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

18-20 January, 2023

Book of Abstracts

University of Szeged

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

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

18-20 JANUARY 2023

SZEGED, HUNGARY

General Information

Date: 18-20 January 2023

Location: Hybrid (University of Szeged, Faculty of Pharmacy, and online MS Teams)

Congress Topics: Pharmaceutical technology, biotechnology and regulatory science

Types of presentations:

1. Oral presentation (10 min + 5 min discussion)
2. Flash presentation (3-5 min, pre-recorded)

Submission of abstracts: gytfi.phd.pharm@szte.hu

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President of the Symposium

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Co-organiser

Foundation for the Development of Pharmacy Education at the University of Szeged

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

January 18-20 2023 - Szeged, Hungary

Greetings

Welcome to our 5th Symposium of Young Researchers on Pharmaceutical Technology, Biotechnology and Regulatory Science!

Once Upon a Time, there was a 12th Central European Symposium on Pharmaceutical Technology and Regulatory Affairs organized in our wonderful Szeged city on September 20-22, 2018.

Most of You, dear Colleagues, attended this event 5 years ago and hopefully, You keep good memories of the scientific and social programs as well. A decision was made then, namely that we wouldn't leave this great network to atrophy. We should keep in touch with each other and bring our new Ph.D. students and young researchers into this community for continuous growth. We all are committed to adding our knowledge and research efforts to find solutions for Global Health challenges, especially within pharmaceutical sciences, and this links us together.

Welcome our new Colleagues here in this network with the sincere hope that You find your mates here and stay with us for possible new cooperations, finding synergies between your research and the presented research projects and representing institutions.

Finally, I wish You a pleasant stay here in Szeged for this period and enjoy the possibility of visiting the ELI-ALPS Laser Research Institute, our laboratory facilities at the Institute of Pharmaceutical Technology & Regulatory Affairs, and the University Main Building's warm and friendly environment.

For those who attend online: please feel free to ask questions and be active; thanks to this digital era, you don't have to feel limited in anything.

Prof. Ildikó Csóka
President of the Symposium

Greetings

On behalf of the Scientific Committee, I am very pleased to welcome the participants of the 5th 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.

This is the fifth time that the Symposium has been organized by the Institute of Pharmaceutical Technology and Regulatory Affairs and the Foundation for the Development of Pharmacy Education, University of Szeged.

The venue of the opening ceremony and the plenary lecture will be held at the ELI-ALPS Laser Institute which clearly shows the importance of this event. The number of participants and presented PhD scientific works, as well as new countries/universities, is increasing every year. The aim of the program is unchanged 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.

We are delighted to welcome 48 PhD students from 16 universities in 12 countries (Charles University, Czech Republic, Heinrich Heine University, Germany, Iuliu Hatieganu University of Medicine and Pharmacy, Romania, Josip Juraj Strossmayer University of Osijek, Croatia, Medical University of Plovdiv, Bulgaria, Omdurman Islamic University, Sudan, University of Belgrade, Serbia, University of Debrecen, Hungary, University of Ljubljana, Slovenia, University of Novi Sad, Serbia, University of Parma, Italy, University of Pavia, Italy, University of Santiago de Compostela, Spain, University of Science and Technology Houari Boumediene, Algeria, University of Szeged, Hungary, Victor Babes University of Medicine and Pharmacy, Romania). The program includes 32 oral and 16 flash presentations. The number of participants is approx. 90.

The 5th symposium, like the 4th, will be held in hybrid form (online and contact). 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

About Szeged

Szeged, the 3rd largest city in Hungary, lies on both sides of the River Tisza, close to the Serbian border. Szeged is the regional center of the southern Great Plain, also referred to as the city where the sun always shines.

Szeged has been inhabited since ancient times. It was founded by the Romans under the name Partiscum. The great flood of 1879 wiped away the whole town, and then a modern city with boulevards and radial avenues emerged from the ruins. The main high street of Szeged (Kárász street) and the central square (Klauzál square) were restored in neo-classical style, for which it received the Europa Nostra Award in 2003.

In 1921 the University of Kolozsvár (now Cluj-Napoca) moved to Szeged, today known as the University of Szeged. Szeged is one of the country's most important centers for research and development, especially in life sciences, biotechnology, laser technology, and information technology.

Today Szeged is a valuable university city, a cultural center, and a tourist attraction. The city center was reconstructed in the spirit of Art Nouveau, transforming Szeged into a city of palaces. The main sights of Szeged, such as the Votive Church, the City Hall, Reök Palace, and the world's 4th largest Synagogue, are all within walking distance from the symposium venue.

Committees

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Head of the Organising Committee

Luca Éva Uhljar

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Bissera Pilicheva, Bulgaria
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Heba Banat
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Patricia Varga
Ranim Saker

Short Program

Wednesday, 18th January – 9:00-16:15 CET

Art Hotel (H-6720 Szeged, Somogyi Street 16.)

8:00 - 8:20	Transfer to the ELI ALPS Research Institute (from Art Hotel)

ELI ALPS Research Institute (H-6728 Szeged, Wolfgang Sandner Street 3.)

8:15 - 9:00	Registration
9:00 - 9:30	**Conference opening - greetings** • *Prof. Gábor Szabó, Managing Director of the ELI ALPS Research Institute,* • *Prof. István Zupkó, Dean of the Faculty of Pharmacy,* • *Prof. Zoltán Kónya, Vice-Rector for Scientific Affairs & Innovation,* • *Prof. Ildikó Csóka, President of the Symposium, Head of Pharmaceutical Technology Doctoral Program*
9:30 – 10:00	**Introduction of ELI ALPS Research Institute** *Prof. Katalin Varjú – Attosecond Science at ELI Scale*
10:00 – 10:45	**Plenary lecture** *Prof. Ildikó Bácskay – Role of 3D printing in the pharmaceutical R&D*
10:45 - 12:00	**Guided tours in the ELI ALPS Research Institute**
12:00 - 12:20	Transfer back

Department of Rector's Office (H-6720 Szeged, Dugonics Square 13.)

12:00 - 13:15	Lunch break
13:15 - 14:30	**Session 1**
14:30 - 14:45	Break
14:45 - 16:15	**Session 2**

JATE Club (H-6720 Szeged, Dugonics Square 13.)

19:00 -	***Gala dinner and Networking event - in person***

Short Program

Thursday, 19th January – 9:00-16:15 CET

Department of Rector's Office (H-6720 Szeged, Dugonics Square 13.)

9:00 - 10:30	**Session 3**
10:30 - 11:00	Break
11:00 - 12:00	**Session 4**
12:00 - 13:30	Lunch break
13:30 - 15:00	**Session 5**
15:00 - 15:15	Break
15:15 - 16:15	**Session 6**
19:00 -	***Game Night - online***

Friday, 20th January – 9:00-13:15 CET

Department of Rector's Office (H-6720 Szeged, Dugonics Square 13.)

9:00 - 10:15	**Session 7**
10:15 - 10:30	Break
10:30 - 12:00	**Session 8**
12:00 - 12:15	**Closing Ceremony**
12:15 - 13:15	Lunch

Schedule

Wednesday, 18th January – 9:00-16:15 CET

8:00-8:20 **Transfer to the ELI ALPS Research Institute** (from Art Hotel)

8:15-9:00 **Registration**

Location: ELI ALPS Research Institute – 3 Wolfgang Sandner Street, Szeged, Hungary

9:00-9:30 **Opening Ceremony:**

Prof. Gábor Szabó (Managing Director of the ELI ALPS Research Institute)

Prof. István Zupkó (Dean of Faculty of Pharmacy, University of Szeged)

Prof. Zoltán Kónya (Vice-Rector for Scientific Affairs & Innovation, University of Szeged)

Prof. Ildikó Csóka (President of the Symposium, Head of Pharmaceutical Technology Doctoral Program, University of Szeged)

