3D printed tablets for the delivery of a poorly soluble drug through mesoporous carriers

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1. Introduction

Poorly soluble drugs comprise a high proportion of the drugs in the market, despite presenting major problems when it comes to their bioavailability. Mesoporous materials can be used for their amorphization, thus increasing their apparent solubility and consequently their bioavailability, while retaining the stability of the system over time. 3D printing has showcased its capabilities in the pharmaceutical field as a fast and facile way to develop patient-tailored drug formulations compared to traditional compounding techniques. Here, a hybrid approach is suggested combining the advantages of the respective techniques. Two mesoporous materials, Mesoporous Magnesium Carbonate (MMC) and a silica-based one (MCM-41), are loaded with the model poorly soluble drug Celecoxib and subsequently extruded into filaments. Finally, the filaments are printed into tablets via the Fused Deposition Modelling technique

2. Drug loading

- Drug loading for MMC = 10%; MCM-41 = 35%

	Specific Surface Area (m^2/g)	Pore Volume (cm^3/g)	Pore Width (nm)
MMC	242.9	0.44	6.84
MMC Celecoxib	187.5	0.37	7.40
MCM-41	1082.0	0.90	3.18
MCM-41 Celecoxib	840.9	0.68	2.95

3. Physicochemical characterization

- No apparent crystallinity post-loading

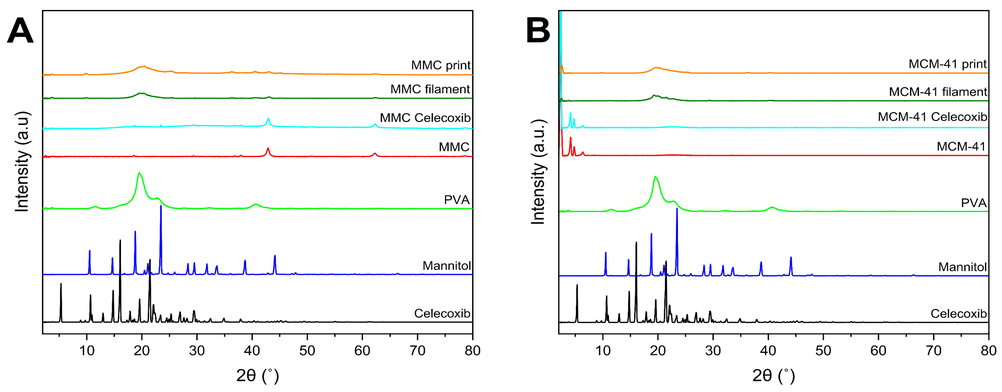

Figure 1. XRD diffractograms of filaments, tablets, and individual components; (**A**) MMC-containing formulations; (**B**) MCM-41-containing formulations.

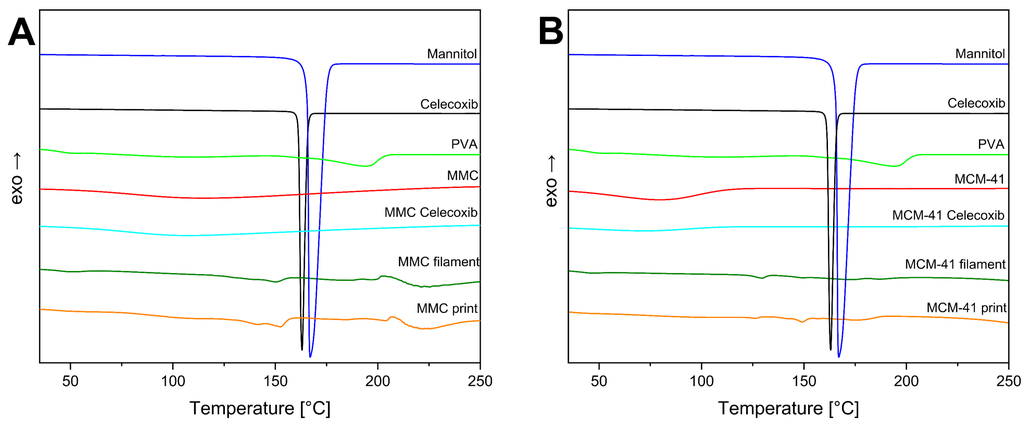

Figure 2. DSC thermograms of filaments, tablets, and individual components; (**A**) MMC-containing formulations; (**B**) MCM-41-containing formulations.

4. Thermogravimetric analysis

- Drug loading for MMC: 9.06%; MCM-41: 11.1%

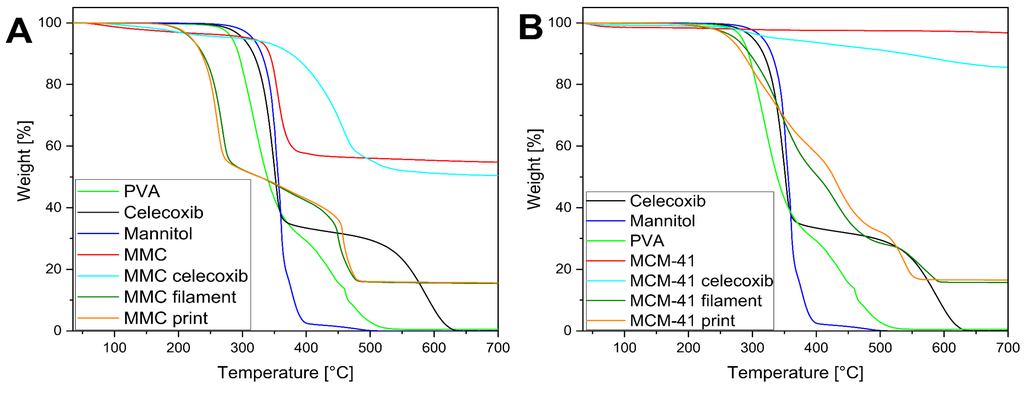

Figure 3. TGA thermograms of filaments, tablets, and individual components; (**A**) MMC-containing formulations; (**B**) MCM-41-containing formulations.

