Univerza v Ljubljani
Fakulteta za farmacijo

Slovensko Farmacevtsko Društvo
SLOVENIAN PHARMACEUTICAL SOCIETY

EUFEPS
European Federation for Pharmaceutical Sciences

EUROPEAN FEDERATION FOR MEDICINAL CHEMISTRY AND CHEMICAL BIOLOGY

BOOK OF ABSTRACTS

9th BBBB International Conference on Pharmaceutical Sciences

Pharma Sciences of Tomorrow

Ljubljana, Slovenia, 15th-17th September, 2022

Impressum

9th BBBB International Conference on Pharmaceutical Sciences
Pharma Sciences of Tomorrow: Book of Abstracts

Editors: Aleš Obreza, Rok Dreu, Alenka Zvonar Pobirk, Barbara Sterle Zorec

Reviewers: Mirjana Gašperlin, Janez Ilaš, et al.

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Prepress design: Barbara Sterle Zorec, Alenka Zvonar Pobirk

Design: Sebastjan Jenko

Publisher: Slovensko farmacevtsko društvo in Univerza v Ljubljani, Fakulteta za farmacijo

URL address: The book of abstracts will be pdf format, available at:
https://bbbb2022.sfd.si/programme/scientific-programme/

Ljubljana, 2022

Kataložni zapis o publikaciji (CIP) pripravili v Narodni in univerzitetni knjižnici v Ljubljani
COBISS.SI-ID **120548355**
ISBN 978-961-94230-4-2 (Slovensko farmacevtsko društvo, PDF)

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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EVALUATION OF DILUTION CAPACITY AND COMPACTION BEHAVIOUR OF THE EXCIPIENTS CO-PROCESSED BY IN SITU FLUIDIZED BED MELT GRANULATION

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1. INTRODUCTION

Co-processing has emerged as a suitable approach to meet the increasing demands for excipients with improved tableting performance. Apart from the most commonly used energy-consuming co-processing methods (e.g. spray-drying and wet granulation), melt granulation as a solvent-free and more environmentally friendly technique has recently gained more attention [1].

The aim of the present study was to investigate the influence of meltable binder particle size and compaction parameters on dilution capacity and compaction behaviour of lactose-based co-processed excipients.

2. MATERIALS AND METHODS

2.1. Materials

Paracetamol (Acros Organics, Belgium) was used as the model drug. Lactose monohydrate (Carlo Erba Reagents, Italy) was used as filler and glyceryl palmitostearate (Precirol® ATO 5 Gattefossé S.A.S, France) as meltable binder.

2.2. Preparation of co-processed excipients

Co-processed excipients were prepared by in situ melt granulation in Mycrolab fluid bed processor (OYSTAR Hüttlin, Germany). Precirol® particles (15%) from the 125–180 μm (≈ 150 μm) or 600–710 μm sieve fraction (≈ 655 μm) were used for granulation of lactose (85%). The inlet air flow rate was 30 m^3/h, and product temperature during agglomeration was 65 °C.

2.3. Particle size and shape analysis

Granule size distribution was evaluated by sieve analysis, and median particle diameter (d_{50}) was calculated by linear interpolation of the cumulative percentage frequency curve. Granule shape was examined by 2D scanned image (4800 dpi resolution) analysis using ImageJ software. The aspect ratio (AR) and circularity (C) were calculated for granule shape evaluation.

2.3. Determination of the Carr index

The bulk and tapped (1250 taps) densities of co-processed excipients and their mixtures with 30, 40 or 50% paracetamol were determined using tap density tester STAV 2003 (J. Engelsmann AG, Germany), and Carr index was calculated.

2.4. Dynamic compaction analysis

Co-processed excipients and their mixtures with paracetamol were compressed on a single punch instrumented tablet press (GTP D series, Gamlen Tableting Ltd, UK). Compacts (100 mg) were compressed under compression load of 200 kg (≈ 70 MPa) or 500 kg (≈ 173MPa), and compression speed of 60 or 120 mm/min. 6 mm flat faced punches were used. The obtained force-displacement curves were used to calculate: net work of compression (NW), detachment stress (DS), ejection stress (ES). Tablet crushing force was determined using tablet hardness tester Erweka TBH 125D (Erweka GmbH, Germany), and the values obtained were used to calculate tensile strength (TS). Elastic recovery (24 h after compression) was calculated, as well.

