A smartphone-enabled 3D printer for fabricating medicines

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INTRODUCTION

3D printing is seen as a disruptive technology with the potential to drive the development of personalised medicines [1]. **Smartphone-based applications** have emerged as alternative platforms to serve affordable and accessible healthcare. A method for directly fabricating pharmaceuticals using one's own mobile phone could be advantageous for **point-of-care manufacturing** of **personalised medicines** at patient's home, on the move or even in resource-limited areas.

AIM

To investigate the feasibility of utilising a smartphone-enabled 3D printer for preparing personalised warfarin sodium Printlets (3D printed tablets) in various geometries.

METHODOLOGY

The smartphone-based printer (M3DIMAKER LUX, FabRx Ltd., UK) (19.5cm x19.5cm x 15cm) contains a building platform, a resin tank, and a container underneath the resin tank for the smartphone (**Figure 1**). Printlets were designed with the same thickness (2.5 mm) but different diameters; size-8 (8 mm diameter), size-11 (11 mm diameter), and size-16 (16 mm diameter). Photopolymer solutions (EOS1) contained 6.92% (w/w) Eosin Y disodium salt 1% (w/v) solution, 7.5% (w/w) triethanolamine, and PEGDA. 5% (w/w) warfarin sodium was added as model drug (EOS2). A Samsung Galaxy A3 smartphone was used as the model and a custom printing mobile app was developed to control the printing process (**Figure 2**).

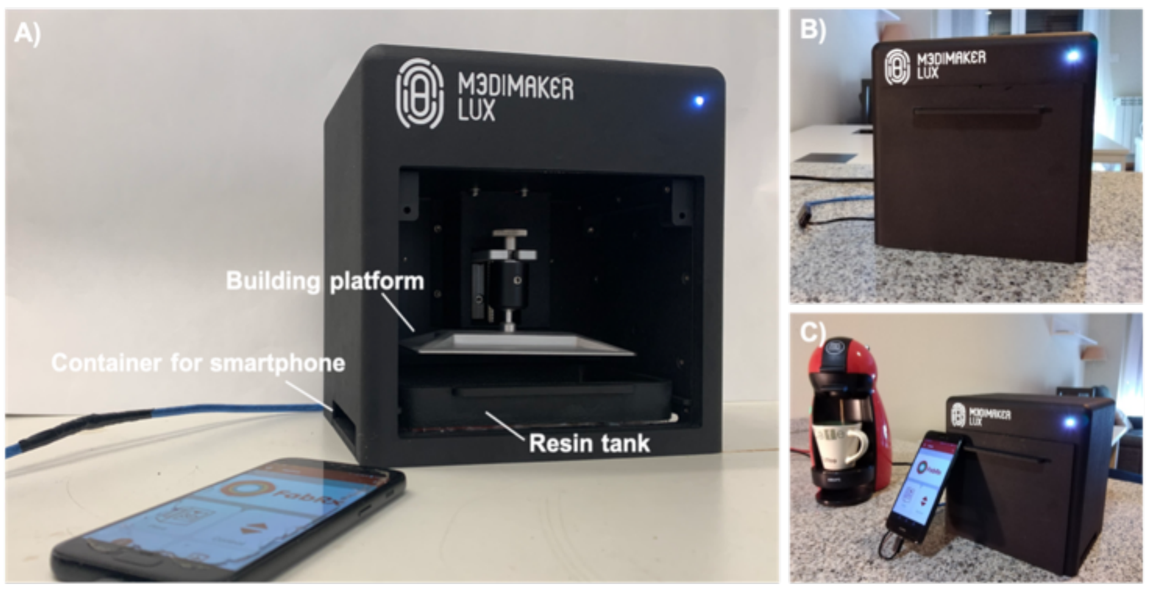

Figure 1. Picture of the **A)** smartphone-based 3D printer alongside a smartphone, **B)** the printer with the smartphone inside it during the printing process, and **C)** comparison of the size of printer with a coffee machine.

