Wissenschaftliche Posterausstellung: Poster 3

Permeation behavior of the NSAID ibuprofen from different poloxamer 407-based formulations through isolated human stratum corneum

S. Schmid and C. C. Müller-Goymann
Institut für Pharmazeutische Technologie, TU Braunschweig

The non steroidal anti inflammatory drug (NSAID) ibuprofen is one of the most frequently used drugs in analgesic and antirheumatic therapy. Since dermal application of NSAIDs may reduce their typical gastro intestinal side effects, topical treatment is an important and effective alternative to a systemic therapy [1].

Quick and efficient pain relief requires an adequate drug permeation across the skin from appropriate vehicles which may influence the flux (= amount of drug permeated per area and time). Poloxamer-based systems have shown high in vitro permeation rates for different active pharmaceutical ingredients (API) [2-3]. Therefore, in the present study ibuprofen (IBU) was chosen as API. Several formulations containing poloxamer 407 (POX), medium chain triglycerides (MCT), isopropanol (IPA), dimethyl isosorbide (DMIS), and water were analyzed with regard to the influence of their quantitative composition on the ibuprofen flux. The results were compared to a commercially available poloxamer-based gel formulation, doc® Ibuprofen Schmerzgel.

Methods: Manufacture of the formulations was performed with a Cito Unguator® 2000 (Konietzko GmbH, D-Bamberg), doc® Ibuprofen Schmerzgel (Hermes Arzneimittel GmbH, D Großhesselohe/Munich) was purchased at a local pharmacy. In vitro permeation studies were carried out in modified Franz cells (37 °C, receiver solution: phosphate buffered saline pH 7.4) with isolated human stratum corneum. The skin samples originated from plastic surgery of healthy female abdomen and were prepared by trypsination [4]. Twelve samples were taken over a period of 32 hours. Quantification of the permeated drug amount was conducted with high performance liquid chromatography (Waters, D-Eschborn) by using a column of Hypersil® ODS 5 µm, 125 x 4 mm (Grom, D-Herrenberg-Kayh) with a mobile phase consisting of acetonitrile/water/acetic acid (55:45:1), a flow rate of 1.7 ml/min, and UV-detection at 246 nm.

Results: The variation of the quantitative composition produced significant differences in IBU permeation behavior [5]. An increased POX/MCT concentration led to a decreased IBU flux due to an increasing amount of poloxamer micelles which enabled partitioning of the API within these micelles and thus a slow API release [6]. In addition, an increase in consistency was observed and contributed to this phenomenon.

An increase in IPA/DMIS concentration produced higher ibuprofen fluxes. It has already been shown that IPA can act as permeation enhancer by fluidization of the lipid bilayer structure of the

stratum corneum [7]. However, high IPA concentrations may damage the stratum corneum so that skin tolerance of the formulations must be considered in the first place.

A doubling of the IBU concentration improved the permeation so that the flux of doc® Ibuprofen Schmerzgel was exceeded, but also changed the macroscopical appearance, mainly in terms of liquefaction, so that these systems may be used as spray formulations.

The present results clearly demonstrate the great influence of the vehicle composition on the in vitro permeation of a drug. Consequently, this queries the common practice of substitution of creams, ointments and gels in terms of the “aut idem” rule.

Acknowledgment: Financial support from Hermes Arzneimittel GmbH (D-Großhesselohe/Munich), supply with Unguator® jars from GAKO® Direkt GmbH (D-Bamberg) and the donation of skin samples from Dr. Schmidt (D-Wolfenbüttel) are gratefully acknowledged.

References:

1. Massey T, Derry S, Moore RA, McQuay HJ. Cochrane Database Syst Rev 2010; (6): CD007402.
2. Grüning N, Müller-Goymann CC. J Pharm Sci 2008; 97(6): 2311-2323.
3. Lusiana, Müller-Goymann CC. AAPS PharmSciTech 2011; 12(2): 496-506.
4. Kligman AM, Christophers E. Arch Dermatol 1963; 88(6): 702-705.
5. Schmid S, Müller-Goymann CC. Aktuelle Derm 2012; 38(12): 499-504.
6. Gilbert JC, Hadgraft J, Bye A, Brookes LG. Int J Pharm 1986; 32(2–3): 223-228.
7. Brinkmann I, Müller-Goymann CC. Skin Pharmacol Physiol 2003; 16(6): 393-404.