ENHANCEMENT OF SKIN PENETRATION OF RHODAMINE 123 BY A MICRONEEDLE DEVICE

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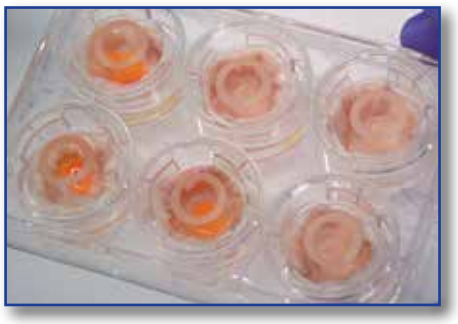
AIMS

Skin constitutes an excellent barrier for the transdermal delivery of hydrophilic or high molecular weight drugs. Low efficacy demonstrated in clinical trials for some topical drugs is mainly due to low skin penetration ability related to the efficient barrier properties of *stratum corneum* (SC). In order to overcome the SC, different chemical and physical methodologies have been investigated to enhance skin penetration. Among the physical methods, one presents the perforation of the SC with microneedles that disrupt the SC barrier of the skin and create pores inducing an increase of penetration. The aim of this work was to evaluate the effect of commercially available microneedle roller device with different needle lengths on the efficiency of skin perforation and the penetration enhancement of Rhodamine 123 in *ex vivo* human skin.

METHODS

Four different models of microneedle roller devices differing by needle lengths (0.2, 0.5, 1 and 1.5 mm) were used. Full-thickness human skin samples were pretreated with microneedle roller device and then treated with Rhodamine 123 (solution 0.1% in DMSO) for 6 hours. Non rolled skin samples were used as controls. Effect of pretreatment with microneedles on skin integrity was evaluated by measuring transepidermal water loss (TEWL) in function of number of roller device passages. At the end of incubation, concentrations of Rhodamine 123 in receptor fluid samples were measured by spectrofluorometry. Distribution of Rhodamine 123 in skin cryosections (6 µm thick) was visualized by epi-fluorescence microscope using a TRITC fluorescence filter cube. Fluorescence related to Rhodamine 123 was analyzed using Image J software.



RESULTS

TEWL increased with the number of passages of the roller device (Figure 1). A marked increase of fluorescence in the skin was observed with all models of microneedle roller devices tested including the model with the shortest needles of 0.2 mm. The results showed that skin fluorescence increased with the needles' length (Figure 2) and the holes created by the different needle models were clearly visible on skin sections (Figure 3). Moreover, concentration of Rhodamine 123 in receptor fluid as well as in skin increased with the length of the needles (Figure 4).

Figure 1 EFFECT OF NUMBER OF PASSAGES OF MICRONEEDLE ROLLER DEVICE ON TEWL

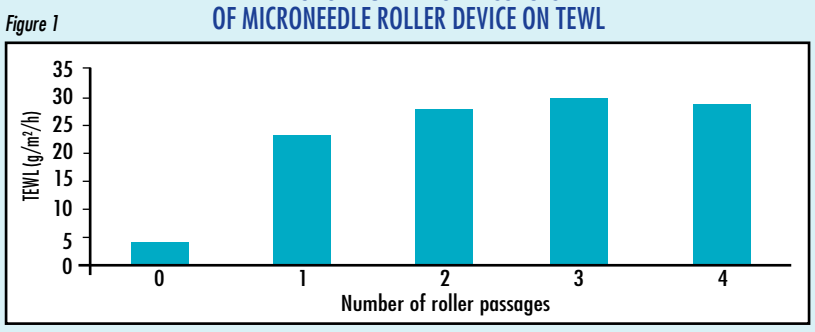


Figure 2 EFFECT OF NEEDLES' LENGTH ON SKIN DISTRIBUTION OF RHODAMINE 123 Skin section

