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3D powder bed tablet printing: From a R&D printer to a scalable GMP printer

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ABSTRACT

Powder bed-based 3D printing has been used to produce pharmaceutical tablets mainly under laboratory conditions. To advance the technology for commercial use, laboratory's proof of principles should be translated to and validated under good manufacturing practice (GMP) conditions. In this study, lactose/starch-based formulations with 10 and 30% w/w API (acetaminophen) drug loading were transferred from the Netherlands Organization for Applied Scientific Research (TNO) R&D printer to a scalable Aprecia GMP printer. First, the critical material attributes (flowability and wettability) of the blends were studied to determine their suitability for small-scale printing. Second, formulations were printed on both the R&D and GMP equipment to study the effect of the printer change on the tablet critical quality attributes, such as dimensions, mass, tensile strength, and API release. We found that tablets with targeted mechanical and dissolution characteristics could be printed with both R&D and GMP equipment while maintaining identical compositions for the powder blends. Nevertheless, the transfer from the R&D printer to the GMP printer required modification of the print settings. The composition of the printing ink was adjusted to accommodate the nozzle requirements of the GMP printer. This adjustment in ink composition resulted in a different balance between the tensile strength and dissolution of certain formulations. Our results demonstrate that the production of lactose/starch-based tablet formulations can be successfully transferred from R&D to GMP printing equipment. Tablets produced on both printers had generally acceptable tensile strengths (above 0.2 MPa) and dissolution characteristics, although the changes in print settings resulted in slightly different product properties.

1. Introduction

Three-dimensional (3D) printing is an emerging technology, in which products are typically manufactured layer by layer on a printing platform based on the input provided by a computer-aided design (CAD) file [1,2]. 3D printing has been increasingly developed and used in a broad range of industries in recent years, and it has been investigated as a potential tool for manufacturing pharmaceutical tablets. Since the introduction of the first FDA-approved 3D printed tablet dosage called Spritam in 2015, interest in the use of this technology for the production of pharmaceuticals has grown further [3]. The number of scientific publications containing the term "3D printing" and "pharmaceutical" has increased from 9 in 2014 up to 242 in 2021 (Scopus search). These numbers reveal that the growth in research on pharmaceutical 3D printing is exponential.

Several printing technologies are available for producing pharmaceutical 3D tablet prototypes [4–6]. However, the only 3D printed FDA-approved drug on the market (Spritam®) is manufactured using drop-on-solid technology, which is better known as powder bed printing. The benefits of powder bed printing are its similarity to the traditional wet granulation process and avoidance of heat. Powder bed printing involves spreading a thin layer of powder on a printing table. The ink (liquid) is sprayed in small droplets onto the powder bed in the shape of the desired object (a circle in the case of a tablet) before the addition of another layer of powder. Thus, a three-dimensional tablet can be created by printing many layers sequentially (Fig. 1).

Different brands of powder bed printers are available; however, the number of printers suitable for pharmaceutical development and good manufacturing practice (GMP) production remains limited. An example of a non-GMP research and development (R&D) printer suitable for pharmaceutical development is the powder bed printer (PBP) Next printer with a Lee valve developed at the Netherlands Organization for Applied Scientific Research (TNO). Z-FREE LAB, Aprecia's lab-scale 3D printer with a Fuji jetting assembly, is a printer designed for product

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development and GMP printing (Supplementary Fig. 1). Both the PBP and the Z-FREE LAB equipment create tablets on a small batch scale (less than 100 tablets per run) following the principle of placing a full layer of powder on the printing table, followed by jetting of small droplets on the printed area. Printing is achieved by repeating the processes of powder addition and wetting. However, there are differences between the two printers, and the main features of each printer are listed in Table 1. The Aprecia system is based on a bed-to-bed system, in which the blend is transferred from the "stock bed" to the "print bed", whereas the TNO system is based on feeding the powder via a hopper (Supplementary Fig. 2). In both cases, the powder is flattened after addition using a counter-rotating roller. Another difference lies in the nozzle that sprays the binder: the Lee valve (of the TNO system) can jet relatively large droplets of low-viscosity liquids such as water. The Fuji nozzle of the Aprecia equipment requires a higher viscosity than that of water, but can jet smaller droplets. In addition, there are scalability differences between the two printing systems. The TNO equipment is only available at the lab scale, whereas the Aprecia equipment has been successfully scaled up from a lab-scale printer (~100 tablets per hour) to a commercial-scale GMP printer (~10,000 tablets per hour). This enables Aprecia to produce small batches required for clinical trials, but it is also easy to scale-up for higher volume commercial-scale manufacturing.

