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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

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

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HOW FORMULATION PARAMETERS AFFECT COMPRESSION BEHAVIOUR OF MULTIPARTICULATE UNITS PREPARED BY SELECTIVE LASER SINTERING?

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1. INTRODUCTION

Selective laser sintering (SLS) represents novel 3D printing technology recently introduced in drug fabrication. It is applicable in different dosage forms preparation, including multiparticulate units (MPUs) (1). The characteristics of the obtained MPUs remain to be described, particularly their compression behaviour and mechanical properties of the obtained compacts.

The aim of this work was to investigate compaction suitability of MPUs prepared by SLS printing and investigate the effect of model drug type, polymer type and MPU size as well as compression pressure on the compression-related parameters (detachment and ejection stress, nett work of compression) and the obtained compacts characteristics (out-of-die elastic recovery, solid fraction and tensile strength).

2. MATERIALS AND METHODS

2.1. Materials

The MPUs were prepared using either ethyl cellulose (EC, Ethocel, Fluka, Switzerland) or methacrylic acid-ethyl acrylate copolymer (1:1) (MA-EA, Eudragit L 100-55, Evonik, Germany) as polymer forming matrices. Ibuprofen (IBU) and caffeine (CAF) were used as model drugs and Candurin® Gold Sheen (CGS, Merck KGaA, Germany) was added as pharmaceutical grade colorant.

2.2. Multiparticulate units preparation

Spherical 3D models were designed and imported as print job file (.stec) to desktop SLS printer Sintratec Kit (Sintratec AG, Switzerland). Samples composition is presented in Table 1 (C-samples contain CAF, while I-samples contain IBU).

Sample	Model drug (10%)	Polymer (87%)	Colorant (3%)	Size (mm)
C1/I1	CAF / IBU	EC	CGS	1
C2/I2				2
C3/I3		MA-EA		1
C4/I4				2

Table 1. Multiparticulate units composition

2.3. Multiparticulate units compression

MPU compacts (100 mg) were prepared on an instrumented tablet press GTP series D (Gamlen Tableting Ltd, UK) in the single compression mode, under the compression loads of 250 and 500 kg, using 6 mm diameter flat punch, at the compaction speed 30 mm/min. The supporting software enabled complete visualization of the upper punch position and force in real time. The measured force-displacement curves were used to calculate nett work of compression, friction force between lower punch and tablet during detachment phase (detachment stress) and friction force between die and tablet in the ejection phase (ejection stress).

Compact dimensions were determined 24 hours after compression. Caliper was used to measure the out-of-die compact thickness (t), while compact diameter (R) and hardness (F) were measured using the hardness tester Erweka TBH 125D (Erweka GmbH, Germany). The obtained values were used to calculate compact tensile strength, solid fraction and out-of-die elastic recovery.

In order to statistically investigate the input parameter effects (polymer type, model drug type and MPU size), experimental design was applied, using software Design-Expert v.7.0 (Stat-Ease Inc, USA).

3. RESULTS AND DISCUSSION

3.1. Multiparticulate units compression

The prepared compact tensile strength was generally higher than 1 MPa and acceptable (2), as represented in Fig. 1, while solid fraction ranged from 67.67 (C4) to 89.46% (C1 and I1). MPUs containing CAF and MPUs with MA-EA exhibited higher increase in solid fraction and tensile strength when compression load was increased, in comparison to samples prepared with IBU or EC, respectively. This indicates better tabletability and compressibility. MPU samples with MA-EA or 1 mm size exhibited higher nett work of compression, but also higher values of elastic recovery. Higher energy input corresponds to higher compressibility and susceptibility to particle consolidation. Ejection stress values did not exceed 3 MPa, which is associated with compact defect propensity (3), while detachment stress was lower than 4 MPa. This indicates that the prepared samples do not stick to punch and die and may be easily detached.

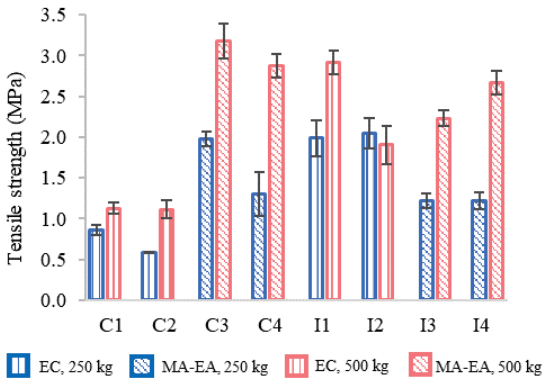

Figure 1. The obtained MPU tensile strength values

All of the investigated factors (model drug type, polymer type, MPU size and compression pressure), as well as model drug-polymer type and model drug-compression pressure interaction significantly affected compact tensile strength ($p<0.0001$). In the case of MPUs containing CAF as model drug and EC as polymer, higher compression pressure increased tensile strength more notably.

In the case of detachment stress, model drug type, polymer type and compression pressure were found as relevant factors ($p=0.0013$), while ejection stress was affected by polymer type, compression pressure and their interaction ($p=0.0097$). Elastic recovery was impacted by all the investigated parameters, as well as model drug type-polymer type and model drug type-compression pressure interaction ($p<0.0001$). Higher compression pressure increased the elastic recovery values more notably in the case of IBU or EC samples. Model drug type, polymer type and compression pressure affected nett work ($p<0.001$), as well as model drug-compression pressure and polymer type-compression pressure interaction. Based on the investigated MPU samples, software-aided prediction recognized IBU, MA-EA and 1 mm-MPUs size as desirable for obtaining compacts with high tensile strength, but also low elastic recovery, low detachment and ejection stress and high nett work values.

4. CONCLUSION

The multiparticulate units were successfully compressed into compacts with good tensile strength values (higher than 1 MPa, generally), low detachment and ejection stress (lower than 3 and 4 MPa, respectively). MPUs containing CAF and MPUs with MA-EA exhibited higher tabletability and compressibility in comparison to samples prepared with IBU or EC, respectively.

Polymer type and compression pressure affected all the investigated compact characteristics (tensile strength, detachment and ejection stress, out-of-die elastic recovery and nett work of compression), while MPU size impact on the observed parameters was the lowest. MPUs containing IBU and MA-EA, with 1 mm size were recognized as preferable for obtaining compacts with favourable characteristics.

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