

Abstract

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Title of diploma thesis: Delivery of protein or peptide into the skin using cubosomes and microneedles

Transdermal transport of high-molecular-weight and hydrophilic substances is complicated by the protective skin layer, the stratum corneum. Physical breaching of this layer using microneedles combined with penetration-enhancing properties of cubosomes was previously reported as an effective approach to transdermal drug delivery and therefore employed in this project. (Rattanapak et al. 2012) Delivering abilities of solid (600 μm), coated (500, 600, 750 μm) and hollow (450, 600 μm) MNs were compared with intradermal injection by hypodermic needle. Cubosomes were prepared from phytantriol, poloxamer 407 and propylene glycol using liquid precursor method and loaded with fluorescent ovalbumin (FL-OVA) or SIINFEKL-TAMRA (ST) peptide. Several formulations for coating of solid microneedles were prepared using various solvents and excipients to investigate quality of coatings and their ability to deliver the drug into skin. Polyvinyl alcohol (PVA) turned out to be the most efficient coating excipient providing equally spread coatings that could be delivered into skin, allowing the drug to permeate to the deeper layers of dermis. As only limited amount of drug can be coated onto the surface of MNs tips, application using NanoPass MicronJet hollow MNs was investigated and resulted in massive fluorescence proving successful delivery by 450 μm long MNs. Solid MNs used to poke through the solution previously poured onto intact skin surface also showed successful delivery. Combination of cubosomes and microneedles is a promising approach to transdermal drug delivery and transcutaneous immunization, however, there is still a need to

tackle several issues e.g. irritability of materials used for preparation of formulations, stability of cubic phase, reproducible way of MNs application, preservation of protein or peptide structure during manufacture, storage and use or possible unwanted immunological effects.