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Soft matter characteristics of topical poloxamer 407-based formulations – the influence of temperature and ibuprofen content

S. Schmid, C. C. Müller.-Goymann

Institut für Pharmazeutische Technologie, TU Braunschweig

Dermal application of non steroidal anti inflammatory drugs (NSAID) is a popular and effective alternative in the short term treatment of pain and inflammation in the muscles and joints reducing gastro intestinal side effects which are a major problem with peroral administration [1]. Poloxamer 407-based formulations with the NSAID ibuprofen (IBU) have already shown high in vitro permeation rates across isolated human stratum corneum [2]. In addition to an adequate drug permeation across skin, rheological properties (e.g. consistency, yield stress) are of great importance to promote comfortable skin application. Therefore, a model formulation containing 24 % poloxamer 407 (POX), 6 % medium chain triglycerides (MCT), 10 % isopropanol (IPA), 20 % dimethyl isosorbide (DMIS), and 40 % water was analyzed with regard to the influence of the ibuprofen content (0, 5, 10, and 14 %) on the rheological characteristics.

Methods: Manufacture of the formulations was performed with a Cito Unguator® 2000 (Konietzko GmbH, D-Bamberg). Rheological studies were performed with a HAAKE Rheo Stress 6000 rheometer (Thermo Fisher Scientific, D-Karlsruhe) equipped with a cone/plate (1 °, 20 mm) shear apparatus. Rotation mode was used to determine flow curves and yield stresses. Since poloxamer-based gel formulations may show thermoreversible gelation [3], the measurements were performed at different temperatures including body and ambient temperature (37 °C and 20 °C, respectively). As pain reduction may be supported by a cooling effect of the vehicle, refrigerator temperature (5 °C) was tested as well. Oscillatory mode was used to investigate viscoelastic properties of the samples. Measurements were performed at 25 °C and 40 Pa (linear viscoelastic range for IBU-free formulation). Complex viscosity at a frequency of 0.5 Hz was determined to describe consistency of the systems. The microstructure was analyzed with a polarizing microscope (Leica DMLM, Leica Microsystem GmbH, D-Wetzlar) equipped with a lambda plate.

Results: The polarizing micrographs showed significant differences in the microscopical appearance of the formulations. Systems with 0 and 5 % IBU were isotropic, those with 10 and 14 % showed anisotropic textures (hexagonal and lamellar, respectively). The changes in microstructure corresponded with an alteration of the rheological properties. 5 % IBU increased the yield stress of the formulation along with its consistency, whereas a further increase in IBU content up to 10 % led to a softening. In contrast, 14 % IBU produced the highest value for complex viscosity despite the lowest yield stress. None of the systems showed thermoreversible

gelation within the temperature range studied. Yield stresses of IBU-loaded formulations decreased with increasing temperature.

Conclusion: IBU as an amphiphilic molecule interacted with the excipients so that a variation in IBU content led to significant changes in microstructure and rheological properties of the formulations. The results illustrate that rheometry is an appropriate method to detect structural changes in semisolid drug delivery systems.

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References:

1. Massey T, et al. Topical NSAIDs for acute pain in adults. Cochrane Database Syst Rev 2010; (6): CD007402.
2. Schmid S, Müller-Goymann CC. Topische Schmerztherapie - Auf die Galenik kommt es an! (Topical NSAIDs - On the importance of the vehicle). Aktuelle Derm 2012; 38(12): 499-504.
3. Schmolka IR. Artificial skin I. Preparation and properties of pluronic F-127 gels for treatment of burns. J Biomed Mater Res 1972; 6(6): 571-582