In previous works, successful proof of principles of 3D powder bed tablet printing was demonstrated using lactose/starch platform formulations [7,8]. These studies showed that a lactose/starch formulation is a suitable platform for creating immediate-release tablets with several tablet dimensions and drug loads. A dosage form fulfilling the target performance requirements of tensile strength (>0.2 MPa) and release (>80% at 30 min) can be achieved by the simultaneous adjustment of formulation and printing setting parameters. The formulations used in these studies were printed on a PBP Next printer with a Lee valve developed by the Netherlands Organization for Applied Scientific Research (TNO). The next step in the technology readiness levels is to transfer the mechanistic understanding of the technology at the research lab scale to an industrially relevant environment, such as a GMP and scalable printer. Currently, there is no literature available on the conversion of a formulation platform between different printers.

The aim of this study is to investigate whether a lactose/starch-based platform formulation developed on an R&D printer can be transferred to an industrial small-scale printer. A hydrophilic model compound acetaminophen at 10 and 30% w/w drug loads was used. To enable smooth technology transfer between the two printers, the flow and wettability, both important critical material attributes (CMAs), of the powder blends were studied. The hardness, mass, and dissolution of tablets produced using the two different technologies were investigated, as these critical quality attributes (CQAs) are indicative of the performance of 3D-printed pharmaceutical tablets.

2. Materials and methods

2.1. Materials

The materials used were milled lactose monohydrate, sodium starch glycolate (Primojel®), fully pregelatinized potato starch (DFE Pharma, Germany), and fine acetaminophen powder with a particle size of x50 = 20–25 μm (Tiefenbacher, Germany). This type and grade of API was selected as model of Biopharmaceutics Classification System (BCS) class 1 API of small particle size.

2.2. Methods

2.2.1. Powder mix preparation

The blends (see Table 2) used for the GMP printer Z-FREE Lab (Aprecia) were prepared by mixing the API and lactose for 15 min at 35 rpm using a Turbula T2F mixer, followed by sieving the API preblend (710 μm sieve). In the second step, the binder (fully pregelatinized potato starch) and the disintegrant (Primojel) were added and mixed for 30 min at 35 rpm. The blends used for the R&D Next printer (TNO) were produced in a similar manner, with the only difference being that a 700-μm sieve was used for sieving, and a Stuart Scientific STR4 rotator drive unit with a drum and a bottle holder was used for blending the mixtures.

2.2.2. Blend characterization

A ring-shear tester (Ring Shear Tester RST-XS, Dietmar Schulze, Wolfenbüttel, Germany) was used to determine the flow of the blends in duplicate. The flow is described by the flow function coefficient (FFC), which is the ratio of consolidation stress to yield strength. The blends were measured at a pre-consolidation stress of 4 kPa, and normal stresses of 1, 2.1, 3.2 kPa were used to shear until failure.

The bulk and tapped density were measured in duplicate according

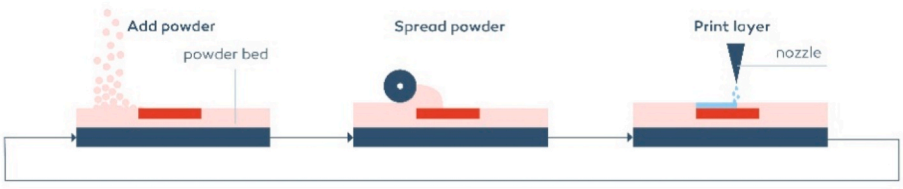

Fig. 1. Powder bed printing process.

Table 1
Overview of differences in printing equipment and standard printing settings.

	R&D printer TNO	R&D/potential GMP printer Aprecia
Printer Name	Next printer	Z-FREE LAB
Scalability	No larger-scale available	Series of printers: ranging from 100 to 10.000 tabs/hour
GMP	No	Yes
Blend feeding	Hopper with screw	Bed-to-bed principle
Nozzle	Lee valve	Fuji jetting assembly
Print ink	Low viscous (1–1.5 cP)	Medium viscous (12.3–14.9 cP)
Number of nozzles	1	>100
Droplet mass	20–24 μg	<150 ng
Batch size	40 tablets (9 mm)	85 tablets (9 mm)
Estimate of the printing speed used in study	100 tablets/hour	500 tablets/hour

Table 2
Overview of the tested blends; percentages are based on % w/w.

