Macedonian pharmaceutical bulletin, 69 (Suppl 1) 169 - 170 (2023)
Online ISSN 1857 - 8969
DOI: 10.33320/maced.pharm.bull.2023.69.03.083
Short communication

3D printing of carvedilol oral dosage forms using selective laser sintering technique

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Introduction

The adjustment of the dose according to the individual needs of the patient is a unique advantage of 3D printing technology, which is of particular importance for the pediatric and geriatric population, due to the diverse needs and characteristics of these groups of patients (Kotta et al., 2018).

Selective laser sintering (SLS) is one of the newest 3D printing techniques that uses powder materials, where the powder particles are connected under the influence of laser beams. The main disadvantage of SLS 3D printing is the high process temperature, which can lead to the degradation of active substances. On the other hand, this technique has many advantages, such as high resolution, the possibility of powder recycling and the absence of pre-processing (Fina et al., 2018; Thakkar et al., 2021).

Materials and methods

The following materials were used in this study: carvedilol (CRV), as a model substance (Hemofarm); Kollidon® VA 64 Fine (vinylpyrrolidone-vinylacetate-copolymerisate K 28, BASF, Germany) as a binding agent; Candurin® Gold Sheen (Merck, Germany) as an agent to improve the absorption of laser energy; CombiLac® (70% alpha-lactose monohydrate, 20% microcrystalline cellulose (MCC) and 10% white, natural corn starch, Meggle, USA) as a vehicle/carrier of the active substance; MicroceLac® 100 (75% alpha-lactose monohydrate and 25% microcrystalline cellulose, Meggle, USA) as a vehicle/carrier of the active substance; Croscarmellose (carboxymethylcellulose sodium, Meggle, USA) as a super-disintegrator and colloidal silicon dioxide (Aerosil® 200, Evonik, Germany) as a flowability improver. The composition of the formulations is shown in Table 1.

Table 1**.** Qualitative and quantitative composition of formulations

Formulation 1	Formulation 2
CRV (10%)	CRV (10%)
Kollidon®VA 64 (10%)	Kollidon® VA 64 (10%)
Candurin®Gold Sheen (3%)	Candurin® Gold Sheen (3%)
Aerosil® (2%)	Aerosil® (2%)
CombiLac® (75%)	MicroceLac® (70%)
/	Croscarmellose (5%)

A cylindrical 3D models of the printed tablets (10.00 mm diameter and 3.00 mm thickness) were designed with Autodesk Fusion 360 software version 2.0.8809 (Autodesk Inc, San Rafael, CA, USA), exported as a stereolithography file (.stl) and printed with Sintratec Kit 3D printer (Sintratec AG, Switzerland). 3D printing of both formulations was performed under the following experimental conditions: the surface layer temperature was 100°C, the chamber temperature was 90°C while the laser

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speed was 180 mm/s. Mass and dimensions of tablets (n=10) were determined using analytical balance (Sartorius, Goettingen, Germany) and a digital caliper (Vogel, Kevelaer, Germany), respectively.

Dissolution testing was performed under non-sink conditions using mini paddle apparatus (Erweka DT 600, Germany) with a paddle rotation speed of 50 rpm for 8 h, in 100 mL of phosphate buffer (pH 6.8). The amount of dissolved CRV was determined by Dionex Ultimate 3000 (Thermo Scientific, USA) HPLC system

Results and discussion

Mass and dimensions of the tablets: Tablets obtained by SLS printing meet the requirements of Ph. Eur. 11.0 in terms of mass variation, i.e., no tablet deviates more than the permitted deviation percentage of 7.5%.

Table 2. Mass, dimensions and thickness of the tablets.

	F1 (average and stdev)	F2 (average and stdev)
Mass (mg)	155.1 ± 2.5	151.81 ± 2.3
Diameter (mm)	10.24 ± 0.19	10.12 ± 0.35
Thickness (mm)	3.28 ± 0.12	3.04 ± 0.15

Tablet disintegration: The tablets (formulation F1) disintegrated in 51 seconds, in 800 mL of distilled water and at a temperature of 37ºC, while the tablets (formulation F2) disintegrated in only 30 seconds, which could be contributed to the presence of super-disintegrator (croscarmellose).

Table 3. Disintegration time of tablets.

Formulation	Time (s)
F1	51 ± 1.15
F2	30 ± 0.57

Tablet hardness: For tablets produced by SLS printing, the hardness values vary between 26.6 N (formulation F1) and 35.3 N (formulation F2). Higher laser speeds have shown a negative effect on tablet hardness.

Table 4**.** Hardness and tensile strengths of tablets.

	F1 (average and stdev)	F2 (average and stdev)
Hardness	35.3 ± 2.05	26.6 ± 1.5
Tensile strength (MPa)	0.67 ± 0.03	0.55 ± 0.04

Dissolution and drug release testing: The formulation F2 contains croscarmellose as a superdisintegrator that leads to a faster release of the active substance. In addition, the formulations contain lactose monohydrate, which has been shown to reduce tablet hardness and increase the rate of drug release. Therefore, the rapid disintegration of tablets and rapid dissolution of CRV can be attributed to the synergistic effect of lactose monohydrate and microcrystalline cellulose, which are part of MicroceLac and CombiLac.

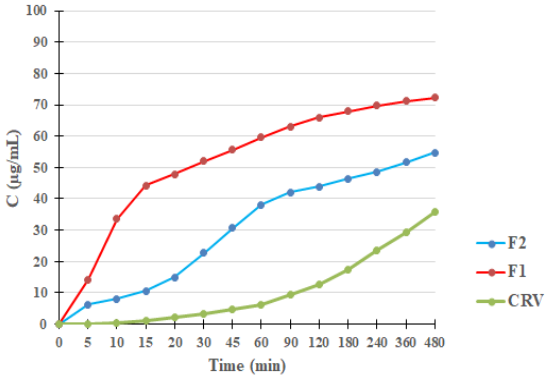

Fig. 1. Dissolution profiles of CRV released from SLS tablets and a sample of the pure drug.

Conclusion

The SLS tablets of formulation F2, containing croscarmellose as a super-disintegrant, disintegrated faster and resulted in a more rapid release of the active substance. Lactose monohydrate, which is an integral part of the excipients used (MicroceLac and CombiLac), also contributes to faster disintegration and thus faster release of CRV from SLS tablets.

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