9:30-10:00 **Introduction of ELI ALPS Research Institute**

Prof. Katalin Varjú – Attosecond Science at ELI Scale

10:00-10:45 **Plenary Session:**

Prof. Ildikó Bácskay – Role of 3D printing in the pharmaceutical R&D

10:45-12:00 **Guided tours in the ELI ALPS Research Institute**

12:00-12:20 **Transfer to the symposium venue**

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

Location: Department of Rector's Office – 13 Dugonics Square, Szeged, Hungary

13:15-14:30 **Session 1 – Chairs: Mahwash Mukhtar, Tamás Sovány**

OP-01 – 13:15-13:30 **Vladislav Frolov,** Eva Snejdrova

Biodegradable depot delivery systems for the local treatment of joint replacement infections

OP-02 – 13:30-13:45 **Luca Éva Uhljar,** Rita Ambrus

Process optimalization of the preparation of PVP-based nanofibrous drug carrier loaded with ciprofloxacin

OP-03 – 13:45-14:00 **Nikolay Zahariev,** Milena Draganova, Plamen Zagorchev, Bissera Pilicheva

Development of daunorubicin-loaded casein nanoparticles as a potential drug delivery system for the treatment of ALL

OP-04 – 14:00-14:15 **Boglárka Szalai**, Orsolya Jójárt-Laczkovich, Mária Budai-Szűcs

Design and optimization of *in situ* gelling mucoadhesive eye drops containing dexamethasone

OP-05 – 14:15-14:30 **Sandra Robla,** Rubén Varela Calviño, Noemi Csaba, Rita Ambrus

Development of rifabutin-loaded protamine nanocarriers for pulmonary drug delivery with improved aerodynamic properties

14:30-14:45 Coffee break

14:45-16:15 Session 2 – Chairs: Marina Tišma, Corina Danciu

OP-06 – 14:45-15:00 **Fanni Falusi,** Szilvia Berkó, Anita Kovács

Influence of polymers and active substances on foam stability

OP-07 – 15:00-15:15 **Balázs Attila Kondoros,** Ildikó Csóka, Rita Ambrus

Investigation of the feasibility and efficiency of solvent-free co-grinding with different active substances

OP-08 – 15:15-15:30 **Silvija Šafranko,** Stela Jokić

Multifunctional biomass-derived and N-doped carbon quantum dots – the versatile nanoparticles for ion sensing with potential biological and pharmacological activity

OP-09 – 15:30-15:45 **Eleonora Sofia Cama,** Milena Sorrenti, Laura Catenacci, Sara Perteghella, Maria Cristina Bonferoni

Preparation and characterization of binary systems with semisynthetic derivatives of β-cyclodextrin for dimethyl fumarate nasal delivery

OP-10 – 15:45-16:00 **Liza Józsa,** Gréta Frei, Ildikó Bácskay, Pálma Fehér

Formulation of external dosage forms containing grape pomace as active ingredient

OP-11 – 16:00-16:15 **Heba Banat,** Ildikó Csóka, Rita Ambrus

Development of a combined nanosystem as a dry powder inhaler for the treatment of pulmonary inflammations

19:00- **Gala dinner and networking event**

Location: JATE Club – 13 Dugonics Square, Szeged, Hungary

Schedule

Thursday, 19th January – 9:00-16:15 CET

9:00-10:30 Session 3 – Chairs: Bissera Pilicheva, Kamel Daoud

OP-12 – 9:00-9:15 **Krisztián Pamlényi,** Géza Regdon Jr., Orsolya Jójárt-Laczkovich, Dániel Nemes, Ildikó Bácskay, Katalin Kristó

Formulation of buccal films in Parkinson's disease

OP-13 – 9:15-9:30 **S P Yamini Kanti,** Orsolya Jójárt-Laczkovich, Ildikó Csóka

Antimicrobial film coated catheters for intravesical drug delivery: factors affecting and future opportunities applying the quality by design concepts

OP-14 – 9:30-9:45 **Yousif H-E. Y. Ibrahim,** Géza Regdon Jr., Tamás Sovány, Katalin Kristó, Gabor Katona

Gum arabic as novel lysozyme carrier polymer

OP-15 – 9:45-10:00 **Rares Iuliu Iovanov,** Andrei Alexe Dobre, Andrea Gabriela Crișan, Sonia Meda Iurian, Ioan Tomuță

3D Printing of prolonged-release tablets containing felodipine

OP-16 – 10:00-10:15 **Ágnes Rusznyák,** Milo Malanga, Ildikó Bácskay, Ferenc Fenyvesi

Formulation and investigation of cyclodextrin polymer-based siRNA delivery systems

OP-17 – 10:15-10:30 **Mirjana Sulejmanović,** Nataša Nastić, Ioannis Mourtzinos, Stela Jokić, Krunoslav Aladić, Anastasia Kyriakoudi, Senka Vidović

Greener approach to the extraction of bioactive compounds from ginger (Zingiber officinale) herbal dust

10:30-11:00 Coffee break

11:00-12:00 Session 4 – Chairs: Svetlana Ibrić, Francesca Buttini, Mirjana Gašperlin

FP-01 – 11:00-11:05 **Radka Boyuklieva,** Bissera Pilicheva

Development of poly-ε-caprolactone nanocarriers for nasal administration of idebenone

FP-02 – 11:05-11:10 **Hala Rayya,** Katalin Kristó, Géza Regdon Jr.

Formulation and investigation of buccal mucoadhesive films for improving buccal absorption

FP-03 – 11:10-11:15 **Rym Benremouga**, Lynda Lamoudi, Kamel Daoud

Extraction of Pistacia lentiscus seeds growing in Algeria and determination of the fatty acid composition

FP-04 – 11:15-11:20 **Tsenka Grancharova,** Stanislava Simeonova, Bissera Pilicheva, Plamen Zagorchev

y-F2O3 nanoparticles as a mediator for photothermal therapy – preparation, characterization and heating ability in muscle tissue phantom

FP-05 – 11:20-11:25 **Affaf Benzahra,** Abdelkader Hadj-Sadok, Kamel Daoud

Polymorphic behavior of hemisynthetic triglyceride-based ingredients intended for pharmaceutical products

FP-06 – 11:25-11:30 **Hadi Shammout,** Krisztina Ludasi, Tamás Sovány

Laser applications in pharmaceutical industry

FP-07 – 11:30-11:35 **Ádám Pannonhalmi**, Balázs Bende, László Szakács

Clinical validation of video-otoscopy based medical device for remote diagnosis of ear complains

FP-08 – 11:35-11:40 **Rabia Ashfaq,** Mária Budai-Szűcs

Design of in situ gelling systems containing natural ingredients for treatment of periodontitis

11:40-12:00 – Q&A

12:00-13:30 Lunch break

Location: Department of Rector's Office – 13 Dugonics Square, Szeged, Hungary

13:30-15:00 Session 5 – Chairs: Senka Vidović, Rita Ambrus

OP-18 – 13:30-13:45 **Dmytro Iefremenko,** Lukáš Lochman, Ondřej Holas

Development of nanoformulations for targeted delivery of obeticholic acid

OP-19 – 13:45-14:00 **Ioana Toma,** Cristina Barbălată, Lucia Tefas, Alina Porfire, Ioan Tomuță

Development and characterization of gemcitabine lipobeads

OP-20 – 14:00-14:15 **Ranim Saker,** Géza Regdon Jr., Tamás Sovány

Investigation of carboxylic acids possible application as linkers on the surface of titanate nanotubes for further functionalization

OP-21 – 14:15-14:30 **Maryana Salamah,** György Tibor Balogh, Gábor Katona

Formulation and optimization of lamotrigine-loaded bovine serum albumin nanoparticles by using full factorial design

OP-22 – 14:30-14:45 **Stefania Glieca,** Angelo Bolchi, Elisabetta Levati, Davide Cavazzini, Valentina Garrapa, Barbara Montanini, Francesca Buttini

Dry powder inhaler of a miniprotein decoy for SARS-CoV-2 infection inhibition

14:45-15:00 Lab tour videos

15:00-15:15 Coffee break

15:15-16:15 Session 6 – Chairs: Peter Kleinebudde, Géza Regdon Jr., Eva Snejdrova

FP-09 – 15:15-15:20 **Gabriela Perković,** Mirela Planinić, Ana Bucić-Kojić

Goat whey as a coating/protective material in the spray drying process of grape pomace extract