Blend	Fully pregelatinized potato starch (% w/w)	Primojel (% w/w)	Lactose (% w/w)	Acetaminophen (% w/w)
Blend 10% API	10	5	75	10
Blend 30% API	10	5	55	30

to USP <616>.

The particle size distribution (PSD) was measured in triplicate using a Helos/KR laser diffraction unit (Sympatec GmbH, Germany). The dry dispersion was measured at a pressure of 1.5 bar using an R5 Fourier lens with a 632.8 nm wavelength He–Ne laser as the light source.

The drop penetration time was measured using a drop shape analyser equipped with a powder sample holder (OCA 50 Dataphysics, Germany). Ten microlitres of print ink were dropped from 4-mm above the powder bed using an ESN16 dispenser unit. The penetration time was recorded as the time between the moment the droplet hit the bed and the moment it was fully adsorbed. Measurements were performed in six times.

2.2.3. Printing process

Two different printers were used in this study. A R&D printer was located at TNO (NL) and a GMP printer was located in the R&D lab of Aprecia (US). The printer located at the R&D lab at Aprecia was not qualified for GMP printing; however, a similar printer could be qualified and placed in a GMP environment to produce tablets in line with GMP requirements. In this study, the R&D printer refers to the TNO printer, and the GMP printer refers to the Aprecia equipment located in the R&D laboratory.

The printing equipment used in this study had differences in powder feeding, print heads, and number of nozzles (Table 1). A different print pattern for each printing equipment was used in order to obtain the two different liquid amounts used per tablet: 60 mg and 83 mg. The R&D print pattern at TNO was created by printing a linearly filled circle. The linespacing (LS) indicates the distance between the droplets; hence, a higher line spacing results in less liquid addition per powder. The GMP printer used multiple nozzles moving in one direction relative to the bed, and thus, no outer line was created (Fig. 2). The distance between the droplets in this equipment is indicated as drops per inch (DPI). The drops created with the Fuji print head used in the GMP printing equipment are smaller than those created with the print head employed in the R&D equipment; therefore, the print pattern needed to be repeated for each layer (double print) to reach 60 and 83 mg per tablet. In summary, the low print ink amount (60 mg) was obtained by using an LS of 0.43 mm for the R&D equipment and printing at 1200 DPI (double print) on the GMP equipment. A high value (83 mg) was obtained using an LS of 0.35 mm for the R&D equipment and printing at 1800 DPI (double print) on the GMP equipment (Table 3).

The R&D and GMP equipment were equipped with different nozzle types, including Lee and Fuij nozzles. The Fuji nozzle used in the GMP equipment is not suitable for printing low-viscosity inks, such as the water/ethanol ink used for the R&D printer equipped with the Lee nozzle. Therefore, the low-viscosity water/ethanol was replaced by a standard Aprecia ink based on water (65.0–72.0% w/w), polysorbate 20 (1.0–2.0% w/w), povidone (8.5–10.0% w/w), glycerin (3.5–4.0% w/w), and IPA (12.0–13.5% w/w). This ink had a higher viscosity (Table 4) and lower surface tension.

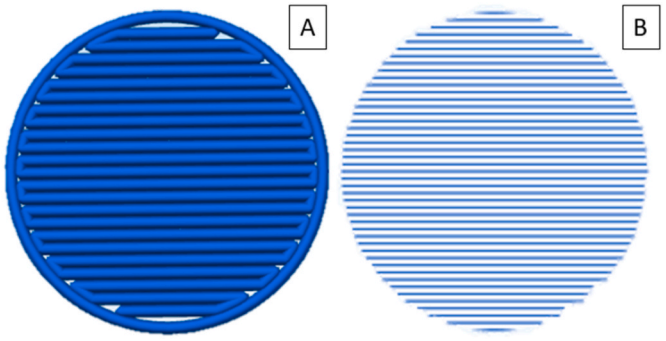

Fig. 2. Schematic representation of the different print pattern used: the R&D pattern is a perimeter that is filled up linewise (A). The GMP pattern has 140 lines in a 9 mm circle (B).

Table 3
Overview of the applied amount of printing ink and the print settings obtained to use the indicated amount of print ink.

