Understanding characteristics essential to the successful design of hollow microneedles for the transdermal delivery of insulin

Fiona Smith[1], Karmen Cheung[2], Joel Segal[3], Faz Chowdhury[2], Frankie Rawson[1], Maria Marlow[1]

[1] School of Pharmacy, University of Nottingham, NG7 2RD, United Kingdom; [2] Nemaura Pharma Limited, LE11 3QF, United Kingdom; [3] Faculty of Engineering, University of Nottingham, NG7 2RD, United Kingdom

Background: Microneedles (MNs) offer the potential for patient-centric drug delivery, including painless administration. More specifically, hollow MNs are well suited to the dose titration of insulin to treat diabetes mellitus, yet there is no approved device. This work evaluated the shortfalls with current commercially available hollow MN devices and the characteristics key to rationally designing a hollow MN device for the administration of insulin.

Methods: Four different hollow MN devices (AdminPen 1500, AdminPen 900, Hydraneedle 20 and Hydraroller 64) were purchased to evaluate their insertion consistency compared to a 4 mm 31-gauge hypodermic needle. Initially, this was assessed using both Parafilm M® and porcine skin models. Later, a 2.65% w/v agarose gel was used with 0.5ml 0.1% w/v methylene blue dye to understand issues with back pressure and leakage. Scanning electron microscopy (SEM) allowed visual inspection.

Thereafter, MiniTab Statistical Software was used to undertake a full-factorial design of experiments to evaluate how the relationship between needle length and the diameter of the hub surrounding the needle, which interfaces with the skin, affects the insertion depth of a single MN. To do so, 4 mm 31-gauge hypodermic needles were modified by attaching 3D-printed components, producing the requisite MNs.

Results: Initial studies with Parafilm M® saw that the Hydraroller 64 was unable to produce uniform insertion, therefore making it obsolete to further investigation. The porcine skin insertion study showed that the maximum insertion efficiency achieved by any device was 47.6% and that MNs only inserted to 42.5-61.9% of their length, depending on the device. Agarose studies demonstrated significant leakage of methylene blue dye, particularly when the AdminPen devices were used, likely due to the high back pressure, further rendering them unsuitable for the reliable delivery of insulin.

Additionally, SEM imaging highlighted the poor standard of manufacturing of hollow MNs, which likely also contributes to poor insertion.

No statistically significant relationship was identified between the hub diameter and the needle length, likely due to the fact the MN insertion has happened before the hub exerted any force on the skin. Unsurprisingly, needle length was identified as a significant factor for insertion depth.

Conclusions: Whilst the insertion profile of existing hollow MN devices is generally poor, the characteristics essential for optimised insertion, and the relationships between them, are still yet to be fully elucidated. Future work will focus on understanding the effects of skin stretching prior to microneedle insertion and the angle of MN insertion.