FP-10 – 15:20-15:25 **Mila Kovačević,** Ilija German Ilić, Alenka Zvonar Pobirk

Optimization of SMEDDS orodispersible tablet formulation

FP-11 – 15:25-15:30 **Assia Benayache,** Lynda Lamoudi, Kamel Daoud

Modeling of film coating thickness with use of artificial neural networks

FP-12 – 15:30-15:35 **Feria Hasanpour,** Szilvia Berkó

3D printing microneedle patch as drug delivery system on the skin

FP-13 – 15:35-15:40 **Gordana Šelo,** Mirela Planinić, Marina Tišma, Ana Bucić-Kojić

The influence of bioprocessing of grape pomace by Rhizopus oryzae on the chemical composition and extractability of phenolic compounds

FP-14 – 15:40-15:45 **Rania Chebani,** Kamel Daoud

Application of pharmacopeia tests on an Algerian Bentonite to assess its potential suitability as a pharmaceutical substance

FP-15 – 15:45-15:50 **Daya Mancer,** Farid Agouillal, Kamel Daoud

Solid lipid particles as carriers for sustained drug release

FP-16 – 15:50-15:55 **Monika Prašnikar,** Maja Bjelošević Žiberna, Pegi Ahlin Grabnar

Formulations for subcutaneous administration: Exploring the influence of monoclonal antibody concentration and addition of excipients on their viscosity

15:55-16:15 – Q&A

19:00- **Online games** (Zoom link sent via email)

Schedule

Friday, 20th January – 9:00-13:30 CET

9:00-10:15 Session 7 – Chairs: Noemi Csaba, Szilvia Berkó

OP-23 – 9:00-9:15 **Andrea-Gabriela Crisan,** Alina Porfire, Sonia Iurian, Tibor Casian, Lucia Rus, Ioan Tomuță

The broadening horizons of pharmaceutical 3D printing – Simple strategies for complex formulations

OP-24 – 9:15-9:30 **Petra Party,** Zsófia Ilona Piszman, Rita Ambrus

High-dose ibuprofen containing carrier-free dry powder inhalers for the therapy of cystic fibrosis

OP-25 – 9:30-9:45 **Josipa Martinović,** Mirela Planinić, Ana Bucić-Kojić

Bioaccessibility of phenolic compounds from grape pomace extracts

OP-26 – 9:45-10:00 **Martin Cseh,** Gábor Katona, Ildikó Csóka

Optimization of design and printing parameters of solid microneedle array produced by SLA printer

OP-27 – 10:00-10:15 **Azza Asim Khalid Mahmoud,** Géza Regdon Jr., Katalin Kristó

Determination of design space for direct pelletization using ProCepT granulator

10:15-10:30 Coffee break

10:30-11:45 Session 8 – Chairs: Mária Budai-Szűcs, Milena Sorrenti

OP-28 – 10:30-10:45 **Alharith A. A. Hassan,** Katalin Kristó, Géza Regdon Jr., Viktória Varga, Tamás Sovány

Preparation and optimization of hydrophobic ion pairing complex of lysozyme

OP-29 – 10:45-11:00 **Bence Sipos,** Márk Benei, Ildikó Csóka, Gábor Katona

Formulation of sustained release sodium alginate beads loaded with antidiabetic drug containing polymeric micelles

OP-30 – 11:00-11:15 **Larisa Bora,** Stefana Avram, Lavinia Lia Vlaia, Ana Maria Muț, Ioana Zinuca Magyari-Pavel, Paula Sfirloaga, Corina Danciu

Oregano essential oil polymeric micelles-based hydrogel as a dermal drug delivery system: in vitro and in ovo assessment

OP-31 – 11:15-11:30 **Sandra Aulia Mardikasari,** Mária Budai-Szűcs, László Orosz, Katalin Burián, Ildikó Csóka, Gábor Katona

Application of albumin-based nanoparticles integrated with thermo-responsive gel systems for enhanced nasal delivery of amoxicillin

OP-32 – 11:30-11:45 **Sofia Milenkova,** Nikolay Zahariev, Maria Marudova-Zsivanovits, Bissera Pilicheva

Chitosan-Casein complexes as carriers for bioactive compounds

11:45-12:00 Lab tour videos

12:00-12:15 Closing Ceremony

12:15-13:15 Lunch

Location: Department of Rector's Office – 13 Dugonics Square, Szeged, Hungary

Abstracts

Plenary lectures

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

January 18-20 2023 - Szeged, Hungary

DOI: 10.14232/syrptbrs.2023.19

Attosecond Science at ELI Scale

Katalin Varjú

Extreme Light Infrastructure - Attosecond Light Pulse Source (ELI ALPS) Research Institute, Szeged, Hungary

The ELI-ALPS facility supports laser based fundamental and applied research at extreme short timescales, operating specialized lasers which drive nonlinear frequency conversion and acceleration processes. The attosecond beamlines based on advanced HHG techniques will be reviewed along with first experiments.

The Extreme Light Infrastructure – Attosecond Light Pulse Source (ELI-ALPS), the Hungarian pillar of ELI ERIC [1], is the first of its kind that operates by the principle of a user facility, supporting laser based fundamental and applied researches in physical, biological, chemical, medical and materials sciences at extreme short time scales.

This goal is realized by the combination of specialized primary lasers which drive nonlinear frequency conversion and acceleration processes in more than twelve different secondary sources. Thus a uniquely broad spectral range of the highest power and shortest light pulses becomes available for the study of dynamic processes on the attosecond time scale in atoms, molecules, condensed matter and plasmas [2,3].

The attosecond secondary sources are based on advanced techniques of Higher-order Harmonic Generation (HHG) [4,5]. Other secondary sources provide THz radiation or particle beams for plasma physics and radiobiology. A set of state-of-the-art endstations will be accessible to those users who do not have access or do not wish to bring along their own equipment.

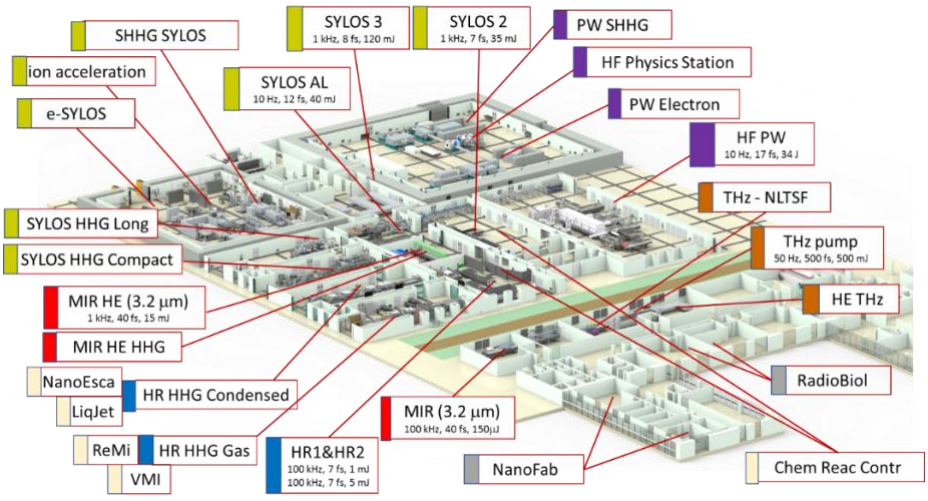

Fig. 1. ELI ALPS Primary and secondary sources with endstations

ELI-ALPS implementation will conclude in 2023, in the meantime various research technology equipment pass commissioning and come online gradually. The talk will give a general overview of the implementation status and access possibilities of the facility, and will focus on the technical aspects of attosecond science driven by high average power few-cycle laser pulses.

At the current phase of the project ELI-ALPS welcomes the submission of proposals [6] for scientific experiments that will support the ramping up of the broad selection of light sources and experimental stations available. ELI-ALPS provides beamtime as well as technical and scientific support for the experiments.