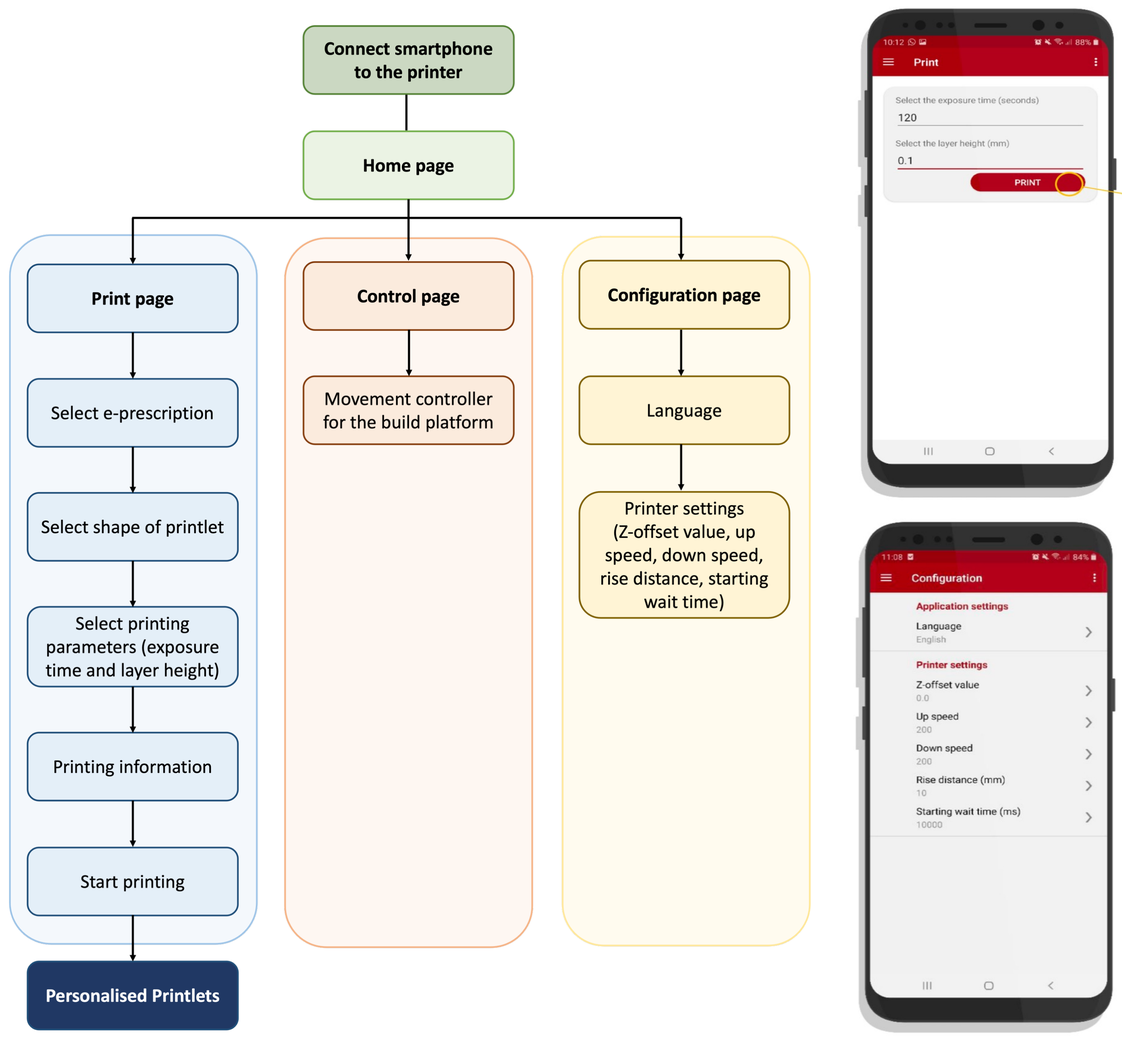

Figure 2. Flow chart of a smartphone-enabled 3D printing process using the custom mobile printing app

RESULTS AND DISCUSSION

Warfarin-loaded Printlets in three different sizes were successfully prepared (**Figure 3A**) with **high resolution and precision**. Printlets with various geometries (**Figure 3B**) and gyroid lattice Printlets (**Figure 3C**) were prepared, demonstrating the **flexibility** of this printer in developing **patient-centric medicines** and illustrating its adaptability to versatile materials.

