III. Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science

20-22 January, 2021

Book of Abstracts

University of Szeged

III. Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science

January 20-22nd 2021 Szeged, Hungary

Greetings

On behalf of the Scientific Committee, I am very pleased to welcome the participants of the 3rd Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science. Special greetings to the young researchers who report on their PhD work at this event.

The symposium series launched before last year was a new initiative of the Institute of Pharmaceutical Technology and Regulatory Affairs, University of Szeged. The aim of this program was to get to know the work of Hungarian and foreign PhD students working at the institute, to master the basic rules of presentation and discussion. Early acquisition of this knowledge/skills is extremely important for mobility programs, conferences, publications and later for defense of theses.

The successful 1st Symposium gave us the idea to invite our cooperative partners to participate in the 2nd Symposium. We were delighted to welcome 16 PhD students from Serbia, Romania, Czech Republic, Bosnia-Herzegovina and Slovenia. 70 colleagues were participated at this symposium and the program included 1 plenary lecture and 39 oral presentations. Since we are past two successful symposia, we decided to continue this series.

The current 3rd Symposium was announced as an online symposium in view of the COVID-19 pandemic. We are very pleased that a large number of participants have registered for this event and 53 PhD students and young researchers from 11 countries (Bosnia and Herzegovina, Bulgaria, Czech Republic, Estonia, Germany, Hungary, Italy, Romania, Serbia, Slovenia, Spain) submit lectures. This is a three-day event provides a good opportunity to discuss the new developments and the future directions of the pharmaceutical sciences.

I am looking forward to having a successful conference with fruitful discussions.

Prof. emer. Piroska Szabó-Révész
Head of Scientific Committee

III. SYMPOSIUM OF YOUNG RESEARCHERS ON PHARMACEUTICAL TECHNOLOGY, BIOTECHNOLOGY AND REGULATORY SCIENCE

20-22 JANUARY 2021

SZEGED
Hungary

General Information

Date: 20-22 January 2021

Location: Microsoft Teams

Congress Topics: Pharmaceutical technology, biotechnology and regulatory science

Oral presentations (10 min) followed by discussions (5 min)

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President of the Symposium
Prof. Dr. Ildikó Csóka

Organiser

University of Szeged, Institute of Pharmaceutical Technology and Regulatory Affairs

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Co-organisers

Foundation for the Development of Pharmacy Education in Szeged

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III. Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science

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III. Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science

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Short-Programme

Wednesday, 20th January – 9:00-16:15 CET

9:00 - 10:15	**Opening Ceremony and Plenary Session**
10:15 - 11:00	**Session 1**
11:00 - 11:20	Break
11:20 - 12:35	**Session 2**
12:35 - 13:30	Lunch break
13:30 - 14:45	**Session 3**
14:45 - 15:00	Break
15:00 - 16:15	**Session 4**
19:00 -	***Networking event***

Thursday, 21st January – 9:30-15:45 CET

9:30 - 10:45	**Session 5**
10:45 - 11:00	Break
11:00 - 12:15	**Session 6**
12:15 - 13:00	Lunch break
13:00 - 14:15	**Session 7**
14:15 - 14:30	Break
14:30 - 15:45	**Session 8**
19:00 -	***Game Night***

Friday, 22nd January – 9:30-14:30 CET

9:30 - 10:45	**Session 9**
10:45 - 11:00	Break
11:00 - 12:15	**Session 10**
12:15 - 13:00	Lunch break
13:00 - 14:15	**Session 11**
14:15 - 14:30	**Closing Ceremony**

III. Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science

January 20-22nd 2021 Szeged, Hungary

Schedule

Wednesday, 20th January – 9:00-16:15 CET

9:00-9:15 **Opening Ceremony**

9:15-10:15 **Plenary Session: Prof. Dr. Csaba Szántay** (Gedeon Richter Plc.)

The hidden role of the human factor in scientific thinking

10:15-11:00 **Session 1 – Chairs: Dr. Barbora Vranikova, Dr. Noemi Csaba**

OP-1 – 10:15-10:30 **Ruba Ismail,** Ildikó Csóka

What are the regulatory aspects surrounding nanopharmaceuticals development?

OP-2 – 10:30-10:45 **Andrea-Gabriela Crișan,** Sonia Iurian, Cătălina Bogdan, Lucia Rus, Alina Porfire, Sebastian Porav, Kinga Ilyés, Ioan Tomuță

Personalized Fused Deposition Modeling 3D printed (FDM-3DP) tablets: a Quality by Design (QbD) approach

OP-3 – 10:45-11:00 **Tamás Kiss,** Gábor Katona, Rita Ambrus

Modifying the release of an antiparkinsonian drug by using mesoporous carrier

11:00-10:20 **Break**

11:20-12:35 **Session 2 – Chair: Dr. Alina Porfire, Dr. Szilvia Berkó**

OP-4 – 11:20-11:35 **Mahwish Mukhtar,** Rita Ambrus

Spray dried hyaluronic acid nanoplexes conjugated with chitosan and its derivatives for the pulmonary administration as dry powder inhalers for tuberculosis

OP-5 – 11:35-11:50 **Merima Sirbubalo,** Amina Tucak, Edina Vranić

Additive manufacturing of PLA microneedles for transdermal durg delivery

OP-6 – 11:50-12:05 **Zorana Mutavski,** Senka Vidović

Potential of vinegar as extraction solvent: can we use it for herbal preparation?

OP-7 – 12:05-12:20 **Črt Dragar**, Tanja Potrč, Sebastjan Nemec, Robert Roškar, Stane Pajk, Slavko Kralj, Mirjana Gašperlin, Petra Kocbek

Development of magnetic nanoparticles for targeted drug delivery

OP-8 – 12:20-12:35 **Reihaneh Manteghi,** Katalin Kristó, Gerda Szakonyi, Ildikó Csóka

Strategies for development of antimicrobial peptides and proteins

12:35-13:30 Lunch break

13:30-14:45 Session 3 – Chair: Dr. Senka Vidović, Dr. Géza Regdon jr.

OP-9 – 13:30-13:45 **Hussein Akel,** Ruba Ismail, Gábor Katona, Ildikó Csóka

Lipid-based nanosystems for the nose-to-brain delivery of biological drug, Insulin

OP-10 – 13:45-14:00 **Zsófia Németh,** Dorina Gabriella Dobó, Edina Pallagi, Ildikó Csóka

Quality-focused formulation - QbD-based liposome design and development

OP-11 – 14:00-14:15 **Stanislava Simeonova,** Tsenka Grancharova, Plamen Zagorchev, Bissera Pilicheva

Near-infrared light-responsive magnetic nanoparticles - preparation and application in photothermal therapy

OP-12 – 14:15-14:30 **Erna Turković,** Jelena Parojčić

Application of artificial neural network in understanding critical material properties governing orodispersible film disintegration

OP-13 – 14:30-14:45 **Kairi Tiirik,** Liis Preem, Kadi Sagor, Marta Putrinš, Tanel Tenson, Karin Kogermann

In vitro and *ex vivo* models for assessing the antibiofilm properties of wound dressings

14:45-15:00 Break

15:00-16:15 Session 4 – Chair: Dr. Wehad Ibrahim, **Dr. Gábor Katona**

OP-14 – 15:00-15:15 **Davide D'Angelo,** Francesca Buttini, Fabio Sonvico

Inhalable cyclosporine powder for immunosuppressive treatment

OP-15 – 15:15-15:30 **Eszter L. Kiss**, Mária Budai-Szűcs, Erzsébet Csányi

Mucoadhesive nanostructured lipid carriers for ophthalmic use

OP-16 – 15:30-15:45 **Gabriela Nistor,** Marius Mioc, Roxana Ghiulai, Roxana Racoviceanu, Codruta Soica

Synthesis of betulinic acid 1,2,4-triazole derivatives suitable for cyclodextrin inclusion complex formulation

OP-17 – 15:45-16:00 **Edit Benke,** Christina Winter, Piroska Szabó-Révész, Eva Roblegg, Rita Ambrus

Effect of solvent compositions on habits and *in vitro* aerodynamic results of spray-dried pulmonary formulations

OP-18 – 16:00-16:15 **Krisztián Pamlényi,** Katalin Kristó, Orsolya Jójárt-Laczkovich, Géza Regdon jr.

Preparation and investigation of permeability and physical-chemical properties of buccal films with sodium alginate

19:00- Networking event

Thursday, 21st January – 9:30-15:45 CET

9:30-10:45 Session 5 – Chair: Dr. Francesca Buttini, Dr. Rita Ambrus

OP-19 – 9:30-9:45 **S. P. Yamini Kanti,** Ildikó Csóka, Orsolya Jójárt-Laczkovich, Livia Adalbert

Analysis of the regulations for medical devices in Europe & future perspectives

OP-20 – 9:45-10:00 **Tsenka Grancharova,** Stanislava Simeonova, Bissera Pilicheva, Plamen Zagorchev

Synergistic effect of magnetic nanoparticles and chemotherapeutic drugs in cancer

OP-21 – 10:00-10:15 **Balázs Attila Kondoros**, Zoltán Aigner

Evaluation of fenofibrate-cyclodextrin complexes prepared by co-grinding method

OP-22 – 10:15-10:30 **Kaisa Põhako**, Karin Kogermann, Tanel Tenson, Külli Kingo

Towards understanding the safety and biocompatibility of electrospun fibers

OP-23 – 10:30-10:45 **Amina Tucak,** Merima Sirbubalo, Edina Vranić, Andreas Zimmer

Solid lipid nanoparticles as drug delivery systems for MicroRNA

10:45-11:00 Break

11:00-12:15 <u>Session 6</u> – Chair: Prof. Dr. Edina Vranić, Dr. Tamás Sovány

OP-24 – 11:00-11:15 **Lucia Ruxandra Tefas,** Cătălina Bogdan, Alina Porfire, Tryfon Digkas, Thomas De Beer, Ioan Tomuță

Development of liposomal drug delivery system as a strategy for improving bioavailability and therapeutic efficacy, by Design of Experiments. A case study.

OP-25 – 11:15-11:30 **Luca Éva Uhljar,** Sheng Yuan Kan, Norbert Radacsi**,** Rita Ambrus

Preformulation studies of ciprofloxacin loaded PVP nanofibers

OP-26 – 11:30-11:45 **Nikolay Zahariev,** Bissera Pilicheva

Application of 32 experimental design in the preparation of casein nanoparticles as potential drug carriers

OP-27 – 11:45-12:00 **Ana Milanović,** Sandra Cvijić

Paediatric PBPK modeling: Prediction of drug exposure following oral dosing of different paracetamol formulations in fasted and fed states

OP-28 – 12:00-12:15 **Stella Zsikó**, Erzsébet Csányi, Szilvia Berkó

New perspectives of skin penetration testing methods

12:15-13:00 Lunch break

13:00-14:15 <u>Session 7</u> – Chair: Dr. Bissera Pilicheva, Dr. Katalin Kristó

OP-29 – 13:00-13:15 **Ernő Máté Benkő,** Ilija German-Ilič, Géza Regdon Jr., Ildikó Csóka, Klára Pintye-Hódi, Stane Srčič, Tamás Sovány

Investigation of drug-matrix interaction in directly compressed matrices

OP-30 – 13:15-13:30 **Roxana Ghiulai,** Marius Mioc, Gabriela Nistor, Roxana Racoviceanu, Codruta Soica

Design and synthesis of betulinic acid gold nano-particles with enhanced pharmaceutical properties

OP-31 – 13:30-13:45 **Chiazor Ogadah,** Šklubalová Zdeňka, Vraníková Barbora

Biorelevant dissolution testing of matrix systems based on combination of mucoadhesive polymers

OP-32 – 13:45-14:00 **Nikolett Kis**, Szilvia Berkó, Erzsébet Csányi

Investigation of dermal semisolid in situ film-forming systems containing lidocaine hydrochloride with QbD approach

OP-33 – 14:00-14:15 **Laura Falkenstein,** Joerg Breitkreutz, Peter Kleinebudde

Deposition studies on a systematically modified paediatric throat geometry

14:15-14:30 Break

14:30-15:45 Session 8 – Chair: Dr. Raphael Wiedey, Dr. Livia Adalbert

OP-34 – 14:30-14:45 **Mercedes Vitek,** Mirjam Gosenca Matjaž, Mirjana Gašperlin, Robert Roškar, Alenka Zvonar Pobirk

Antioxidant efficacy of vitamins loaded lipid-based delivery systems with different microstructure for dermal application

OP-35 – 14:45-15:00 **Fanni Falusi,** Anita Kovács, Erzsébet Csányi

Investigation of foams for topical use

OP-36 – 15:00-15:15 **Yousif H-E. Y. Ibrahim,** Katalin Kristó, Géza Regdon jr., Tamás Sovány

Development and optimization of the coating processes of lysozyme loaded pellets for oral delivery

OP-37 – 15:15-15:30 **Nguyen Viet Khan,** Ivo Laidmäe, Karin Kogermann, Andres Meos, Duc Viet Ho, Ain Raal, Hoai Thi Nguyen, Jyrki Heinämäki

