

Influence of Micelle Solubilization by Tocopheryl Polyethylene Glycol Succinate (TPGS) on Solubility Enhancement and Percutaneous Penetration of Estradiol

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Abstract

The effect of micellar solubilization on the enhancement of the solubility and percutaneous penetration of estradiol by the surface-active agent, tocopheryl polyethylene glycol succinate (TPGS) was characterized in this study. Results show that the solubility of estradiol was improved in the presence of TPGS through micellar solubilization. The critical micelle concentration (CMC) of TPGS increased with increasing ethanol concentration in the medium. With the flux corrected to the saturated level ($J(\text{corrected})$) of the free form of estradiol, an increase in the alcohol content of the medium resulted in an increase in $J(\text{corrected})$ for all levels of TPGS examined. For the same level of alcohol content, an increase in the TPGS concentration mostly led to a small extent of decrease in $J(\text{corrected})$. However, the extent of decrease was more obvious in media containing more than 60% alcohol. We also confirmed that only an insignificant amount of TPGS was transported across the skin (below the detection limit of 2 microg/ml). Permeabilities ($P(\text{eff})$), which describe the overall effects (DK/H) on the stratum corneum (SC), decreased with increasing TPGS concentration for media containing 0, 40, 60, and 80% alcohol, whereas they increased then decreased with increasing TPGS concentration for media containing 10 and 20% alcohol. The enhancement ratios based on $P(\text{eff})$ assuming that the medium contained 0% TPGS and alcohol as unity did not increase accordingly with increases in TPGS concentration at the same level as alcohol. Likewise, the enhancement ratios for the same level of TPGS increased with low alcohol content, but then decreased with increasing alcohol content. We concluded that micellar solubilization by TPGS was able to improve the solubility of estradiol, but it only had an insignificant influence on the skin. Interfacial coverage of TPGS with increasing TPGS concentration and hindrance of the partitioning of estradiol by the increasing alcohol content might play a role in influencing the permeability of estradiol.