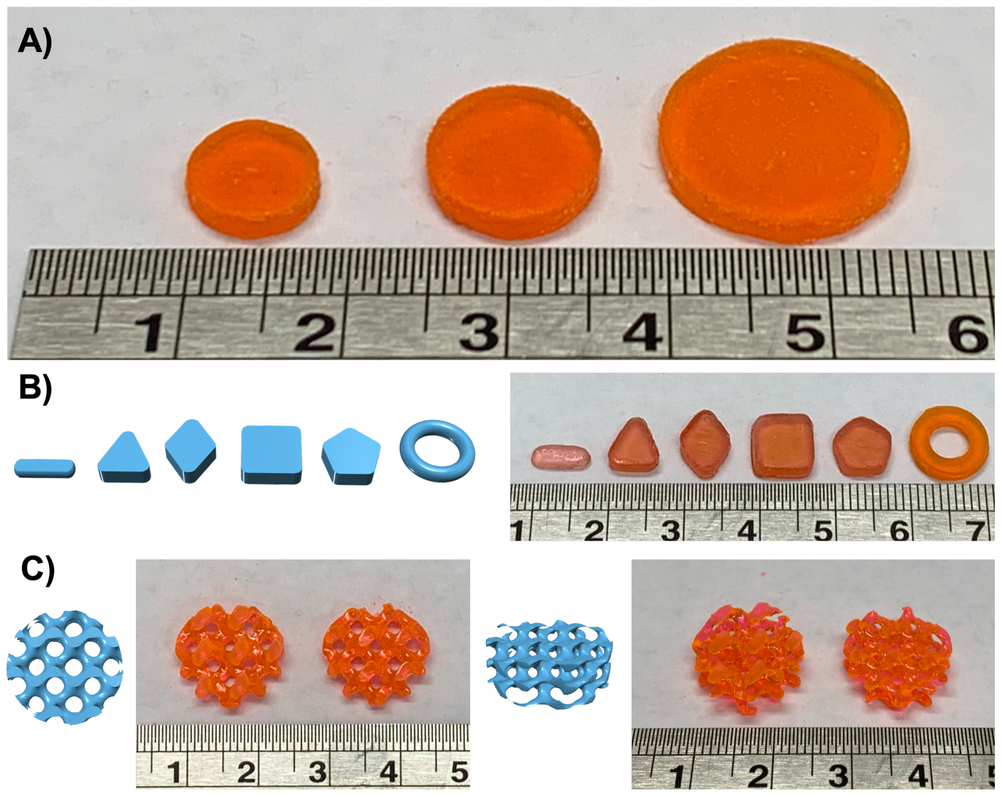

Figure 3. A) Photographs of (from left to right) size-8, size-11, and size-16 Printlets; 3D models (left) and photographs (right) of **B)** Printlets in various geometries, and **C)** gyroid lattice Printlets. Scale shown in cm.

XRPD and DSC analyses were performed to investigate the physical state of warfarin in EOS2 Printlets and the results suggested the drug is present in an amorphous phase **(Figure 4).**

