Depot-Forming Dissolving Microarray Patches for the Non-invasive Delivery of a Model Hydrophobic Drug

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Introduction:

Prolonged release dosage forms are becoming increasingly attractive due to their ability to provide continuous release of medications following their administration. This increases patients' compliance to their treatment regimens and, thus, improve their quality of life [1]. However, to achieve prolonged release over more than 24 hours, injections or implants are required. Such systems are invasive and difficult to terminate upon the development of toxic or adverse events [2]. Therefore, in this project, microarray patches (MAPs) containing a model hydrophobic drug; atorvastatin (ATR), are being developed to deposit a therapeutic dose intradermally to provide a sustained systemic absorption over a prolonged period.

Methods:

- Moulds were firstly prepared, then dissolving MAPs were fabricated in a bilayer-casting technique [3], as shown in Figure 1.

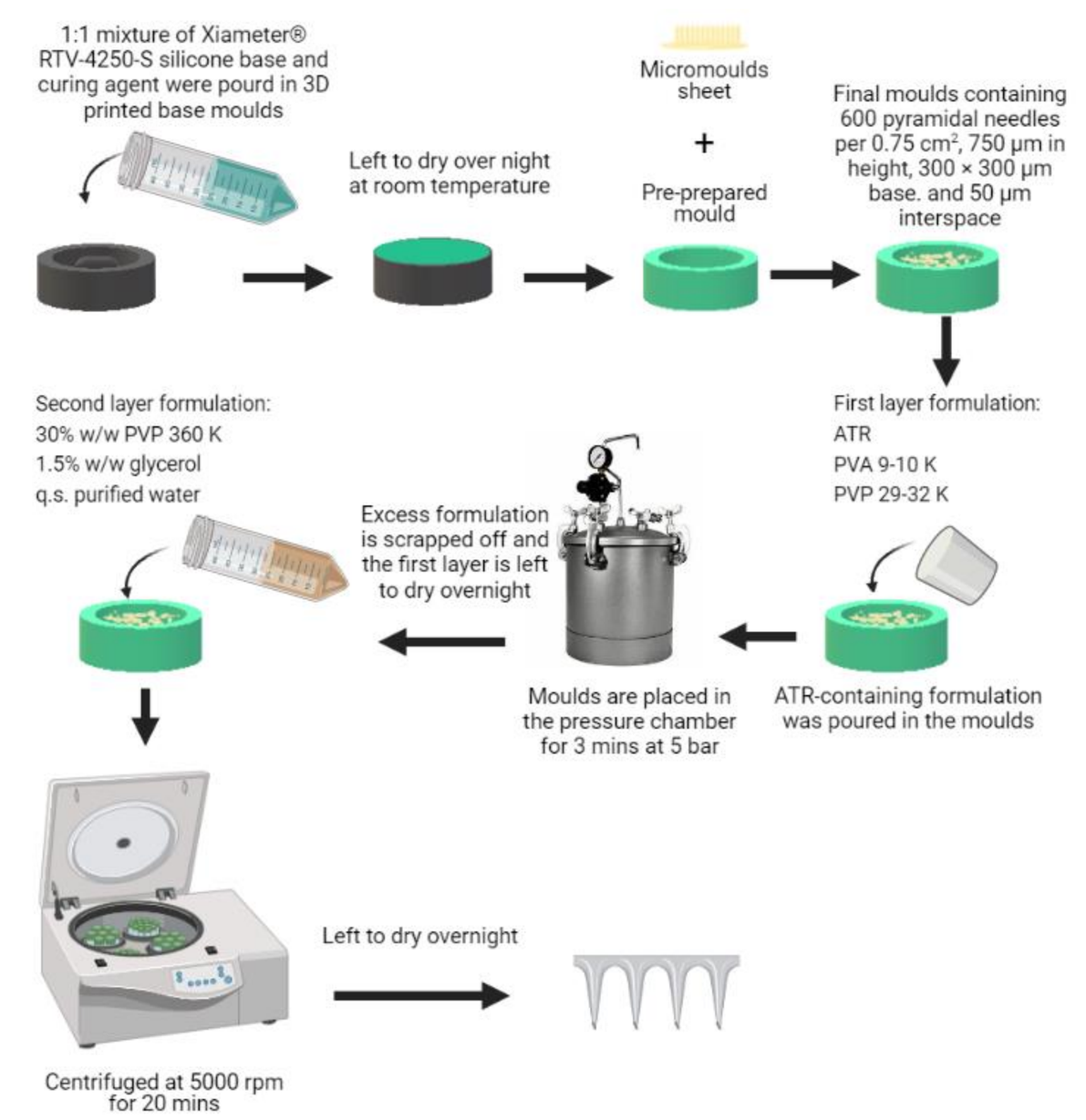

Figure 1: Schematic representation of steps required to prepare moulds and cast dissolving MAPs.

- The moulds were comprised of 600 pyramidal needles per 0.75 cm2, 750 µm height, 300 × 300 µm base and 50 µm interspace.
- MAPs were firstly characterised in terms of their mechanical strength, drug content and in situ insertion efficiency.
- Afterwards, an ex vivo skin deposition studies for 4 and 24 hours were conducted using Franz-cells, as described in Figure 2, to quantify ATR deposited intradermally.

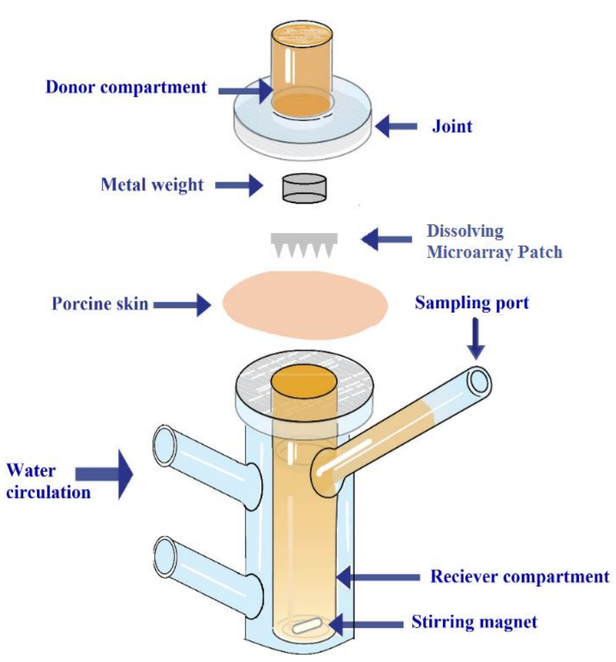

Figure 2: Schematic representation of Franz cells set up.

Results:

- MAPs were found to contain a mean of 5.15 ± 0.4 mg of ATR/MAP. Their tips were efficiently inserted into excised neonatal porcine and reached ~ 500 µm depth in skin. MAPs were also able to dissolve *in situ* within 60 minutes.

