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Lipid-based Ionic Liquid is a Novel Biocompatible Carrier for the Transdermal Peptide Drug Delivery

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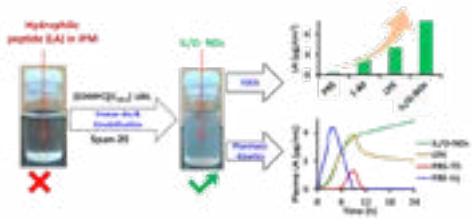
Transdermal drug delivery system has become an attractive alternative to the conventional oral or needle-based delivery system because of their self-administration association, patient preferable, avoidance of first-pass metabolism, and achievement of controlled and sustained delivery for local or systemic action. The transdermal delivery of large hydrophilic molecules is challenging due to the inherent diffusive barrier of the skin. Recently, Lipid-mediated nanocarrier have attracted in transdermal drug delivery systems (TDDSs) because of their lipophilic character. To address this issue, a new biocompatible pharmaceutical formulation was developed and stabilized by a blend of lipid-based ionic liquids (LBIL-containing 1,2-dimyristoyl-sn–glycerol-3-ethyl-phosphatidylcholine as its cationic part and a fatty acid-stearic, oleic, or linoleic acid as its anionic part) and Span-20, which covered a hydrophilic peptide drug "Leuprolide acetate" and was dispersed in isopropyl myristate (IPM). This is the first-time reported application of LBILs, and the formulation was dubbed as ionic liquids in oil nano dispersions (IL/O-NDs).

For these purposes, a water-in-oil emulsion process was used to create the drug-IL complexes, which was then freeze dried to remove the water and cyclohexane. The complexes were then dispersed in isopropyl myristate (IPM) and stabilized with sorbitol laurate (Span-20). Ionic liquid-in-oil nano dispersions (IL/O-NDs) were made using different weight ratios of LBILs and Span-20 as the surfactant and co-surfactant, respectively. TDD and pharmacokinetic parameters were measured on the skin and in the blood of BALB/C mice using Frans-diffusion cells and an enzyme-linked immunosorbent assay (ELISA). Furthermore, the biocompatibility of IL/O-NDs was investigated using MTT-assay and skin histopathological observation on a human artificial lab-Cyte EPI model as well as a BALB/C mouse model.

Keeping the overall surfactant in IPM constant at 10%, a 5:5 wt. percent ratio of surfactant (IL) and cosurfactant (Span-20) in the IL/O-NDs significantly ($p<0.0001$) increased the physiochemical stability, drug loading capacity, and drug encapsulation efficiency. IL/O-NDs significantly increased in vitro and in vivo peptide delivery across the skin ($p <0.0001$) when compared to non-IL-treated groups. Based on the pharmacokinetic parameters, [EDMPC][Linoleate]/O-ND was deemed the most preferable LBIL-based formulation for a TDDS. When compared to the aqueous delivery vehicle, the transdermal delivery flux with [EDMPC][Linoleate]/O-ND was increased 65-fold. The IL/O-NDs were able to deform the lipid and protein arrangements of the skin layers, enhancing the peptide's transdermal permeation. The biocompatibility of the LBIL-based formulations was revealed by in vitro and in vivo cytotoxicity studies of the IL/O-NDs. These findings suggested that IL/O-NDs are potentially biocompatible carriers for lipid-peptide TDDSs.



Recent Publications

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Biography

Shihab Uddin has received his PhD in Engineering on Chemical System and Engineering (leading to Biomedical Engineering) from the Kyushu University, Fukuoka, Japan in 2021. Currently, he is working in the Kyushu University, Fukuoka, Japan as a postdoctoral research fellow in the Dept. of Applied Chemistry and very soon he will join in the University of the British Columbia, Vancouver, Canada as a postdoctoral research fellow at the faculty of the Pharmaceutical Sciences. He is a highly motivated and innovated research scientist with demonstrated academic and industrial experienced in synthetic/material chemistry, pharmaceutical-formulations, nano biotechnology, and lipid-based nano drug delivery. He is expert in synthetic biology, methods developments and validations, pharmacokinetics, pharmacodynamics, drug delivery, and targeted tumor immune therapy. He is serving as an editorial board member of "Pharmacotherapy and Pharma science Discovery" journal. He has several publications in well repeated journal of RSC, ACS, Springer, and Elsevier and many of them are noted as front cover pages. He is focusing his research on the developing and translating innovative drug delivery technologies to clinical use and educating the next generation of scientist in the drug delivery field.

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