Electrospun amphiphilic nanofibers for stigmasterol-loaded delivery systems

OP-38 – 15:30-15:45 **Fakhara Sabir**, Gábor Katona, Ruba Ismail, Ildikó Csóka

Nose to brain delivery of n-propylgallte loaded lipid nanoparticles for targeting glioblastoma multiforme via QbD approach

19:00- Game Night

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Friday, 22nd January – 9:30-14:30 CET

9:30-10:45 **Session 9 – Chair: Dr. Jelena Djuriš, Dr. Erzsébet Csányi**

OP-39 – 9:30-9:45 **Anže Zidar,** Julijana Kristl

Challenges in nanofiber testing *in vitro*

OP-40 – 9:45-10:00 **Carla Garcia-Mazas,** Marcos García Fuentes, Noemi Csaba

New polymeric nanocomplexes against glioblastoma initiating cells

OP-41 – 10:00-10:15 **Stefana Suciu**, Sonia Iurian, Rita Ambrus, Catalina Bogdan, Ioan Tomuță

Milk oral lyophilisates with loratadine: screening for new excipients for paediatric use

OP-42 – 10:15-10:30 **Bence Sipos,** Gábor Katona, Ildikó Csóka

Nose-to-brain applicability of Meloxicam-loaded Soluplus polymeric micelles

OP-43 – 10:30-10:45 **Alharith A. A. Hassan**, Katalin Kristó, Tamás Sovány

Printing of peptide-loaded hybrid nanoparticles for oral delivery

10:45-11:00 **Break**

11:00-12:15 **Session 10 – Chair: Prof. Dr. Codruta Soica, Dr. Urve Paaver**

OP-44 – 11:00-11:15 **Marija Djuranović,** Svetlana Ibrić

Application of deep learning tools in prediction of printability of 3D printed tablets

OP-45 – 11:15-11:30 **Martin Cseh,** Zsolt Geretovszky, Zoltán Veréb, Ferenc Bari

The 3D Printing Center of the University of Szeged: opportunities and challenges

OP-46 – 11:30-11:45 **Petra Party,** Rita Ambrus

Preparation and characterization of carrier-free dry powder inhalers containing nanosized active ingredient

OP-47 – 11:45-12:00 **Sandra Robla,** Jose Manuel Ageitos, Rubén Varela Calviño, Sulay Tovar, Noemi Csaba

Bioinspired pollen microcapsules to overcome mucosal barriers

OP-48 – 12:00-12:15 **Siniša Simić,** Jelena Vladić

Overview: Supercritical carbon dioxide versus subcritical water extraction of bioactive compounds from herbal material

12:15-13:00 **Lunch break**

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13:00-14:15 **Session 11 – Chair: Prof. Dr. Mirjana Gašperlin, Dr. Mária Budai-Szűcs**

OP-49 – 13:00-13:15 **Patrícia Varga,** Rita Ambrus, Csilla Bartos

Development of spray-dried meloxicam-containing microcomposites using biocompatible matrix

OP-50 – 13:15-13:30 **Marius Mioc,** Roxana Ghiulai, Gabriela Nistor, Roxana Racoviceanu, Codruta Soica

Structural design of triterpenic acid 1,2,4-triazole linked gold nanoparticle bioconjugates, as potential treatment for malignant melanoma

OP-51– 13:30-13:45 **Sebastian Pohl,** Peter Kleinebudde

Transfer of twin-screw granulation process using a shear stress description of screw configuration

OP-52 – 13:45-14:00 **Sheila Barrios Esteban,** Sonia Reimondez-Troitiño, Ruman Rahman, Cameron Alexander, Marcos Garcia-Fuentes, Noemi Csaba

Protamine-based nanoparticles: an attractive gene delivery system for 2D and 3D glioblastoma models

OP-53 – 14:00-14:15 **Yasmin Ranjous,** Dóra Kósa, Zoltán Ujhelyi, Géza Regdon jr., Krisztina Anita Nagy, Zoltán Kónya, Ildikó Bácskay, Tamás Sovány

Optimization of the functionalization method of titanate nanotubes in order to use them as drug delivery systems

14:15-14:30 **Closing Ceremony**

Abstracts

III. Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science

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OP-1

DOI: 10.14232/syrptbrs.2021.op1

What are the regulatory aspects surrounding nanopharmaceuticals development?

Ruba Ismail[1,2], Ildikó Csóka[1,2]

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[2]Department of Applied and Environmental Chemistry, Institute of Chemistry, Faculty of Science and Informatics, University of Szeged, Szeged, Hungary

Tremendous effort has been devoted over the last two decades for developing nanomedicine-based products particularly in the field of drug delivery systems. Nanopharmaceuticals, due to their special their physiochemical characteristics and behaviour, have proved to hold fantastic potential for addressing the questions of unmet clinical needs. But still and all, nanopharmaceuticals R&D needs a complex and comprehensive global critical thinking not to mention that there are still many challenges in their regulations. Hence, this presentation aims at providing an overview on the regulatory needs and risks of nanopharmaceuticals with a focus on the Food and Drug Administration (FDA) and European Medicine Agency (EMA) regulations. Towards boosting the translation of nanopharmaceuticals to clinical applications, Quality by Design (QbD), as a risk-based methodology, is greatly recommended to be followed. In addition to considering the risk assessment focused design, the whole research needs to be performed with great attention to its complexity and multidisciplinary character.

Acknowledgements: This work was supported by the Ministry of Human Capacities, Hungary (Grant TKP-2020) and Gedeon Richter Ltd – GINOP project (2.2.1-15-2016-00007).

References

1 Ismail R. PhD Thesis, University of Szeged (2020).
2 Ismail R.; Sovány T.; Gácsi A.; et al. Pharm. Res. 36, 16 (2019).
3 Pallagi I.; Ismail R.; Paál T.L.; Csóka I. Eur. J. Pharm. Sci. 122, 160-169 (2018).
4 Csóka I.; Pallagi E.; Paál T.L. Drug Discov. Today. 23,1340-1343 (2018).

OP-2

DOI: 10.14232/syrptbrs.2021.op2

Personalized Fused Deposition Modeling 3D printed (FDM-3DP) tablets: a Quality by Design (QbD) approach

Andrea-Gabriela Crișan[1*], Sonia Iurian[1], Cătălina Bogdan[2], Lucia Rus[3], Alina Porfire[1], Sebastian Porav[4], Kinga Ilyés[1], Ioan Tomuță[1*]

1. Department of Pharmaceutical Technology and Biopharmacy, Faculty of Pharmacy, University of Medicine and Pharmacy „Iuliu Hațieganu", Cluj-Napoca, Romania
2. Department of Dermopharmacy and Cosmetics, Faculty of Pharmacy, University of Medicine and Pharmacy "Iuliu Hațieganu", Cluj-Napoca, Romania
3. Department of Drug Analysis, Faculty of Pharmacy, University of Medicine and Pharmacy „Iuliu Hațieganu", Cluj-Napoca, Romania
4. National Institute for Research and Development of Isotopic and Molecular Technologies, Cluj-Napoca, Romania

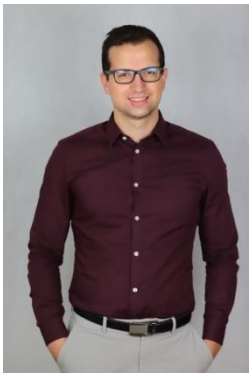
Pharmaceutical manufacturing by three-dimensional printing (3DP) provides unique advantages, including individualization potential by associating customizable doses of various active pharmaceutical ingredients (APIs) with different release profiles in one drug delivery system (DDS). One of the most promising techniques is fused deposition modeling (FDM). The aim of this research was to explore FDM-3DP for the development of personalized immediate release (IR) DDSs with diclofenac sodium (DS) by applying the quality-by-design (QbD) approach.
High drug loaded (50%) FDM 3D printable filaments were prepared by hot melt extrusion. Regarding the printing process, a systematic assessment of the influence of the selected independent variables (design feature, dosage form size and printing resolution) on the quality attributes of the 3D printed DDSs was conducted. By adjusting the dimensions of the digital models, tablets with API content in the range of 32-75 mg were produced. The optimum formulation represented by a concentric ring design tablet with a DS content of 50 mg presented 78% drug release after 5 minutes and 90% drug release after 10 minutes. A correlation between the investigated factors and the dissolution performance of the dosage forms was found as high-resolution printing (0.1 mm) and greater tablet dimensions promoted faster release of the API.
In conclusion, by employing the QbD approach to investigate the influence of the printing parameters and the dimensions of the DDS on the dissolution performance and API content of the dosage forms, preparation of tablets with very rapid dissolution and adjustable doses of API was completed.

Acknowledgements: This project was supported by "Iuliu Hațieganu" University of Medicine and Pharmacy internal doctoral research grant 1680/34/19.01.2018 and by The European Social Found, Human Capital Operational Programme 2014-2020, project no. POCU/380/6/13/125171.

Supervisor: Prof. Ioan Tomuță

OP-3

DOI: 10.14232/syrptbrs.2021.op3



Modifying the release of an antiparkinsonian drug by using mesoporous carrier

Tamás Kiss, Gábor Katona, Rita Ambrus

Institute of Pharmaceutical Technology and Regulatory Affairs, Faculty of Pharmacy, University of Szeged, Szeged, Hungary

The mesoporous silica-based materials are utilized in different field of pharmaceutical technology. One of the remarkable applications is based on the incorporation of active pharmaceutical ingredients (APIs) molecules into the mesopores. If the drug release rate is limited, it can be accelerated after loading drug into the mesoporous silica thanks to its stabilized amorphous state, the increased contact surface and the improved aqueous wetting ability of the excipient. The deceleration of a highly soluble API dissolution by mesoporous silica is a less investigated area.

Our aim was to explore the possibilities of per os administered drug release regulation by using hydrophobized mesoporous silica. The highly soluble model API was the levodopa methyl ester hydrochloride (LDME) which was loaded into the pores of SYLOID 3050 XDP and its sylilated derivatives. The sylilation was executed with trimethylchlorosilane (TMCS). The reaction resulted in products with lower aqueous wetting ability. The hydrophobization reaction was reproducible after standardizing the adsorbed water content of silica, the occurence of the process was proven with FT-IR, charge titration and contact angle measurements.

The LDME was loaded into the pores of silica with different hydrophobization extent in the range of 5-20 w/w% API. The drug was stable amorphous during the 1-month investigation period at 40 °C and 70% relative humidity (ICH Q1A (R2) guideline). The API was homogenously distributed in the products. The drug release could be regulated by controlling the wetting ability of silica. The hydrophobization extent effect was more remarkable when the loading degree was lower.

Acknowledgement: Ministry of Human Capacities, Hungary grant, TKP-2020

Supervisors: Gábor Katona, Rita Ambrus

OP-4

DOI: 10.14232/syrptbrs.2021.op4

Spray dried hyaluronic acid nanoplexes conjugated with chitosan and its derivatives for the pulmonary administration as dry powder inhalers for tuberculosis

Mahwash Mukhtar, Rita Ambrus

Institute of Pharmaceutical Technology and Regulatory Affairs, Faculty of Pharmacy, University of Szeged, Szeged, Hungary

The current therapies fail to deliver the drug to the alveolar macrophages in lungs, where causative agent resides, for the treatement of tuberculosis [1]. Hence, the ineffective drug delivery approaches lead to the drug toxicity and organ damage. Dry powder inahlers (DPIs) have recently shown promising results for the site specific drug delivery in the infectious diseases. Therefore, we developed nanoplexes based DPIs comprised of biocompatible polymer hyaluronic acid (HA) complexed with chitosan (CS), thiolated chitosan (TC) and mannsosylated chitosan (MC) individually to explore their affinity for alveolar macrophages to achieve higher drug deposition in deeper tissues of lungs. Nanoparticles were prepared by ionic gelation method [2] and later optimized by Design of Experiment (DoE), Box-Behnken design, prior to spray-drying to obtain nano-DPIs encapsulated with isoniazid. The size, morphology, physico-chemical properties, *in-vitro* release profile, *in-vitro* permeation, aerodynamic profile and i*n-silico* drug deposition of the nano-powders were promising. Furthermore, biocompatibility assay revealed the safety profile of nanoplexes. Moreover, spray drying enhanced the rheological properties of nano-powders. Altogether, DPIs highlighted promising results based on the preliminary fundamental outcomes with enhanced drug encapsulation efficiency and drug deposition profile.

Acknowledgements: This work was supported by the GINOP-2.3.2-15-2016-00036 ('Development and application of multimodal optical nanoscopy methods in life and materials sciences'), and Ministry of Human Capacities, Hungary grant TKP-2020.

