Deformation Behavior of Transfersomes Dispersed in Deep Eutectic Solvent during Stratum Corneum Penetration

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The stratum corneum (SC), outermost layer of the skin, is known as a skin barrier. SC consists of corneocytes and intercellular lipid lamellar. Various drug carriers, such as microemulsions, bicelles, liposomes, and transfersomes (TFs), have been used to improve the skin permeability of drugs. Liposomes are vesicles comprising unilamellar and multilamellar lipid membranes. However, their skin permeability is low because of their large size, which makes it challenging to permeate through intercellular lipids in the SC. TFs comprise phospholipids and a single-chain surfactant that acts as an "edge activator." Consequently, TFs can penetrate the narrow intercellular spaces of the SC. Recently, transdermal delivery using deep eutectic solvents (DESs) has gained attention because DESs enhance the solubility and skin permeability of some drugs. DESs are formed by the self-association of two or more components that self-associate through hydrogen bonding interactions. Hydrated DESs are produced by the incorporation of water. Compared to unhydrated DESs, the hydrated counterparts exhibit significantly reduced viscosity. Furthermore, they improve long solvent-transfer times and slow molecular diffusion In this study, TFs dispersed in hydrated DESs were prepared. This system is presumed to improve skin permeability through two mechanisms: the deformation of TFs and the disruption of the SC lipid structures by DESs. As a model drug, we selected an antioxidant compound, β-carotene, renowned for its health benefits, which include deactivating highly reactive oxygen species under ultraviolet (UV) irradiation. The concentration of β-carotene in TFs and liposomes that penetrated hairless mouse skin was evaluated. β-carotene did not thoroughly pass through the skin. The results clearly indicate that the topical delivery of β-carotene through TFs was higher compared to that through liposomes. TFs dispersed in DES/water = 8/2 accumulated the most in the SC among all the prepared samples. Therefore, in subsequent studies, DES/water = 8/2 was selected as the sample solvent. Small angle X-ray scattering (SAXS) results showed that TFs and liposomes dispersed in DES/water = 8/2 formed multilamellar structures with a repeat distance of around 6.9 nm. Dynamic light scattering (DLS) and transmittance electron microscopy (TEM) results showed that the diameters ranged from approximately 250 to 500 nm for liposomes and > 500 nm for TFs. Finally, structural changes in the TFs and liposomes after application to the SC were observed. We examined six positions where strong peak intensities of TFs and liposomes were detected. In the case of TFs, the peak area varied significantly depending on the irradiation time and position (Fig.1 top). Conversely, the peaks of liposomes exhibited less changes compared to those of TFs (Fig.1 bottom). These findings indicate that TFs penetrate the SC while being deformed, while liposomes undergo minimal deformation. Consequently, the topical delivery of β-carotene through TFs was higher than through liposomes.

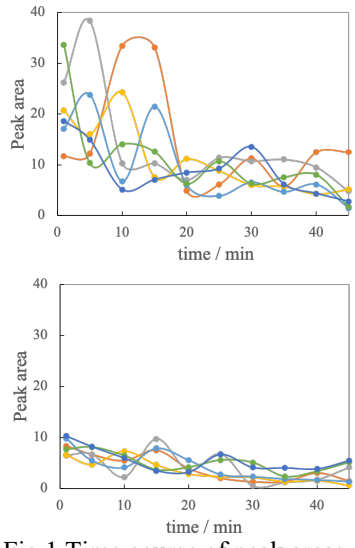

Fig.1 Time course of peak areas of TFs (top) and liposomes (bottom) from 1 to 45 min after application to the SC.

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