Investigation of Various Polymers for SLS 3D-Printing of Solid Oral Dosage Forms

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Purpose

- Selective laser sintering (SLS) is promising for printing oral dosage forms.
- Print ranges for commonly used pharmaceutical polymers not yet established for additive manufactured medications.
- Evaluate dedicated polymers for pharmaceutical applications.

Objectives

- Determination of optimal print conditions for various pharmaceutical-grade polymers (PVA 4-88 (Parteck® MXP), PVP-VA[1] (Kollidon VA64®), PVP-VA[2] (Plasdone™ S-630)).
- Usage conditions of dedicated PVA based polymers P1 (PVA3-82) and P2 (PVA5-74) in SLS printing and impact of hydrolysis degree on printing performance.

Methods

Materials and composition

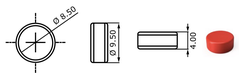
- 10% API (indomethacin)
- 88.5% polymer (PVA, PVP-VA[1], PVP-VA[2], P1, and P2)
- 0.5% excipient (silicon dioxide colloidal)
- 1% colorant (silica-based effect pigment)

SLS of dosage forms

- 36 tablet batches created with the same conditions:

Layer Height (µm)	Perimeter Offset (µm)	Hatching Space (µm)	Hatching Offset (µm)	Number of Perimeters
125	50	50	150	3

- Prints done with three temperatures and three laser scan speeds: 75 °C, 100 °C, & 125 °C and 200 mm/s, 300 mm/s, and 400 mm/s, respectively.
  - For some materials, 125 °C was too high, so 112.5 °C was used
  - Tablets designed using Fusion360 modelling software:

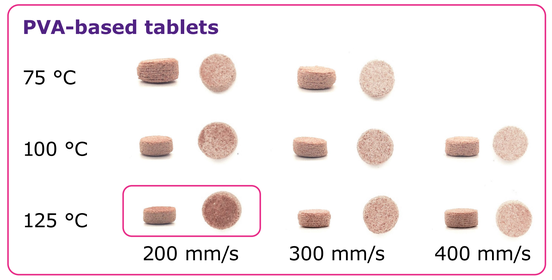


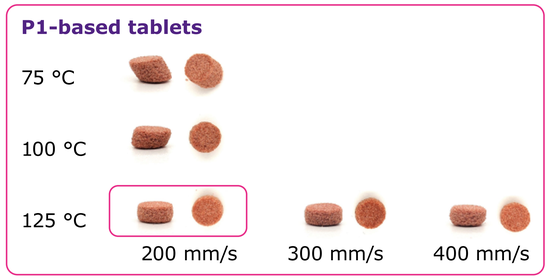
- Printing occurs in layer-by-layer fashion in print bed (tablets fully submerged in powder post-printing, collected via sieving, and dedusted).
- 2.3 W diode (λ=455 nm) laser used.

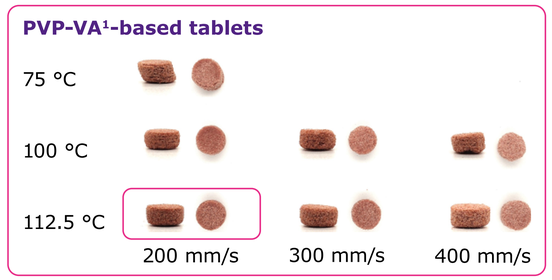
Characterization

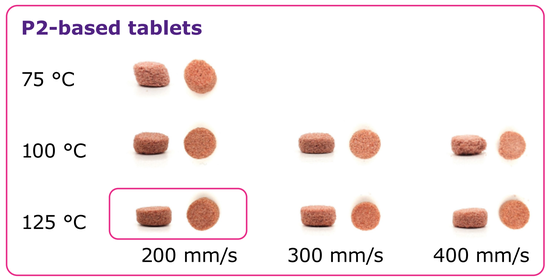
- XRD, DSC, friability, mass and size analysis, HPLC, dissolution.

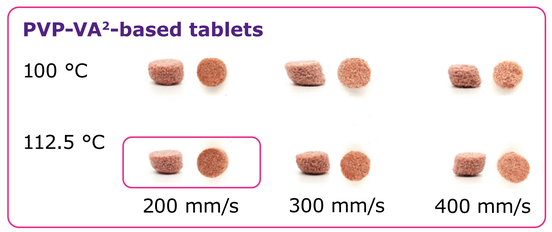
Results











- Evidence of amorphous nature in all of the best print condition samples for each polymer.
- Trends of lower temperature and high laser scan speeds showed more evidence of crystallinity of the API.

Number of Outliers for each configuration												
	75 °C, 200 mm/s	75 °C, 300 mm/s	75 °C, 400 mm/s	100 °C, 200 mm/s	100 °C, 300 mm/s	100 °C, 400 mm/s	112.5 °C, 200 mm/s	112.5 °C 300 mm/s	112.5 °C, 400 mm/s	125 °C, 200 mm/s	125 °C, 300 mm/s	125 °C, 400 mm/s
PVA 3-82	–	–	–	2	4	18	–	–	–	1	2	1
PVA 5-74	1	–	–	0	3	–	–	–	–	0	1	0
PVP-VA[1]	13	–	–	0	9	13	5	3	7	–	–	–
PVP-VA[2]	–	–	–	4	9	12	2	4	10	–	–	–
PVA 4-88	4	19	–	1	4	1	–	–	–	2	5	7

Table 1.
Number of outliers for each printed batch, with less outliers being the ideal case.

- Printable tablets for each of the polymers tested with the best print by characterization and visual standard indicated via a red box.
- Tablets exhibit higher level of sintering at lower laser scan speeds and higher temperatures (within an appropriate temperature window).
- Mass deviation for the tablets with the best print parameters fell within Ph. Eur. 2.9.5-Uniformity of Mass of Single-Dose Preparation standards for traditional tablets.
- Number of outliers for tablets with the best print parameters did not always meet Pharmacopeia requirements (<2 outliers), but all viable samples were measured (standards require just 20 at random).
- Friability, while not fully meeting Ph. Eur. criteria for traditional tablets, performed well in some cases, especially for PVA-based tablets.

Friability comparison of each identified configuration												
P1	–	–	–	12.0	51.9	–	–	–	–	2.3	9.3	22.9
P2	–	–	–	11.0	–	–	–	–	–	4.5	9.5	15.9
PVP-VA[1]	–	–	–	7.8	34.9	–	4.1	–	–	–	–	–
PVP-VA[2]	–	–	–	7.0	–	–	4.5	22.6	–	–	–	–
PVA	11.2	–	–	4.3	20.2	–	–	–	–	2.0	9.1	–

Table 2.
Friability for each printed batch, with lower friability being the ideal case.

Conclusions

- Higher temperatures within the print window for the polymers and lower laser scan speeds within the range tested generally led to superior samples.
- PVA based polymers were able to perform within a broad processing window (75–125 °C), whereas PVP-based polymers tested show an optimal upper limit of 112.5 °C.
- Best friability results were obtained using PVA grades.
- Most robust samples per batch tended to meet or come close to meeting current Pharmacopeia standards for traditional oral dosage forms.

Funding

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