Mazita Mohd Diah et al., J Nanomed Nanotechnol 2016, 7:5 (Suppl)
http://dx.doi.org/10.4172/2157-7439.C1.043

Skin permeation characterization for conjugated carboxymethyl-oligochitosan carboxymethyl-5-fluorouracil nanoparticles

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Nanoparticulate drug delivery systems refer to systems in which drugs are physically incorporated into nanoparticles or nano entities. Nanoparticles, being small with a large specific surface area, increase solubility, enhance bioavailability, improve controlled release and enable precision targeting of the entrapped compounds. In this study, carboxymethyl-oligochitosan (CM-oligochitosan) as polymeric permeation enhancer was conjugated to a polar pro-drug, carboxymethyl-5-fluorouracil (CMFU) through succinate linker, to increase the skin drug permeation. CM-oligochitosan-CMFU conjugate was then transformed into nanoparticles (NP) via spray drying technique. Skin drug permeation was profiled through treating the Sprague Dawley rat's skin (*in vitro*) with CM-oligochitosan-CMFU NP and CMFU and, had the skin characterized using ATR-Fourier transform infra-red (ATR-FTIR) spectroscopy, differential scanning calorimetry (DSC) and scanning electron microscopy (SEM) techniques. The nanoparticles were characterized by particle size: 229.10±57.05 nm, polydispersity index: 0.60±0.15, zeta potential: -55.92±24.48 mV and drug content: 2.29±0.27% w/w. The level of skin drug permeation of CM-oligochitosan-CMFU NP was higher than CMFU, which had no conjugation to CM-chitosan and nanoparticulation, following 24 hours of study. ATR-FTIR spectra of the untreated skin showed characteristic CH stretching vibrational peaks (asymmetric and symmetric CH2) associated with the lipid alkyl chains of epidermis at 2918.63±0.02 and 2850.56±0.15 cm-1. Similar peaks were not obtainable in skin samples treated with CM-oligochitosan-CMFU NP, while CH peak of lipid was noted in epidermis treated with CMFU. The interaction of CM-oligochitosan-CMFU NP with CH regime of epidermis could have disrupted and loosened the lipid packing thus facilitating skin drug permeation. Through treating the skin with CM-oligochitosan-CMFU NP, the amide I band of skin was shifted to lower wavelength from 1646.83±1.08 cm-1 to 1642.40±3.72 cm-1 unlike cases of CMFU. The band shift indicated that corneocytes perhaps dehydrated and shrunk, thereby leading to the formation of larger intercellular aqueous pores and better nanoparticles permeation. The ATR-FTIR outcome was further supported by thermal and morphological analysis. DSC analysis showed that the melting temperature and enthalpy of endotherm at 65.92±0.57^{0}C related to lamellar lipid structure were reduced when the skin was treated with CM-oligochitosan-CMFU NP. The skin lipid packing became disordered and this was not observable in study using CMFU. Using SEM, the skin treated with CM-oligochitosan-CMFU NP was characterized with pore formation, while the surfaces of skin remained intact when it was treated with CMFU.

Biography

M M Diah is now pursuing her PhD in Drug Delivery at Non-Destructive Biomedical and Pharmaceutical Research Centre, iPROMISE, Universiti Teknologi MARA, Malaysia. She got her Master's in Chemistry degree (Zeolitic Material Catalysis) in 2002 from Universiti Teknologi Malaysia. She is also a Senior Researcher at Industrial Biotechnology Research Centre, SIRIM Berhad, Malaysia. Her research interests are in bioactives' isolation from natural product for cosmeceutical and pharmaceutical application and in delivery technology. She has published papers and patents especially for bioactives that are applied in skin whitening products.

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