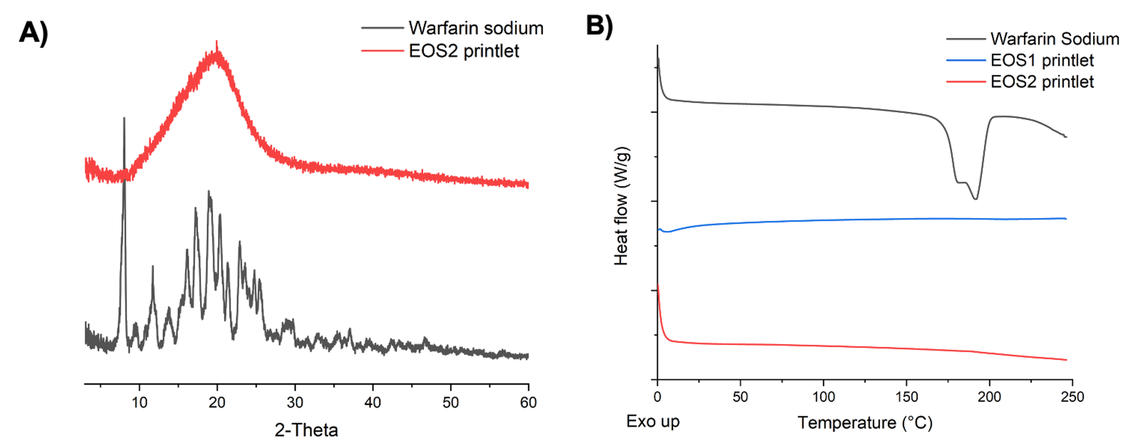

Figure 4. A) X-ray powder diffractograms, and **B)** DSC thermograms of warfarin, EOS1 Printlet, and EOS2 Printlet.

The Printlets were tested in an *in vitro* dynamic dissolution model to evaluate the warfarin release rates **(Figure 5).** The release of warfarin commenced slowly in the gastric phase during the first 2 h and the release rates increased in the intestinal phase and continued throughout the remaining 22 h.

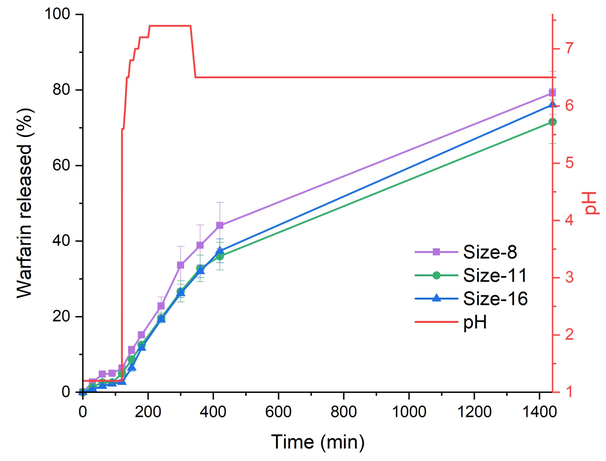

Figure 5. Cumulative release profiles of EOS2 size-8, size-11, and size-16 Printlets. Data values represent mean ± SD (n=3).

CONCLUSION

In this study, a compact smartphone-based 3D printer and a customised printing app were developed and used for the preparation of warfarin-loaded Printlets. The printer is **portable and easy to operate**, making it suitable for use, even in the absence of professional knowledge on 3D printing. The findings of the present study establish a proof-of-concept for the potential of this 3D printing system, however several safety and regulatory concerns should first be addressed to enable its translation into real-world healthcare benefits.

REFERENCES

[1] Seoane-Viaño, I., et al., Translating 3D printed pharmaceuticals: from hype to real-world clinical applications. Advanced Drug Delivery Reviews, 2021, 174, 553-575.

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3D printed dexamethasone-loaded punctal plugs for dry eye disease

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INTRODUCTION

Dry eye disease is a common ocular disorder that is characterised by tear deficiency or excessive tear evaporation. Common treatment involves the use of eye drop however ocular bioavailability is usually poor (<5%) [1]. **Punctal plugs** are non-invasive and non-surgical medical devices to mitigate dry eye syndromes **(Figure 1). 3D printing** has been forecast to become a revolutionary technology within the pharmaceutical sector for preparation of **personalised medicines** [2].

