3D PRINTED MICRONEEDLE PATCHES FOR DRUG DELIVERY

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Dennis is currently a Professor in Pharmaceutical Technology & Process Engineering and for the last 5 years his research has focused on three main areas including Continuous Manufacturing of Pharmaceutical Processes, Nanotechnology and Medical Devices. Dennis received a prestigious award for my "Outstanding Scientific Contribution" in Pharmaceutical Processes and invited to deliver the Award Lecture, sponsored by AstraZeneca, at the Academy of Pharmaceutical Sciences' 'PharmSci 2017' conference. He has joined the Editorial Boards of more than six international journals including the Wiley's Editorial Board for the edition of a series in "Advances in Pharmaceutical Technology". Dennis has published 87 full papers, 4 patents, 5 book chapters and 2 book editions.

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Sophia is a PhD student at the University of Kent working on the design and 3D printing of microneedles for drug delivery purposes.

3D printing comprises of a family of distinct technologies that use a layer-by-layer process to create a physical object based on a virtual Computer Aided Design (CAD) model. Since its launching in the 1980s, it has changed the outlooks of manufacturing in numerous industrial and scientific fields, enabling the fast and accurate production of structures and components with levels of complexity that are unreachable through conventional techniques. Medical scientists envisioned the unique prospects of 3D printing to fundamentally alter how patients are treated, aiming in taking modern therapeutics from the massively produced to the customised. Implants and prosthetics have been 3D printed with tailored, patient-specific characteristics. In pharmaceutics, the investigation on this cutting-edge technology's potential to manufacture drug delivery systems has already been fruitful, with the first 3D printed oral administration tablet, Spritam, to gain FDA approval and the term 'pharmacoprinting' to be introduced.

Lately, applications of 3D printing on the field of Transdermal Drug Delivery (TDD) have started to be explored. Modern TDD systems are vastly based on the concept of microneedles, which are miniature puncturing devices that can painlessly pierce the skin and convey drugs directly into the dermal microcirculation. Microneedle systems are an appealing alternative to traditional oral and injection-based drug administration routes that tackle common drawbacks such as needle phobia, pain and degradation in gastric acids, yielding high degrees of bioavailability. 3D printing aims to revolutionize microneedle fabrication strategies since typical methods such as micromoulding and micromachining are commonly multistep and difficult to scale-up.

Key highlights of 3D printed microneedles:

- Rapid fabrication of complex designs with high resolution
- Delivery of various therapeutic agents at high drug load
- Use of a biocompatible printable resin

Among the various 3D printing technologies, Stereolithography (SLA) is a user-friendly, straightforward, cost-effective technology that uses a UV laser beam to selectively polymerize photosensitive polymers. Due to its high-resolution capability, SLA permits the creation of complex structures with great accuracy and reproducibility. It also endows the design and prototype stage with versatility since multiple designs can be built simultaneously with no material losses associated with the fabrication of moulds.

In this study, the SLA technology was employed to fabricate four prototypes of solid microneedle arrays with different needle shapes. The arrays were designed using the SolidWorks® 3D CAD engineering software and featured cone, cross, pyramid and spear shaped microneedles (Fig. 1).

The four designs were printed via a photopolymerization process using a Class I FDA approved resin leading hardened plastic patches with strong mechanical properties. The complete fabrication process including post-printing washing and curing under UV radiation lasted less than two hours.

The 3D printed microneedle arrays demonstrated excellent piercing capacity. Piercing tests through full thickness porcine skin were conducted, measuring the force required for each design to fully penetrate. All the designs successfully pierced the skin and no needle failure was observed. Very low forces of penetration (<5 N) were needed for all the designs, with the cone-shaped needles to require the minimum force value. A major advantage of the microneedles patches is the rapid release rates of therapeutic agents even at high drug loading. The study demonstrated that 3D printing when combined with coating or 'poke and patch' strategies is a promising technique for the fabrication of solid microneedles for transdermal drug delivery. Future developments will focus on the co – printing of drug/polymer blends with the drug substance embedded in the polymeric structure.

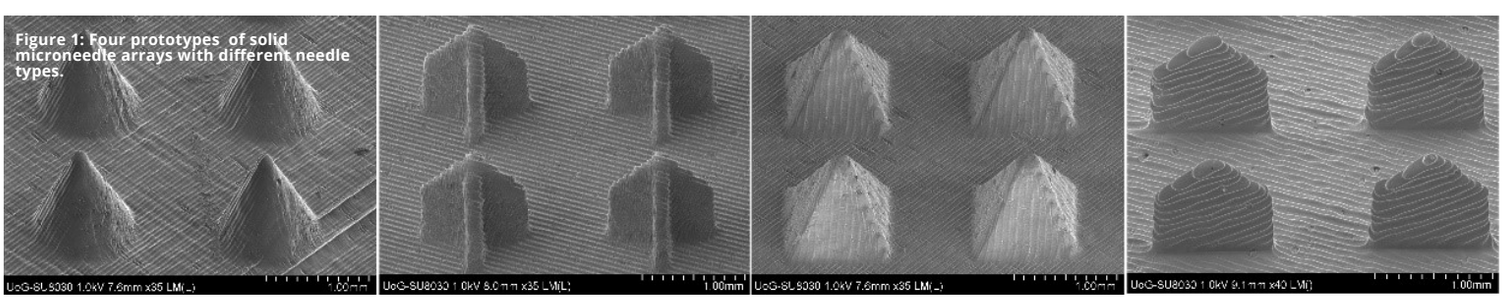

Figure 1: Four prototypes of solid microneedle arrays with different needle types.