References

1. https://eli-laser.eu/
2. S. Chatziathanasiou et al., “Generation of Attosecond Light Pulses from Gas and Solid State Media”, Photonics **4**, No 26 (2017)
3. M. Reduzzi et al., “Advances in high-order harmonic generation sources for time-resolved investigations”, Journal of Electron Spectroscopy and Related Phenomena 204, Page 257-268 (2015)
4. S. Kuhn et al., “The ELI-ALPS facility: the next generation of attosecond sources.”, Topical Review, Journal of Physics B **50** 132002 (2017)
5. S. Mondal et al., “Surface plasma attosource beamlines at ELI-ALPS”, JOSA B **35**, A93-A102 (2018)
6. https://www.eli-alps.hu/en/Users-2/User-Call-2

DOI: 10.14232/syrptbrs.2023.21

Role of 3D printing in the pharmaceutical R&D

Ildikó Bácskay, Petra Arany

Healthcare Industry Institute, University of Debrecen, Debrecen, Hungary
Department of Pharmaceutical Technology, University of Debrecen, Debrecen, Hungary

Since the appearance of the 3D printing in the 1980s it has revolutionized many research fields including the pharmaceutical industry. The main goal is to manufacture complex, personalized products in a low-cost manufacturing process on-demand. In the last few decades, 3D printing has attracted the attention of numerous research groups for the manufacturing of different drug delivery systems. The drug delivery systems are sub-grouped into tablets, capsules, orodispersible films, implants, transdermal delivery systems, microneedles, vaginal drug delivery systems, and micro- and nanoscale dosage forms. Since the 2015 approval of the first 3D-printed drug product, the number of publications has multiplied. In our lecture, we focused on summarizing the technologies and the requirements of 3Dprinting. Different possibilities of the wide application field of 3D printing are also presented. In the last part of our talk, we will give a brief introduction to the 3D printing researches at the Department of Pharmaceutical Technology, University of Debrecen.

References:

1. Bácskay I., Ujhelyi Z., Fehér P., Arany P. Pharmaceutics, 14, 1312. (2022)

Abstracts

Oral presentations

OP-01

DOI: 10.14232/syrptbrs.2023.23

Biodegradable depot delivery systems for the local treatment of joint replacement infections

Vladislav Frolov, Eva Snejdrova

Department of Pharmaceutical Technology, Charles University, Hradec Kralove, Czech Republic

Musculoskeletal infections which commonly accompany orthopaedic surgery are still a major problem and require effective therapy. Currently, this consists of a combination of systemically and locally applied antibiotics in the form of targeted delivery systems with prolonged drug release. Antibiotics administered locally provide a high drug concentration at the target site. This approach benefits from minimizing systemic drug exposure and potentially reduces resistance development [1, 2].

The aim of this work was to formulate and characterize vancomycin loaded PLGA nanoparticles (NPs) for impregnating bone grafts used in treatment of musculoskeletal infections. Commercial or non-commercial PLGA were used in NPs preparation by water-in-oil-in-water double emulsion solvent evaporation technique. Polyvinyl alcohol or poloxamer were used for emulsion stabilization of primary emulsion.

Size, polydispersity and zetapotential of prepared NPs were determined using a Zetasizer Nano ZS. Encapsulation efficiency was estimated by UV-spectrophotometry directly by measuring the amount of encapsulated drug after dissolution of NPs in organic solvent and extraction of drug by water. Thermal behaviour of blank PLGA nanoparticles and drug-loaded nanoparticles was studied using a DSC. The drug release into the PBS pH 7.4 at 37°C was measured.

As a result of our work, NPs up to 300 nm in size and polydispersity below 0.2 were successfully obtained. The created NPs will be used in further tests connected with impregnation of morselised bone grafts after optimalization of other parameters, such as encapsulation efficiency and drug loading.

References:

1. Andersson DI, Hughes D Nat Rev Microbiol 8: 260 – 271. (2010).
2. Prokes L, Snejdrova E. Molecules, 27, 6487. (2022)

OP-02

DOI: 10.14232/syrptbrs.2023.24

Process optimalization of the preparation of PVP-based nanofibrous drug carrier loaded with ciprofloxacin

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Nanotechnology is one of the most intensively investigated fields within pharmaceutical technology. Therefore, a wide range of nanosized drug delivery systems is available. Nanofibers have numerous advantages such as the great variety of suitable polymers, small diameter, large surface area, and tailorable drug release. These properties can be exploited to develop medicines and medical devices. In the latter case, nanofiber applications range from protective clothing to wound management and tissue engineering. Electrospinning (ES) is the simplest technique used for producing nanofibers. The traditional ES setup contains a high-voltage supply, a polymer container, a pump, a nozzle, and a collector. The single nozzle configuration is the simplest and most common ES method. But to increase productivity, it requires scaling up or switching to nozzle-free ES.

In this work, we aimed to produce ciprofloxacin-loaded nanofibers with rapid dissolution and long-term stability. Initially, the traditional single-nozzle ES method was used, and then the process was optimized in three steps. As the first step, the optimization of the single-nozzle ES took place by comparing the morphology and the physicochemical properties of the different nanofibers. Also, the solubility and the dissolution of the drug were studied [1]. In the second step, the ciprofloxacin concentration was increased inside the fibers [2]. As the third step, the productivity was improved by using a nozzle-free ES method. Additionally, rapid dissolution was earned in every case and the samples were stable for 16 months [2].

In summary, the production of ciprofloxacin-loaded nanofibers was optimized, and homogenous, stable nanofiber mats with rapid drug dissolution were earned.

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OP-03

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Development of daunorubicin-loaded casein nanoparticles as a potential drug delivery system for the treatment of ALL

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The aim of this study was to develop nanosized-casein carriers by the method of spray drying and to evaluate their potential as a tool for delivery of daunorubicin in the treatment of acute lymphocytic leukaemia (ALL). Full 3^2 factorial design was applied to evaluate the optimal production parameters (concentration of the polymer and the crosslinker) for the preparation of blank casein nanoparticles. Nine batches of unloaded particles were developed and characterized in terms of particle size, size distribution, surface morphology and compatibility between the drug and the polymer. Based on an optimized "placebo" model of casein nanostructures, four batches of daunorubicin-loaded particles were synthesized at varied drug-polymer ratios. The obtained structures have average particle size within the range 127 to 167 nm, and encapsulation efficiency was between 42.8% and 61.8%. Delayed drug release was demonstrated, which correlates with the results of the cytotoxicity study on lymphoblast cells.

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OP-04

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Design and optimization of *in situ* gelling mucoadhesive eye drops containing dexamethasone

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Many factors limit the bioavailability of topical ocular formulations, such as blinking, tear dilution, and the structure of the tear film and the ocular surface [1]. Bioavailability can be improved by increasing the residence time on the eye surface and the penetration of the active pharmaceutical ingredient. This study aimed to formulate *in situ* gelling mucoadhesive ophthalmic formulations [2]. To increase the residence time, the formulations were based on a thermosensitive polymer (Poloxamer 407 (P407)) and were combined with two types of mucoadhesive polymers. Dexamethasone (DXM) was solubilized by complexation with hydroxypropyl-β-cyclodextrin (HPBCD). The effect of the composition on the gel structure, mucoadhesion, dissolution, and permeability was investigated using 3^3 full factorial design. These parameters of the gels were measured by rheological studies, tensile test, dialysis membrane diffusion, and *in vitro* permeability assay. The dissolution and permeability of the gels were also compared with DXM suspension and CD-DXM solution. P407 strongly determined gelation; however, the mucoadhesive polymers also influenced it. Mucoadhesion increased with the polymer concentration. The first phase of drug release was similar to that of the CD-DXM solution, then it became prolonged. The permeability of DXM was significantly improved.