References

1 Mukhtar, M. et al. Expert Opin. Drug Deliv, 17(9), 1239-1257 (2020).
2 Mukhtar, M. et al. Int. J. Biol. Macromol. 165, 3007-3019 (2020)

Supervisor: Rita Ambrus

OP-5

DOI: 10.14232/syrptbrs.2021.op5

Additive manufacturing of PLA microneedles for transdermal drug delivery

Merima Sirbubalo, Amina Tucak, Edina Vranić

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As physical permeation enhancers, microneedles (MNs) can modificate *stratum corneum* by creating microchannels, that are large enough to enable drugs, including macromolecules, to enter the skin while being small enough to avoid pain, irritation, and needle phobia [1,2]. Great emphasis is placed on the production process of microneedles itself, the selection of the most suitable materials as well as their shape, density, and size. This work aimed to fabricate biodegradable PLA MNs using additive manufacturing, more precisely fused deposition modeling (FDM) technology, and investigate the effect of varying geometry and print settings on the printed MNs in order to develop microneedles of optimal shape, density, and height.

Ultimaker 5S 3D printer (Ultimaker, Netherlands) was used to print triangular and cylindrical MNs with different heights (0,6 mm, 1,2 mm, and 1,8 mm) and different number and orientation of single arrays on the base (5x5, 3x3, 1x5) using 2.85 mm PLA filament (3D Republika, Serbia). The results showed the ability of Ultimaker 5S to successfully print MNs with different shapes, where the triangular shape was chosen to be more acceptable for transdermal delivery. 1.8 mm height was chosen as the optimal height for the MNs, while the 5 x 5 orientation of single arrays on the base resulted in more accurately printed MNs without a lot of waste material between the needles. Based on the results obtained, it can be concluded that FDM printing parameters can easily be adjusted to develop MNs of optimal shape, density, and height for transdermal drug delivery.

References

1 Quinn, H.L. et al. Expert Opin. Drug Deliv. 11, 1769-802 (2014)
2 Mikolajewska, P. et al. Pharm Res. 27, 2213–2220 (2010)

Supervisor: Prof.Edina Vranić

OP-6

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Popential of vinegar as extractio solvent: can we use it for herbal preparation?

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Apple cider vinegar (ACV) is widely used around the world as a flavoring and as a food preservative. Also, its use has been proposed in folk medicine as a health benefit for obesity and overweight, arthritis, asthma, cough, diarrhea, eczema, diabetes, and high cholesterol, and other disorders and diseases. It is produced by alcoholic and acetic fermentation (double fermentation). The ACV chemical composition is affected by the chemical composition of the apples used as a raw material, and by the applied fermentation process. According to the available data, ACV contains various organic acids-dominantly acetic acid, phenolic compounds, minerals (like potassium, sodium, calcium, and iron), vitamins (C and B group), and pectin.

In this study, ACV was used as an extraction solvent for the extraction of phenolic compounds from the black elderberry fruit. Conventional modified maceration and ultrasound-assisted extraction were used as the extraction techniques. The potential of several different ACVs as the extraction solvents was investigated. For the obtained ACV elderberryextracts, the analysis of phenolic compounds (TP), flavonoids, and anthocyanins were performed. Also, the effect of applied extraction process on the changes in pH and changes in sensory properties of obtained extracts was assessed. It has been observed that the ability to use ACV as an extraction solvent predominantly depends on the ACV production process, its chemical composition and microbiological status. The type of ACV production process affected the value of ACV pH, total solids, sugar content, acetic acid content, initial TP content, and sensory properties, which further affects the efficiency of extraction of phenolic compounds from black elderberry fruit, microbiological status and sensory properties of obtained extracts.

Supervisor: Senka Vidović

OP-7

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Development of magnetic nanoparticles for targeted drug delivery

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Among several types of nanoparticles, iron-oxide-based magnetic nanoparticles (MNPs) have shown great potential for their use as targeted drug delivery systems [1]. Despite numerous advantages, some limitations of MNPs need to be overcome before their application in clinical practice, including ineffective spatial guidance, poor colloidal stability, usually low drug loading, and inadequate drug release [1,2].

The aim of our work was to prepare MNPs based on the controlled assembly of superparamagnetic iron oxide (γ-Fe_2O_3) nanocrystals. Thus, we had developed a one-pot method for the preparation of MNPs composed of several nanocrystals, tetradecan-1-ol, model drug, and surfactant (Brij®L4 or our own surfactant N^1,N^1-dimethyl-N^2-(tricosan-12-yl)ethane-1,2-diamine (SP11)). The method is based on hot homogenization of the hydrophobic phase containing a nonpolar surfactant into the aqueous phase, using ultrasonication. The resulting MNPs showed good colloidal stability and relatively high drug loading capacity (up to 7.6 wt. %). The surfactant selection influenced the MNPs morphology, drug release profile, and MNPs surface charge, whereas the MNP size, iron oxide content, and drug loading were comparable among investigated formulations.

To sum up, the specific composition gives these MNPs promising characteristics for application in nuclear magnetic resonance imaging and magneto-thermally-triggered targeted drug delivery [3,4]. They are therefore attractive candidates as novel nanotheranostics.

References

1 Kralj et al. Current Medicinal Chemistry, 24(5), 454-469 (2017).
2 Dragar et al. Materials, 12(3), 1-14 (2019).
3 Brezaniova et al. J. Control. Release, 241, 34-44 (2016).
4 Roy Chowdhurry et al. Biomed. Pharmacother, 84, 291-304 (2016).

Supervisor: Petra Kocbek

OP-8

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Strategies for development of antimicrobial peptides and proteins

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Due to the several unresolved challenges of antimicrobial peptide and protein agents including low bioavailability, high manufacturing cost and toxicity concerning their delivery to the target site, their potential has yet to be concerned [1].
Novel chemical modification approaches and novel formulations within the limits of nanotechnology offer several opportunities to overcome these barriers. However, these approaches hide several risks. To avoid these risks and control the quality of the final product, this study presents a Quality by Design (QbD) based peptide and protein modification and formulation design.
Evaluation of the potential risks in the peptide PEGylation process through the example of PGLa as well as, the effective delivery of proteins with antimicrobial activity was accomplished through the example of lysozyme in a novel formulation strategy as layer-by-layer polyelectrolyte core-shell nanoparticle [2]. The precipitation method was applied for the formulation of core and the second step was the layering of polymers according to the factorial design. The samples were lyophilized and then analytical investigations were performed such as e.g. measurement of FTIR and zeta potential. The particle size, encapsulation efficiency, content of α-helix structure and enzyme activity were the optimization parameters.

Acknowledgements: This work was supported by the Ministry of Human Capacities, Hungary (Grant TKP-2020).

References:
1 Marr, A. et al. Curr. Opin. Pharmacol. 6, 468–472 (2006)
2 Kristó, K. et al. Int. J. Pharmaceut. 573, 118825 (2019)

Supervisors: Prof. Ildikó Csóka, Gerda Szakonyi

OP-9

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Lipid-based nanosystems for the nose-to-brain delivery of biological drug, Insulin

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Lipid-based nanosystems with the aim of direct nose-to-brain delivery of therapeutics are of great interest nowadays for both biomolecules and abiotic molecules. The hormone insulin, administered nasally, could be promising for Alzheimer's disease therapy, which only has fruitless treatments that interfere with its progression. Insulin may play this role by either being involved in the clearance of beta-amyloid from the brain or increasing memory performance. Since insulin is a macromolecule polypeptide with a delicate and hydrophilic nature, its delivery to the brain is limited by the lipophilic blood-brain barrier (BBB) not to mention the low stability issue. Encapsulation of insulin in solid lipid nanoparticles (SLNs) holds great potential in boosting insulin ability to reach the brain, owing to their nanosize, biocompatibility, and lipophilicity. Further coating of SLNs with a mucoadhesive polymer, chitosan, can improve the drug release profile, mucoadhesion to the olfactory region and permeation through the nasal mucosa, which are the three key steps for any nasally applied drug to be delivered to the brain.

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References:

Akel, H. et al. Eur. J. Pharm. Biopharm. 148: 38-53. (2020)
Ferreira, L. S. et al. Frontiers in neuroscience, 12, 830. (2018).
Pardeshi, C. V., Belgamwar, V. S. Materials Technology, 35(5), 249-266. (2020)

Supervisor: Prof. Ildikó Csóka

OP-10

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Quality-focused formulation - QbD-based liposome design and development

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Formulations should carry the quality designed into the products to meet the pharmaceutical requirements. The Quality by Design (QbD) approach ensures the quality of medicines by developing and manufacturing products following statistics-, analytics- and risk-management-based methodologies [1].

This research aims to systematise the characteristics of the components (material attributes, MAs) and the preparation settings (process parameters, PPs) in case of the thin-film hydration liposome preparation technique. Furthermore, the study specifies the quality target product profile of a liposomal formulation and the critical quality attributes of the liposomes. Also, it identifies those MAs and PPs that influence the characteristics of the vesicles [2].

The theory was supported with practical research; the effect of the working temperature, the phosphatidylcholine-cholesterol ratios, the PEGylated phospholipid concentration, the type of the hydration media and the cryoprotectants were studied in different formulations. The results present the key points of a Risk Assessment (RA)-based experimental design, and the impacts of the critical factors mentioned above based on the investigation of the liposomal characteristics (size, surface charge, thermodynamic behaviours and structural investigations).

The study revealed the relevance of the QbD-based RA in the thin-film hydration-based liposome preparation process and shown the main effects of the tested critical factors. The results ensure that the understanding and the application of the QbD elements in the pharmaceutical developments help to influence and to reach the aimed quality of the formulated product.

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References

1 Pallagi, E. et al. Int. J. Pharm. 562, 11-22 (2019)

2 Németh, Zs. et al. Pharmaceutics. 12,1164 (2020)

Supervisors: Edina Pallagi, Prof. Ildikó Csóka

OP-11

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Near-infrared light-responsive magnetic nanoparticles - preparation and application in photothermal therapy

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One of the non-invasive techniques used in the fight against cancer is conventional hyperthermia, which, despite being very effective in destroying tumor cells, has low spatial selectivity and severely affects healthy tissues. Photothermal therapy (PTT), which uses near-infrared absorbing magnetic nanoparticles to generate heat from optical energy, is of great interest as the method is controllable, highly efficient, less invasive and poses much fewer side effects compared with standard approaches such as chemotherapy and radiotherapy. The combination of photothermal therapy with hyperthermia mediated by magnetic nanocomposites can also help in eliminating inflammatory macrophages and enhancing tumor-cell permeability and retention effect.

Over the last decade, scientists worldwide have focused on improving the PTT effects of magnetic nanoagents by optimizing synthesis and coating methods with appropriate near-infrared (NIR) -sensitive materials. In order to develop an effective PTT mediator, the carriers created must meet the following criteria: small size, photostability, facile synthesis, non-toxicity and dual modality. The magnetic materials irradiated under a NIR laser must make full usage of the resulting thermal energy to destroy cancer cells without affecting healthy tissues. An optimal combination of materials, synthesis methods, and coating approaches are presented in this study focusing on Fe_3O_4 magnetic nanoparticles. In addition, the possibilities for optimizing the effects of magnetic hyperthermia are considered.

Supervisors: Bissera Pilicheva, Plamen Zagorchev

OP-12

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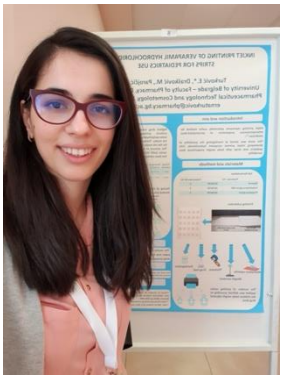

Application of artificial neural network analysis in understanding critical material properties governing orodispersible film disintegration

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Orodispersible films (ODF) are thin strips that are intended to disintegrate within seconds upon contact with liquid. Critical material properties (CMP) affect ODF disintegration, but due to complexity of data, film performance is difficult to predict. The aim of this work was to develop artificial neural network (ANN) model as tool for prediction of ODF performance based on its CMP.

Dataset values for building ANN model were based on the in-house experimental results and included following input parameters: concentration of active ingredient, its solubility, molecular weight and polymer ratio, ratio of superdisintegrants, plasticizers, film surface-area, weight, thickness, mechanical properties (Young's modulus, tensile strength, % elongation and complex modulus) and disintegration time as output. Preprocessing operators were applied to filter examples, select attributes and set roles of attributes. Split validation is performed to estimate how accurately model performs on unseen data. Root-mean-square error (RMSE) is used to compare prediction errors of data.

ANN model with one hidden layer showed accurate predictions, while higher number of layers led to overfitting therefore higher RMSE values for testing data. ODF mechanical properties as input are highly related with film disintegration as the selected performance indicator, accompanied with high predictability. ANN was able to perform prediction on ODF disintegration time with high accuracy characterized with RMSE 0.871 and 0.176 for training and testing set, respectively.

The results obtained indicate that it is possible to build predictive ANN which could lead to better understanding of complex relationship between ODF properties and their effect on film disintegration.

Supervisor: Prof. Jelena Parojčić

OP-13

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In vitro and *ex vivo* models for assessing the antibiofilm properties of wound dressings

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Insufficient infection treatment in chronic wounds is associated more and more with the presence of biofilm, thus, novel biofilm targeting wound care products are being developed. It is of importance to have appropriate analytical methods to quantitatively evaluate these wound care products for their anti-biofilm properties. The aim of present study was to develop *in vitro* and *ex vivo* biofilm models for assessing the antibiofilm properties of electrospun wound dressings.

