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Effect of disintegrants and tablet infill on release behaviour of 3D printed tablets

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Abstract: The polymer hypromellose (HPMC) is widely used for 3D printing of pharmaceutical dosage forms. This paper deals with the study of acceleration of drug release from 3D printed HPMC tablets. Polyvinylpyrrolidone (PVP) was added and the infill of the tablets was also varied. Both, lower infill and addition of PVP, can accelerate the drug release of caffeine from 3D printed HPMC tablets.

I. Introduction

3D printing manufacturing techniques include many different types of processes. One of them is fused deposition modeling (FDM). In FDM printing, a thermoplastic polymer is melted and the mass is deposited through a nozzle onto a build plate with the help of the moving print head. Here, the polymer solidifies and can be shaped into the desired form. The FDM 3DP offers various advantages over other additive manufacturing techniques. Of particular note is the use of relatively simple and inexpensive printers [1].

Originally in the technical field, 3D printing is also finding more and more applications in the medical/pharmaceutical field. Compared to conventional tableting, 3D printing offers the advantage that individual shapes can be printed, which in tableting can either not be represented at all or in some cases only with a very high technical effort. The hydrophilic polymer hypromellose (HPMC) has been investigated in numerous publications [2–4]. Nonetheless, the polymer HPMC has the disadvantage that - in accordance with its field of application - it forms a hydrogel matrix on contact with release medium, thus leading to prolonged release. This polymer is therefore not suitable for the preparation of immediate-release dosage forms without further modification. To alter the release characteristics, either the internal and external structure of the dosage form can be changed or disintegration-accelerating additives can be incorporated. Structural changes to the dosage form include varying the fill rate and changing the fill pattern [3, 5].

The aim of this work is to investigate the influence of the infill rate of the tablets as well as the influence of the hydrophilic binder polyvinylpyrrolidone PVP K12 on the drug release of 3D printed cylindrical tablets. The objective is to accelerate the drug release compared to a 100 % filled HPMC tablet.

II. Material and Methods

II.I. Material

Hypromellose (HPMC, Affinisol® HME 15 LV) was kindly gifted by Dow Chemicals (Midland, USA). Caffeine was used as a model drug (Fagron, Germany). Additives were PEG 6000 (Merck, Germany), fumed silica (Fagron, Germany) and magnesium stearate (Sigma-Aldrich, Germany). PVP K12 (Carl Roth GmbH + Co. KG, Germany) was used as a disintegrant. The composition of each batch is shown in Table 1.

Table 1: Composition of the tested batches (each batch contains 2.5 % magnesium stearate and 0.5 % fumed silica).

Batch	HPMC	Caffeine	PEG 6000	PVP K12
	%			
HPMC	77.0	10.0	10.0	-
HPMC_PVP	67.0	10.0	10.0	10.0

II.II. Filament production

The powder mixtures were mixed with a turbula mixer (Turbula T2F, System Schatz, Germany, 49 rpm at 5 min). Subsequently, processing into filaments was carried out by hot melt extrusion. A twin-screw extruder was used (Three-Tec ZE 12, Switzerland). The extrusion temperature was set between 155 and 170 °C and a nozzle size of 2.8 mm was used.

II.III. 3D printing

The filaments were printed into cylindrical tablets with outer dimensions h = 5 mm and d = 10 mm (designed with FreeCAD v. 0.18). Cura was used as slicing software (v. 3.6.0, Ultimaker, Netherlands). The Ultimaker 3

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(Ultimaker, Netherlands) was used as the printer, and it was equipped with a 0.4 mm diameter nozzle. The printing temperature was 200 °C. The layer height was set to 0.1 mm and the printing speed to 70 mm/s. The infill rate was varied to 20 % (HPMC_20 and HPMC_PVP_20) and 100 % (HPMC_100 and HPMC_PVP_100).