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OP-05

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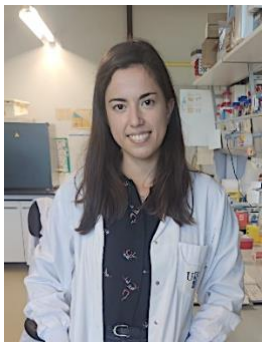

Development of rifabutin-loaded protamine nanocarriers for pulmonary drug delivery with improved aerodynamic properties

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Tuberculosis is an infectious respiratory disease that constitutes a significant public health challenge. The extended administration of high doses of drugs in its oral antibiotic therapy has difficult patient compliance and has promoted resistance to these treatments [1]. Therapeutic strategies based on microparticle administration in the form of dry powder inhalers (DPIs) constitute a promising alternative for pulmonary delivery and patient adherence. The controlled agglomeration of nanoparticles into micron-sized particles allows their transport to the alveoli, where redispersion and release of the nanoparticles take place. [2]. In this work, rifabutin-loaded protamine nanocapsules (NCs) were prepared by solvent displacement method and were physicochemical, *in vitro,* and aerodynamic characterized after their spray-drying procedure. Protamine NCs presented a size of around 200 nm, positive surface charge, and drug association of up to 54%. They were stable as a suspension under storage, as well as in biological media and as a dry powder after lyophilization in the presence of mannitol. The developed NCs presented a strong capacity to internalize and activate alveolar macrophages and showed good compatibility with red blood cells. Moreover, rifabutin-loaded protamine nanoparticles could be successfully incorporated in microparticles by co-spray drying with mannitol for the obtention of a dry powder with adequate aerodynamic properties. The developed ready-to-use pulmonary dry powder system holds great promise of interest for inhalable therapy of pulmonary tuberculosis.

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OP-06

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Influence of polymers and active substances on foam stability

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Foams are becoming increasingly attractive delivery systems in the field of dermatology due to their beneficial properties, such as easy spreading, pleasant skin sensation, and applicability in certain skin conditions.

Because of its applicability, the selection of proper stabilizing agents is a fundamental factor in the formulation of foams. One possible approach for enhancing stability is to delay the liquid drainage of liquid films from the foam structure, which can be accomplished by adding macromolecular polymers.

Examples of such polymers include xanthan gum, which is a widely used excipient in pharmaceutics. Hyaluronic acid is derived from natural sources and has moisturizing and water-retaining properties.

Our research aimed to investigate the effect of two popular polymers (xanthan gum and hyaluronic acid) as well as two potential dermatological active ingredients (dexpanthenol and niacinamide) on foam formation and foam stability.

Rheological amplitude sweep test, surface tension, microscopical investigations, and cylinder test were used to investigate foam formation. The stability of the foams was assessed using the rheological frequency sweep test and the spreadability test.

The addition of macromolecular polymers increased the stability of dermal foams. The rheological results were in correlation with the results of the spreadability and cylinder tests. Among the active substances, dexpanthenol promoted foam formation, while niacinamide had no measurable effect on foam structure. In conclusion, the combination of xanthan gum and dexpanthenol can be an ideal combination in terms of foam formation and stability.

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OP-07

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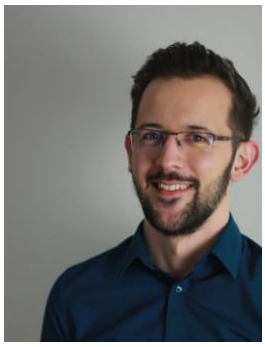

Investigation of the feasibility and efficiency of solvent-free co-grinding with different active substances

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Cyclodextrin (CD) complexation is widely used to improve the solubility of active pharmaceutical ingredients (API). The use of polymers as a third component can further enhance the beneficial effects of CDs. Production of CD complexes via solvent-free methods (e.g., co-grinding (CG)) is an environmentally and economically desirable technology. This work deals with the CG CD complexation of different APIs, the changes in physicochemical properties during the process, the in vitro evaluation of final products, and finally the comparison with different solvent methods.

For these reasons, we used Terbinafine Hydrochloride [1] and Fenofibrate [2] as model APIs and different types of amorphous CD derivatives with and without applying polymers as a third component. CG preparation methods were performed both manually and with laboratory mills. The products were systematically investigated in the solid phase by X-Ray Powder Diffractometry (XRPD), Differential Scanning Calorimetry (DSC), Thermogravimetry (TG), Scanning Electron Microscopy (SEM), Fourier-Transform Infrared spectroscopy (FTIR), Raman microscopy and in vitro dissolution, diffusion, and – for selected products – cytotoxicity studies.

With both APIs, amorphous products have been produced, as confirmed by XRPD, DSC, and TG studies. The intermolecular interactions were presumed by FTIR, and these results were supplemented by Raman spectroscopy if needed. Based on these, selected CDs were able to host the APIs as guest molecules, forming complexes. These presumed complexes were further studied by in vitro studies, showing better dissolution, modified diffusion, and cytotoxicity values. Overall, the results suggest that the preparation of CD complexes without solvent by co-grinding is easy to perform and the products obtained have similar improved properties as those prepared by solvent-based methods.

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OP-08

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Multifunctional biomass-derived and N-doped carbon quantum dots – the versatile nanoparticles for ion sensing with potential biological and pharmacological activity

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The aim of this study was to prepare, characterize and investigate the potential application of carbon quantum dots (CQD) derived from *Citrus clementina* peel. The prepared nanoparticles by hydrothermal synthesis using citric acid and amino acids of different complexity (Ala, Arg, Asn, Gln, Glu, Gly, His, Leu, Lys, Phe, Ser i Trp) represented model systems. The samples obtained from citric acid and amino acids Ala, Arg, His, Leu, Lys, and Trp showed great properties with calculated quantum yield (QY) from QY= 12.97% - 36.43% under investigated pH=7. Hence, these amino acids were selected for the biomass-derived CQD preparation from *Citrus clementina* peel. The results indicated the versatility among the prepared samples regarding optical, physical and chemical properties of nanoparticles, as well as on the biological activities, compared to the model systems. Furthermore, the best-performing samples from each series of synthesis were extensively studied regarding chemical (solubility, EDS), physical (AFM, FTIR, PXRD), optical (spectrofluorimetry, UV-Vis spectroscopy), biological and pharmacological properties. The biological activities of prepared samples were investigated by spectrophotometric methods of antiradical activity (DPPH method), inhibition of protein denaturation (bovine serum albumin and egg albumin), and biocompatibility/cytotoxicity was investigated on tumor cell lines (HeLa, NCI-H385, CaCo-2, D54). The samples were also utilized as fluorescent nanoprobe for selective and sensitive detection of Fe^{3+} ions and developed models were tested for the Fe^{3+} ion detection in real well-water samples. This research could be a good example of sustainable biomass waste utilization with potential for biomedical analysis and ion sensing applications.

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OP-09

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Preparation and characterization of binary systems with semisynthetic derivatives of β-cyclodextrin for dimethyl fumarate nasal delivery

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Relapsing-remitting multiple sclerosis is a chronic inflammatory disease of the central nervous system. Solid dosage forms in capsules of dimethyl fumarate (DMF) are currently used as first line treatment [1], [2]. However, the gastrointestinal side effects, the limited solubility and the low stability, limit its therapeutic efficacy. To overcome this issues, binary systems of DMF and semisynthetic derivatives of β-cyclodextrin (β-CD), in particular hydroxypropyl (HPβCD) and randomly methylated β-CD (RAMEB) were prepared with the aim to improve its bioavailability and allow its administration by the nasal route [3].

Complexes by kneading method, at 1:1 and 1:2 molar ratios, were prepared and characterized by means of differential scanning calorimetry (DSC) supported by FT-IR analyses in order to point out the solid-state interaction between the two components. Phase solubility studies were performed according to Higuchi and Connors method, with a concentration of CD ranging from 0 to 200 mM.

Stability studies have been performed in order to verify how much the presence of CD can influence the degradation process of the drug; the results within 14 days showed that the binary systems slowed down the DMF degradation process.

Solutions of DMF and the kneading products were freeze-dried, according to a design of experiment plan, to evaluate the effect of complexation on relevant stability aspects and quantify the presence of degradation products monomethyl fumarate and fumaric acid. RAMEB:DMF at 2:1 molar ratio seemed the most suitable system for DMF stabilization.

The present work highlights how CDs can be a valid tool to increase the water solubility and stability of the drug, with interesting perspectives in relation to a possible nasal application.

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OP-10

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Formulation of external dosage forms containing grape pomace as active ingredient

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The wine industry and the grape industry produce a large amount of by-products, grape pomace, which are proven sources of phenolic compounds with antioxidant and antimicrobial effects. For this reason, there has recently been an increasing interest in the use of these winemaking wastes [1,2].