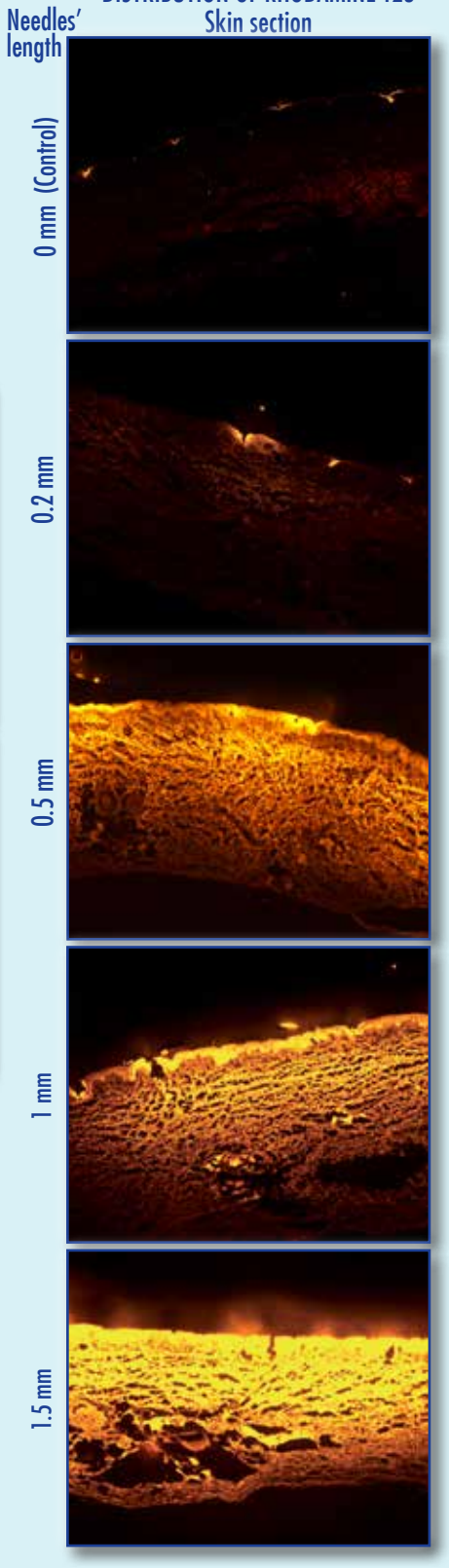


Figure 3 VISUALIZATION OF HOLES CREATED BY THE MICRONEEDLE ROLLER DEVICE

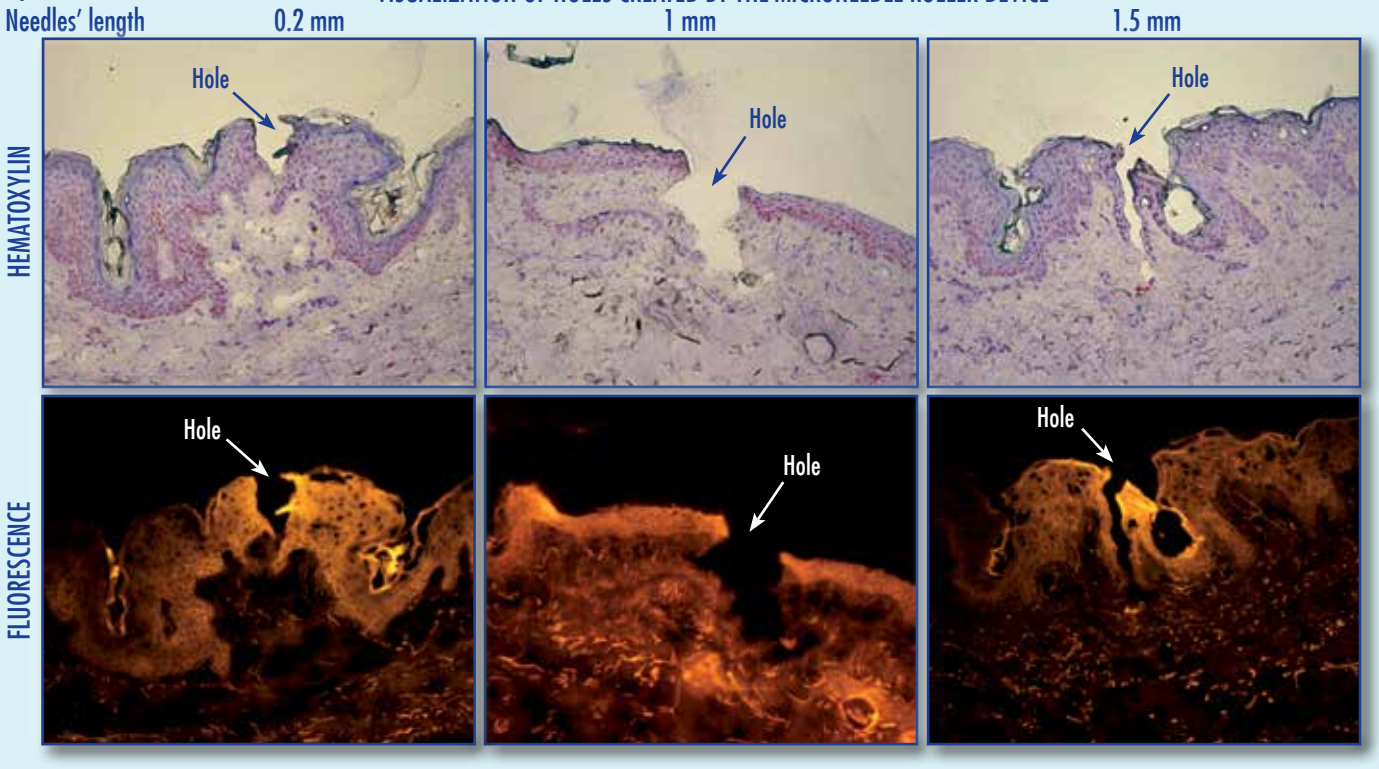
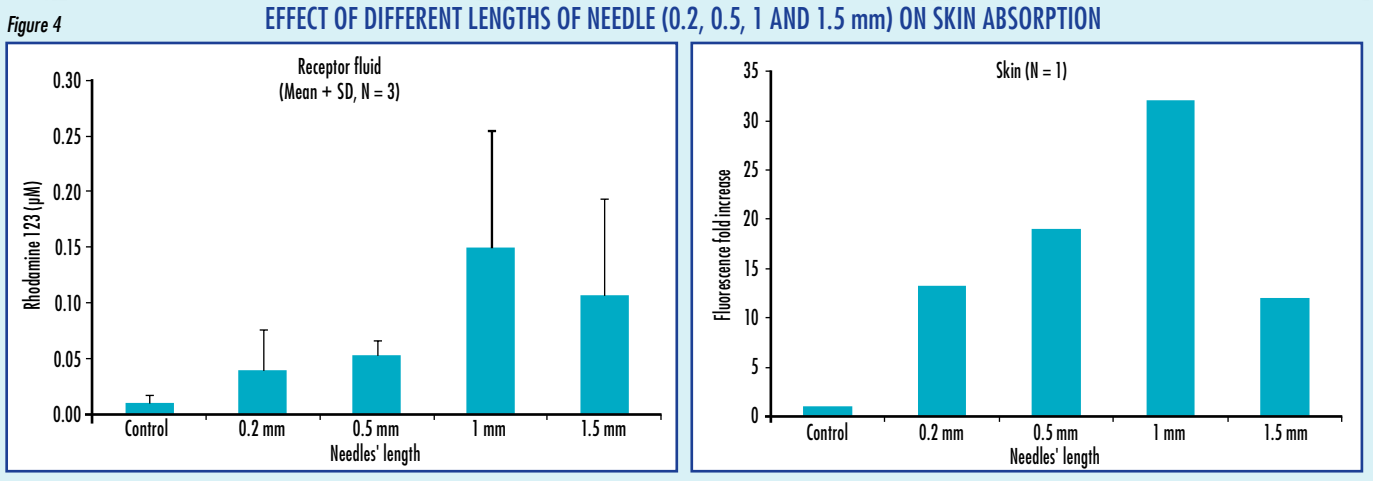


Figure 4 EFFECT OF DIFFERENT LENGTHS OF NEEDLE (0.2, 0.5, 1 AND 1.5 mm) ON SKIN ABSORPTION



CONCLUSION

This work shows that microneedles considerably increased the absorption and distribution of Rhodamine 123 in *ex vivo* human skin samples. Therefore, microneedles can be suitable devices for clinical and preclinical use in order to enhance dermal delivery of test compounds.

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