Weight print fluid/per tablet	Settings R&D printer	Settings GMP printer
60 mg	Linespacing 0.43	1200 dpi double print
83 mg	Linespacing 0.35	1800 dpi double print

2.2.4. Next printer (R&D) located at TNO (NL)

The formulations were printed using a PBP Next printer, developed at TNO (Eindhoven, the Netherlands) with a Lee valve INKA2476210H (nozzle diameter 0.178 mm). The powder mixture was automatically deposited from a hopper onto the powder platform and spread into a layer of even thickness using a counter-rotating roller. A water/ethanol (95/5% v/v) solution was jetted onto the powder bed with an average drop mass of 22 μg. The tablets were printed with a layer thickness of 0.4 mm and a line spacing (being the distance between the centre of two printed droplet lines) of 0.35 mm (narrow spacing; hence high liquid addition) and 0.43 mm (wide spacing; hence low liquid addition) (Table 3). The perimeter was printed before the infill pattern (Fig. 2A). Each layer, and thus the printing pattern, was rotated by 15° compared to the previous layer. A maximum of 40 tablets was printed in a single printing run. The powder deposition and solution jetting were repeated until a flat tablet with a diameter of 9 mm and a height of 2.8 mm was created, which was dried overnight at 50 °C in an oven.

2.2.5. Z-FREE LAB printer (GMP) located at aprecia (US)

The formulations were printed using an Aprecia Z-FREE LAB printer. The powder mixture was spread onto the powder bed in 0.4-mm layers by transferring the powder from a feed bed using a counterrotating roller. A water-based solution (Table 4) was jetted onto each layer of the powder bed as the bed moved beneath a fixed printhead of >100 nozzles. Therefore, each tablet was printed with multiple lines of droplets with an average drop mass of <150 ng, starting at the leading edge of the circle and ending at the trailing edge (Fig. 2B). To add the required amount of liquid, printing was performed twice at either 1200 or 1800 DPI (Table 3). A maximum of 85 tablets were printed in a single run. The powder deposition and solution jetting were repeated layer by layer until a flat tablet with a diameter of 9 mm and a height of 2.8 mm was created, which was dried overnight at 50 °C in an oven.

2.2.6. Tablet characterization

The tablets were analysed for weight, diameter, thickness, and hardness using an automated tablet tester (Sotax HT100, Germany). The tablet breaking force was measured at a constant speed of 2 mm/s, and the maximum force required to break the tablets was used as the crushing force. The measurements were performed ten times.

Tablet dissolution was analysed six times using a USP II dissolution

Table 4
Overview of the used inks.

Ink used for	Components	Viscosity (cP)	Surface tension (mN/m)
R&D printer	Water/ethanol (95/5% v/v)	1–1.3	56–73
GMP printer	Water/Isopropyl alcohol/glycerin/polysorbate 20/povidone k29/30	12.3–14.9	31.6–32.9

tester (Vankel) in combination with a UV-VIS spectrophotometre (PerkinElmer Lambda 25, the Netherlands) at a wavelength of 243 nm. The dissolution profiles were measured in 900 mL 0.05 M phosphate buffer pH 5.8 at 37 °C with a paddle speed of 50 rpm.

3. Results and discussion

3.1. Blend characterization

The flowability and wettability of powder blends are considered critical material attributes (CMA) in powder bed 3D printing. Therefore, these CMAs were investigated prior to manufacturing the 3D printed tablets [9–12]. The flow, expressed as the FFC, was measured using a shear cell. Table 5 shows that the blends containing 10% and 30% w/w API have FFC values of 5 and 3, respectively. For reference, the FFC of a similar placebo blend containing lactose and fully pregelatinized starch was 8, as determined in previous studies [7]. Therefore, as the percentage of API in the blend increased, the powder flowability decreased. To interpret these results, the thresholds of the flow required for printing are presented. FFC $\geq$3 and >5 are typically required for printing tablets on a small scale and for scale-up, respectively (personal communication with Aprecia). We can therefore anticipate that the 10% w/w API blend will be suitable for both small-scale printing and for scaling-up. Although the 30% w/w API blend would be sufficiently flowing for small-scale manufacturing, it would face challenges in the scale-up phase. Possible remedies to improve the flow could be increasing the PSD of the API, adding a glidant, or further customising the lactose grade.