The objective of our experimental work was to formulate external preparations that contained an extract made from grape pomace as a natural active ingredient. As pharmaceutical dosage forms, ointments and gels were formulated using penetration-enhancing surfactants and gel-forming substances. The different pharmaceutical forms were subjected to texture analysis, the results of which can predict the degree of bioavailability of the active ingredient. The release of the active substance from the carrier and its penetration through the membrane are determined using a Franz diffusion cell and a UV-VIS spectrophotometer. A cytotoxicity test was performed with 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) dye on a human keratinocyte (HaCaT) cell line to verify the biocompatibility of the compositions. The *in vitro* antioxidant capacity of the preparations was detected using the 2,2-diphenyl-1-picrylhydrazyl (DPPH) method, while the anti-inflammatory effect was detected using the human TNF-α ELISA Kit on the HaCaT cell line.

Based on the results of the conducted experiments, it can be concluded that the cream containing the sugar ester SP 70 surfactant and Transcutol HP penetration enhancer and solubilizer has a more favorable diffusion profile compared to the gel. In the case of the former, the bioavailability of the active ingredient approached 45% after 90 minutes. With the help of the MTT test, we determined that our preparations do not produce a significant decrease in cell viability, and their biocompatibility is adequate. Based on the results of the DPPH test, there is no significant difference between the antioxidant effect of the gel and the cream. Treatment with the cream reduced the amount of the proinflammatory cytokine TNF-α by 48%, while the gel reduced it by 36% compared to the control samples, which proves the significant anti-inflammatory effect of the preparations containing pomace when tested on the HaCaT cell line. Based on our results, it can be concluded that we managed to produce formulations with valuable effects from an industrial by-product, thereby making our Earth more sustainable.

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OP-11

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Development of a combined nanosystem as a dry powder inhaler for the treatment of pulmonary inflammations

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Many pulmonary diseases are listed as major death-causing diseases in the world, therefore, developing new treatments is a mounting need. Local delivery of drugs by inhalation has shown higher effectiveness with less systemic side effects. Mannitol is an osmotic agent used as a mucolytic to improve the clearance of mucus, and it is available in the market as a dry powder inhaler. Since respiratory inflammations are mostly engaged with mucus accumulation, we aimed to develop a combined nanosystem for inhalation by combining mannitol with a well-known non-steroidal anti-inflammatory drug (NSAID) that can be administered to fight pulmonary inflammation. This nanosystem can be used to target mucus-obstructive pulmonary diseases such as cystic fibrosis, bronchitis, and bronchiectasis. The formulation process was in two stages: (i) a top-down method (wet-media milling) was used to produce nanosuspension containing NSAID, (ii) followed by co-spray drying with mannitol. During the formulation, different mannitol ratios were studied. The powder characterizations were investigated in terms of particle size, zeta potential, distribution index and morphology. Moreover, powder yield and drug content were calculated. Physical, structural, and thermal analyses were carried out. Also, in vitro release test and in vitro lung deposition characterization were assessed. The resulting powder was roughly spherical in shape and nano in size which enabled a high lung deposition and showed an enhanced release profile. Hence, we successfully developed two active agents loaded in a single nanosystem as a promising combination therapy that has the potential to increase mucus clearance while simultaneously treating inflammation and improving patient adherence.

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OP-12

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Formulation of buccal films in Parkinson's disease

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Parkinson's disease (PD) is the second most common movement disorder [1]. The current treatment of PD focuses on replacing the dopamine level from an external source (Levodopa-L-DOPA) or on applying a dopamine agonist API, which can stimulate the dopamine receptors in the central nervous system. The advantages of buccal films include that the patients do not have to swallow the dosage form, so they can be used in the case of swallowing problems, which is a common symptom in this disease [2, 3].

In this work, we applied an anti-Parkinson's disease drug as an active agent in the polymer film system, which can also be used on the buccal mucosa to improve the success of the current Parkinson's therapy.

The buccal films were prepared at room temperature with the solvent casting method. To prepare the films, different polymers were used as film forming agents, and plasticizer, too. The physical properties, the interactions between the components of the films and the release of the API from the films were examined with different analytical methods (the permeation of the API into the buccal cells, biocompatibility, Raman mapping, etc.). The entire amount of the active ingredient is fast dissolved from most film compositions.

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OP-13

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Antimicrobial film coated catheters for intravesical drug delivery: factors affecting and future opportunities applying the quality by design concepts

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Over the years, catheter-associated urinary tract infections (CAUTI) have been one of the most common nosocomial infections and can also lead to several other complications. In this case, antimicrobial-coated catheters were developed, offering great potential for the prevention of catheter-related urinary tract infections and other complications. Intravesical drug delivery can treat CAUTI by introducing drugs directly into the bladder via a catheter. [1]

Although these new solutions exist for the intravesical delivery of drugs via antimicrobial film-coated catheters, some problems still exist in their treatment. Current urinary catheters are consistently failing to prevent or treat several issues such as - physical risks (CAUTI, sepsis and bladder cancer), lifestyle restrictions (restriction of clothing or daily activities) or psychological factors (changes in self-esteem and confusion). Catheter users must be kept at the centre of innovation, and any advances that can change clinical practice must consider biology, psychology and economics in addition to technology and physics.[2]

Therefore, it is very important to understand the general design constraints and their associated implications for the patients, to gain insight into future innovations.[3] To achieve our goal and to solve unmet clinical need, it is a must to address these issues by understanding the factors that affect catheter performance and the concept of quality by design to overcome these issues and provide better quality care to patients.

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OP-14

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Gum arabic as novel lysozyme carrier polymer

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Pharmaceutically, natural carbohydrate polymers have been increased attention, particularly in the field of drug technology, as carrier systems for the reason of their approved safety, biocompatibility, and biodegradability [1]. The present work aimed to prepare Gum Arabic (GA)-loaded Lysozyme via a simple solvent evaporation method. The prepared solutions/films had investigated for the minimum film formation temperature (MFFT), biological activity, tensile strength, mucoadhesivity, thickness, surface free energy (SFE), moisture content, FTIR spectra, water uptake capacity, disintegration and dissolution. The obtained films demonstrate good enzyme activity, novel mucoadhesive properties, and high tensile strength values with improved elasticity. Moreover, the moisture content and thickness were adequate regarding long-term stability and convenient oral applicability respectively. FT-IR reveals no serious chemical interactions. Furthermore, the prepared samples elicit high water-absorbing capacity and short disintegration time with two phases of enzyme release; an immediate release followed by a slow release pattern, which may be attributed to gel formation after a complete hydration. It concluded; GA presented an innovative biopharmaceuticals carrier system with novel properties such as superior mucoadhesivity and conformation stabilizing property on the incorporated enzyme.

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OP-15

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3D Printing of prolonged-release tablets containing felodipine

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3D printing technology is a modern manufacturing process, called additive manufacturing. The most common method used to manufacture 3D printed drugs is through fused deposition modeling (FDM). This uses drug loaded filaments previously obtained by hot melt extrusion (HME).

The objectives of this work were: to formulate polyvinyl alcohol-based filaments containing felodipine through HME technique, were the API remains stable at the extrusion temperature; to determine the maximum concentration of felodipine from which usable filaments can be obtained; to prepare 3D printed felodipine tablets through FDM using different filament types and infill percentages and to assess the *in vitro* release profile of felodipine from the prepared imprints.

Two types of filaments containing 5% and 15% felodipine were prepared. These showed appropriate properties to be used in 3D printing of tablets and the API remained stable during the HME and FDM process. Six types of tablets were 3D printed using the two filaments and three infill percentages for each filament type (10%, 50%, 80%). All the tablets were tested for the *in vitro* release of felodipine.

It was determined that increase of felodipine concentration from 5% to 15% in the filament used in 3D printing, decreases the release rate of the API during the *in vitro* dissolution test, most probably due to the low water solubility of felodipine. Also a higher infill determined a release prolongation, most likely due to the difficulty with which the dissolution medium penetrates through the free spaces of the imprint.