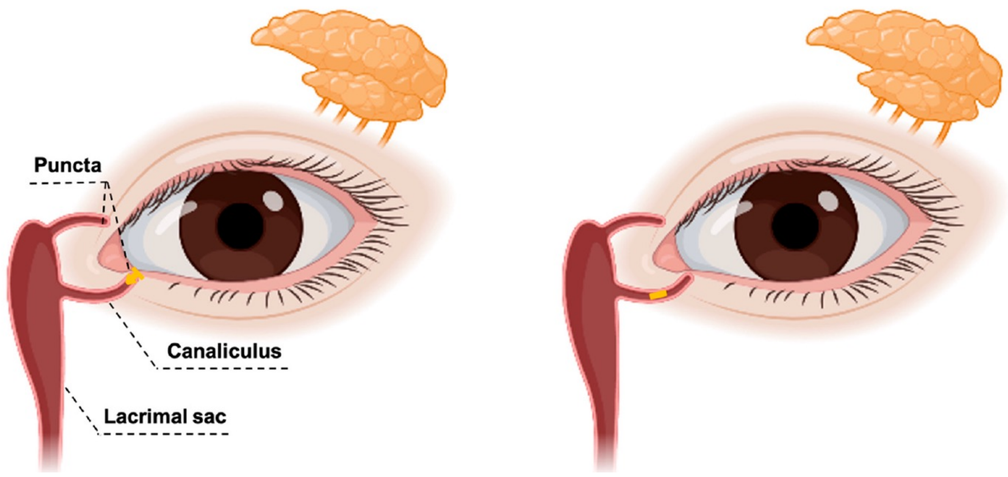

Figure 1. Schematic illustration of punctal plug in the punctum (left) and in the canaliculus (right) of the eye.

AIM

To employ **digital light processing (DLP)** 3D printing to fabricate drug-loaded punctal plugs for controlled drug delivery. **Dexamethasone**, a corticosteroid, was incorporated because of its anti-inflammatory properties and wide applications in corneal disease treatment, including dry eye symptoms.

METHODOLOGY

The punctal plug was designed to be inserted in the punctum of the eye with a configuration similar to those of commercially available punctal plugs. Photopolymer solutions contained 2.0% (*w*/*w*) Irgacure 819, 1.0% (*w*/*w*) β-carotene, and dexamethasone, PEGDA, and PEG 400 as shown in **Table 1**.

Table 1. Compositions (% w/w) of the drug-loaded photopolymer resins.

	Dexamethasone	PEGDA	PEG 400
D10	10.0	87	0.0
D20	20.0	77	0.0
D10PEG	10.0	69.6	17.4
D20PEG	20.0	61.6	15.4

All the punctal plugs were printed with a commercial DLP 3D printer (Titan2 HR, Kudo3D Inc., Dublin, CA, USA) equipped with an HD DLP projector. *In vitro* release kinetics of the punctal plugs were evaluated using an in-house flow rig model that mimics the subconjunctival space [3] **(Figure 2).**

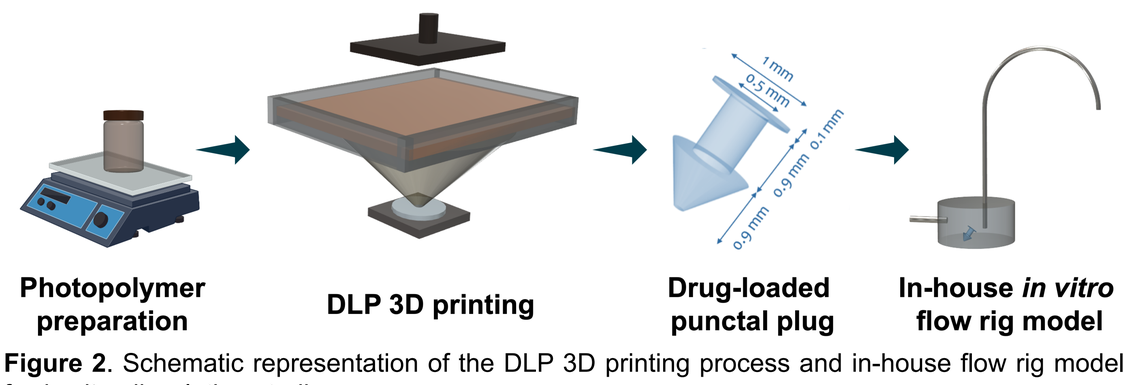

Figure 2. Schematic representation of the DLP 3D printing process and in-house flow rig model for *in vitro* dissolution studies.

RESULTS AND DISCUSSION

Different dexamethasone-loaded punctal plugs were successfully fabricated via DLP 3D printing with good resolution and reproducibility **(Figure 3).** XRPD and DSC results showed that a small fraction of dexamethasone was in crystalline state in the D20 and D20PEG 3D printed formulations **(Figure 4).**

