352c Transdermal Drug Delivery Via Coated Microneedles

Harvinder S. Gill and Mark R. Prausnitz

Transdermal drug delivery has the advantage of eliminating the first pass effect of the liver and providing a large surface area and ease of accessibility for drug administration. However, to date transdermal drug delivery for systemic effects is limited to very few drugs, all of which have low molecular weights and high to moderate lipophilicity. Skin's topmost layer called the stratum corneum offers most resistance to transport of drugs across the skin. Different chemical and physical methods like chemical enhancers, ultrasound, electric energy, pressure driven flow, and lasers have been tried to disrupt the mass transfer resistance barrier of stratum corneum to deliver larger molecular weight and/or hydrophilic compounds. However, these methods have found limited success. Microneedles are microscopic needles a few hundred microns in size, and they have been shown to increase transdermal flux of large molecular weight compounds by many fold. One of the ways in which this is achieved is to coat the compound onto microneedle shafts and insert them into the skin where they deposit their payload. This study focused on solid stainless steel microneedle fabrication, controlled dip coating of different drugs onto microneedle shafts and their subsequent release into porcine skin in vitro. Stainless steel microneedles of different shapes and size were fabricated using laser cutting followed by electropolishing. This fabrication process was shown to be extremely versatile and can be used to fabricate microneedles of intricate designs to incorporate different functionalities like improved penetration and retention in skin. Next, drugs were coated onto microneedle shafts using a dip coating method. At the sub-millimeter length scales of microneedles, surface tension of the coating liquid becomes important and makes it difficult to localize the coating solution only onto the needle shafts and not contaminate the supporting base and other structures. To address this difficulty we have developed a coating technique based on controlled coating solution viscosity, needle-coating solution surface tension, and the method of physical contact between the coating solution bath and microneedles. This coating technique allows coating of a large variety of drugs independent of their molecular weights onto desired regions of microneedle shaft with good spatial control. Representative molecules of calcein, riboflavin, bovine serum albumin, and luciferase DNA plasmid were successfully dip coated onto microneedle shafts and imaged using a fluorescent microscope. To quantify the amount of drug that can be coated on a single microneedle, riboflavin was used as a model drug for dip coating microneedles. Microneedle arrays containing five microneedles in a single row were dip coated with riboflavin, using coating solutions of different riboflavin concentrations. The amount of riboflavin in the coatings was determined by dissolving the riboflavin containing coatings off the microneedles and measuring riboflavin concentration using fluorescence spectroscopy. It was found that a maximum dose of 2.2 micrograms of riboflavin could be coated onto each microneedle using the solution concentrations tested in the study. In vitro release tests performed in porcine skin and aqueous solution showed that drug comes off microneedles completely in less than 10 seconds. Post insertion histological examination of porcine skin showed “footprints” of the microneedle insertion site and its payload (i.e. calcein), demonstrating that microneedles penetrate porcine skin and delivers their payload. In conclusion, stainless steel microneedles were fabricated and dip coated with different water soluble molecules, and a high drug loading of 2.2 micrograms of riboflavin per microneedle was obtained using the dip coating method developed. Histological examination confirmed insertion of microneedles and delivery of coated drugs. Thus, coated microneedles can be used to deliver drugs to the skin requiring sub-milligram doses, for example vaccines and protein therapeutics.

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