The second CMA for the powder bed is wettability [9,13], as the rapid wetting of the powder bed is a prerequisite for printing tablets without defects. The results of the binder liquid ink penetration times revealed that the composition of the binder liquid had a crucial impact on wettability. The GMP ink had a penetration time ten times slower than that of the R&D ink (based on water/ethanol), owing to the higher viscosity of the GMP ink (12.3–14.9 cp) compared to that of the R&D ink (1–1.3 cP) (Table 4). Moreover, regardless of the ink used, the liquid penetration times moderately increased at higher API loadings (10 vs. 30% w/w API). A higher drug loading results in a reduction of the particle size of the blends (x10 = 10.3 and 4.9 μm at 10% w/w and 30% w/w API, respectively), which in turn reduced the porosity of the powder, and subsequently, the ability of the ink to penetrate. The effect of x10 on wettability was also observed when studying different particle sizes of lactose. When the x10 of lactose decreased below 10 μm, a rapid increase in penetration time was observed [7]. Additionally, the difference in the hydrophilicity of the filler and API affects the penetration times.

Previous studies have shown that for small-scale powder bed printing, a powder wettability of less than 2 s is preferred for low-viscosity inks [14]. Slower wettability results in poor adhesion and "rolling" of the binder ink, and the consequent irregular build-up of the tablet structure. However, such rapid liquid penetration is not required in the GMP setup. In this case, it is believed that the intrinsically slower penetration time of the ink is compensated for by the small droplet size used during tablet manufacturing. Owing to their size, the nanodroplets (<150 ng) jetted to the powder bed during 3D GMP printing are expected to be absorbed into the powder more rapidly than the microdroplets (22 μg) used in the R&D set-up. Hence, the GMP printer can operate with a more viscous and potentially slower penetrating ink than that in the R&D printer.

In conclusion, based on flow, the powder blend formulations at both high and low drug loading are suitable for printing on the R&D and GMP printers. Moreover, based on the wettability results, it appears that the ink requirements of the two printers are different. The much higher viscosity and slower liquid penetration of the GMP ink compared to the R&D ink are compensated for by the smaller droplet size used in the printing equipment. Overall, both the R&D and GMP inks are likely to be suitable for printing the two powder blends.

3.2. Tablet characterization

The two different blends (containing 10% w/w and 30% w/w acetaminophen) were used for the comparison between the GMP printer and the R&D printer. The tablet mass, strength, and dissolution are some of the most important critical quality attributes (CQAs) of pharmaceutical tablets. The tablet mass and tensile strength are directly linked to the dose and resistance of the tablet to handling and packaging. Dissolution provides an indication of the rate and extent of drug absorption in the body.

3.3. Tablet dimensions, mass, and tensile strength

Formulations at 10 and 30% w/w drug loading were printed with both the R&D and GMP printers using two ink levels (i.e. 60 and 83 mg per tablet). Tablet dimensions, mass, and tensile strength are strongly related to the amount of print ink, which was kept constant for a fair comparison between printer performance.

The GMP printer yielded tablets with slightly smaller diameters for both low and high ink levels. By contrast, the tablet thickness was higher for the tablets produced with the GMP printer, especially when more ink was used (Fig. 3). These differences could be due to the different printing patterns of the two devices. The R&D printer first prints an outer circle, which is then filled line-wise, resulting in a relatively high amount of print ink on the brim of the tablet, and hence a higher likelihood of the movement of print ink to the side of the tablet. This ink binds the powder outside the intended print pattern, resulting in a larger diameter. Additionally, the greater thickness of the tablets produced with the GMP printer can be attributed to the smaller ink droplet size used by this printer. Smaller droplets are jetted more homogenously, and can better fill the small pores within the powder bed even below the intended print pattern, thus binding more powder in the axial direction (i.e. thicker tablets).

Considering the tablet mass (Fig. 4A), the GMP printer yielded heavier tablets than the R&D printer with both levels of ink. A possible explanation can be related to the print ink. The GMP ink is a solution

Table 5
FFC, penetration time, bulk density, and PSD of the blends used for printing at the GMP equipment. Percentages are based on % w/w.

