Influences of Microemulsion Types on the *In Vitro* Release, Skin Penetration and Retention of Benzophenone-3

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ABSTRACT

The aims of this thesis were to investigate the phase behavior of systems composed of acceptable pharmaceutical components; to formulate and characterize benzophenone-3 loaded microemulsions; to investigate the stability of benzophenone-3 loaded microemulsions; and to evaluate the effect of microemulsion type on the *in vitro* release, skin penetration and retention of benzophenone-3 from microemulsions. For the phase behavior examination, the dispersion systems were composed of Tweens (20, 40, 60 and 80) as surfactants, Eutanol G as oil phase and sterile water as aqueous phase. With the aid of ternary phase diagram, the microemulsion regions were determined. It was found that microemulsion regions were achieved with every studied system. The microemulsion system consisted of Tween 80 provided the largest microemulsion regions followed by the system composed of Tween 20. Therefore, these two systems were selected for further investigation. Both systems were incorporated with a co-surfactant, isopropyl alcohol (IPA), at weight ratios of 1:1 and 2:1. Overall, six microemulsion formulations at ratio of 18:72:10 (oil: surfactant or mixtures of surfactant and co-surfactant: water) were selected from these systems. Each blank microemulsion formulation was then incorporated with 5% w/w benzophenone-3, a sunscreen agent. These prepared microemulsions were evaluated for type and physicochemical property (viscosity, pH, zeta potential, particle size and morphology). Using dilution test and electrical conductivity, the type of these microemulsions were assessed. The two blank microemulsion formulations which did not contain IPA were indicated as w/o whereas; the four blank microemulsions containing IPA were classified as o/w microemulsions. The types of microemulsion systems did not change after the incorporation of the sunscreen. All studied microemulsions displayed Newtonian flow characteristics. The microemulsions without IPA had much higher viscosity than the microemulsions with IPA did. The pH values of both blank and benzophenone-3 loaded microemulsions were in the ranges of 7.43 to 8.20. The average particle sizes

of both blank and benzophenone-3 loaded microemulaions were found to be lees than 300 nm. The microemulsion droplets were uniform as indicated by a low polydispersity index. The negative values of zeta potential were obtained. The morphology of all benzophenone-3 loaded microemulaions was investigated by transmission electron microscope (TEM). The TEM results showed the spherical shapes. For the stability study, both physical and chemical stabilities of the studied microemulsions were evaluated at various temperatures (6 °C, room temp (about 30 °C) and 45 °C for up to two months. There were some changes in pH, viscosity, particle size, and zeta potential values of the stored microemulsions. Nevertheless, all microemulsions remained transparent and no phase separation was observed. The color changes were found in the samples kept at 45 °C. The HPLC analysis revealed that the content of benzophenone-3 of all stored microemulsions did not differ significantly from that of the freshly prepared formulations. From the *in vitro* release study through synthetic membrane using modified Franz diffusion cell, the results showed that the plots of cumulative released of benzophenone-3 were fitted best to zero order kinetic ($r^2 > 0.99$). The greatest release rate was achieved with the o/w microemulsions which contained 1:1 Tweens:IPA. The release rates of the w/o formulations and the o/w microemulsions which contained 2:1 Tweens:IPA were not significantly different. For the *in vitro* skin permeation through excised newborn pig skin, the o/w microemulsions gave higher skin permeation of benzophenone-3 than the w/o microemulsions. In addition, the o/w microemulsions with 1:1 Tweens:IPA provided higher trandermal flux than those with 2:1 Tweens:IPA. The natures of microemulsions (types and compositions) played a crucial role in controlling the release and the percutaneous absorption of the sunscreen. The *in vitro* skin retention study demonstrated that benzophenone-3 could be accumulated in the skin. The skin accumulation of the o/w microemulsions containing 2:1 Tweens:IPA appeared to be higher than the other formulations. The rank order of the ratio between skin retention and skin permeation was found to be o/w microemulsions (2:1 Tweens:IPA) > w/o microemulsions > o/w microemulsions (1:1 Tweens:IPA). In the present study, the o/w microemulsions with 2:1 Tweens:IPA may be promising carrier systems for topical delivery of benzophenone-3.