In conclusion felodipine was released in a prolonged manner over a period of 5 hours, from the 3D printed tablets.

OP-16

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Formulation and investigation of cyclodextrin polymer-based siRNA delivery systems

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Cyclodextrin polymers are widely used excipients mainly in the pharmaceutical industry for increasing the water solubility of lipophilic drugs, as well as monomeric cyclodextrin molecules.

Cyclodextrin-based systems are also used as siRNA delivery agents [1], so we aimed to investigate the siRNA carrying capacity of two cyclodextrin polymers, quaternary amino beta-cyclodextrin polymer (QABCDP) and amino beta-cyclodextrin polymer (NHBCDP) and the polyethyleneimine (PEI).

The different polymer solutions effects on Caco-2 cell proliferation were measured by RTCA method. The properties of the formulated polyplexes were investigated by dynamic light scattering technology (DLS) and zeta potential measurements. The cellular uptake of the polyplexes was investigated by confocal microscopy and flow cytometry.

Based on our RTCA studies, it can be stated that 50 and 100 nM polymer solutions did not affect cell proliferation. The complexation was successful, as the size and zeta-potential of both siRNA and polymer changed after complexation. Confocal microscopy and flow cytometry experiments revealed, that QABCDP polyplexes are taken up by cells and localized in the cytoplasm. Complexes formed with PEI were found along the cell membrane, even polyplexes formulated with NHBCD polymer were not taken up.

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OP-17

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Greener approach to the extraction of bioactive compounds from ginger (*Zingiber officinale)* herbal dust

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In the recent years, the usage of non-conventional extraction techniques, in order to obtain the highly valuable products that would be used in the various branches of industry, is expanding. Besides, in the line with improving sustainability, the intensive studies have been undertaken to convert various by-products and wastes into the highly valuable products. Therefore, this research integrates several different advanced eco-friendly extraction techniques (Supercritical CO_2 extraction, Ultrasound-assisted extraction, and Subcritical water extraction) with aim to utilize ginger (*Zingiber officinale*) herbal dust which represents by-product of the filter tea factory.

The ginger herbal dust is produced in the filter factory sites during the processing (grinding and fractionating) of the raw material, and it is generated on the level up to 20%. Ginger is highly valuated medical plant as it possesses several strong health beneficial effects such are antioxidant, anticancer, and anti-inflammatory. Gingerols, shogaols, and essential oil are the main responsible bioactive compounds enabling these effects.

Thus, the study evaluated the perspective of extraction process integration, as the efficient way for maximal isolation and exploitation of the ginger bioactives. The integration enabled the extraction of non-polar and low polar ginger bioactives in the first utilization phase, while second process stage is focused on the polar constituent's isolation. This way several different high quality products could be obtained, enabling maximal utilization of the starting material. The study evaluates the effect of process parameters on the each bioactive isolation. Chemical characterization of isolated compounds and extracts is investigated using HPLC and GCMS techniques.

OP-18

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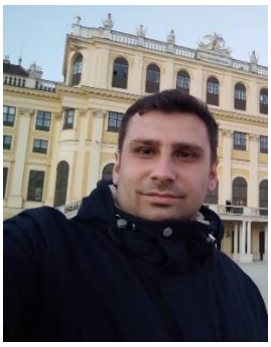

Development of nanoformulations for targeted delivery of obeticholic acid

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Nanosized materials such as nanospheres play an important role in personalized medicine. Their benefits include the possibility of targeting, enhanced bioavailability, reduced side effects, and site-specific controlled drug release. They can effectively encapsulate a wide range of therapeutic and diagnostic agents and deliver them into specific cells, reducing their non-specific action. PLGA is an FDA-approved, biocompatible, biodegradable tunable polymer with an excellent safety profile [1]. PLGA nanospheres are one of the most effective and safe polymeric nanoparticles for targeted delivery. The aim of this work was to develop PLGA nanoparticles with incorporated FXR agonist (obeticholic acid; OCA), for the targeted delivery into macrophages. Macrophages are key homeostasis regulators and their targeting could be exploited for the treatment of metabolic liver disorders. Desired nanoparticles for macrophage-specific delivery should be within a size range of 100 nm to 300 nm. Nanospheres were prepared using nanoprecipitation method and size, polydispersity, and zeta-potential were determined. Spectrophotometrical and HPLC assay for OCA was developed. OCA was extracted from PLGA nanoparticles using an ethanol/acetone extraction system. The dependence of the size and polydispersity index of PLGA nanoparticles from different types of water phases used during nanoprecipitation was studied. As a water phase, buffers with various pH ranges were used. For PLGA 50:50, with the increasing pH from 2.5 to 10, size decreases from 189 ± 3.87 nm to 42 ± 1.51 nm. For PLGA 75:25 with the increasing pH from 2.5 to 10, size decreases from 194 ± 2.27nm to 35 ± 0.74 nm. In vitro release of OCA from PLGA nanoparticles was studied. At physiological pH (7.3), around 86.63 % ± 0.61 % OCA was released from OCA-loaded PLGA nanoparticles in a 4 h study. At lysosomal pH (4.5) around 88.27 % ± 1.67 % OCA was released from OCA-loaded PLGA nanoparticles in a 355 h study.

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OP-19

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Development and characterization of gemcitabine lipobeads

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The entrapment of anticancer agents in drug delivery systems (DDS) for tumor targeting improves drug pharmacokinetics, toxicity, and efficacy. DDS development is a complex process which requires careful design and evaluation to ensure their safety and efficacy [1]. Lipobeads (LB) are structures consisting of a hydrogel core enclosed within a lipid bilayer [2]. LB borrow from liposomes the well-established preparation techniques, diversity of lipids to control lipid bilayer properties, biocompatibility of the lipid bilayer, ability to vary size and morphology, accessibility for attachment of various ligands, and efficacy of encapsulation of both hydrophilic and hydrophobic molecules [3]. Gemcitabine (GEM) is a chemotherapeutic agent that presents an increased hydrophilicity and short half-life, being an ideal candidate for entrapment in LB [4]. The aim of this study was the development and characterization of GEM-LB. The hydrogel core of LB was obtained using the precipitation/dispersion polymerization method and the lipid bilayer was obtained by thin film hydration method. An optimization study was performed using the Design of Experiments (DoE) methodology employed to study the impact of formulation factors (NIPA and PL concentration) on LB attributes. GEM-LB showed adequate characteristics in terms of size (< 200 nm), homogeneity (PDI<0.30), zeta potential (approx. – 30 mV) and drug encapsulation (13-67% GEM). The DoE showed the relation between the formulation factors and LB attributes. In conclusion this study reports the successful formulation and characterization of GEM-loaded LB using the DoE approach.

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OP-20

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Investigation of carboxylic acids possible application as linkers on the surface of titanate nanotubes for further functionalization

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The novel characteristics of newly manufactured nanomaterials and their tremendous potentials that could be invested in numerous fields make them highly presented in many aspects of the modern life. Recently, titanate nanotubes (TNTs) are creating a new chapter in the field of nanotechnology with their unique structure and preferred properties like high mechanical strength, good wettability and biocompatibility which make them one of the most promised nanoparticles that were recently discovered.

As many of the requested applications of these nanoparticles could be achieved through manipulation of their surface, this study aims to enhance or adapt some of their properties by surface functionalization. Different types of carboxylic acids (trichloroacetic acid, citric acid and acrylic acid) were investigated as possible linkers on the surface of TNTs for further functionalization later with additional molecules like polyethylene glycol (PEG) which supposed to improve aqueous solubility, prolong circulation time, reduce toxicity and prevent aggregation. The determination of functionalization success, and the nature of TNTs-acids interactions were examined basically by FT-IR spectroscopy. The results revealed that binding carboxylic acids to the surface could be done through weak interactions like hydrogen bonds but this type of functionalization is probably not enough as the functionalizing agent could detached easily. For this reason, stronger interaction is more preferable which will be investigated with acrylic acid using free radical polymerization reaction.