Blend	FFC	Penetration time (sec) (R&D ink)	Penetration time (sec) (GMP ink)	Bulk density (g/ml)	X10 (μm)	X50 (μm)	X90 (μm)
10% API	5	1.9	13.1	0.62	10.3	60.4	125.6
30% API	3	2.4	23.0	0.45	4.9	42.8	116.6

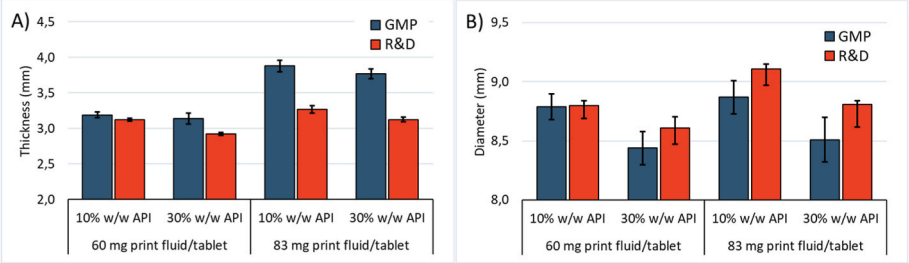

Fig. 3. Average tablet thickness (A) and diameter (B). Percentages are based on % w/w.

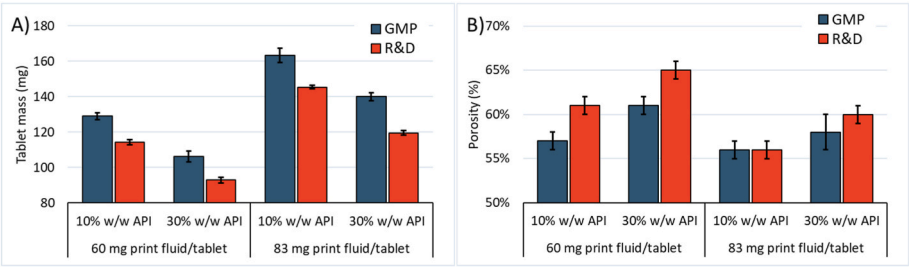

Fig. 4. Average tablet mass (A) and porosity (B). Percentages are based on % w/w.

containing povidone, glycerin and polysorbate resulting in 13–16% w/w solids in the solution. The R&D printer only contains water and ethanol, and hence 0% solids in the liquid. For example, these solids result in a tablet mass increase of 7–10 mg for a low amount of print ink. Another reason for the differences in tablet mass is the method of powder addition during printing. In the R&D equipment, the blend freely flows from a hopper onto the printing platform, while in the GMP process, the so-called bed-to-bed principle [15] is used, where a more settled blend is moved from one bed to another. The difference in powder addition could result in a different bulk density of the blend deposited on the printing table, yielding a different tablet mass. In agreement with this theory, heavier and denser tablets produced by the GMP printer generally have lower porosity (Fig. 4B). Nevertheless, the porosity of the tablets was in range of values reported in literature, which are normally between 50 and 60%, and in some cases even exceeding 80% [16]. Intermediate levels of tablet porosity, as shown here, should guarantee a good balance between the mechanical robustness of the tablets (promoted by low porosity) and rapid disintegration (promoted by high porosity).

The mechanical robustness of the tablets was satisfactory, as most formulations had a tensile strength >0.2 MPa, as shown in Fig. 5A. A tensile strength of >0.2 MPa was taken as the target value, given that demonstration tablets from the powder bed printed technology produced on a full-scale GMP scale (ZipDose) had a strength of 0.15 MPa [8]. Stronger tablets were obtained at lower drug loadings for both the printers, which was expected because the relatively higher concentration of soluble lactose in the low drug-loaded formulations contributed to an increased binding ability. The tensile strengths of the tablets produced by both printers were similar for high ink levels. However, at a lower amount of ink, the R&D printer yielded weaker tablets than the GMP printer, particularly at a higher drug load of 30% (Fig. 5A). This result can be explained from the fact that with a low amount of print ink and less binding capacity, the differences in printing ink become more pronounced and discriminative. Aprecia printing ink (GMP) contains povidone, which helps in binding the tablet; while R&D tablets only contain water/ethanol as printing ink. Additionally, GMP tablets have lower porosity, which generally results in higher tensile strength. Finally, another factor that could contribute to the higher tensile strength of the tablet obtained with the GMP printer is the more homogenous distribution of the binder liquid (nanodroplets) compared with the R&D printer (microdroplets). Previous studies on wet granulation have shown that the droplet size of the binder can affect the hardness of granules [17]. Similarly, in 3D powder bed printing, the size of the ink droplet is a critical process parameter that affects the tensile strength of the tablet.

In conclusion, the printing equipment and process parameters affect the final tablet properties. The tablet mass, diameter, thickness, porosity, and tensile strength were different, which was the result of specific differences in the printing process used (e.g. printing pattern, blend feeding mechanism, ink droplet atomisation) and/or in the print ink composition between the two printers. Nevertheless, both printing equipment were able to produce robust lactose/starch-based tablets with tensile strength >0.2 MPa, in most cases.

