Accepted Manuscript

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PII: S0022-3549(17)30498-7

DOI: 10.1016/j.xphs.2017.07.002

Reference: XPHS 867

To appear in: *Journal of Pharmaceutical Sciences*

Received Date: 5 June 2017

Revised Date: 27 June 2017

Accepted Date: 6 July 2017

Please cite this article as: Rossana P, De Gennaro B, Gaudino D, Grizzuti N, On the use of non-steroidal anti-inflammatory drugs as rheology modifiers for surfactant solutions, *Journal of Pharmaceutical Sciences* (2017), doi: 10.1016/j.xphs.2017.07.002.

On the use of non-steroidal anti-inflammatory drugs as rheology modifiers for surfactant solutions

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Abstract. Surfactant molecules can give rise to different morphological structures, depending on numerous parameters such as temperature, surfactant concentration and salinity. Specifically, the salt content can be easily tuned in a way to induce morphological transitions and modulate the rheological response. It is shown that non steroidal anti-inflammatory drugs can be used in the same way as classical binding salts in changing the rheological properties of the resulting gel-like system. On the one hand, the experimental results show that by tuning small details in the molecular conformation of the drug and its concentration in the micellar solution it is possible to obtain the desired mechanical response. On the other hand, the results prove that rheology can be considered as a powerful tool to detect the drug release content, with obvious consequences on possible applications.

Surfactants are peculiar molecules made up of a hydrophobic chain and a hydrophilic head, used in different areas of applications, from detergency and pharmaceutical products to oilfield formulations. When dispersed in water above a critical concentration (the so-called critical micellar concentration), they can assemble in various morphologies, trying to minimize the exposition of the hydrophobic part to the water [Israelachvili *et al* (1976)]. The morphology depends upon the packing factor, a geometrical parameter related to the head and to the relative size of the tail. Spherical aggregates, worm like micelles, bilayers and other morphologies can be obtained [Larson (1999)]. Their assembly can be easily tuned by addition of a binding salt (usually based on aromatic groups), which is able to change the packing parameter of the surfactant molecules, due to its insertion into the surfactant micellar palisade [Dreiss (2007), Gaudino *et al* (2015)]. On the one hand, the resulting morphology confers to the solutions specific rheological properties. On the other hand, the mechanical response can be used as a tool for detecting the relative amount of the penetrating molecule. This principle has been used very recently to detect the drug content released from an inorganic support into a micellar solution used as a model system for a topical gel formulation [Pasquino *et al* (2016)]. Indeed, non steroidal anti-inflammatory drugs (NSAIDs) can act as binding salts for surfactant molecules and change the rheological response, thus materializing the possibility of using the viscosity level as a parameter to measure the effective drug release from potential supports. The current work aims to study the effect of drug concentration on a specific micellar solution and to understand the influence of the molecular conformation of the drug on the resulting rheological response. We are interested, in particular, into model topical systems based on surfactant molecules. At the best of our knowledge, solutions for topical applications are usually based on aqueous polymer solutions and they are not surfactant-based [Moore *et al* (2000)]. The topical use, moreover, has been very little exploited in literature, in particular concerning the interactions between the suspending fluid and the drugs.

Micellar solutions based on a widely used surfactant molecule, Cetylpyridinium Chloride (CPyCl – Applichem Panreac), were prepared by using distillate water and by adding two NSAIDs, Diclofenac and Ibuprofen in their sodium form (Farmalabor and Sigma-Aldrich, respectively), and the more commonly used binding salt Sodium Salicylate (NaSal - Applichem Panreac). CPyCl is present in many commercial products, such as toothpastes and medical sprays, and is mainly used for its antiseptic and antibacterial properties. Chemical structures of the penetrating salts are shown in Figure 1. They are all aromatic cosolutes.