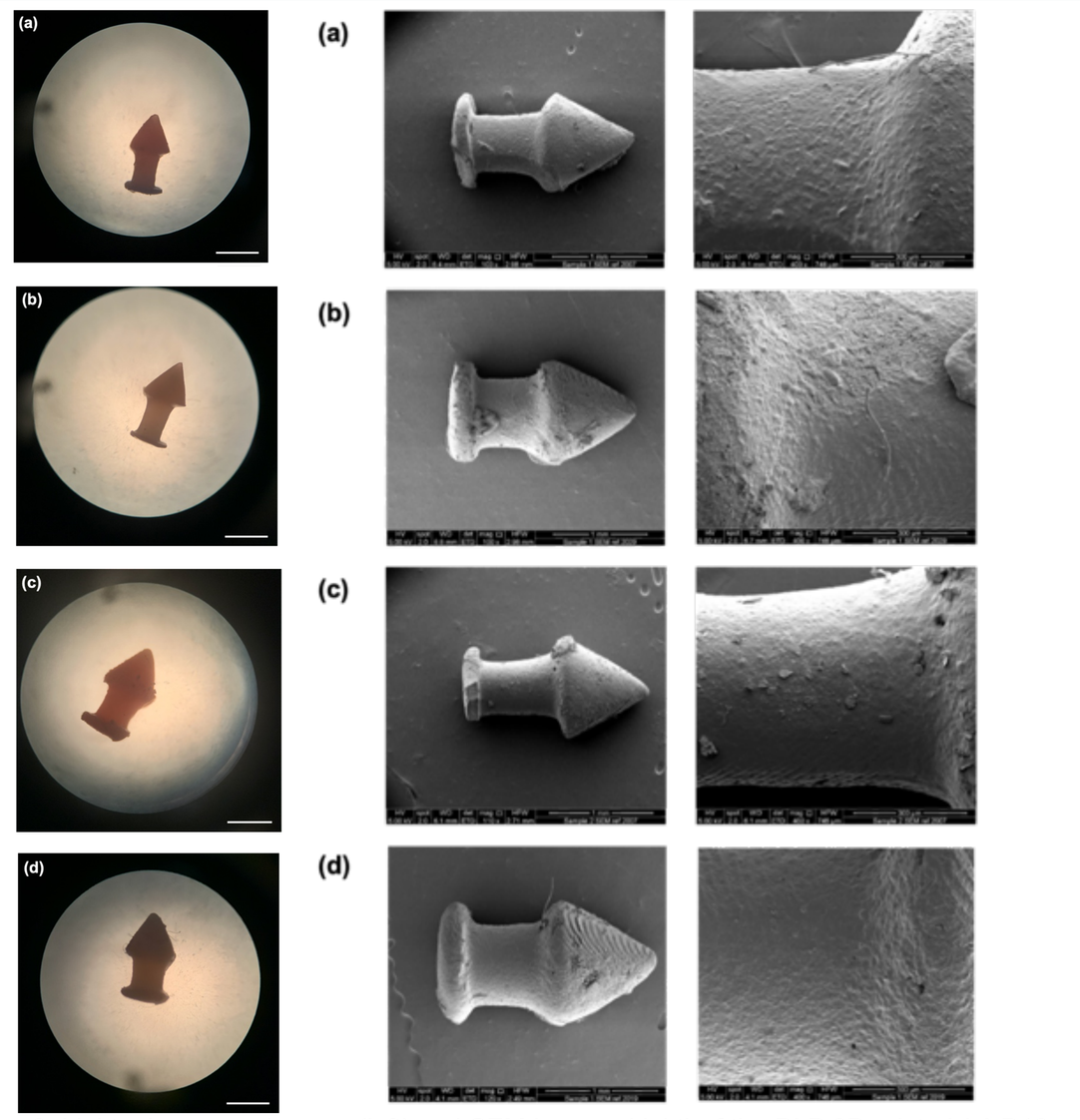

Figure 3. Light microscope images (left) and SEM images (right) of the DLP 3D printed **(a)** D10, **(b)** D10PEG, **(c)** D20, and **(d)** D20PEG punctal plugs. The scale bar is equivalent to 1mm.

