# Rapid Intradermal Drug Delivery by a Dissolvable Micro-Needle Patch

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ABSTRACT SUMMARY:

The versatile TheraJectMAT™ transdermal patch consists of dissolvable micro-needles composed of drug or vaccine in an inert GRAS matrix. The system can deliver hundreds of micrograms of drug rapidly through the stratum corneum into the epidermal tissue. This technology may be ideal for skin immunization.

## INTRODUCTION:

It is generally recognized that skin immunization is more effective and more efficient for vaccination[1-2] than standard intramuscular or subcutaneous syringe injection. It is the Langerhans cells in the skin that initiate the immune response. The dissolvable transdermal micro-needle technology can effectively overcome the stratum corneum barrier function[3-4] and deliver an effective vaccine payload to the appropriate tissue. TheraJect's proprietary micro-needle patch techniques provide simple, syringe-, blood- and pain-free delivery to the epidermis. The model drug lidocaine and human cadaver skin were used to demonstrate the potential for skin immunization with TheraJectMAT™, by visual observation of needle penetration and rapid dissolution as well as extraction and measurement of lidocaine concentration in epidermal tissue.

## EXPERIMENTAL METHODS:

Lidocaine HCl from Sigma and sodium carboxymethyl cellulose (CMC) from Hercules were dissolved in D.I. water at a predetermined ratio. The resulting gel was cast into a mold by centrifugation and dried under ambient conditions. When dried, the micro-needle matrix was separated from the mold and cut into 7/16"diameter discs each having 25 micro-needles. The stratum corneum is thermally separated from cadaver skin dermatomed to ~300 μm in thickness. The separated layer was replaced onto the dermal skin layer and positioned on a ¼" thick shock-absorbing base to which the lidocaine micro-needle patch was applied by a spring injector at ~4 m/s injection velocity. At predetermined intervals (5, 10, 15 and 30 minutes), the stratum corneum and remaining micro-needle system were separated for visual inspection. The dermal layer was extracted in 3 ml of D.I. water for lidocaine content quantitative analysis by HPLC.

## RESULTS AND DISCUSSION:

Table 1 shows average drug delivery for different percentages of drug-loaded micro-needles (1.5 mm length for 30 minutes). Fig.1 shows the amount of drug released over 30 minutes. As expected, micro-needles containing a higher percent composition released more drugs per unit time. Fig. 2 (a) and (b) are images of micro-needle penetrating the stratum corneum. The estimated drug delivered after 30 minutes is in reasonable agreement with the measured delivery amount. The estimated delivery in table 1 was calculated based on the visual observation that 55% of the conical micro-needles penetrated the skin and the penetrated portion was fully dissolved (Fig.3).

Table 1: Delivery of Lidocaine in 30 minutes from 1.5 mm micro-needle injection.

| Drug loading % w/w | Actual Delivery (μg) | Estimated delivery* (μg) |
|---|---|---|
| 10% | 99 ± 20 | 95 |
| 20% | 192 ± 90 | 191 |
| 40% | 394 ± 33 | 381 |

*based upon 55% of total conical needle volume penetrated and dissolved (visual observation)

Fig.1: Lidocaine Delivered into Skin over 30 Minutes

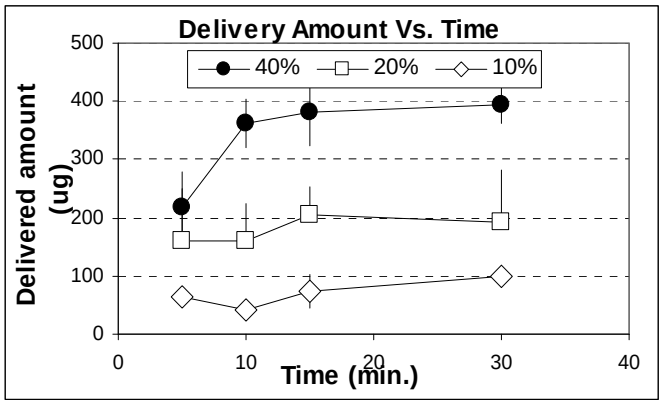



Fig.2: Micro-Needle Penetration of Stratum Corneum.

(a) 5 minutes (b) 30 minutes

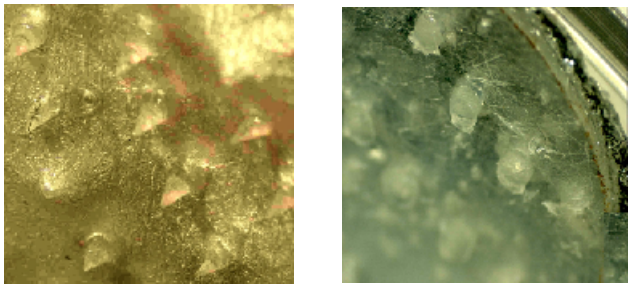
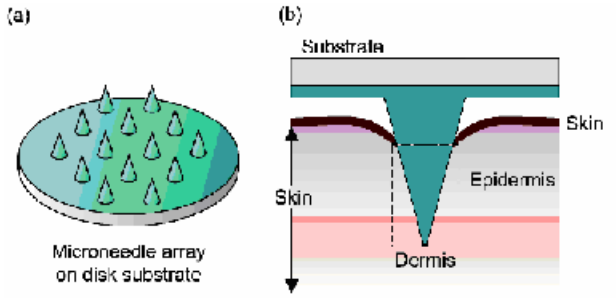


Fig.3: Micro-Needle Skin Penetration




The data is consistent with a portion of the micro-needles penetrating the skin and the embedded portions (within dashed line) dissolving within 30 minutes (Fig. 2 b).

The intradermal delivery for different needle dimensions was also evaluated (Table 2). As expected, longer micro-needles were more effective in delivery and alternative compositions are also likely to have an effect. The sensation for injection with these micro-needle systems was mild and no micro-bleeding was observed in placebo human tests (data not shown).

Table 2: Effect of Micro-Needle Dimensions on Lidocaine Delivery (20% lidocaine)

| Length / Base diameter (μm) | Tip angle | Delivery(μg) in 15 minutes |
|---|---|---|
| 1500 / 670 | 30° | 205 ± 49 |
| 960 / 480 | 30° | 181 ± 21 |
| 900 / 300 | 20° | 103 ± 16 |
| 630 / 230 | 30° | 25 ± 7 |

CONCLUSION: *In-vitro* data clearly show that micro-needle patches composed of drug in a fast-dissolving matrix can rapidly deliver payload into skin. The human trivalent HA influenza vaccine dose is 45μg. So it appears that the depth, speed, and deliverable amount of TheraJectMAT™ are ideal characteristics for intradermal vaccine delivery.

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