In vitro model was created using thermally crosslinked electrospun gelatine (GEL) matrix as an artificial skin and for *ex vivo* model pig ear skin was used. Different pathogenic bacteria, isolated from wounds, were used to develop a biofilm. The model was set up in 24-wellplates on top of GEL matrix or pig skin bacterial dispersion was added and after that chloramphenicol (CAM)-loaded electrospun wound dressings were applied. These systems were incubated for 24 and 48 h, subsequently planktonic bacteria were removed, biofilm disrupted and quantified.

The results show that GEL matrix is suitable to be use as an artificial skin in *in vitro* biofilm model, as bacteria adhered to its surface and formed a biofilm. Compared to GEL matrix, the *ex vivo* model on pig skin appeared to be a better and preferred surface for the biofilm formation. Application of CAM-loaded wound dressings effectively reduced the biofilm formation in both models. To conclude, designed *in vitro* and *ex vivo* models allow comparing and evaluating the antibiofilm properties of wound dressings.

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Supervisors: Marta Putrinš, Tanel Tenson, Karin Kogermann

OP-14

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Inhalable cyclosporine powder for immunosuppressive treatment

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Our research brings to the development of a high respirable powder for inhalation of Cyclosporine A (CsA) with improved dissolution rate. This powder was produced by spray drying using a low amount of excipients. Different powders were produced starting from aqueous solutions containing 10-20 % (w/w) of mannitol; 0-5% (w/w) of glycine and 60-45% (v/v) of ethanol according to a design of experiment. The aerodynamic performance was analyzed throw fast screening impactor and next generation impactor using RS01 inhaler. The dissolution profile of CsA powders was evaluated with a vertical diffusion cell apparatus (RespiCell™) across a polycarbonate membrane. Curves obtained from dissolutions were linearized by the Weibull distribution.

Twelve powder were characterized and the best results in terms of dissolution profile and respirability were obtained using a 20 % of mannitol for powder construction. In this way, 59.7 ± 2.8 minutes were requested to dissolve 63.2% of CsA. This value was significantly lower compared to the one of CsA raw material (169,5 ± 29 min). The CsA-Mannitol spray dried powder was successfully emitted by the powder device (>87%) and the fine particle fraction was higher than 70%.

In conclusion, the work leads to the production and characterization on an inhalation powder with the potential to be administered directly to the lung for the prevention of rejection following lung transplantation and the containment of the inflammatory process due to SARS-CoV-2 infection.

Supervisors: Francesca Buttini, Fabio Sonvico

OP-15

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Mucoadhesive nanostructured lipid carriers for ophthalmic use

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Today, the development of an effective ophthalmic drug delivery system is a major challenge. The most commonly used ophthalmic preparations are eye drops, which have low bioavailability due to the complex structure and elimination mechanism of the eye [1].
Nanostructured lipid carrier (NLC) is second-generation solid lipid nanoparticles that contain a lipid matrix of mixed solid and liquid lipids. These systems are ideal for the incorporation of drugs with low water solubility, such as corticosteroids [2].
The aim of the study was to incorporate dexamethasone (DXM) into mucoadhesive polymer-containing nano lipid carriers to increase drug bioavailability. A 2^3 factorial experimental design was used in which the three factors were polymer, DXM, and emulsifier concentrations. The particle size, Zeta potential, polydispersity index, and Span value of the samples were analyzed. The biocompatibility of the formulations was assessed by human corneal toxicity tests and immunoassay analysis. Potential increases in bioavailability were analyzed using mucoadhesivity study, *in vitro* drug diffusion, and various penetration tests such as corneal-PAMPA model, human corneal cell penetration, and *ex vivo* porcine corneal penetration by Raman mapping. The results showed that DXM can be incorporated into stable mucoadhesive NLC systems that are non-toxic. Mucoadhesive NLCs can create a depot on the surface of the cornea that can predict better bioavailability.

References

1 das Neves, J. et al. Eds., New York: Springer (2014)

2 Kovacs, A. et al. Eur. J. Pharm. Sci., 99, 246-257 (2017)

Supervisors: Mária Budai-Szűcs, Erzsébet Csányi

OP-16

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Synthesis of betulinic acid 1,2,4-triazole derivatives suitable for cyclodextrin inclusion complex formulation.

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Pentacyclic triterpenes are natural compounds with a large plethora of described pharmacotherapeutic effects. Betulinic acid (BA) stands as a widely studied compound of this class, exhibiting multiple therapeutic effects such as: antiinflammatory, antiviral and antiproliferative. The low bioavailability o BA represents a major drawback which represented a starting point of multiple research directions, having the sole purpose of increasing BA's bioavailability. One direction employed by the literature in this regard represents the synthesis of cyclodextrin (CD) inclusion complexes (1). Knowing that BA is a large pentacyclic structure herein we propose the synthesis of a BA-1,2,4-triazole derivative that can be easily incorporated into CD and can exhibit an improved antiproliferative effect as compared to BA. The proposed derivatization requires obtaining a BA halogenated derivative by allylic bromuration (C-30), that ca be subsequently used as an alkylating agent against a 3-thiol-1,2,4-triazole derivative. 30-bromo-BA was obtained according to previously reported methods using NBS (2). The obtained compound was purified by flash column chromatography. The BA derivative was later reacted to 5-(4-metoxifenil)-4H-1,2,4-triazol-3-thiol, in presence of EtOH and EtONa. The completion of the reaction was monitored by TLC. The obtained compound was purified by flash column chromatography. FT-IR and LC-MS analysis confirmed the formation of 30-[3-(4-metoxiphenyl)-1H-1,2,4-triazol-5-yl-sulfanyl]-betulinic acid. Docking studies of the BA derivative an BA using CD as targets revealed that indeed our obtained compound shows a theoretical stronger affinity towards CD as compared to BA. The obtained compound and its CD formulations will be subjected to further biological assessments.

References

1 Soica, CM., Int J Mol Sci. 5(5):8235–55 (2014)

2 Sidova, V., Plos ONE, e0171621 (2017)

Supervisor: Prof. Codruta Soica

OP-17

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Effect of solvent compositions on habits and *in vitro* aerodynamic results of spray-dried pulmonary formulations

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In the case of carrier-free dry powder inhalation systems (DPIs), the formulations can be prepared by various technological methods to bring the particles of the samples in the internationally recommended range of 1-5 microns. In addition to traditional particle size reduction technologies (such as milling), appeared sample preparation procedures (spray-drying, spray-freeze-drying, and supercritical-fluid technology) to ensure the aerodynamically favorable particle morphology. Among the latter production methods, spray drying is already widespread, as it compares its advantages and disadvantages and proves to be a very promising production solution. The choice of the solvents used in spray drying and their proportions are in many cases based solely on the solubility of the drug and applied excipients, but it may also be noteworthy that each solvent composition may affect the habit of DPI powders and thus *in vitro* aerodynamic results. Observations in this regard have been reported in a few studies in the international literature [1, 2]. The present work aims to investigate the different concentrations of a given organic solvent, how it affects the physical properties, and the *in vitro* aerodynamic results of the prepared DPI powders. Based on the results, it can be concluded that due to the changes in the micrometric properties of the samples, the *in vitro* aerodynamic results can be tripled. Thus, in the development of spray-dried DPI, the solvents used in the production and their mixtures are of paramount importance.

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References

1 Gilani, K. et al. J. Pharm. Sci. 94, 1048-59 (2005)
2 Ji, S. et al. Int. J. Pharm. 513, 175-82 (2016)

Supervisor: Rita Ambrus

OP-18

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Preparation and investigation of permeability and physical-chemical properties of buccal films with sodium alginate

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Nowadays the buccal administration of active ingredients is an innovative method. Mucoadhesive films represent one of these possibilities of drug administration. Mucoadhesive films can be used to introduce the API to the systemic circulation. By this way of drug administration, the API enters the circulation without degradation and avoids the first pass effect of the liver [1]. Besides, this drug delivery system can be applied in pediatrics and geriatrics. The bases of buccal mucoadhesive preparations are polymers which have mucoadhesive properties [2].

Our work was focused on preparing buccal mucoadhesive polymer films which were based on sodium alginate (SA) and contained cetirizine dihydrochloride (CTZ). Our main aim was the preparation and the physico-chemical investigation of the prepared mucoadhesive films.

In our present work SA and HPMC were used as film forming agents. Glycerol was added as plasticizer to the films, and CTZ was the API. The polymer films were prepared with solvent casting method at room temperature. The mechanical and physical-chemical properties of the films were investigated with different methods, such as thickness, tensile strength and in vitro mucoadhesion of films. The chemical properties were examined by FT-IR and Raman spectroscopy. The dissolution and permeation of the API were also tested. The results showed that almost all film compositions have sufficient mechanical properties. The API can distribute homogeneously in the films. In view of the above findings, we can find promising compositions.

References:

1 Castán, H. Drug Deliv. 22, 869–876 (2015)

2 Kelemen, A. Molecules 25(22), 5248. (2020)

Supervisors: Katalin Kristó, Géza Regdon jr.

OP-19

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Analysis of the regulations for medical devices in Europe & future perspectives

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This presentation aims to provide a structural & functional understanding of regulations for medical devices in the European Union. Medical Devices (MD) in the European Union are regulated by the European Commission based on their proposal in order to ensure the safety and efficacy of Medical Device, thus facilitating patient's access to device in the European market.

MD s are any instruments, appliances, software, implant intended to be used for medical purposes alone or in combination for diagnosis, prevention, prediction, treatment, replacement, of any disease, injury or disability or physiological/pathological state. **In-Vitro MD** is reagents, calibrators, instruments, software or system used alone or in combination to examine specimens (e.g.: blood & tissue) to provide further information for physiological/pathological state, congenital impairments, to track treatment response and to monitor therapeutic measures.

The New Medical Device Regulations (EU) 2017/745 (MDR) & In Vitro-Diagnostics Medical Device Regulations (EU) 2017/746 (IVDR) aims to give national regulators much more control & oversight of Medical device industry. Companies should proactively comply with these upcoming changes; if they do not then they could possibly result in losing their license to operate. Hence, it is very important to develop a new model for the industry to get them quick market access according to the new Medical Device rules.

In clinical practice, incidents including the breast implant and the hip replacements crisis have made it necessary to improve the regulatory & compliance approaches for the industry and hence raising a question about the quality aspect of the MD. Such incidents along with the understanding and addressing the critical factors of the pharmaceutical industry, namely the expectation of the patients and the requirements of the current legislations will determine of the quality of the MD.

Applying new approaches, by implementing the quality-by-design (QbD) could efficiently increase the quality of MD fitting in the ever-changing regulatory landscape. Tailoring the early development phases of MD by adding elements that are currently widely applied, but not yet included in the QbD model in a structured way would allow a more conscious development. In this way the continuous development & innovation of MD could be facilitated in the life cycle of the device.

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Supervisors: Prof. Ildikó Csóka, Orsolya Jójárt-Laczkovich,Livia Adalbert

OP-20

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Synergistic effect of magnetic nanoparticles and chemotherapeutic drugs in cancer

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Magnetic nanoparticles (MNPs) are a clinically available biomedical tool and have been approved to serve as magnetic resonance contrast agents. MNPs are of great interest in a wide range of applications due to their unique physical properties. High surface to volume ratio allows MNPs functionalization with different ligands and coatings for various biomedical applications. Due to their magnetic properties, MNPs can be used as magnetic-guided drug delivery carriers. Conventional chemotherapeutics suffer several drawbacks such as nonspecific targeting, toxicity to the healthy cells, reduced stability, and drug resistance by the cancer cells. To overcome these limitations, MNPs with attached specific ligands (markers or molecules with tumour binding capacity) are used for targeted delivery of chemotherapy drugs to the cancer cells keeping the healthy cells unaffected. Moreover, nanocarriers have the potential to overcome chemotherapy drug resistance by bypassing the ABC-transporter mediated drug efflux mechanisms. Another promising application of MNPs in cancer therapy is via magnetic hyperthermia. Tumour cells are known to be more sensitive to temperature increase than normal cells. When used in conjunction with chemotherapy, magnetic hyperthermia offers substantial synergistic effects. Recent publications in the field reveal that combined chemo-phototherapy based on NIR laser irradiation using MNPs results in lower tumour growth and cancer regression due to efficient drug penetration in the tumour tissue.

References:

Kumar, P.; Srivastava, R. Nanomedicine for Cancer Therapy (2017)
Hervaultab, A.; Thanh, N.T.K. Nanoscale, 6, 11553-11573 (2014)

Supervisors: Plamen Zagorchev, Bissera Pilicheva

OP-21

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Evaluation of fenofibrate-cyclodextrin complexes prepared by co-grinding method

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Cyclodextrins (CD-s), and CD derivatives are widely used for the improvement of the physicochemical properties of poorly water soluble active pharmaceutical ingredients (API-s). Several methods (e.g., co-precipitation, kneading) require organic solvents to prepare these complexes. Nevertheless, complexation can be achieved via mechanochemical activation by co-grinding method. Generally, complexation with amorphous CD-derivatives requires shorter grinding time and results stable amorphous products.

