

Synergistic effect of Iontophoresis and Soluble Microneedles for Topical Delivery of Methotrexate: A Microdialysis Study

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Purpose: To determine the effect of microneedles alone, iontophoresis alone, or the combination on the in vivo topical delivery of methotrexate using intracutaneous microdialysis.

Methods: A MTX gel (15 mg/ml, pH 7.4 in 0.25 M phosphate buffer with 1% HEC) was placed in a cartridge designed for iontophoresis. The cathode from a constant current source was connected to the cartridge and the anode was connected to a Trans Q (IOMED, Inc.) inactive electrode. Cathodal iontophoresis (0.4 mA/cm² for 1hr), soluble microneedles (500 micron) or the combination was tested in the hairless rat microdialysis model. The microneedles were used to porate the skin prior to application of the drug with or without iontophoresis. The dialysate samples collected were analyzed using HPLC. Potential skin irritation was monitored using chromameter, laser doppler velocitometry (LDV) and transepidermal water loss (TEWL).

Results: Methotrexate was used as a model drug in these studies, but published data shows its clinical efficacy when delivered iontophoretically to psoriatic skin. After 1hr of iontophoresis, the concentration of methotrexate in the dialysate (adjusted for recovery) was 42.5 µg/ml. The concentration of methotrexate in the dialysate after iontophoresis in combination with microneedles was 100.1 µg/ml. The increase in concentration with iontophoresis alone was 16-fold ($p < 0.05$) and with the combination of microneedles was 37-fold ($p < 0.05$) when compared to delivery with microneedles alone (2.7 µg/ml). The methotrexate concentration decreased after the iontophoresis was stopped. The average depth of microdialysis probe is 0.54 mm from the skin surface as determined by ultrasound imaging (Dermascan). The chromameter and LDV values did not show any change, whereas TEWL values increased from a baseline reading of 5.5 to 11.3 g/m²h after iontophoresis, 8.9 to 11.2 g/m²h for microneedles and 6.5 to 10.9 g/m²h for their combination.

Conclusion: From these results it can be concluded that iontophoresis alone or in combination with microneedles can significantly increase the topical delivery of methotrexate in vivo. This can lead to potential applications for psoriatic or other skin disorders.

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