ENHANCING TRANSDERMAL DELIVERY USING A ONE-STEP HYDROGEL FORMING MICRONEEDLE DEVICE: A CONCEPT STUDY

Aaron RJ Hutton, Melissa Kirkby, Ryan F Donnelly

School of Pharmacy, Queen's University Belfast, BT9 7BL, N. Ireland

Background: Hydrogel-forming microneedles (MN) consist of drug-free, micron scale polymeric needles situated in perpendicular orientation on a base plate to which a separate drug containing reservoir is attached. In its current form, this MN device requires the addition of water (10 μL) prior to skin insertion both *in vitro* and *in vivo* to permit the adhesion of the drug containing reservoir to the MN. Evidently, this current method of application would not be feasible in a clinical setting. For this reason, this concept study aims to develop a hydrogel-forming MN device which can be inserted into the skin in a one-step process.

Methods: In this study, a 3D printed TPU 95A housing was created, into which the MN, lyophilised wafer containing a model compound and a neatly single folded water-containing reservoir were added. These components were then secured in place using a 3D printed lid. Parafilm® M and polyethylene were considered appropriate polymeric films for the production of water-filled reservoirs. Using a heat-sealing method, individual sheets of both polymeric films were cut to size (60 x 26 mm) and folded over once. The two adjacent sides were heat sealed for 10 secs, followed by the addition of 600 μL of water. The top opening was folded and heat-sealed to produce a water-tight polymeric pouch. The volume of water released from both films was quantified following application of a 32 N force for 30 secs. MN insertion into an artificial membrane was also tested using two different hydrogel-forming MNs, comprised of 400 μm and 600 μm needle heights respectively.

Results: To quantify the volume of water released from Parafilm® M (PR) and polyethylene (PER) reservoirs, the mass of a single 3D printed MN device containing the polymeric pouch was recorded before and after application of a 32 N force. In this case, the mass difference represented the volume of water released. Although both reservoirs were of the same size and encased the same volume of water, PR was observed to release a statistically greater volume of water (383 ± 26.7 μL) compared to PER (294 ± 32.2 μL), equivalent to a total % water release of 63.86 ± 4.45% and 48.97 ± 5.37% respectively ($p = 0.0209$). To determine the ability for MNs to insert into an artificial skin membrane using a one-step application, two different MN types comprised of different needle heights, namely 400 μm and 600 μm were tested. After applying a 32 N force for 30 secs to a 400 μm MN, 100% needle insertion into the first layer (126 μm) of Parafilm® M was observed with all four setups, namely PR design, PER design, MN & wafer and MN alone. Furthermore, there was no significant difference between all four setups in the second layer and third Parafilm® M layer ($p > 0.05$). 100% insertion in layers 1 and 2 was observed with all four setups using 600 μm MNs. Although the PR design displayed the highest percentage insertion in layer 3, there was no significant difference between all four setups ($p = 0.2527$). Again, in layer 4, representing an insertion depth of 504 μm, no significant difference in needle insertion was observed between all four setups ($p = 0.3912$).

Conclusions: With the end user at the forefront of this study, a 3D printed MN housing was designed to permit a one-step application process. Comparing 2 different polymeric films, it was observed that PR released a greater volume of water following application of a 32 N force. In addition, it has been shown that this delivery device does not adversely affect needle insertion into an artificial skin membrane. The next phase in this study will include *in vitro* testing of model compounds to determine whether the greater volume of water released from this design enhances or adversely affects permeation across dermatomed neonatal porcine skin when compared to the current two-step application process.