Our aim was to prepare API-CD complexes by co-grinding and use analytical techniques to describe the complexation process as a function of grinding time. In this study heptakis(2,6-di-O-methyl)-β-cyclodextrin (DIMEB), an amorphous CD-derivative was used as a complexation agent, and fenofibrate (FEN), a BCS II. API was chosen as a model drug. FEN-DIMEB physical mixture was prepared in 1:1 molar ratio. Co-grinding was performed in a mortar for 60 minutes, and samples were taken at predetermined intervals. Original components and samples were characterized by DSC, XRPD, FTIR methods. Dissolution properties of API, physical mixture, kneaded product, and co-grinded samples were also investigated.

DSC investigation showed that the endothermic peak indicating the melting point of the API decreased continuously with increasing co-grinding time. Meanwhile, a new, continuously growing exothermic peak appeared at a higher temperature after 30 minutes of grinding time. XRPD studies showed a linear trend of decreasing peaks with the increasing grinding time, after 60 minutes the product was totally amorphous. Based on FTIR results, presence of molecular interactions was detected between the host and gest molecules. The product obtained by co-grinding showed similar dissolution property compared to the kneaded product due to the presence of stable amorphous molecular complex.

Supervisor: Zoltán Aigner

OP-22

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Towards understanding the safety and biocompatibility of electrospun fibers

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Every year the number of patients with chronic wounds increases because of population aging and non-efficient wound treatment methods. Most chronic wounds are infected with bacterial biofilms. The presence of bacterial biofilms and the lack of good topical antimicrobial treatment options make the wound care even more difficult. Therefore, new strategies for wound management are needed. One wound dressing solution could be the antimicrobial electrospun nanofibers which enable to incorporate different drugs into their structure and deliver these successfully into the wound area. With this new potential treatment, it is important to test the safety and biocompatibility of these electrospun fibers before their administration to patients.

The aim of this study was to test the safety and biocompatibility of electrospun fibrous matrices with and without antimicrobial agents on different eukaryotic cells. Three different eukaryotic cell lines were used (baby hamster kidney cells (BHK-21), human lung fibroblasts (MRC-5) and primary fibroblasts obtained from patients). The study had all relevant ethical committee permissions. Experiment setup was based on modified MTS assay that measures the cell viability. Morphology of fibers and biocompatibility were evaluated with scanning electron microscopy (SEM). The results showed that all tested electrospun fibers were safe and biocompatible. However, there were some differences in the viability of cells when pristine polymeric matrices and matrices with antimicrobial agents were compared. Furthermore, the behaviour of different cells varied. Further studies will test the cell migration, proliferation and differentiation on electrospun matrices in more depth in order to understand better the cell-fiber interactions.

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Supervisors: Karin Kogermann, Tanel Tenson, Külli Kingo

OP-23

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Solid Lipid Nanoparticles as Drug Delivery Systems for MicroRNA

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MicroRNA-based medicines have drawn attention as a promising tool for the treatment of various diseases. Due to the poor biomembrane permeation, cellular uptake, and enzymatic instability of naked microRNA, the clinical success of gene therapy is mostly dependent on formulating efficient and safe transfection vectors [1]. Therefore, we aimed to develop cationic solid lipid nanoparticles (SLN) for gene therapy purposes.

SLN containing 0.15% of stearylamine, 4.85% of Precirol ATO 5 (solid lipid), 1% of Tween 80, and 1% of Poloxamer 188, as non-ionic surfactants, were produced using a high-pressure homogenization process (800 bar and three cycles). microRNA 27-a was further complexed with SLN in the following SLN/microRNA ratios: 1:5, 1:2.5, 1:1, 2.5:1, 5:1, 10:1, 25:1 and characterized using dynamic light scattering, electrophoretic light scattering, and gel retardation assay.

The SLN had a mean diameter of 112 ± 0.5 nm (PDI of 0.202 ± 0.011) and a zeta potential (ZP) value of +30.6 ± 1.25 mV. Complexation of SLNs with microRNA decreased a particle size from 244.8 ± 2.7 to 120.4 ± 0.4 nm with an increasing weight ratio of SLNs, while the biggest particle size was observed in 1:1 ratio (1146 ± 110.2 nm) due to low ZP values (3.45 ± 0.2 mV). Further, ZP increased from -14.3 ± 0.4 mV to + 39.7 ± 0.5 mV. Both ELS data and gel retardation assay results revealed that complete complexation could be attained above the weight ratio of 5:1. Our investigations suggest that SLN poses a high potential to be non-viral gene carriers in miRNA replacement therapy.

References

1 Zhang, Y. et al. J Control. Release. 172, 962−74. (2013)

Supervisors: Prof. Edina Vranić, Univ.-Prof. Andreas Zimmer

OP-24

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Development of liposomal drug delivery system as a strategy for improving bioavailability and therapeutic efficacy, by Design of Experiments. A case study

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There is mounting evidence for the anticancer effects of all-*trans* retinoic acid (ATRA) in different types of malignancies. However, ATRA treatment is usually associated with side effects, and most importantly with retinoid acute chemoresistance. Furthermore, ATRA shows reduced physicochemical stability, aqueous solubility and plasma half-life. Nanocarriers have emerged as promising strategies for delivering drugs to tumors. Therefore, this study aimed at developing an ATRA-based liposomal formulation with enhanced stability and therapeutic efficacy.

ATRA-loaded liposomes (L-ATRA) were prepared by ethanol injection from egg phosphatidylcholine and cholesterol. Design of Experiments (DOE) was employed to study the influence of several formulation factors on the quality attributes of L-ATRA. 11 formulations were prepared according to a 2^3 full factorial design, and characterized in terms of size, polydispersity, ATRA content and entrapment efficiency. An optimum liposomal formulation with desirable characteristics was evaluated *in vitro* regarding ATRA release.

L-ATRA exhibited a mean size of 200-400 nm, and a narrow size distribution (polydispersity index < 0.25). ATRA was successfully loaded into the liposomes with an efficiency of 70-80%. According to the DOE statistical analysis, L-ATRA attributes were mainly influenced by the concentrations of phospholipid and ATRA. The *in vitro* release study showed a maximum percentage of 72.5% ATRA released after 48h in a mixture of PBS pH 6.5 and ethanol 1:1 (v/v) at 37°C.

Overall, this study reports the successful formulation and preparation of an ATRA-loaded liposomal formulation by DOE. L-ATRA could be a promising candidate for effective and safe delivery of ATRA in cancer patients.

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Supervisor: Prof. Ioan Tomuță

OP-25

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Preformulation studies of ciprofloxacin loaded PVP nanofibers

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Ciprofloxacin is a worldwide-used, broad-spectrum antibiotic with low water-solubility [1]. To earn higher solubility, and better bioavailability, nanofibers were fabricated as an amorphous solid dispersion with the polymer, polyvinylpyrrolidone (PVP). For the production, needle and needleless electrospinning methods were used [2]. The fiber size and morphology were observed by scanning electron microscopy (SEM). Physicochemical properties were characterized by X-ray powder diffraction (XRPD), differential scanning calorimeter (DSC), and Fourier-transform infrared spectroscopy (FTIR). The results proved the amorphous state of the CIP inside the nanofibrous mats. The solubility, *in vitro* dissolution rate, and *in vitro* diffusion were remarkably higher in the case of the nanofibers compared with the CIP powder or the physical mixture of the two components. The solubility of the CIP demonstrated a significant increase both in water (pH 6.3) and phosphate buffer solution (pH 7.4). In addition, fast-dissolving formulations were developed, while 94±6% of the CIP was released in the first 5 min. Moreover, *in vitro* diffusion from pH 6.8 to pH 7.4 also showed a notable increase. The stability of the nanofibrous samples was studied by SEM and *in vitro* dissolution. In conclusion, fast-dissolving formulations were built up which can be further investigated to develop appropriate pharmaceutical forms.

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References

1 Caço, A.I. et al. Ind. Eng. Chem. Res. 47,8083–8089 (2008)
2 Keirouz, A. et al. Med. Eng. Phys. 71,56-67 (2019)

Supervisor: Rita Ambrus

OP-26

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Application of 3^2 experimental design in the preparation of casein nanoparticles as potential drug carriers

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Production of nanoparticles by nano spray drying is strongly influenced by the process parameters - polymer concentration, solubilizing agent concentration, inlet temperature, pumping speed, spray rate, as well as the spray mesh size.

The aim of the present study was to establish the optimal process parameters - polymer concentration and crosslinking agent concentration required to produce casein nanoparticles with optimal structural and morphological characteristics for use as drug carriers.
A full 3^2 factorial design was used to study the influence of process parameters. Three different concentrations of casein solution were varied: low concentration 0.05%, medium concentration 0.1% and high concentration 0.15%. The influence of the crosslinking agent concentration ($CaCl_2$, Mw = 110.98 g/mol) was also investigated: low concentration 0.5 M, medium concentration 1.0 M and high concentration 1.5 M. A spray membrane with a mesh size of 4.0 µm was used and the following spray conditions were applied: inlet temperature 40 °C, solution feed rate 50%, spray intensity 70%, drying gas speed 120 L/min, pressure 30 nbar.
Using the nano spray drying method, nine models of nanoparticles were obtained, which were characterized based on shape, size and size distribution, surface morphology and yield. Optimal conditions to produce casein nanoparticles were derived and promising models were selected to be studied as potential drug-delivery systems.

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Supervisor: Bissera Pilicheva

OP-27

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Paediatric PBPK modelling: Prediction of drug exposure following oral dosing of different paracetamol formulations in fasted and fed states

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In recent years, physiologically-based pharmacokinetic (PBPK) models have been increasingly used in paediatric drug development. Moreover, the value of such approach has been recognized by the regulatory authorities (1).

The aim of this study was to evaluate paracetamol absorption and disposition in children following oral administration of sustained-release hot-melt coated (HMC) granules and tablets made of HMC granules (2,3) in comparison to immediate-release uncoated granules and tablets made of uncoated granules, using PBPK modelling. Paracetamol-specific PBPK model was firstly developed and validated for adults, and then extrapolated to five paediatric age groups: neonates/12 days, infants/18 months, children/2 years, children/6 years, and adolescents/12 years. Simulations were performed for fasted and fed states (different age-appropriate meal types). The simulated plasma concentration-time profiles indicated delayed paracetamol absorption from HMC formulations in comparison to immediate-release formulations. Also, the simulations revealed that co-administration of food is not expected to affect paracetamol absorption following oral administration of HMC formulations, in contrast to immediate-release formulations whereas marked food effect was anticipated.

According to the simulations results, HMC granules and tablets made of HMC granules can provide prolonged drug effect, irrespective of the presence of food, and consequently better compliance of paediatric patients.

References

1 Verscheijden, L.F.M. et al. Pharmacol. Ther. 211:107541 (2020)
2 Milanovic, A. et al. J. Drug Deliv. Sci. Technol. 46, 274–284 (2018)
3 Milanovic, A. et al. Eur. J. Pharm. Sci. 142:105121 (2020)

Supervisor: Sandra Cvijić

OP-28

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New perspectives of skin penetration testing methods

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Modelling penetration through the skin is a specific challenge. In the permeation analysis of dermal formulations, human skin is defined as a standard by regulatory agencies. However, there are artificial membranes which can replace human skin to some degree. Academicians and pharmaceutical firms are focusing on developing structured procedures and safe, effective alternatives to human skin in permeability studies. In my research work, I examined specific *in vitro* experiments to test semisolid preparations. In this study hydrogel and two forms of creams have been investigated as the most widely used dermal preparations. The parallel artificial membrane permeability assay (PAMPA) and Raman mapping methods were compared to the gold standard Franz cell process. The diffused amount of drug showed similar results for the different formulations. These findings are well aligned with the results of the Raman mapping. Our results indicate that any early screening experiments can be carried out using model tool Skin PAMPA complemented by method Raman mapping as a semi-quantitative process.

References

1 Zsikó, S. et al. Pharmaceutics. 11(07), 310 (2019)
2 Zsikó, S. et al. Sci. Pharm., 87(3), 19 (2019)
3 Zsikó, S. et al. Pharmaceutics. 12(9), 803 (2020)

Supervisors: Erzsébet Csányi, Szilvia Berkó

OP-29

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Investigation of drug-matrix interaction in directly compressed matrices

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Personalized medicine is recently emerging trend, therefore pharmaceutical industry faces a new challenge on providing solid dosage forms, which as still the most favourable medicines, with tailorable properties. A novel approach may be the utilization of drug-polymer interactions in the development of solid delivery matrices.

A line of chemically similar drugs with increasing acid strength were mixed various matrix forming agents and directly compressed with an instrumented IMA Kilian SP300 tablet press. Kawakita and Walker analysis were made to evaluate the composition's compressibility. Compressibility studies showed an increment in the energy value needed for deformation, which may be due to particles attracted to each other causing chemical interactions.

The presence of solid-state drug-polymer interactions based on the formation of H-bonds were confirmed by FT-IR spectroscopy.

