Complex and personalised dosage forms: a multi-material hot-melt inkjet 3D printed solution

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1. Background

- Polypharmacy is a common medication regime used for the treatment of chronic or elderly patients and can involve the regular consumption of anywhere from 8 and up to 60 medicines.
- This can lead to a low patient compliance (32.6% among older patients) and mistakes in medication, with consequential increased risk of adverse reactions and unwanted drug interactions.

2. Aim

Development of a new solvent free 3D printing system capable of fabricating personalised multi-material solid dosage forms with complex delivery profiles via the jetting of melted inks.

3. Results and Discussion

3.1 Printer development

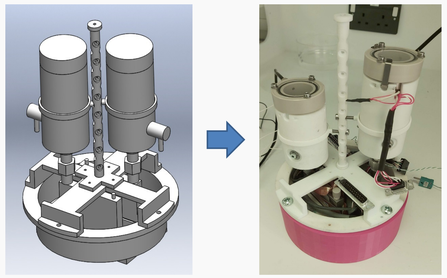
A commercially printer, a PiXDRO LP50, was modified extensively to achieve the required dual dispersing capabilities. The single printing unit was redesigned to Include two separate reservoirs and printheads within the printers mechanical, space, weight, and software limitations.

Hardware implementation

- Second reservoir
- Coupling system
- Head mounting system
- Temperature control unit

Software implementations

- Temperature control code
- Dual head control system
- Calibration
- 3D object design and slicing



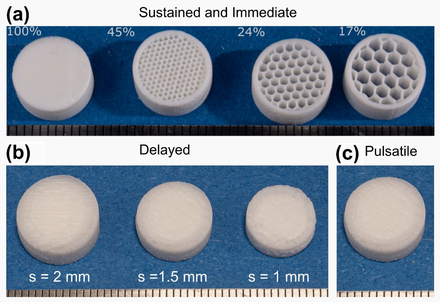
CAD design of multimaterial unit

Final multimaterial unit

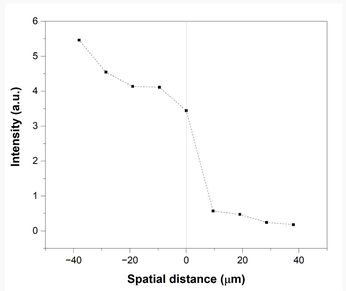
3.1 Tablet characterisation

To demonstrate the printer and to understand the effect of tablet geometry and drug localization on drug release we prepared three sets of tablets. Single material tablets with varying physical infill (100%, 45%, 24% and 17%) and multimaterial tablets with single or double drug reservoirs encapsulated in a drug free shell.

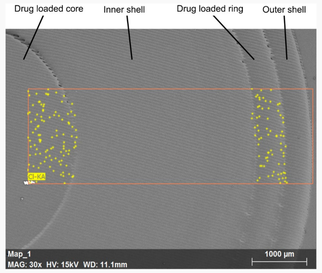
Drug free ink: Compritol HD5 ATO, Drug loaded ink: Compritol HD5 ATO and Fenofibrate 10% (w/w).



Optical images of Sustained, Immediate, Delayed and Pulsatile release tablet.



Raman linear map confirming the presence of the drug only in the core region (-40-0 μm) and not in the shell (0-40 μm) of a delayed release tablet.

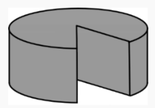


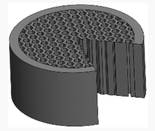
EDX analysis of Pulsatile release tablet. Highlighted the drug distribution (yellow).

3.2 Tailored drug release

3.2.1 Immediate and sustained drug release

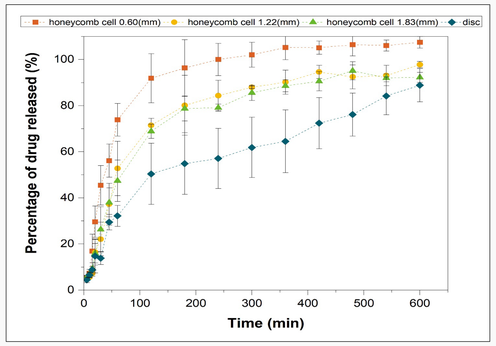
SLOW DRUG RLEASE



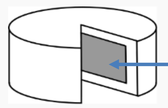


FAST DRUG RLEASE

Cumulative *in vitro* drug release data shows that the tablet with the smallest channel diameter (0.6 mm) releases the drug at the fastest rate (full release in ca. 2hrs) with the solid (100% infill) tablet taking ten hours. This demonstrates the ability to modify drug release rates via geometry control.

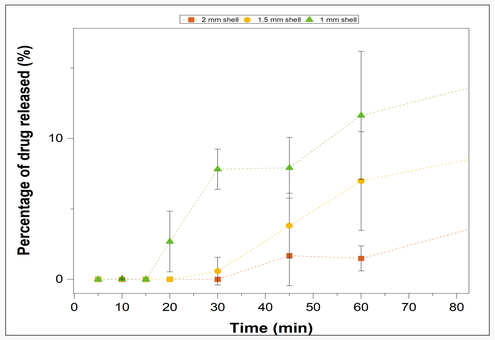


3.2.2 Delayed drug release

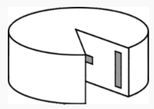


DRUG LOADED REGION

Delayed release tablets with fixed drug-loaded core geometry (8mm x 2mm) and varying shell thickness (1, 1.5, 2 mm) showed an initial delay proportional to the shell thickness and followed by a drug release phase that lasted for the rest of the experiment.

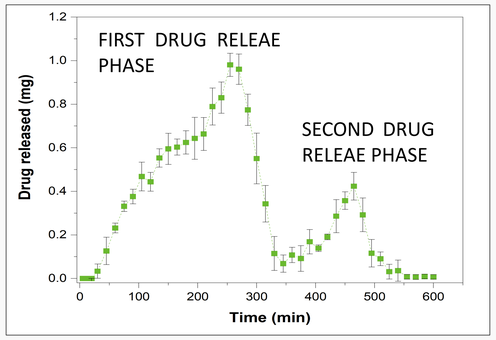


3.2.3 Pulsatile drug release



TWO SEPARATE DRUG LOADED REGIONS

Using the dual head printer two separate regions (centre and rim) of drug loading in the tablet allowed a pulsatile drug release profile. Control of location and amount of drug would allow an arbitrary release profile to be achieved.



4. Conclusions

- We have successfully designed and implemented the changes in the electronics, hardware and software necessary to produce a working **dual head hot-melt inkjet 3D printing unit.**
- We have demonstrated the potential of this new system in the production of tablets showing tailored drug release profiles depending on geometry and location of the encapsulated drug.

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