5. Morphological assessment

- High printing accuracy.
- The mesoporous particles are surrounded by molten polymer.

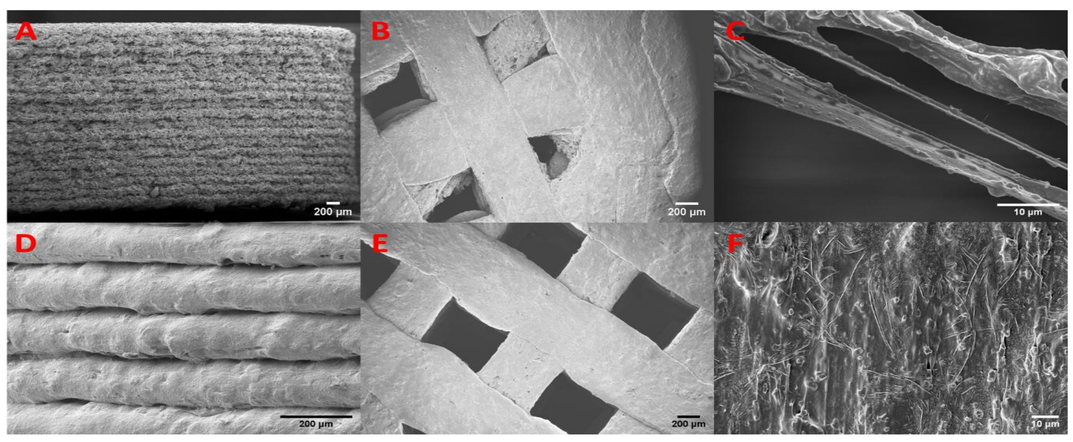

Figure 4. SEM images of printed tablets. Top row: MMC tablet; (**A**) side view, (**B**) top view, (**C**) fiber within the structure of the tablet. Bottom row: MCM-41 tablet;(**D**) side view, (**E**) top view, (**F**) magnified view of the surface of the top layer.

6. In-vitro drug release

- Rapid drug release from the mesoporous materials and supersaturation.
- Higher concentration and drug % released from tablet formulations.

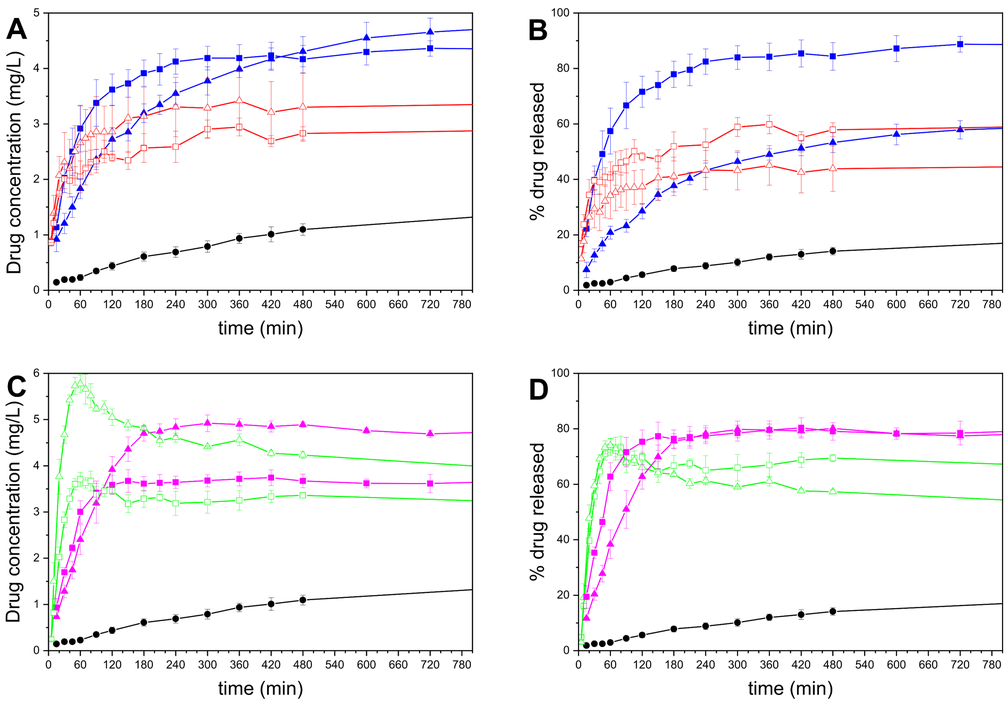

Figure 5. Drug release curves. (A) MMC formulations; (B) MCM-41 formulations. (A), (C) concentration of drug released over time; (B), (D) % drug released over time. . Crystalline celecoxib: ●, MMC-50: □, MMC-70: △, MMC-T50: ■, MMC-T70: ▲, MCM-41-50: □, MCM-41-70: △, MCM-41-T50: ■, MCM-41-T70: ▲.

7. Conclusions

A novel combinatorial 3D printed drug delivery system was developed. The drug was successfully loaded and amorphized within the pore system of the mesoporous materials. The FDM produced tablets showed great promise, as the drug concentrations and % of drug released were significantly higher compared to the crystalline drug. This approach is suggested as a promising alternative for the delivery of poorly soluble drugs in 3D printed formulations.

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