A custom-made device was applied to perform dissolution tests to obtain information on the effect of interactions on the drug liberation kinetics. The results of dissolution tests proved that strength of interactions have increased due to formation of polyelectrolyte complexes which exerted considerable influence on both the quantity of liberated drug and the speed of drug liberation.

According to the findings it may be concluded that inclusion of the physico-chemical properties of raw materials and careful evaluation of their potential interactions during the development phase of the drug delivery systems may open new ways to provide medicines with tailored properties.

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Supervisors: Tamás Sovány; Prof. Ildikó Csóka

OP-30

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Design and synthesis of betulinic acid gold nano-particles with enhanced pharmaceutical properties

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Betulinic acid (BA) is a pentaciclic triterpene, exhibiting strong cytotoxic activity but low water solubility, which affects its bioavailability and biological activity. Extensive studies have been carried out for increasing the solubility and bioavailability of BA, one option being BA-bioconjugates with gold nanoparticles (GNP). The synthesis of BA GNP bioconjugates was achieved by using cysteamine as a linker between the organic molecule and the metallic surface of GNP. BA's carboxylic group was condensed to the amine group of cysteamine using DCC and DMAP in dichlormethane. The completion of the reaction was monitored by means of TLC. The obtained BA amide was purified by flash column chromatography. FT-IR and LC-MS analysis confirmed the identity of the synthesized compound. Synthesis of GNPs was conducted accordingto a previously published procedure. The synthesis is achieved by reducing chloroauric acid ($HAuCl_4$) withtrisodium citrate dihydrate ($C_6H_5O_7Na3{\cdot}2H_2O$) using a $HAuCl_4$:$C_6H_5O_7Na3$molar ratio of 1:3.5. The obtained clear ruby-redsolution was cooled at room temperature. Purificationwas accomplished by repeated steps involving centrifugationfollowed by washing with deionized water. The finalproduct was lyophilized and resuspended in methanol. A methanolic solution of BA-cysteamine amide was added drop wise to the methanolic suspension of GNPs, under continuous stirring for 24h, allowing the thiol group to attach to the metallic surface. After the completion of the reaction, methanol was slowly evaporated under reduced pressure and the obtained formulation was washed with deionized water, centrifuged and lyophilized. The obtained product was refrigerated. This current nanoformulation will be further investigated for its proposed anticancer activity.

Supervisor: Prof. Codruta Soica

OP-31

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Biorelevant Dissolution Testing of Matrix Systems Based on Combination of Mucoadhesive Polymers

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Matrix tablets represent the most favourable form of the modified release drug delivery systems intended for oral administration, due to their cost-effectiveness and easy preparation. The formulation of matrix systems using mucoadhesive polymers (such as guar gum) leads not only to prolonged drug release, but also enables targeting and localizing them to a specific site in the gastrointestinal tract (*e.g.*, colon) [1]. It is well known that the conditions for drug vary along the gastrointestinal tract (GIT). Consequently, the dissolution characteristics of these systems should allow for the drug to be released in a controlled manner over the different segments of the GIT. This highlights the importance of dissolution testing in media, which simulate the changes in the composition of GIT fluids (i.e., biorelevant media). Therefore, the main aim of this study was to investigate the effect of two mucoadhesive polymers and their combinations without any additional excipients (*e.g.,* fillers, lubricants) on the dissolution profile of a model drug, theophylline. To simulate the passage of the systems through the GIT, three biorelevant media simulating the fasted state gastric, intestinal, and colon fluids (FaSSGF, FaSSIF, and FaSSCoF) of pH 1.6, 6.5, and 7.8, respectively, were used. The results demonstrated that the formulations could sustain the release of the drug for 24h in all media and the influence of pH differences of media on the drug release patterns were negligible.

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Reference

1 Tugchu-Demiroz F. J Drug Target. 12(2), 105-112 (2004)

Supervisors: Šklubalová Zdeňka, Vraníková Barbora

OP-32

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Investigation of dermal semisolid in situ film-forming systems containing lidocaine hydrochloride with QbD approach

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Recently, research has been focused on developing dermal local anesthetic treatment to decrease pain before a surgical intervention. This treatment is non-invasive and painless, therefore provides an attractive alternative to injection. Lidocaine hydrochloride (LID-HCl) is a commonly used drug in local anesthesia, but its effective time is short. Film-forming system (FFS) is an innovative drug delivery system, which forms a film after application, dries fast, and has good mechanical properties. These advantages make FFSs a promising choice in local anesthesia.

The aim of my research work was to develop LID-HCl containing semisolid in situ FFSs using the Quality by Design (QbD) approach. The FFSs were developed from the silicone containing blank formulations, which were used in my previous research. They were investigated regarding the effect of LID-HCl on the film-forming properties and the skin permeation of the active ingredients. The QbD approach was used to ensure the quality-based development.

During the research, initial risk assessment identified four high-risk critical quality attributes (CQAs): in vitro drug release, in vitro drug permeation, drying properties and mechanical properties, and three medium-risk CQAs: pH, viscosity, and film appearance. Furthermore, four high-risk critical material attributes (CMAs) were also considered during the formulation: permeation enhancing excipients, drying excipients, film-forming excipients, and emollients. These parameters were investigated during the work.

Results show that LID-HCl has great impact on FFSs. The silicone content can improve the applicability of formulations and has a favorable effect on the permeation rate of LID-HCl.

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References

1 Anita K. et al. Drug Des Devel Ther. 14, 5059-5076 (2020)

Supervisors: Szilvia Berkó, Erzsébet Csányi

OP-33

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Deposition studies on a systematically modified paediatric throat geometry

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Inhaling drugs seems to be an upcoming therapy option in many indications due to various advantages: less active pharmaceutical ingredient (API) is needed to achieve an effective dosage, a rapid onset of action and a therapy opportunity in case of inability to swallow.
Because of age- dependent differences in upper airway geometries and breathing patterns it is difficult to predict the pulmonal deposition of API´s, especially in paediatric inhalation therapy. Assessing the pulmonal deposition is especially important in evaluating the efficacy of therapy and dosage finding.
A few geometry models, which should improve the knowledge about the particle deposition, were introduced in literature which try to reflect the tracheobronchial region of children. However, none depicts the age-specific differences.
Therefore, a known paediatric throat geometry was modified in different dimensions and realized via 3D-printing. Constrictions were built in systematically to investigate the particle deposition in the upper airways and to determine the amount of API which is able to reach the lungs. Aerodynamic assessment was performed with the Next Generation Impactor (NGI) according to the Ph. EUR 2.9.18 using the example of "Cyclocaps® Salbutamol sulphate 200µg"and the modified throat geometries instead of the sample induction port (SIP).

Supervisors: Prof. Joerg Breitkreutz, Prof. Peter Kleinebudde

OP-34

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Antioxidant efficacy of vitamins loaded lipid based delivery systems with different microstructure for dermal application

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Nowadays, the interest in the development of novel dermal delivery systems for efficient therapy of skin weaken by various environmental stressors is steadily growing. Namely, environmental agents activate cutaneous inflammatory pathways and induce oxidative stress particularly by lowering the levels of antioxidants, which is associated with various skin diseases. Supporting the endogenous skin antioxidant system has been thus recognized as extremely beneficial [1, 2].

The purpose of the present work was to evaluate and compare different lipid based delivery systems for dermal administration of vitamins with antioxidant properties in terms of their stability and antioxidant activity. Dermally applicable lyotropic liquid crystals and microemulsions, all composed of the same ingredients but with different microstructure, were selected as carrier systems for simultaneous delivery of hydrophilic vitamin C and lipophilic vitamin E. The influence of selected delivery systems on the stability of incorporated antioxidants was assessed by HPLC method while their antioxidant capacity was investigated using DPPH assay.

Obtained results revealed differences in the stability among incorporated vitamins in correlation to the type of the delivery system, with lyotropic liquid crystals as most perspective formulation. Additionally, the study also demonstrated that the antioxidant efficacy of studied vitamins depends on their concentration and that the internal structure of the delivery system to some extent affects ability of incorporated vitamins to neutralize radicals.

References

1 Gašperlin M.; Gosenca M. Expert Opin Drug Deliv. 8(7), 905–919 (2011)
2 Kim K. E. et al. Life Sci. 152, 126–136 (2016)

Supervisors: Mirjam Gosenca Matjaž, Prof. Mirjana Gašperlin, Robert Roškar, Alenka Zvonar Pobirk

OP-35

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Investigation of foams for topical use

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The use of foams is becoming increasingly popular in the pharmaceutical and cosmetic fields. Foams are colloidal systems in which gas bubbles are dispersed in a solid or liquid dispersion medium. Pharmaceutical foams are usually applied topically, through dermal, vaginal, or rectal routes [1]. Foams have many beneficial properties over conventional carrier systems, which increases patient adherence, such as rapid and convenient application, even on extensive or hirsute, on sensitive and inflamed skin surfaces [2]. The aim of my work is to determine the investigation methods suitable for studying the physicochemical, structural properties and stability of dermally applied foams.

In the course of my research, the foam formulas were developed on the basis of literature and then I studied their characteristics by macroscopic, microscopic, rheological and structure analysis methods. Through microscopic examination the structure and bubble size of the foams were determined. The structure of foams was also studied by oscillometric rheology, during the measurements I proved what deformations would occur in the structure of the foam due to deforming forces. Furthermore, using Texture analyzer, I investigated the spreadability of the foams to model the dermal application.

Based on the results, it can be said that the selected instruments and the applied test methods are suitable for studying the properties and stability of foams.

References

1 Farkas et al. APH 89:5 (2019)

2 Parsa et al. Current Opinion in Colloid & Interface Science (2019)

Supervisors: Anita Kovács, Erzsébet Csányi

OP-36

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Development and optimization of the coating processes of lysozyme loaded pellets for oral delivery

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Increasing attention has been raised towards biopharmaceutical drugs in the last two decades as a result of known advantages compared to the small drug entities [1]. The design space of lysozyme loaded pellet production was optimized in the frame of raw material attributes by applying a special granulation chamber (Opulus®, Hungary) to take the encountered thermal shocks generated by the mechanical stress during the production steps into account as prescribed by [2]. The aim of the present work is to optimize the consecutive coating process in a manner to preserve pellet quality. The coating processes were performed based on 23 full factorial design with a center point. The effects of atomizing pressure, drying air temperature and drying air pressure were set as investigated factors, and pellet properties were set as optimization parameters. It was found that pellets demonstrated good thermal stability at the applied coating temperatures. Atomizing pressure was found as main factor affecting enzyme activity, moisture content, hardness, and release behaviour. Also, it is recommended to increase spheronization time to improve sphericity and then film homogeneity. In addition, increasing coating thickness is crucial to prevent premature drug release. Based on the biological activity and release pattern, the optimization of the coating process was successful, and the delivery system may be utilized for treating GI infections or as adjuvant regimen for controlling inflammatory bowel disease.

References
1 Ibrahim, J. et al. DARU J. Pharm. Sci. 28, 403–416 (2020)
2 Kristó, K. et al. EJPS. 95, 62–71 (2016)

Supervisors: Katalin Kristó, Géza Regdon jr., Tamás Sovány

OP-37

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Electrospun amphiphilic nanofibers for stigmasterol-loaded delivery systems

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Stigmasterol (STIG) among the most plentiful plant sterols has been demonstrated to possess a wide range of biological activities. However, the therapeutic use and efficacy of this plant sterol are limited due to its poorly water-soluble characteristics. To overcome these challenges, the present study was undertaken to formulate novel amphiphilic electrospun nanofibers (NFs) loaded with STIG, phosphatidylcholine and polyvinylpyrrolidone. The chemical structure of STIG, surface morphology, physical solid state, and drug–polymer interactions of NFs were characterized using nuclear magnetic resonance (NMR) spectroscopy, scanning electron microscopy (SEM), Fourier transform infrared (FTIR) spectroscopy, X-ray powder diffraction (XRPD), and differential scanning calorimetry (DSC), respectively. The drug release of NFs was investigated *in vitro* using an in-house dialysis-based dissolution method. The STIG-loaded NFs presented a nano-scale size of 297 ± 56 nm. The liposomes with a diameter of 436 ± 64 nm were spontaneously formed as the NFs were exposed to water. The entrapment efficiency of liposomes was 57%. In conclusion, the present amphiphilic NFs loaded with STIG enable a promising alternative approach for drug delivery of the present poorly water-soluble plant sterol.

