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Welcome letter

Dear colleagues,

We warmly welcome you to the 9th BBBB Conference in Ljubljana, where we have decided to continue the tradition of organizing international BBBB conferences after a break due to the Covid-19 pandemic. Unfortunately, the situation did not allow us to hold the meeting in 2021, when we celebrated three anniversaries, the 100th anniversary of the University of Ljubljana, the 70th anniversary of the Slovenian Pharmaceutical Society and the 60th anniversary of continuous pharmacy studies at the University of Ljubljana. The theme of this year's symposium is "Pharma sciences of tomorrow". The program consists of plenary and keynote lectures from different areas of pharmaceutical sciences, coming from all BBBB partners and broader scientific community. There will also be plenty of opportunity for younger researchers to present their results in the form of oral and poster presentations in an international environment. The conference will offer opportunities for exchange of scientific ideas between young and established scientists and professionals, as well as between people from academia, industry and regulatory authorities. At the conference, we invite you to also visit the capital of Slovenia, which was designated as the European Best Destination 2022 for 2022.

Conference Chair
Prof Dr Aleš Obreza

Chair of the Scientific Committee
Prof Dr Rok Dreu

General Secretary or the Conferece:
Assoc Prof Dr Alenka Zvonar Pobirk

CONTENT

(Photo: Zmajski most / The Dragon bridge; Luka Esenko, Ljubljana Tourism photo library)

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ORAL DOSAGE FORMS WITH CARVEDILOL FABRICATED BY SELECTIVE LASER SINTERING (SLS) 3D PRINTING TECHNIQUE

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1. INTRODUCTION

When it comes to pharmacy, 3D printing has gained immense popularity in recent years due to its revolutionary use in printing drugs tailored to individual patient needs [1,2]. Selective laser sintering (SLS) is an industrial 3D printing technique which uses a powder bed to build up the 3D object thanks to a laser which binds the powder particles together. Advantages of SLS technique include the fact that it is a solvent-free process and offers relatively fast production. Until today, a limited number of studies investigating the production of drug dosage forms using SLS have been reported [2,3].

2. MATERIALS AND METHODS

2.1. Materials

Carvedilol (CRV) was used as a model substance in this study and it was donated by Hemofarm (Vršac, Serbia). The following excipients used to obtain 3D printing tablets: polyvinyl alcohol (PVA, Merck), mannitol (Parteck® M, Merck), Ludipress® (coprocessed excipient consisting of 93% lactose monohydrate, 3.5% crospovidone (Kollidon® CL) and 3.5% povidone K30 (Kollidon® 30), BASF), talc (Merck) and candurin (Candurin® Gold Sheen, Merck).

2.2. Preparation of formulations

The compositions of the formulations are shown in Table 1.

Table 1. Composition of the formulations

Material	Formulation 1	Formulation 2
CRV	10%	10%
PVA	55%	55%
Parteck® M	30%	/
Ludipress®	/	30%
Talc	2%	2%
Candurin® Gold Sheen	3%	3%

Powder for 3D printing was obtained by mixing all the components of the formulation and sifting through a sieve with a diameter of 180 μm.

2.3. 3D printing of oral dosage forms

A cylindrical 3D models of the printed tablets (8.00 mm diameter and 2.00 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). The printing parameters were controlled using Sintratec 3D printer software. After a series of variations in temperature and laser speed, the optimal values of these parameters used in the 3D printing process were established and shown in Table 2.

Table 2. SLS 3D printing process parameters

Surface Temperature (◦C)	Chamber Temperature (◦C)	Laser speed (mm/s)	Hatch space
80 ºC	70 ºC	60	250 μm

2.4. Mechanical properties of 3D tablets

Tablets (n = 10) were weighed on a Sartorius BP 210 D analytical balance (Sartorius, Goettingen, Germany) and measured (diameter and thickness) using a digital caliper (Vogel, Kevelaer, Germany).

2.5. Powder X-ray diffraction analysis (PXRD)

PXRD analysis was performed to assess whether the laser induced amorphization of any of the compounds, especially amorphization of poorly soluble CRV. Samples were collected using a Philips PW-1050 (Philips, The Netherlands) diffractometer, operated at 40 kV and 30 mA, using Ni-filtered Cu Kα radiation.

2.6. Dissolution and Drug Release Analysis

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 HPLC method using Dionex Ultimate 3000 (Thermo Scientific, USA) HPLC system.

3. RESULTS AND DISCUSSION

3.1. 3D printing process

It was shown that SLS printer was able to fabricate 3D tablets with CRV, as well as that success of the printing process depended on the used printing parameters.

3.2. Mechanical properties of 3D tablets

The dimensions of the obtained 3D tablets were in accordance with the defined values of the created 3D models (F1: 8.10 ± 0.08 mm diameter and 2.10 ± 0.13 mm thickness, F2: 8.13 ± 0.09 mm diameter and 2.10 ± 0.12 mm thickness). Significant variations in tablet weight between formulations were not observed (m_1=0.146 ± 0.04; m_2=0.136 ± 0.03).

3.3. Powder X-ray diffraction analysis (PXRD)

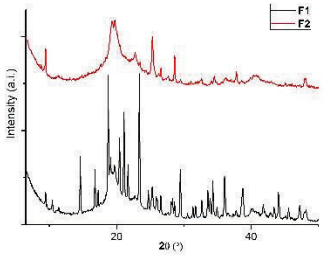

Figure 1. The X-ray powder diffraction of F1 and F2.

3.4. Dissolution and Drug Release Analysis

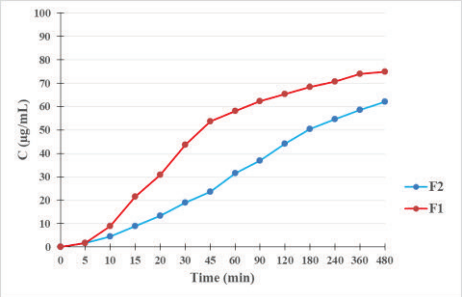

Figure 2. Dissolution profiles of 3D printing tablets

4. CONCLUSION

SLA represents a new chapter in 3D printing of solid oral dosage forms and in individualized therapy in particular. By adjusting the formulation and process parameters, it was possible to produce SLS tablets with co-amorphous CRV and PVA as a main polymer. Complete drug release was achieved under non sink conditions after 8 hours in phosphate buffer. The tailoring of drug release might be achieved by varying formulation factors as well as process parameters, although it could be governed by the composition of the whole formulation.

5. REFERENCES

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