II.IV. Characterization of the filaments and printed tablets

Photos of the filaments as well as the printed tablets were taken using a reflected light microscope (Zeiss Stemi 2000-C with Zeiss CL 1500 ECO, AxioCam and AxioVision software, all Carl Zeiss Microscopy GmbH, Germany). Pharma Test DT70 paddle apparatuses (Pharma Test Apparatebau AG, Germany) were used as release apparatuses. The dissolution medium used was 900 mL phosphate buffer pH 7.4 (USP), which was tempered to 37 °C. The rotation speed was set to 75 rpm. The tablets were weighted with spiral sinkers. Caffeine was detected using a flow-through UV-Vis photometer (Cary 8454 UV-Vis Diode Array System, Agilent Technologies, USA), cuvette 1 mm, wavelength 272 nm, baseline correction: 500 nm.

III. Results and Discussion

The above batches were successfully extruded at temperatures of 155-170 °C and printed at temperatures of 200 °C. Fig. 1 shows exemplary images of the HPMC filament and the tablets of batch HPMC_20.

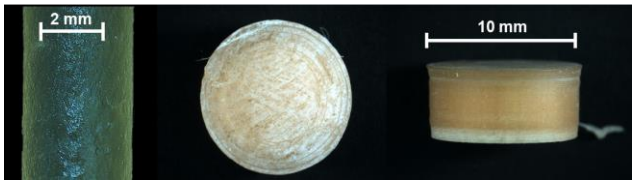

Figure 1: Reflected light images of the HPMC filament (left side) and the printed HPMC_20 tablets (middle - top view; right side - side view).

Fig. 2 shows the release data of the individual batches. A comparison between the batches HMPC_20 and HPMC_100 shows that the tablets of batch HPMC_20 release the active ingredient caffeine more quickly. HPMC is a hydrophilic matrix former that initially swells in water and then slowly dissolves over time. A possible explanation for the faster release at a low infill rate would be that the lower fill rate provides more surface area when the tablet dissolves. The greater surface area would allow the drug to dissolve out of the matrix more quickly.

When the PVP K12 was added, it can be observed that the drug release can also be accelerated. PVP K12 is readily soluble in aqueous media. This property could lead to a disruption of the inner matrix structure of the HPMC and to an additional surface enlargement.

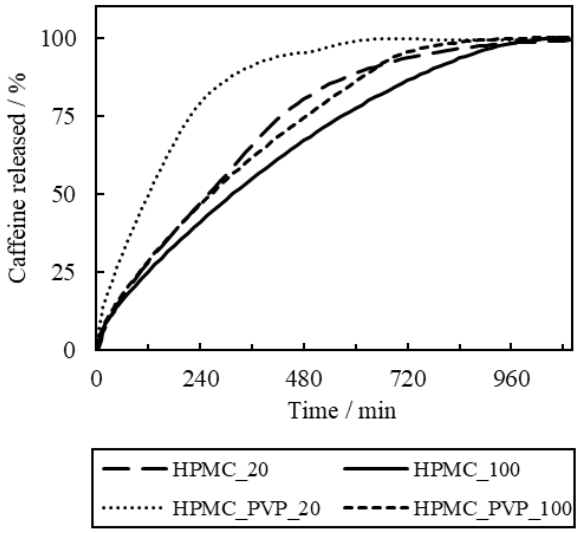

Figure 2: Drug release graphs of the different 3d printed batches with 20% and 100% infill and addition of PVP K12 (mean of n=6).

IV. Conclusion

In this work, 3d printed tablets of HPMC and caffeine were successfully fabricated. To summarize, drug release from HPMC-based 3d printed tablets can be achieved firstly by reducing the filling rate. Moreover, the addition of highly water-soluble substances such as PVP K12 can further accelerate the release. The combination of PVP K12 and a low fill rate of 20 % is particularly promising for producing tablets with accelerated release compared to pure HPMC tablets. From these results, it would be interesting to see how further increasing the surface area would affect the release. Here, for example, the outer walls of the tablet could be omitted and only a lattice structure printed, where the inner layers would then come into direct contact with the medium.

AUTHOR'S STATEMENT

Conflict of interest: Authors state no conflict of interest.

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