Supervisors: Prof. Ain Raal, Prof. Hoai Thi Nguyen, Prof. Jyrki Heinämäki

OP-38

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Nose to brain delivery of *n*-propylgallte loaded lipid nanoparticles for targeting glioblastoma multiforme via QbD approach

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This study aimed to develop liposomes and solid lipid nanoparticles (SLNs) encapsulated with *n*-propylgallate (PG) as potential platforms for nose-to-brain delivery of anticancer drugs. The lipid formulation loaded with PG was not studied previously through this administration route, therefore its investigation and optimization is promising. The liposomes, solid lipid nanoparticles were developed by direct pouring method and solvent injection method respectively following the Quality by Design approach. The risk assessment strategy was used to screen and rank the critical quality attributes that can affect the final PG loaded nanoparticles. The 3-factor Box Behnken Design and Response surface Quadratic models was used to optimize the formulations of liposomes and solid lipid nanoparticles respectively. The lipid nano-formulation showed good compatibility according to results of XRPD, FTIR and DSC. The PG-SLNs showed encapsulation efficiency of 84±0.5%, particle size of 103±46.04 nm with polydispersity index of 0.16±0.001 and zeta potential of -36±4.78 mV. The PG-liposomes showed 90 ± 3.6% encapsulation efficiency, 167.9 ± 3.5 nm average hydrodynamic diameter, 0.129 ± 0.002 PDI and -33.9 ± 4.5 zeta potential. *In vitro* drug release and permeation studies of both formulation in simulated nasal conditions were performed. Both lipid nanoformulations resulted in enhanced nasal permeability and sustained release of nanoformulation compared to the PG solution. The optimized formulations showed high potential to be used to target the brain via intranasal route.

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References

Sabir, F et al. Drug Discov. Today 25(1): 185-194. (2020)

Supervisor: Prof. Ildikó Csóka

OP-39

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Challenges in nanofiber testing *in vitro*

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Nanofibers provide unique opportunities for drug delivery and tissue engineering. Despite many advantages of nanofibers, they are not yet in clinical use, mainly due to insufficient data about safety. Exploring nanofiber safety starts with in vitro testing, but unlike nanoparticles that have a clearly defined assay cascade by European Nanomedicine Characterisation Laboratory, tests need to be established or modified to account for additional considerations. We identified three main areas of challenges in *in vitro* testing of nanofibers namely pre-processing, cell culture experiment and evaluating the results. Challenges in pre-processing start with preparation of nanofibers (aseptic work) with constant nanofiber mat thickness, and clean nanofiber sample edge. MTS proliferation assay has proven to be sensitive to nanofiber sample orientation, size, and nanofiber collector material. Challenges in evaluating MTS proliferation assay results remain due to cell infiltration in nanofiber mat, formazan dye absorption into nanofibers and absorbance determination. Experimental nanofiber mats were made with an electrospinning device collected on glass or aluminium base. A model *in vitro* test was MTS proliferation assay performed in 96 and 48 well microtiter plates with primary blood derived cells. Experiments were designed using “Design of Experiments” approach to evaluate the influence of individual assay configurations. Most of the challenges can be overcome in the pre-processing phase with optimised nanofiber mat thickness, accurate nanofiber cutting or limiting the assay area with a microtiter insert glued to the nanofiber mat. Formazan dye absorption can be determined with additional experiments to measure the absorption capacity of nanofibers. With optimisation of described experimental parameters we expect more accurate in vitro results.

Supervisor: Prof. Julijana Kristl

OP-40

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New polymeric nanocomplexes against glioblastoma initiating cells

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Gene therapy emerged as an alternative to small drugs and proteins in the treatment of a large variety of diseases. However, the administration of nucleic acids still remains a challenge due to the biological barriers that need to be overcome before reaching the target cells. Indeed, polynucleotides are very sensitive to degradation and cannot cross cell membranes. To overcome these obstacles, nucleic acids are often included in viral, lipid or polymeric particles. Polymeric gene nanocarriers offer chemical flexibility and good protection for the therapeutic genes, but the materials used still need to the optimized to achieve improved efficiency in the gene delivery process.

Considering this background, the objective of this work has been the development of new prototypes of polymeric nanoparticles for their use in gene therapy and to test their potential for the treatment of glioblastoma. For this, a variety of synthetic cationic polymers have been combined with plasmid DNA or with both plasmid and an endosomolytic polymer. The nanoparticles were characterized for their physicochemical properties, for their toxicity and transfection efficiency in cell cultures. The polymer having primary amines and hydrophobic side groups, combined with the endosomolytic polymer provided some of the best results regarding their transfection/toxicity ratio. This advanced prototype was used with a therapeutic plasmid encoding Bone Morphogenic Protein-4 as a potential treatment against glioblastoma. These therapeutic nanoparticles showed the capacity to suppress glioblastoma growth in a murine xenograft model when combined with Temozolomide, due to the synergistic effect between those two treatments administered together.

Supervisors: Marcos García Fuentes, Noemi Csaba

OP-41

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Milk oral lyophilisates with loratadine: screening for new excipients for paediatric use

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Milk-based formulations are promising approaches for drug delivery. Its nutritional function, considerable effect on the drug solubility and taste masking capacity, recommended milk as potential excipient. This work aimed to investigate the properties of milk for paediatric oral lyophilisates (OLs) preparation and its influence on the quality profile.
A D-Optimal screening experimental design, with three independent variables: suspended active pharmaceutical ingredient (API) dose - loratadine, alveolae volume and the type of milk (1.5% and 3.5%) was generated and led to 16 formulations. The OLs were characterized for the disintegration time, texture and dissolution profile and particle size analysis upon reconstitution.
The independent variables included into the experimental design had significant influences on the output and gave robust models for all responses. A good OL excipient should allow fast disintegration and good mechanical profile. Disintegration was facilitated by high API content, small alveolae and low fat milk, correlated to weaker mechanical structures. However, appropriate mechanical profiles with hardness over 600g were obtained for most formulations, especially for the ones containing low doses of API. Dissolution was favoured by high API content and low fat milk. Low particle sizes upon reconstitution could improve both palatability and API dissolution and were granted by high alveolae volumes and low lipid content.
These results showed the feasibility of milk structures that meet OLs' quality criteria, indicated a rational way to choose the type of milk and highlighted the effects of the API dose and product volume.
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Supervisors: Sonia Iurian, Prof. Ioan Tomuță

OP-42

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Nose-to-brain applicability of Meloxicam-loaded Soluplus polymeric micelles

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Non-steroidal anti-inflammatory agents, such as meloxicam (MEL), play a key role in the treatment of the Alzheimer's Disease-associated neuroinflammation which leads to the loss of physiological functions.

Our aim was to develop MEL-loaded Soluplus® polymeric micelles and to test the application of them for the auspicious nose-to-brain drug delivery pathway in order to be a potential therapeutical nano system in the therapy of neuroinflammation.

To decrease the need of in vivo testing, various in vitro methods were used to investigate dissolution and permeability throughout this pathway. In vitro drug release at nasal conditions were tested in simulated nasal electrolyte solution. Cellular uptake and viability were investigated on human RPMI 2650 nasal epithelial cells. Using rapid equilibrium dialysis and parallel artificial membrane permeability assay, passive diffusion was investigated as the determining transport through penetration of the blood-brain-barrier. IVIVC was calculated based on these results.

Based on the in vitro results, we found that the nanoparticles tend to follow this pathway more favourably compared to the initial MEL. The formulation is viable to nasal epithelial cells with high trans-epithelial transport capacity. Rapid release kinetics paired with high flux and permeability values were determined at axonal conditions. A significantly higher simulated cerebral concentration of MEL was detected in the case of the nanoparticles.

In conclusion, it can be claimed that by encapsulating MEL into a polymeric micelle, prosperous pharmacokinetics can be achieved which can be used in the treatment of neuroinflammation.

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Supervisors: Prof. Ildikó Csóka, Gábor Katona

OP-43

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Printing of peptide-loaded hybrid nanoparticles for oral delivery

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Oral delivery of biopharmaceuticals has been representing an extensively active area of research during last decades. Part of this increasing interest comes from the superiority of this route over the parenteral one in terms of patients' convenience and compliance. However, biopharmaceuticals are delegate materials and are liable to degradation and inactivation during manufacturing and transit in the GIT after administration. Several studies utilised a variety of nanocarriers systems to deliver those macromolecules through this route. Among them, hybrid nanoparticles constitute a promising approach to achieve this mission. Based on the physicochemical properties of the loaded drug and the required features of a platform, a variety of one-step and two-step methods have been employed to fabricate these hybrid nanocarriers. Printing technology, recently introduced to the pharmaceutical field, seems to have the potentiality to prepare such systems.

This project aims the investigation of the emerging area of additive manufacturing, namely syringe extrusion technique and inkjet printing, for the construction of orally delivered peptide-loaded hybrid nanocarriers. In this study, the principles of Quality by Design and Design of Experiments will be exploited to investigate the process parameters and material attributes that affect the characteristics and the performance of the printed hybrid nanocarriers. The physical characteristics of the nanocarriers and the biological activity of the peptide will be examined. After that, the design space for the optimized response will be determined and verified.

References

1 Kristo, K. *et al*. Int. J. Pharm. 573, 25-39 (2019)

2 Ihalainen, P. *et al.* Int. J. Pharm. 494, 585-592 (2015)

Supervisors: Tamás Sovány, Katalin Kristó

OP-44

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Application of deep learning tools in prediction of printability of 3D printed tablets

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Fused deposition modelling (FDM) is an additive manufacturing technology that utilizes a 3D design to create an object by depositing molten materials on a platform in a layer-by-layer manner. The feedstock of the FDM printers is called filament and it is created using a hot melt extrusion process (HME) [1]. Although, FDM coupled with HME process has been intensively researched and developed in recent years, printability and various parameters affecting printability is still an unknown field.

The aim of this study was to evaluate influence of mechanical properties of filaments on printability through three-point bend test. The parameters that were observed were maximum force (N), maximum stress (N/mm2) and maximum displacement (mm).

After integrating obtained data for all 90 samples in a data mining environment software RapidMiner Studio version 9.7.0 (Boston, USA) and after analysing it via visual tools (Decision tree model) the correlation between maximum displacement, maximum force and printability was found. It was observed that filaments with the maximum displacement greater than 1.09 mm had a tendency to be printable, while filaments with the maximum displacement bellow this value were not printable. Additionally, if maximum force was lower than 9.61 N, filaments were printable. Otherwise, if maximum force was greater than 9.61 N, even with maximum displacement greater than 1.09 mm, printing was impossible. The method achieved an overall accuracy of 84.85%.

This study showed that the three-point bend test can be successfully used as an initial predictor of printing abilities of obtained filaments.

Reference

1 Basit, A., Gaisford S, eds. 3D Printing of Pharmaceuticals. Vol. 31. 109, Springer (2018)

Supervisor: Svetlana Ibrić

OP-45

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The 3D (Printing) Center of the University of Szeged: opportunities and challenges

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Personalized medicine is about to become the most efficient and sustainable way of practice both in prevention and treatment. A key enabling technology of personalized medicine is 3D printing, or Additive Manufacturing (AM) as more commonly known, nowadays. The conceptually simple, but radically new approach of AM roots in building objects additively, i.e. layer-upon-layer from a digital blueprint. The material of the object could either be plastic, metallic or even certain human tissue, depending on the AM technology used.

The 3D Printing Center of the University of Szeged (3DC) has been recently launched to merge and increase the knowledge of relevant research teams within the University and open up opportunities to those who are new to resolving the potential of AM.

The main emphasis of the 3DC is on life science and is equipped with high-end imaging and 3D printing instrumentation. Our metal printer is capable to print in an extensive portfolio of high-tech materials but can also be run with medical-grade titanium and stainless-steel alloys, appropriate for implants and medical instruments. We have two professional, high-resolution resin 3D printers capable to print even biocompatible materials. The 3DC is addressing bioprinting with a mechanical and a pneumatic printer, while teaching is assisted by several of our desktop printers of SLA and FDM technology. Last, but not least a metrological 3D scanner is also available, along with several other auxiliary instruments, such as a 3D optical microscope, a dynamic mechanical tester, to mention but a few.

OP-46

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Preparation and characterization of carrier-free dry powder inhalers containing nanosized active ingredient

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Pulmonary drug delivery provides rapid onset of action, large surface area for absorption and limited drug degradation. With the development of innovative dry powder inhalers, we could improve the therapeutic effect. The non-steroidal anti-inflammatory meloxicam was the active ingredient, which could be useful for the treatment of lung cancer, cystic fibrosis and chronic obstructive pulmonary disease.

Our aim was to produce dry powder inhalers containing nanonized meloxicam. We targeted different regions of the lung with micrometric particles prepared by Mini Spray-Dryer and nanometric samples produced by Nano Spray-Dryer.

We used a two-step preparation method. The nanosuspension was prepared with wet milling, using meloxicam and polyvinyl alcohol. The powders were obtained with spray-drying of the nanosuspension and using leucine. We measured the following properties: particle size (laser diffraction, DLS), morphology (SEM), true density, structure (XRPD), thermoanalytical properties (DSC), *in vitro* dissolution, *in vitro* absorption, *in vitro* lung deposition (Andersen Cascade Impactor).

We worked out a powder preparation method, using wet milling and spray drying. We managed to nanonize the active ingredient and prepare 3-4 µm particles by Mini Spray-Dryer and 500-800 nm particles by Nano Spray-Dryer. The particles were spherical with low density. Thanks to the improved surface area and amorphization, released and absorbed amount of meloxicam increased. The *in vitro* aerodynamic measurements proved that with the microsized particles we targeted the bronchioles and with the nanosized we reached the alveoli.

