

## ABSTRACT

### DEVELOPMENT AND CHARACTERIZATION OF POLYMERIC FORMULATIONS AND MICRONEEDLES FOR DERMAL DRUG DELIVERY

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Skin provides an attractive route for drug delivery, as transdermal delivery systems can ensure noninvasive and sustained delivery of medication across the skin into systemic circulation. Although the skin is a convenient site for drug administration, it only permits passive penetration of permeants with certain physicochemical properties. As a result, different strategies or devices have been developed to enhance the drug permeation into and across skin.

The first aim of this study was to evaluate the efficacy of multiple dosing of trolamine salicylate (TS) as a topical analgesic on *in vitro* skin permeation. Also, the effect of sonophoresis on topical delivery of analgesic was evaluated. Results suggested that the multiple dosing ( $17.4 \pm 4.1 \mu\text{g}/\text{cm}^2$ ) delivered a significantly higher amount of drug than the single dose ( $6.5 \pm 0.6 \mu\text{g}/\text{cm}^2$ ). Also, the use of ultrasound enhances topical absorption of TS into and across skin.

In the second aim, we focused on developing a new formulation to reduce the frequency of application of topical analgesics. A Poly lactic-co-glycolic acid (PLGA) based bio-adhesive polymeric solutions were prepared successfully and formed a thin

film upon application *in situ*. A significantly higher amount of TS was delivered from a formulation containing 20% PLGA ( $45 \pm 4 \mu\text{g}/\text{cm}^2$ ) as compared to PLGA-free counterpart ( $0.6 \pm 0.2 \mu\text{g}/\text{cm}^2$ ).

In the third aim, hyaluronic acid (HA) microneedles (MNs) were fabricated with and without magnesium ascorbyl phosphate (MAP) to facilitate the delivery of the active agent into and across the skin. The results showed that successful fabrication of HA MN, and the application of the current MN technology enhanced the delivery of MAP into skin ( $96.8 \pm 3.9 \mu\text{g}/\text{cm}^2$ ) compared to passive delivery ( $44.9 \pm 16.3 \mu\text{g}/\text{cm}^2$ ).

In the fourth aim, the feasibility of transdermal delivery of heparin, a hydrophilic macromolecule, through laser-microporated skin was investigated. There was no passive permeation of heparin across the skin. However, permeation of heparin from the laser-treated group delivered  $13.4 \pm 0.62 \mu\text{g}/\text{cm}^2$  after 24 h. Furthermore, heparin was not delivered to either the epidermis or dermis passively, whereas the laser-treatment group enabled delivery of heparin to the epidermis as well as the dermis.