Effect of surfactant concentration on sonophoresis of proteins through rat skin

A. Dahlan, H. O. Alpar and S. Murdan
Department of Pharmaceutics, School of Pharmacy, University of London, 29-39 Brunswick Square, London WC1N 1AX, UK. Email: afendi.dahlan@ulsop.ac.uk

The synergistic effect of sodium lauryl sulphate (SLS) normally at 1% and lowfrequency ultrasound (US) in transdermal drug delivery has been established (Mitragotri et al 2000). However, due to the potential skin irritancy of SLS, the use of 1% surfactant concurrently with US could be pharmaceutically unacceptable. The aim of this study was to explore the relationship between surfactant concentration and enhancement of transdermal protein delivery by low-frequency ultrasound. Permeation studies using Franz cells were conducted using full-thickness rat skin as the membrane, and the receptor phase (4mL) was phosphate buffered saline (PBS). The donor compartment was filled with 20mL of coupling medium (water or SLS aqueous solution at different concentrations: 0.001, 0.004, 0.01, 0.04, 0.1 and 1%) and ultrasound (30% amplitude, 0.5 s on, 0.5 s off pulse wave for a total sonication time of 2min) was applied with the transducer being 5mm from the skin surface. Following ultrasound application, the coupling medium was removed from the donor compartment and the skin was rinsed and blotted dry, and 50 _L of iodine-125 labelled bovine serum albumin (BSA) was applied onto the skin. After 24 h, the levels of radioactivity in the receptor compartment (e.g., 0.1%), protein permeation into skin was increased despite the lack of pits formed on aluminium foil. This indicates that protein was permeating through the skin via pathways that could not be related to pits formed on aluminium foil. This study has shown that very low concentrations of SLS (e.g., 0.001%) resulted in similar protein permeation to those achieved by 1% SLS. The lower SLS concentration has advantages, such as lower toxicity.

Mitragotri, S. et al (2000) J. Pharm.Sci. 89: 892–900

and in the skin were measured using a gamma counter. Gel electrophoresis on the receptor phase confirmed BSA presence. It was found that when 0.001% and 0.004% SLS solutions were used as the coupling medium, protein permeation into the receptor phase was similar to those obtained when water was used as couplingmedium. Surprisingly, an increase in SLS concentration to 0.01% and 0.04% resulted in a marked decrease in protein permeation. A further increase in SLS concentration to 0.1% to 1% resulted in increased protein. To understand the protein permeation profile at the different surfactant concentrations, the surface tension of the different SLS solutions were measured and aluminium foil pitting experiments were conducted. The latter are conducted by applying ultrasound waves to an aluminium foil using different SLS solutions as coupling medium and counting the number of pits formed on the aluminium foil. The number of pits gives an indication of the damage caused to skin by ultrasound. There seems to be some correlation between surface tension of SLS solutions and number of pits formed and protein permeation at low SLS concentrations. Increasing surfactant concentration from 0 to 0.04% led to decreased surface tension, decreased number of pits and decreased protein through the skin. The reduced damage caused to skin (equivalent to fewer pits on aluminium foil)may be responsible for the decreased protein permeation. At higher SLS concentrations