylenglicol, poloxamer and permeation terpene enhancers. Later refrigeration was carried out as above, but gel formation does not occur when left at laboratory temperature. The rheological properties of the gels and solutions were studied using an ARES-RFS III (Advanced Rheometric Expansion System) Rheometric Fluid Spectrometer, TA Instruments.

In vitro membrane and skin permeation studies were carried out using a section of the abdominal skin (skins were obtained from male mice 6-8 weeks old removed from donor mice and placed as membrane in vertical Franz diffusion cells, obtaining a permeation area of 1.0 cm² and a receptor cell volume of 7.0 ml. These cells were maintained in a water bath at 35 °C ± 2 °C. The cell receptor compartment contained a phosphate isotonic solution pH 7.2 and was maintained under stirring at 500 rpm. Three hundred mg of each gel was placed on the epidermal side of the skin facing the donor compartment. After a 60 minutes temperature stabilization period 300 µL aliquots from the receptor compartment were taken through the sampling port of the cells at scheduled intervals over a 24 hours time period.

A discussion is presented about results obtained from above mentioned studies.