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COMBINED EFFECT OF *l*-MENTHOL AND 89 kHz ULTRASOUND ON THE SONOPHORETIC TRANSPORT OF HYDROPHILIC COMPOUNDS ACROSS THE HAIRLESS RAT SKIN

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ABSTRACT

Sonophoresis is known as a physical enhancing technique using an ultrasound for transdermal drug delivery. In the present study, we studied a dependency of acoustic amplitude of 89 kHz ultrasound and a combined effect of the ultrasound and *l*-menthol as a chemical enhancer on the transdermal transport of calcein across the hairless rat skin. Transdermal flux of calcein was increased by application of ultrasound for 10 min and recovered after cessation of the ultrasound application in a transient manner. When deuterium oxide (D₂O) was used as solvent instead of water, D₂O flux was also increased in the transient manner. The maximal flux achieved by 89 kHz ultrasound was dependent of the acoustic amplitudes up to 80 V_{p-p} (volt peak-to-peak). Ultrasound application at 20 V_{p-p} in the presence of 5% *l*-menthol induced 5-times higher calcein flux compared to that without *l*-menthol. Transient pattern of the increase in calcein flux was conserved in case of the combined application, although the calcein flux after ultrasound application was higher than that without *l*-menthol. No obvious skin surface damage was observed after combined application of ultrasound and *l*-menthol. These findings suggest that combined application of low-frequency ultrasound and chemical enhancers such as *l*-menthol can be useful to effectively bring out the sonophoretic enhancement for hydrophilic compounds.

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