2.4. Experimental Design

In order to investigate the influence of binder particle size, paracetamol content and compression speed on the abovementioned compaction properties, compacts were prepared, at compression load of 500 kg, according to 2^3 full factorial design.

3. RESULTS AND DISCUSSION

3.1. Particle size and shape

Larger initial binder particle size led to formation of larger and more spherical granules (Table 1).

Table 1. The size and shape of the co-processed excipients' particles.

Binder PS (μm)	d_{50}	AR	C
150	564.9	1.33	0.81
655	846.2	1.14	0.86

3.2. Flowability

The Carr index values obtained indicated considerably better flowability of the co-processed excipient prepared by using larger binder particles (P655) in comparison with the excipient prepared with smaller binder particles (P150). This might be ascribed to more spherical and larger particles of P655. However, the addition of paracetamol led to an increase in Carr index values and less pronounced differences between two excipients (Fig. 1).

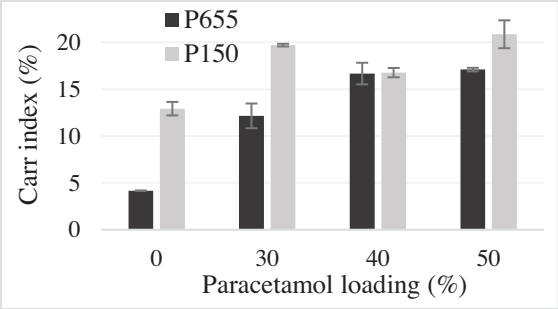

Figure 1. The influence of paracetamol loading on flowability of co-processed excipients.

3.3. Compaction behaviour

The results obtained revealed better mechanical properties of P150 in comparison with P655 compacts, irrespective of the compression pressure applied. The addition of paracetamol, as the model API with poor compaction properties, led to decrease in tensile strength of the compacts prepared with both excipients, and paracetamol content showed statistically significant influence on TS ($p < 0.0001$). Acceptable tensile strength (> 1 MPa) could be achieved for compacts with 30% paracetamol compressed at higher compression pressure (≈ 173 MPa).

Paracetamol content, compression speed and interaction between binder particle size and paracetamol content were found to significantly affect NW. The influence of binder particle size was more pronounced at higher paracetamol content, with lower NW observed in the case of P655. Higher compression speed led to higher NW.

Relatively low values of detachment and ejection stress (< 3.5 MPa) indicate good antiadhesive and lubricating properties of the investigated excipients. Lower values of both parameters were observed in the case of P655 which could be related to different agglomeration mechanisms involved. Besides binder particle size, compression speed and paracetamol content were found to significantly influence these properties.

Elastic recovery values of the investigated samples ranged between 12 and 28%. In the case of both excipients, higher elastic recovery values were obtained at higher compression pressure. ER values of the compacts prepared at higher compression pressure were significantly affected by compression speed and interactions of the investigated variables.

4. CONCLUSION

The results obtained show that meltable binder particle size affects granule size and shape, and consequently may influence flowability and compaction behaviour of the co-processed excipients. Interactions between binder particle size and compaction variables were also found to affect compaction properties of the investigated excipients.

5. REFERENCES

1. Ćirin-Varađan, S., et al., *Comparative evaluation of mechanical properties of lactose-based excipients co-processed with lipophilic glycerides as meltable binders.* Journal of Drug Delivery Science and Technology, 2022. 67: 102981.

ACKNOWLEDGMENT

This research was funded by the Ministry of Education, Science and Technological Development, Republic of Serbia through Grant Agreement with University of Belgrade-Faculty of Pharmacy No: 451-03-68/2022-14/200161.