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.

Authors: Stanislav Gobec, Hatice Yeşim Karasulu et al.

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)

P49

APPLICATION OF SUPPORT VECTOR MACHINE LEARNING FOR ORODISPERSIBLE FILMS DISINTEGRATION TIME PREDICTION

Erna Turković, Ivana Vasiljević, Dragana Vasiljević, Svetlana Ibrić, Jelena Parojčić

Department of Pharmaceutical Technology and Cosmetology, University of Belgrade – Faculty of Pharmacy, Serbia

1. INTRODUCTION

Orodispersible films (ODF) have emerged as innovative dosage forms that provide wide variety of advantages for patients and manufacturers over conventional dosage forms. The prominent characteristic of ODFs is fast disintegration followed by good patients acceptability [1]. Therefore, relevant disintegration time (DT) is usually considered as ODF critical quality attribute. Extensive research on ODFs is generating a lot of data, but lack of standardization is the main obstacle that limits their comparative evaluation. The following work aims to explore literature data on ODFs characteristics using the predictive data-classification algorithm Support vector machine (SVM) and assess its applicability in pharmaceutical development based on the set of experimentally obtained data.

2. MATERIALS AND METHODS

2.1. Materials

Hydroxypropyl cellulose (Klucel GF, Ashland, USA), ethanol (≥99.8%, Honeywell, Charlotte, NC, USA) and glycerol, 85% (w/w) (Ph. Eur.) were used for preparation of printing and casting dispersion.

2.2. Data pre-processing

Comprehensive data exploration has been conducted in the PubMed database using most common synonyms for ODFs with fifteen synonyms in singular and plural. Built database had following attributes: manufacturing approach, polymer selection, polymer molecular weight (KDa), polymer load (%), mechanical properties (tensile strength (MPa), Young's modulus (MPa), elongation at break (%)), disintegration method and disintegration time (DT) (s).

2.3. ODF preparation and characterisation

Polymer dispersions for solvent casting and semi-solid extrusion 3D printing were prepared by dispersing HPC in ethanol:glicerol solution followed by continuous stirring on the magnetic stirrer. Prepared dispersions were: (i) casted on a unit-dose plexiglas plates, or (ii) printed using Ultimaker 2+ (Ultimaker, , Netherlands). ODFs were characterized in terms of mechanical properties using Z-LX Table-Top Testing Machine (Shimadzu, Japan) and DT using adapted compendial tester (Erweka ZT52, Germany) with a weight.

3. RESULTS AND DISCUSSION

3.1. Data pre-processing

274 papers (without reviews) were identified via search, of which 112 were included in the database.

Table 1. Classification of disintegration testing and manufacturing methods

Disintegration testing methods	Manufacturing methods
Compendial method for solid dosage forms – 1	Solvent casting – 1
Adapted compendial method (with clamp/frame) – 2	Inkjet printing – 2
Adapted compendial method (with clamp/frame and weight) – 3	3D printing – 3
Drop method / Slide frame method (without weight) – 4	Electrospinning – 4
Drop method / Slide frame method (with weight) – 5	Hot-melt extrusion – 5
Petri dish / Beaker / Glass vial method (with agitation) – 6	
Petri dish / Beaker / Glass vial method (without agitation) – 7	
Other – 8	

Nominal data from literature was transformed into numerical, using coding operator so that each nominal data had corresponding numerical value. Critical attributes for films fast disintegration were derived. 18 polymers were included as categorical data and were further differentiated on the basis of molecular weight. Values for most commonly evaluated mechanical properties were included as

numerical data. Different DT methods were classified in seven classes (Table 1), while the manufacturing methods were classified in five classes. RapidMiner Studio 9.10 (RapidMiner, Dortmund, Germany) was used to transform data and employ SMV algorithm.

3.2. SVM model prediction

Attributes with the highest weight were polymer load and DT method employed (Figure 1). The polymer type and characteristic did have conclusive effects on DT as their weight varied during data mining. This can be attributed to inconclusive data provided in papers and lot of missing values for those attributes. Mechanical properties had low weight, which can be explained with the broad value range for those attributes. Different research groups had different approach to disintegration testing, which lowered model precision as it was reported that SVM does not have high accuracy when data is imbalanced [3]. Relative error value was 20%, which can be considered as high, but, having in mind great diversity in presented data and methodology, obtained value is still acceptable for the pilot study.

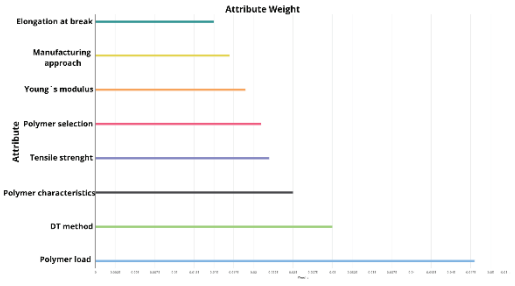

Figure 1. Attribute weight in predicting model

3.3. Experimental validation

HPC-based films prepared by 3D printing had tensile strength, elongation at break and Young's modulus of 3.5 MPa, 137% and 5 MPa, respectively. Average DT was 69 s. For casted films, relevant values were 3.4 MPa, 105% and 3 MPa, and DT was 27 s. Experimentally obtained results were entered into model simulator (Figure 2) to simulate situation reflecting the experimental set up in which HPC-based films were prepared by 3D printing and solvent casting, and relevant attribute values obtained by samples characterization. In the case were manufacturing method was set to be 3D printing (coded as 1) predicted DT value was close to experimentally obtained value, i.e. 71.7 and 69 s, respectively.

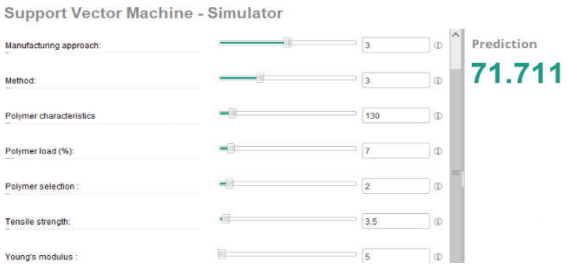

Figure 2. Model simulator used to predict DT of 3D printed HPC-based films

When solvent casting method was considered, predicted DT value was remarkedly higher than the experimentally obtained one, indicating bad predictability. It might be assumed that good predictability obtained in the case of 3D printed films is associated with lower data variability due to more simple sample composition and robust preparation method. In the case of casted films, data was much more complex due to a higher number of research papers and approaches to characterisation.

4. CONCLUSION

The obtained results indicate that SVM algorithm can be employed to predict ODF DT value based on the dataset created using literature data. However, in order to obtain meaningful predictions, larger dataset, with fewer inconsistences and less missing values would be advantageous.

5. REFERENCES

1. Scarpa, M., et al., *Key acceptability attributes of orodispersible films.* European Journal of Pharmaceutics and Biopharmaceutics, 2018. 125: 131-140.
2. Preis, M., et al., *Comparative study on novel test systems to determine disintegration time of orodispersible films.* Journal of Pharmacy and Pharmacology, 2014, 66: 1102–1111.
3. Wu,G and Chang,E.Y. *Adaptive feature-space conformal transformation for imbalanced-data learning.* Proceedings of the 20th ICML, Washington DC, 2003. 816-823.

ACKNOWLEDGMENT

This work was financially supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia (project 451-03-68/2022-14/200161).