Abstract

Omiganan is a novel 12 amino acid synthetic cationic peptide from the cathelicidins family. Omiganan possesses antimicrobial action against a wide range of microbes, including gram-positive and gram-negative bacteria and fungi. Omiganan mainly acts by depolarizing the cytoplasmic membrane, resulting in cellular disruption and death. While, DPK-060 is a synthetic, 17 amino acid peptide, structurally derived from the human protein kininogen. DPK-060 mainly acts by membrane disruption mechanism, thus demonstrating strong broad-spectrum antimicrobial activity against both gram-positive and gram-negative bacteria, including *methicillin-resistant S. aureus (MRSA) in-vitro* and *in-vivo.* The positive results were obtained phase II clinical trial to treat atopic dermatitis (AD) patients but found not statistically conclusive due to the instability of DPK-060 as a drug substance in the formulation.

The aim of this study was to overcome the challenges associated with dermal delivery of Omiganan and DPK-060 i.e., proteolytic degradation, poor permeation profile, twice-a-day application, etc. via development and characterization of their suitable dermal formulations such as liposomes and NLCs. The nanocarrier based formulations of Omiganan and DPK-060 were successfully prepared and optimized to have maximum drug entrapment and minimum particle/vesicle size. The *in-vitro* characterization revealed uniform size distribution, spherical shape and favorable zeta potential, pH, viscosity and spreadability along with the prolonged release profile and higher cellular uptake. Additionally, Omiganan and DPK-060 loaded nanocarrier gel-based formulations were demonstrated potent antibacterial activity and resistance to proteolytic degradation. These formulations have no cytotoxic potential and are hemocompatible. *Ex-vivo* study revealed enhanced permeation of Omiganan and DPK-060 loaded nanocarrier gel-based formulations. Moreover, the results of pharmacodynamic studies demonstrated strong anti-psoriatic potential of Omiganan loaded nanocarrier gel-based formulations in Imiquimod induced psoriatic animal model. While, strong efficacy was also observed in Ovalbumin induced atopic dermatitis/eczema animal mode by both Omiganan and DPK-060 nanocarrier gel-based formulations. In a nutshell, the optimized nanocarrier gel-based formulations of Omiganan and DPK-060 were found to possess potent antibacterial and anti-inflammatory activities along with quality attributes in desired range as defined in QTPP and therefore seems suitable for once daily application in psoriasis or eczema.