3D PRINTING OF MICROBICIDE VAGINAL RINGS: A PROOF-OF-CONCEPT STUDY

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WHAT WE LEARNED

1. 3D printing can be used for the fabrication of single dose vaginal rings and MPTs with controlled diffusion based drug release obeying $t^{1/2}$ kinetics up to Day 28.

2. A higher rate of release can potentially be achieved from 3D printed vaginal rings compared to conventionally injection moulded rings using liquid silicone rubber, however this theory requires examination.

3. By diversifying the materials used to encapsulate APIs, a broader spectrum of therapeutic compounds could be explored for delivery from vaginal rings and MPTs.

BACKGROUND

3D printing based on fused deposition modelling (FDM) technology can be used to achieve control over an object's design through the manipulation of geometry, density and surface area. This creates exciting opportunities for the development of customizable medicines that cannot be achieved using conventional thermoplastic processing techniques.

OBJECTIVES

1. Determine the feasibility in using 3D printing as an alternative manufacturing technique in the production of a viable drug delivery device that is capable of delivering a pharmaceutically relevant dose of drug.

2. Produce a multipurpose prevention technology (MPT) with discrete layers that can be used to deliver a microbicide and a hormonal contraceptive.

METHODS

A Makerbot Replicator 2 3D printer was used to manufacture single dose vaginal rings and MPTs using dapivirine (DPV) (20% w/w) and/or levonorgestrel (LNG) (20% w/w) loaded filament blends of poly lactic acid (PLA) and thermoplastic polyurethanes (T87) (1:4).

In vitro analysis (n=4) was carried out for each formulation over 28 days in water with 0.25% w/w Tween® 80. Samples were placed in a shaking incubator at 37˚C and 60 min^{-1}. Release samples were taken daily and analysed using high pressure liquid chromatography (HPLC).

RESULTS

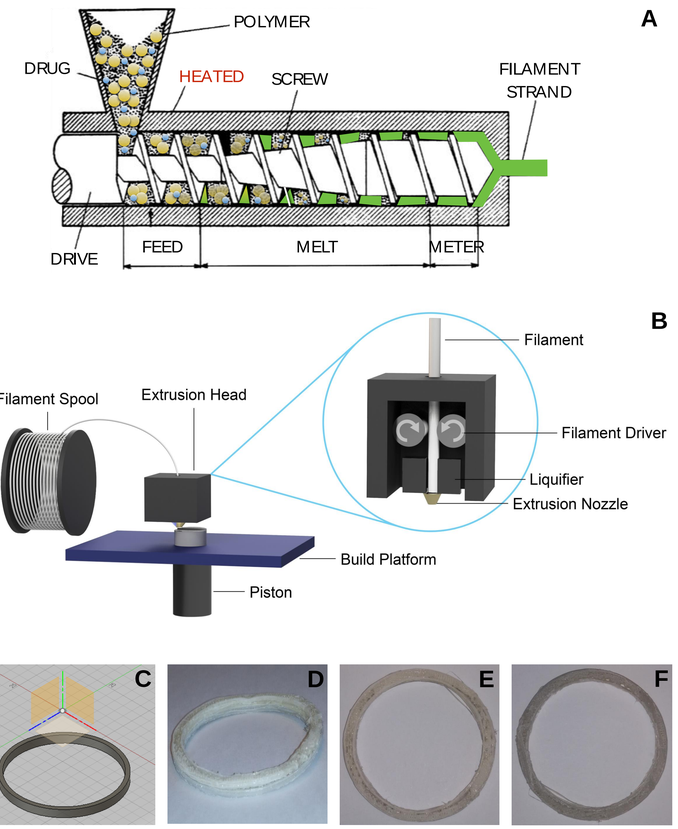

Fig. 2. Schematic showing the key components of a (A) hot melt extruder and a (B) 3D printer based on FDM technology; and the (C) computer aided design (CAD) for a vaginal ring (outer diameter 54 mm, inner diameter 50 mm, height 4 mm) which was used to 3D print (D) a combination ring with two discrete layers loaded with either (E) DPV 20% w/w or (F) LNG 20% w/w

Table. 1. Mechanical and content analysis of 3D printed vaginal rings

Ring	Model Drug	Compression Force (N)	Drug Content (mg)
DPV	DPV	0.29 ± 0.04	174 ± 13
LNG	LNG	7.53 ± 1.65	249 ± 18
Combination (DPV and LNG)	DPV	1.70 ± 1.01	58 ± 5
	LNG		143 ± 7

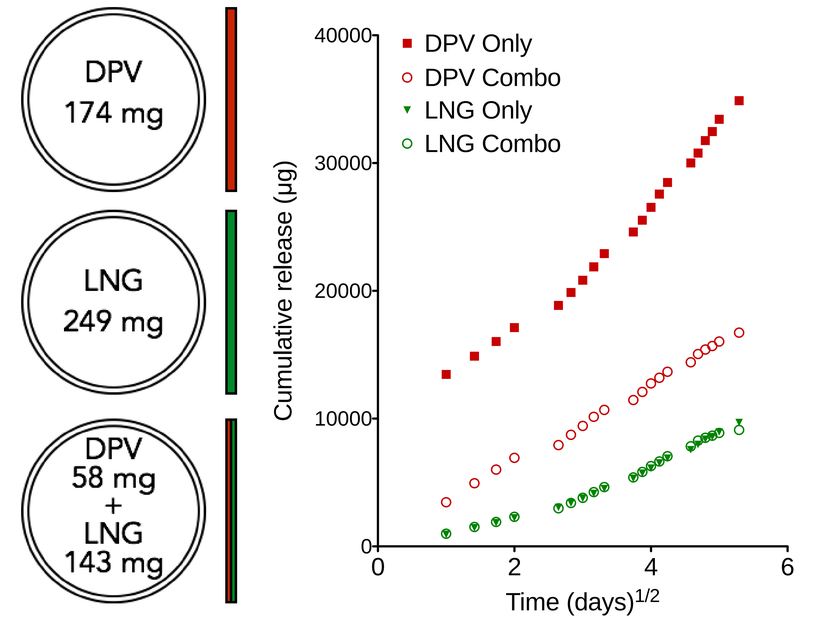

Fig. 3. *In vitro* analysis of vaginal rings (outer diameter 54 mm, inner diameter 50 mm, height 4 mm) 3D printed using PLA : T87 (1:4) filament with DPV 20% w/w, DPV 20% w/w in combination ring, LNG 20% w/w and LNG 20% w/w in combination ring