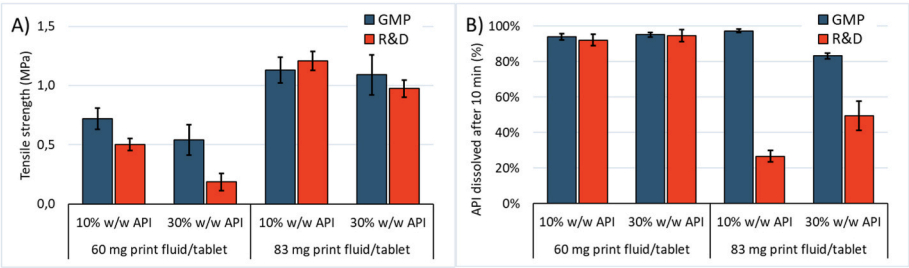

Fig. 5. Average tensile strength (A) and dissolution speed (B). Percentages are based on % w/w. Note that the dissolution data of the R&D printer at 10% w/w drug load were also presented in our previous publication [7].

3.4. Tablet dissolution

Tablet dissolution is an important CQA as it relates to the bioavailability of the API. In general, powder bed printing of oral dosage forms has a distinctive advantage over other 3D printing technologies in that it enables producing porous tablets that disintegrate quickly [14]. However, this advantage on dissolution of powder bed 3D printing can be partially lost for certain formulations. In a previous study conducted with the TNO R&D printer, we have shown that the concomitant use of starch as binder and a high amount of print ink could lead to the formation of a viscous cloud on dissolution [7]. The cloud formation could lead to irregular and slower release of the API.

The dissolution rates of tablets printed on the R&D and GMP equipment were similar at lower ink levels, but showed significant differences at higher ink volumes (Fig. 5B). With 83 mg/tablet of ink, the GMP tablets had a higher dissolution rate than those of the R&D prints. This can be explained by the different compositions of printing inks used. The R&D ink is based on a water/ethanol mixture, whereas the GMP ink used by Aprecia contains additives such as polysorbate 20. Increasing the amount of print ink leads to an increase in the wetting of the amylose component, which in turn enhances the starch binder properties and facilitates the bridging (i.e. "gluing") of other ingredients during the printing process. Consequently, the amylose forms a gelling cloud upon dissolution. Polysorbate 20 inhibits the gel formation ability of starch [18], maintaining a high dissolution rate even with larger amounts of print ink. Generally, tablets with low amounts of print ink showed limited cloud formation during dissolution, and therefore, provided a fast dissolution rate for both printers.

Overall, the release rate of tablets was affected by the amount of print ink used. The variation in release was significantly more pronounced with the R&D ink than with the GMP ink. Thus, the platform offered by the GMP printer and ink appears to be more suitable for the formulation of fast-dissolving immediate release tablets than the R&D platform.

4. Conclusions

A critical phase in the advancement of pharmaceutical 3D printing from the laboratory to clinical applications is the validation of technology transfer from research laboratories to industrially relevant environments. To convert lab-scale proof-of-concept into industrial applications, it is important to investigate the differences between tablets produced on an R&D printer and those produced on GMP equipment. We demonstrated that transferring technology from R&D to GMP can be done without significant formulation adjustments. Tablets of good quality were produced with both R&D and GMP printers using identical powder blends. However, switching printers necessitated modifying the liquid binder ink composition due to different printing heads.

Moderate variations in the physical properties (diameter, thickness, tablet mass, and porosity) of the tablets produced with the two printers were identified. These differences can be attributed to differences in the printer setup (such as powder addition), print pattern, and nozzle type. The GMP printer was also superior to the R&D printer in yielding tablets of consistently favourable tensile strength (high) and dissolution rate (fast), irrespective of formulation variables.

Overall, our results demonstrated that 3D printing of pharmaceutical immediate-release tablets using conventional lactose/starch-based formulations is not only possible at the R&D scale, but can be smoothly transferred to a GMP environment for subsequent scale-up steps.

Authors statement

KvH: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing - original draft; AB: Writing - original draft, Supervision, Investigation; LBB: Formal analysis, Investigation, Data curation, Writing - review & editing; BHD: Writing - review & editing; Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jddst.2023.104865.

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