

Microneedle Enabled Intradermal Delivery of Biologics

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Abstract

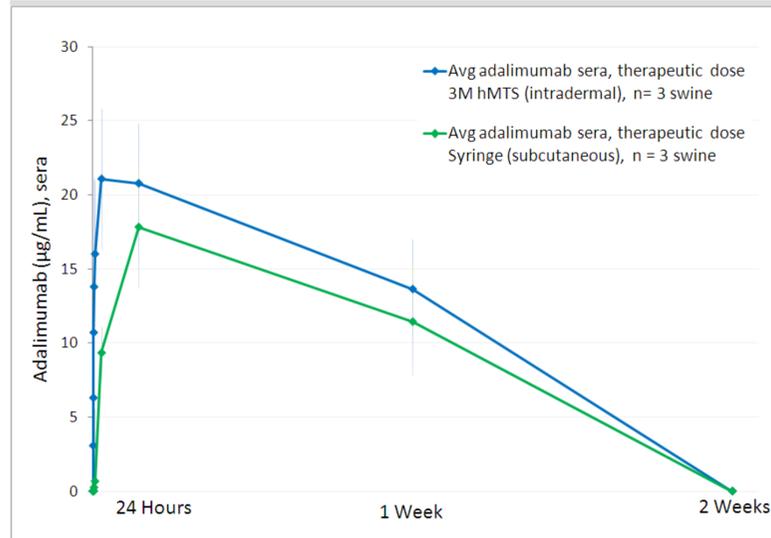
PURPOSE: 3M's has developed a microneedle-based drug delivery platform, collectively referred to as MTS (Microstructured Transdermal Systems). Using solid or hollow microneedles, drugs are delivered into the dermis and/or epidermis. Microneedle-enabled intradermal delivery may provide therapeutic advantages over traditional injection-based delivery devices such as syringes and autoinjectors. This research describes pharmacokinetic features of intradermal delivery that may be different from subcutaneous or intramuscular delivery.

METHODS: Between 2-200 mcg of API was coated on solid microneedles using a dip-coating process and characterized via HPLC. The microneedles were applied to swine and drug was allowed to dissolve off the tips of the structures. Blood samples were collected at designated time points and analyzed using an ELISA assay. Residual drug was measured using HPLC. Liquid drugs or dyes were administered to swine using 3M's integrated hMTS device or via a proof-of-concept device consisting of a hollow microneedle array and a syringe pump. Between 0.8-2mL of formulation was delivered into the dermis over the course of minutes. Drug levels were quantified in blood using an ELISA assay. In both cases (solid and hollow microneedles), a second group of swine were administered drug by subcutaneous injection. Blood samples were collected and analyzed as described above.

RESULTS: Most large molecule drugs administered via solid or hollow microneedles evidenced a PK profile that was slightly different than that observed when the same drugs were administered via subcutaneous injection. Generally, a higher Cmax (up to 150%) and an earlier Tmax were observed, indicating faster absorption of the drug into the systemic circulation. In some cases, a higher AUC (e.g. ~120%) was also observed. Both of these observations may be explained by the higher density of lymphatic capillaries, and the higher rate of interstitial fluid exchange, in the dermis versus the subcutaneous tissue.

CONCLUSION: The viability of microneedle-based intradermal drug delivery is demonstrated for drug formulations currently administered via subcutaneous or intramuscular injection. Differences in the PK profiles between these delivery technologies suggest minor physiological differences in the target tissue. APIs that benefit from faster absorption or higher bioavailability may be good targets for delivery technologies like 3M's MTS.

Results: hMTS ID versus SC Delivery of a Therapeutic Dose of HUMIRA®



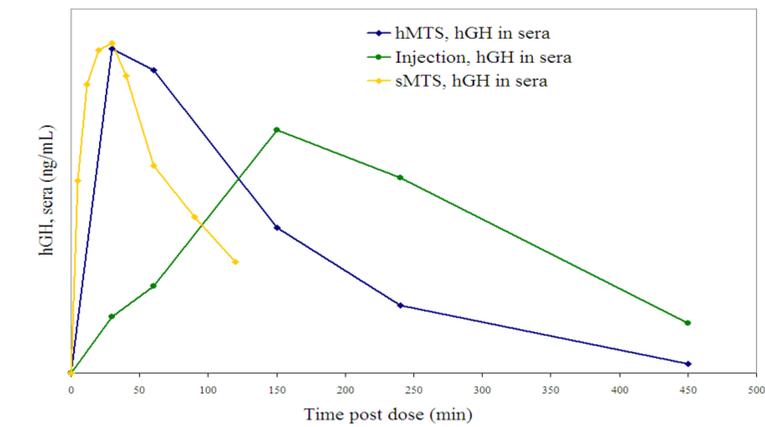
1) **Cmax:** Through 4.5 hours, blood levels associated with hMTS delivery were significantly higher than those associated with SC injection.

2) **Tmax:** Blood levels for hMTS subjects reached a plateau between 4.5 and 24 hours; all SC injection Profiles evidenced a Tmax at 24 hours.

3) **AUC:** Although not statistically significant, the AUC associated with the hMTS delivery was 20% higher than the average AUC associated with injection.

These differences likely result from faster, more complete lymphatic uptake of this large protein in the dermis versus the subcutaneous tissue. The dermis is a very dynamic environment with a high rate of fluid exchange and a high density of lymphatic and circulatory capillaries.

