COMPLEX AND PERSONALISED DOSAGE FORMS: A MULTI-MATERIAL HOT-MELT INKJET 3D PRINTED SOLUTION.

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Background: Polypharmacy is the most commonly used type of treatment used for chronic or elderly patients and can involve the regular consumption of anywhere from 8 and up to 60 medicines. While this approach can be effective, it can lead to low compliance (32.6%) among older patients and misconsumption, with consequential increased risk of adverse reactions and drug interactions. Thanks to its versatility, 3D printing offers a potential elegant manufacturing solution to this problem by enabling the production of personalised, multi-drug dosage forms with complex delivery profiles. Of particular interest would be the possibility to utilise lipidic materials as the main excipients for the solid dosage forms, especially for enhancing the delivery of poorly soluble drugs. Hence, this work aimed to develop a novel thermal jetting apparatus for multi-material printing for pharmaceutical application.

Methods: We developed a new approach for a solvent free 3D printing system capable of fabricating multi-material solid dosage forms via the jetting of melted materials. For this purpose, we modified a commercially available printer (PiXDRO LP50) to include a dual reservoir unit capable of dispensing two different materials during the same additive process. This included the design and development of complementary reservoir, support structures alongside with support temperature control unit and power supply. A commonly used pharmaceutical lipid, Compritol HD5 ATO (matrix material) and Fenofibrate (model drug) were used to prepare both drug-free and drug-loaded inks with drug concentrations varying between 5% and 30% (w/w). Using our bespoke system, we produced several proof-of-concept multi-material solid dosage forms with tailored dosing and release. This included single and multi-material complex 3D patterns with defined localised drug loading whereby drug-free ink is used as a release-retarding material. Various characterizations were performed to optimize the 3D printed tablet formulation.

Results: DSC, TGA, Shear viscosity analysis were used to ensure the ink printability. SEM, EDX, ATR-FTIR, Raman Spectroscopy and XRPD showed that the printlets demonstrated the required physical properties regardless of geometry and composition with the drug being found mostly in its amorphous state. *In vitro* release studies showed tailored release patterns and displayed immediate, extended, delayed and pulsatile drug release depending on drug localisation within the printed formulations and tablet geometry.

Conclusions: Using our novel system, we were able to produce several proof-of-concept multi-material solid dosage forms, with complex geometries and drug distributions able to demonstrate ‘programmable’ drug release patterns in *in vitro* studies.