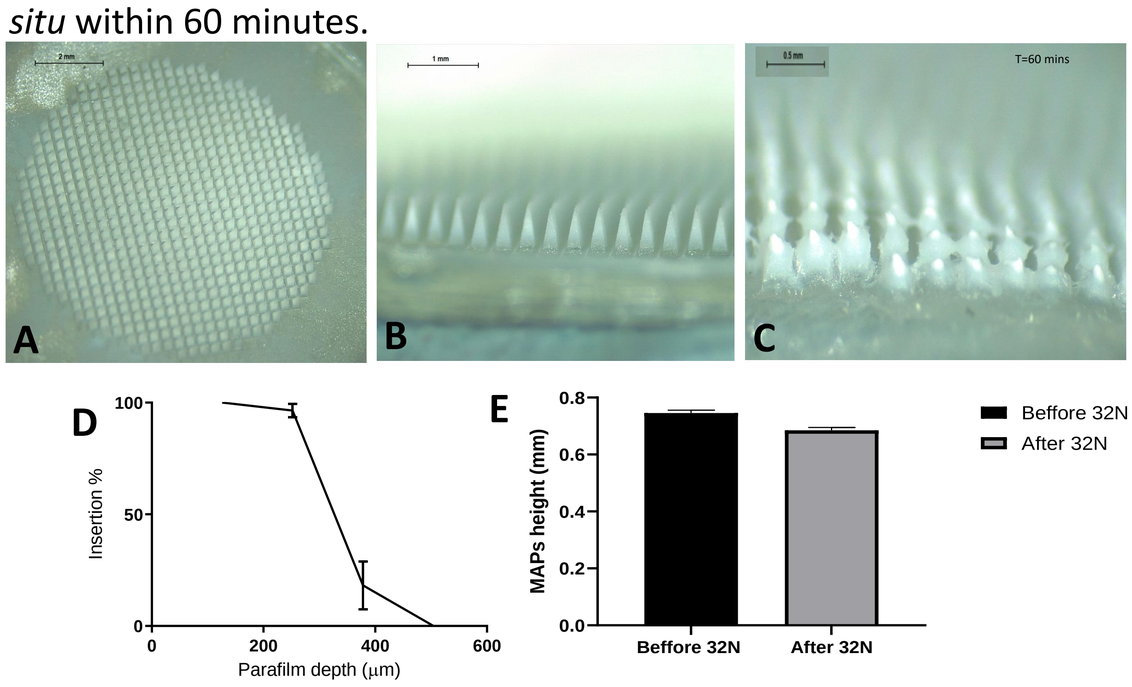

Figure 3: Microscopic images for ATR-containing dissolving MAPs prior to their insertion into the skin (A, B), and at t=30 mins (C). The *in vitro* insertion profile of the MAPs (D) and the height reduction percentage after the application of 32 N force, which was only 8% (E) .

- Skin deposition studies showed that a total amount of ATR delivered after 24 hours was found to be 2.0 ± 0.33 mg, which represents 38.7 ± 6.7% of the initial amount loaded in each MAP. After 4 hours, an overall quantity of 1.45 ± 0.15 mg ATR, which stands for 28 ± 0.79% of the initial ATR amount loaded in each MAP.

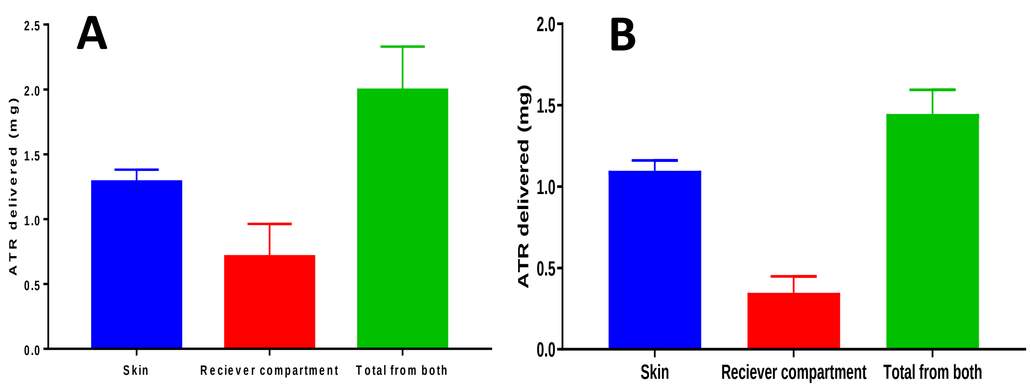

Figure 4: Illustrates the percentage delivered into skin and receiver compartments of Franz cells at (A) 24 hours and (B) 4 hours following MAPs insertion into the skin. Mean ± SD, n=3.

Conclusions:

Those findings demonstrate the efficiency of MAPs to successfully deposit hydrophobic ATR intradermally for its subsequent systemic release. Oral bioavailability of ATR after 40 mg oral dose is known to be ~14% [4]. Therefore, a weekly therapeutic dose can potentially be deposited into the skin using a reasonable patch size of ~14.7 cm^2. Future *in vivo* study to be conducted to evaluate ATR delivery over two weeks.

References:

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