The samples are suitable for pulmonary delivery; therefore, our products could treat different respiratory diseases in the future.

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Supervisor: Rita Ambrus

OP-47

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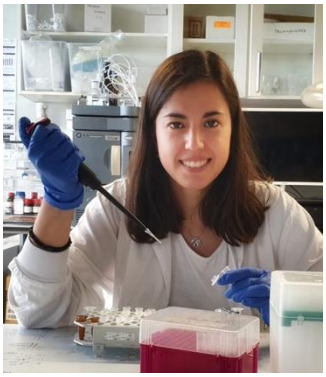

Bioinspired pollen microcapsules to overcome mucosal barriers

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Premature removal of nanocarriers in mucosal tissues, their enzymatic degradation and elimination by intestinal immune cells constitute current limitations on nanocarrier-mediated oral delivery of biopharmaceuticals [1]. Herein we present a strategy to overcome these limitations based on a biomimetic multi-stage delivery platform, using natural pollen-derived biomaterials [2].

For this purpose, we produced hollow pollen microcapsules (HPMs) with the same external structure as intact pollen grain, but free of internal compounds and potential contaminants, and we loaded them with non-biodegradable model nanoparticles of different sizes and surface charges. Association efficacy was studied by different techniques and lack of allergenicity was analyzed in the presence of immature dendritic cells and macrophages. Mucointeraction was also evaluated *in vivo* upon oral gavage to healthy rats. Results showed that 200 nm non-biodegradable model nanoparticles reached an optimal internal loading (around 85%) and a controlled release profile during the initial 8 h followed by a continuous release up to 120 h in simulated intestinal fluid. Further, this platform did not present allergenic effects, while their specific 3D surface morphology enabled an efficient and prolonged interaction with the intestinal mucosa upon oral administration, preserving intestinal tissue integrity. These characteristics places this pollen microcapsules as interesting multistep delivery platform candidates for the oral delivery of biopharmaceuticals.

References

1 Traidl-Hoffmann, C. et al. Allergy Immunol. 131:1–13 (2003)

2 Thwala, L.N. Expert Opin. Drug Deliv. 14:23–36 (2007)

Supervisors: Noemi Csaba, Sulay Tovar

OP-48

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Overview: Supercritical carbon dioxide versus subcritical water extraction of bioactive compounds from herbal material

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In order to meet the requirements of the constantly growing market for high quality medicinal plant products, the extraction and separation techniques that provide these products are in a state of constant development and improvement. Traditionally, the products of aromatic medicinal plants have been obtained by classical extraction methods such as hydrodistillation and Soxhlet, which are used to separate the fat and volatile fractions of these plants. These traditional methods, although well-known and documented, have a number of negative characteristics that can affect product quality such as toxic solvents residue, non-selective extraction and high energy consumption due to long extraction time as well as thermal degradation of high-value products. In order to neutralize the problems of traditional extraction techniques, new extraction methods have been introduced, such as supercritical carbon dioxide extraction and subcritical water extraction, which are aligned with strict requirements of the market and green chemistry. In this study, aromatic medicinal plants were extracted using supercritical carbon dioxide extraction and subcritical water extraction to demonstrate the advantage of using these modern and green extraction methods. Considering that obtaining the product with highest content of bioactive components was the primary goal, the advantages and disadvantages of the applied process were classified based on the chemical characterization of the extracts.

Supervisor: Jelena Vladić

OP-49

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Development of spray-dried meloxicam-containing microcomposites using biocompatible matrix

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Meloxicam (MEL) could relieve acute pain by absorbing through a highly vascularized alternative route: the nasal mucosa. However, there is an issue that requires a solution: the poor water-solubility of MEL. Chitosan can help to overcome this problem and because it is mucoadhesive, capable of opening the epithelial tight junctions and can achieve controlled drug delivery, there is a growing interest in it as a biocompatible matrix for nasal drug delivery in pharmaceutical developments [1]. The aims of this work were to prepare non-cross-linked and cross-linked drug-free and MEL-containing chitosan-based microparticles by spray drying while optimizing the process parameters and the composition of the formulation. The effect of inlet air temperature and pump rate on the particle size distribution and morphology of drug-free chitosan particles was investigated to determine the optimal parameters. After that, the micrometric properties, structural characterization and *in vitro* drug release of MEL-containing samples were studied. Sodium tripolyphosphate (TPP) was used in different amounts as the cross-linking agent. Micronized chitosan particles were successfully prepared regardless of the process parameters and the concentration of TPP. Nearly spherical habit could be observed in the case of drug-containing samples. The highest amount of molecularly dispersed MEL dissolved from the non-cross-linked formulation, controlled drug release was observed. Based on the mentioned results, spray-dried chitosan microparticles containing MEL may offer an opportunity to reduce acute pain or enhance analgesia through the nasal route.

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References

1 Bernkop-Schnürch, A.; Dünnhaupt, S. Eur. J. Pharm. Biopharm. 81 463–469. (2012)

Supervisors: Rita Ambrus, Csilla Bartos

OP-50

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Structural design of triterpenic acid 1,2,4-triazole linked gold nanoparticle bioconjugates, as potential treatment for malignant melanoma.

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Pentacyclic triterpenes are natural occurring compounds with well described pharmacotherapeutic potential but have some pharmacodynamic drawbacks such as low bioavailability [1]. To address this inconvenience, previous studies have attempted various formulations in order to increase their bioavailability and antitumor activity [2,3]. The current study proposes the structural design of a series of new gold nanoparticle (GNP) based bioconjugates in which each component can exert a synergic antiproliferative effect.

In our current work, based on their antiproliferative activity against malignant melanoma, ursolic acid, oleanolic acid and betulinic acid were chosen to be formulated as GNP bioconjugates. In order to bind to the GNP surface, the use of linker molecules is required. For the conceptualization of chemically suitable linkers that are also potentially active in melanoma, we choose the 3-mercapto-4-amino-1,2,4-triazole ring as a starting point template. In this regard, a virtual compound library was constructed (3-mercapto-4-amino-5-R-1,2,4-triazole derivatives) for the purpose of obtaining a selection of potentially active molecules, using molecular docking based virtual screening. The target proteins chosen are key nodes in melanoma active signalling pathways. The 3D structures of the targets were obtained from the RCSB database: EGFR (1XKK), MEK1 (3EQG), AKT1 (4GV1), mTOR (4JT5) and PI3Kα (6GVF). After docking the compound library in the mentioned targets, using PyRx, based on the obtained docking scores and binding site pose analysis, five compounds were retained as possible candidates with theoretical antiproliferative potential: 4-amino-5-(4-ethoxyphenyl)-1,2,4-triazole-3-thiol, 2-(4-amino-5-sulfanyl-1,2,4-triazol-3-yl)phenol, 4-amino-5-(4-nitrophenyl)-1,2,4-triazole-3-thiol, 4-amino-5-(2-naphthyl)-1,2,4-triazole-3-thiol, 4-amino-5-(4-quinolyl)-1,2,4-triazole-3-thiol. These molecules will be used as linkers in the synthesis of future pentacyclic triterpene-GNP bioconjugates.

References

1 Prades, J. Biochim Biophys Acta 1808(3):752–60 (2011)
2 Soica, C.M. Int. J. Mol. Sci. 5(5):8235–55 (2014)
3 Dutta, D. Sci. Rep. 9(1):11506 (2019)

Supervisor: Prof. Codruta Soica

OP-51

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Transfer of twin-screw granulation process using a shear stress description of screw configuration

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Factors like liquid-to-solid ratio (L/S), screw configuration and barrel fill level have crucial impact on the extent of granule formation [1]. Strategies that allow successful process transfers onto twin-screw granulators of different barrel diameters, without necessity of numerous experiments, are rare and still challenging [2,3].
Aim of this study was to transfer a TSG process using a newly developed equation that numerically describes the screw configuration as shear stress (τ)

$$\tau \left[\frac{N}{m^2}\right] = \frac{\dot{m}_{tot} \cdot n \cdot \pi \cdot D_{screw}}{L/S} \cdot \sum \left(\left(\frac{A_{contact}}{V_{free}} \right)^2 \cdot \frac{L_{screw}}{D_{screw}} \cdot sin(\alpha) \right)$$

$\dot{m}_{tot}$	total material throughput
n	screw speed
$A_{contact}$	contact area screw-barrel
V_{free}	free volume
L_{screw}	element length
D_{screw}	element diameter
L/S	liquid to solid ratio
α	stagger angle of kneading elements or aperture angle of conveying elements

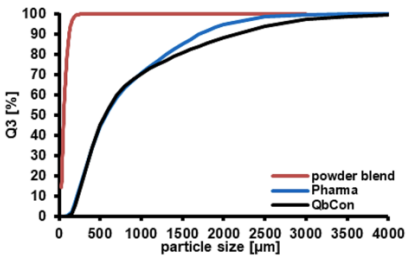

Fig. 1. GSD of a process transfer approach.

Two granulators of different barrel diameters (Pharma: 16 mm, QbCon: 25 mm) were used. The granule size distributions (GSD) of the original granules were compared only in the first place (Fig. 1). The GSD curves were comparable to each other with regard to their characteristics. Deviations were noticed above approx. 1000 µm only, resulting in higher x90 values for the granules produced on the QbCon. In a second step and to draw a final conclusion, process transfers were performed, where the original and turbo-sieved granules as well as tablets were characterized according to the European Pharmacopoeia. Very similar characteristics could be revealed. A successful transfer can be assumed.

References
1 Thompson, M.R. Drug Dev Ind Pharm, 41 1223-1231 (2015)
2 Iveson, S.M. et al. Powder Technol, 117, 3-39 (2017)
3 Osorio, J.G. et al. AIChE Journal, 63, 921-932 (2017)

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OP-52

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Protamine-based nanoparticles: an attractive gene delivery system for 2D and 3D glioblastoma models

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Glioblastoma multiforme is one of the most aggressive brain tumors. Its treatment combines surgical resection, chemotherapy, and radiotherapy, at expense of severe side-effects. Gene therapy holds great promise due its capacity to target specific pathways within glioblastoma cells by the introduction of exogenous tumor suppressor sequences, which are rendered therapeutically effective by using nanocarriers. Protamine:Dextran nanoparticles have become an attractive gene delivery system due to their intrinsic ability to encapsulate and protect nucleic acids, and the delivery efficacy. These NPs present spherical morphology, size below 150 nm and positive surface charge. They present long-term stability for one month under storage conditions (4ºC) and short-term stability for 4h when diluted in simulated physiological media (37ºC, pH=7.4). The association of different nucleic acids to these NPs was studied by agarose gel electrophoresis, showing high encapsulation (≥90%). *In vitro* cell-viability studies were optimized using U87MG cells and spheroids models, then followed by assessment using primary patient-derived glioblastoma cells. Toxicity was studied with proliferation and cell-death assays indicating low/non-toxicity for this nanosystem. Particle uptake in both glioblastoma models was tested with fluorescently labelled-nanosystem using confocal microscopy and quantified by Flow Cytometry. The studies revealed an uptake efficiency of 99%. The transfection of different doses of pDNA was carried out with a model plasmid encoding the Enhanced Green Fluorescent and Luciferase Proteins. These studies showed the capacity of NPs to efficiently transfect U87MG cells and spheroids at doses greater than 1 ug/well. This new formulation could be considered as a promising gene-nanocarrier for glioblastoma treatment.

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Optimization of the functionalization method of titanate nanotubes in order to use them as drug delivery systems

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In the first step of the study, the production process and product quality of TNT composites with atenolol and hydrochlorothiazide [1] were successfully optimized. Nevertheless, to use titanate nanotubes (TNTs) as drug delivery systems, the tailoring of their surface characteristics and hydrophilicity may be essential. Trichlorooctylsilane (TCOS), trichloroocatdecylsilane (TCOdS) and Mg stearate (MgSt) were used as functionalizing agents to increase their permeability through the GIT.

In this step, the functionalized TNTs were characterized by using a vario EL cube elemental analyzer to determine the H, C, N, and S contents and an optical contact angle tester to investigate the surface free energy. Furthermore, Caco-2 cell lines were utilized to test the cytotoxicity of the functionalized TNTs with MTT assay as well as permeability, where the concentration of the permeated amount was determined with an X-ray fluorescent analyzer.

According to the OCA results, for silane-based materials there was no significant difference in the polarity of TNTs when using the different molecular sized TCOS and TCOdS. There was a proportional linear relationship between the concentration of the agent and the polarity of TNTs, and the maximum hydrophobicity was achieved by using 100 µL of both, therefore, the functionalization reagent may be selected on an economical basis. In contrast, the surface characteristics of TNTs showed a sigmoidal relation to MgSt, which enables the use of less St and more uploaded drug molecules. Furthermore, functionalization with MgSt is a water-based green method, and altogether seems to be a better choice to achieve the targeted aims.

References

1 Ranjous Y. et al. Nanomaterials, 9(10), 1406 (2019)

Supervisors: Tamás Sovány, Géza Regdon jr., Zoltán Kónya

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Thank you for participating!