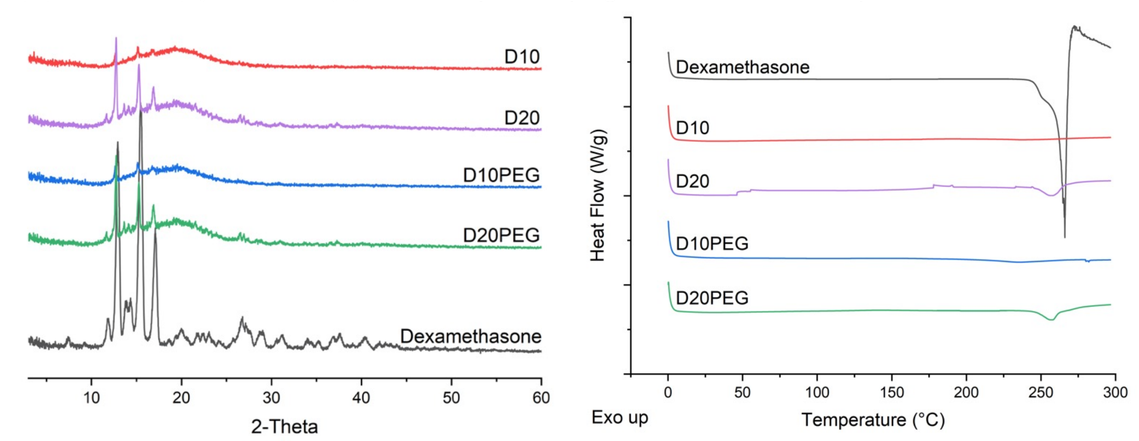

Figure 4. X-ray powder diffraction patterns (left) and DSC scans (right) of dexamethasone and DLP 3D printed formulations.

In vitro release results showed sustained release of dexamethasone for up to 7 days from D10PEG and D20PEG punctal plugs, while punctal plugs made with D10 and D20 exhibited **prolonged releases** for more than 21 days **(Figure 5).**

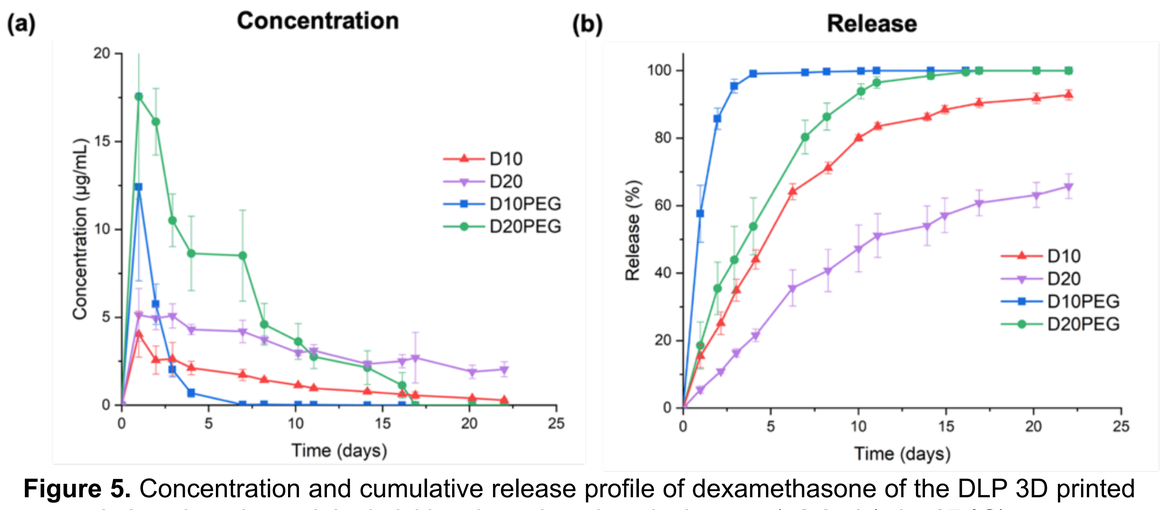

Figure 5. Concentration and cumulative release profile of dexamethasone of the DLP 3D printed punctal plugs in a rig model mimicking the subconjunctival space (~2.0 μL/min, 37 °C).

CONCLUSION

This study demonstrated that DLP 3D printing represents a potential manufacturing platform for fabricating personalised drug-loaded punctal plugs for patients with dry eye disease. The opportunities could be extended to adapt other ocular therapeutics for **drug delivery to the front eye** with extended release characteristics.

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