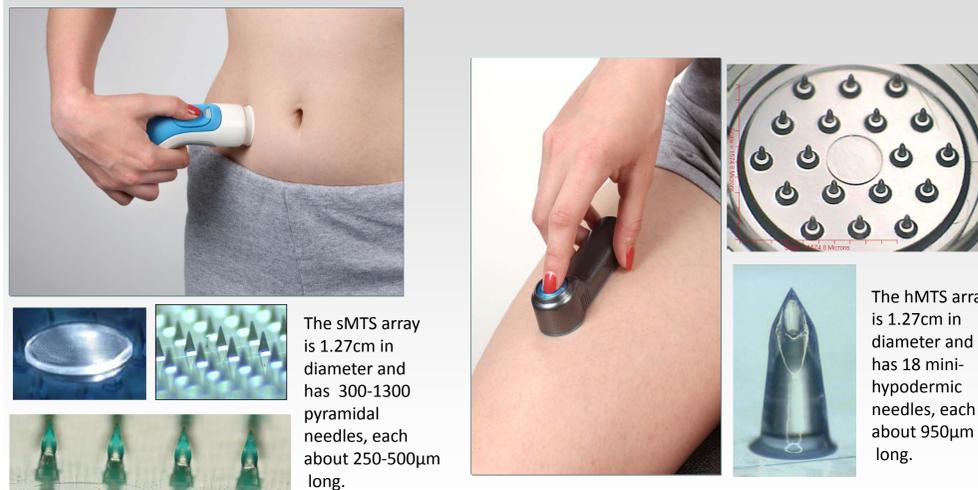
Results: sMTS and hMTS ID versus SC Delivery of hGH



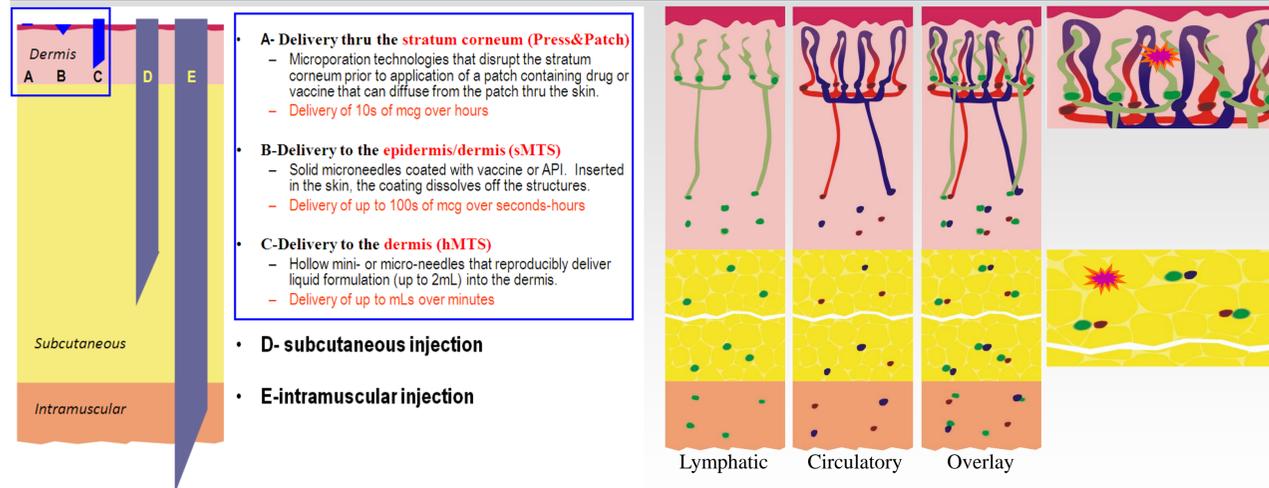
Tmax: hGH Blood levels in swine that received MTS administration was achieved at 30 minutes, significantly sooner than those observed in swine that received hGH administration by SC injection (150 min).

A lower dose of hGH was administered to swine treated by sMTS. Swine that received the hMTS administration showed a higher Cmax than those that received hGH subcutaneously. The AUC was very similar.

hMTS and sMTS Delivery Systems



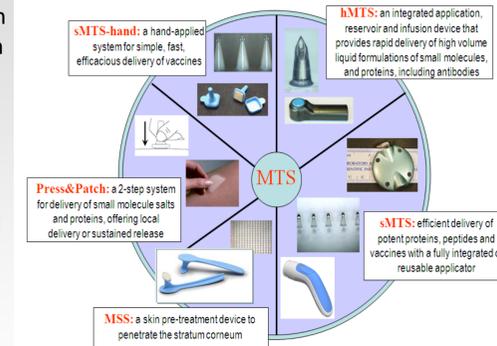
Skin Physiology



Conclusions

3M's MTS is a microneedle-based delivery system designed to provide convenient, self-administration options for transdermal delivery of molecules, such as biopharmaceuticals, not compatible with conventional transdermal delivery technologies.

The MTS platform accommodates both liquid and solid formulations and efficiently and quickly accesses the intradermal space. Biopharmaceutical delivered into this compartment often show and earlier Tmax, a higher Cmax and, in some cases, a higher bioavailability. This rapid, efficient absorption can be attributed to the high density of blood and lymphatic capillaries, and the rapid fluid exchange in the dermis.



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