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OP-21

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Formulation and optimization of lamotrigine-loaded bovine serum albumin nanoparticles by using full factorial design

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Lamotrigine (LAM) as a BCS II class anti-epileptic drug with poor water solubility, is applied alone or in combination with other drugs to control seizures and to prevent the extreme mood swings of bipolar disorder in adults. The application of albumin nanoparticles means a promising approach for nose-to-brain delivery of LAM and to improve its bioavailability.

In this study, our aim to develop and optimize was LAM-loaded bovine serum albumin (BSA) nanoparticles (LAM-NPs) for nose-to-brain delivery via quality by design (QbD) approach. The main objective was the optimization of particle size (<250 nm) and encapsulation efficiency (>50%) of LAM-NPs using 3^3 factorial design. Then, the effect of different types of crosslinking agents (glutaraldehyde, glucose and 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride (EDC)) was studied on the selected formulations.

The optimized formulations were characterized regarding to particle size, PDI, zeta potential (before and after freeze-drying), encapsulation efficiency (EE%), *in vitro* blood-brain barrier permeability (BBB-PAMPA) and rapid equilibrium dialysis (RED) as well as *in vitro* drug release. The optimized LAM-NPs showed 168.9 ± 2.15 nm particle size with a zeta potential of -45.4 ± 0.43 mV and 0.078 ± 0.007 of PDI before freeze-drying, whereas 171.9 ± 0.3 nm particle size, -41.8 ± 0.7 mV zeta potential and 0.118 ± 0.007 of PDI after freeze-drying. The EE% was 81.94%. PAMPA result showed an increase in the permeability of LAM through the BBB. In addition, LAM-NPs showed higher drug both at nasal (pH=5.6) and at cerebrospinal fluid condition (pH = 7.4) in comparison to initial LAM.

The optimized formulation could be a promising for enhancing bioavailability of LAM through nose-to-brain delivery and to ensure sustained drug release.

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OP-22

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Dry powder inhaler of a miniprotein decoy for SARS-CoV-2 infection inhibition

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A novel approach that has been proposed for the treatment of SARS-CoV-2 infection is the use of a small protein which interacts with the receptor binding domain (RBD) of the spike protein, avoiding the virus entry into the human cells, thus preventing the multiorgan failure induced by the virus [1]. The aim of this project was the development and characterization of a dry powder inhaler containing the LCB1 small protein.

A quality by design approach has been applied for the formulation of the spray dried powder, investigating the effect of the critical material attributes and process parameters on the quality of the powder. The LCB1 was expressed as described in literature [2], and then was spray dried using a mini Spray Dryer B-290.

The lead powder, composed by 5.7% of LCB1, 15% of L-leucine, 78.3% of trehalose and 1% of buffer salts provided an emitted fraction (the fraction of the powder leaving the device after aerosolization) of 86.6% and a respirable fraction (the fraction of the powder with an aerodynamic diameter less than 5 µm) of 50.6%, parameters obtained using a Next Generation Impactor. In addition, it was evaluated whether the protein maintained its conformation, and ability to interact with the RBD. For this purpose, SDS-page, SEC and ELISA assay were employed, and they revealed no differences between the protein in the powder and the native one.

In conclusion, the process parameters adopted, combined with the addition of trehalose, favoured the respirability and structural integrity of LCB1 inhalation powder.

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The broadening horizons of pharmaceutical 3D printing – Simple strategies for complex formulations

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The undeniable potential of 3D printing in the pharmaceutical field has been highlighted due to the notable extent of research triggered by the possibility to deliver personalized drug products. We aimed to support the translation of fused deposition modeling into a flexible pharmaceutical dosage form manufacturing platform by providing simple strategies that enable the customization of the obtained products. Thus, we developed a tablet that allowed the immediate release of the drug due to two major factors. The first one is the unique design (honeycomb structure) that granted a high surface area to volume ratio, while the second one is the low polymer content of the filaments employed for the printing process. These findings were further applied to obtain a product of increased complexity, namely a tablet that assured the sustained release of the API. A bilayer tablet geometry was designed, consisting of a fragment with a honeycomb structure and another fragment with 100% infill. The former was destined to assure the immediate release of an API dose and it was fabricated using the previously mentioned drug-loaded filaments with low polymeric content, while the latter was considered to enable the slow dissolution of another API dose and was manufactured using a drug loaded filament with an increased polymeric fraction. Our investigations provided novel approaches that could further be used to bring the fused deposition modeling technique closer to real-life applicability in the pharmaceutical domain.

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OP-24

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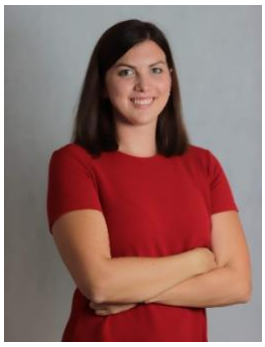

High-dose ibuprofen containing carrier-free dry powder inhalers for the therapy of cystic fibrosis

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Cystic fibrosis (CF) is characterized by inflammation, which contributes to lung damage. The nonsteroidal anti-inflammatory ibuprofen (IBU) significantly slows the progression of the illness. IBU should be taken in large doses, therefore inhalable particles could be beneficial to administer IBU directly to the lung.

We aimed to develop a carrier-free dry powder inhaler (DPI) system containing IBU. Inhalable powders were formed by wet milling and spray drying. We hypothesized a spherical shape, enhanced drug release, and optimal aerodynamic properties to provide a local treatment for CF.

The IBU was milled in a high-performance planetary mill. Solid particles were formulated from the microsuspension by spray-drying (Büchi Mini and Nano Spray-dryer). The following investigations were implemented: laser diffraction, scanning electron microscopy, density, solubility, X-ray powder diffraction, differential scanning calorimetry, dissolution test (Watchglass/PTFE disk assembly), and aerodynamic investigation (Andersen Cascade Impactor).

Wet milling led IBU to become micronized. The particle sizes of the spray-dried formulations were in the required pulmonary size range. The shape of the particles appeared spherical with hollows. The rheology measurement presented low density values. The structural analysis revealed that IBU becomes amorphous. The formulations demonstrated enhanced solubility and drug dissolution. The in vitro aerodynamic investigation showed proper lung deposition.

We successfully formulated high-dose ibuprofen containing DPIs. We aimed to improve the water solubility by reducing particle size. The particle size, shape, and density properties resulted in an efficient in vitro aerodynamic behavior. The compositions could offer a novel therapy for CF.

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OP-25

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Bioaccessibility of phenolic compounds from grape pomace extracts

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Grape pomace is the solid residue of the winery, rich in phenolic compounds. Phenolic compounds have great potential to exert multiple pharmacological effects when they reach the target site (intestine) in the body where they can be absorbed. Since the bioavailability of phenolic compounds in the body is relatively low, their encapsulation can increase their bioaccessibility in the digestive system and eventually improve the bioavailability. In this work, a phenolic rich-extract from pomace of Cabernet Franc variety was encapsulated by ionic gelation with 3 % sodium alginate as excipient and 0.25 M calcium chloride as curing agent. Also, 5 % gelatin and 1.5 % chitosan were used as additional excipients in combination with sodium alginate. The freeze-dried hydrogels were subjected to simulated digestion *in vitro* during the oral, gastric and intestinal phases to evaluate the bioaccessibility index of individual phenolic compounds from grape pomace extracts.

Encapsulation efficiency was improved by 31.3 % and 40.4 % with the addition of gelatin and chitosan to sodium alginate, respectively. The highest release of was observed in the intestinal phase. Ten individual phenolic compounds were identified by UHPLC analysis, of which five were phenolic acids (gallic, 3,4-dihydroxybenzoic, syringic, ellagic, and o-coumaric acid) and the other five were flavan-3-ols (epicatechin, catechin, epicatechin gallate, gallocatechin gallate, and procyanidin B2). The highest bioaccessibility index is observed at the end of the intestinal phase for o-coumaric acid in all samples (386.5 - 766.3 %).

OP-26

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Optimization of design and printing parameters of solid microneedle array produced by SLA printer

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Microneedles are widely investigated in both pharmaceutical and cosmetical sciences. These sub-millimetre structures tend to pierce the stratum corneum and deliver pharmaceutically active ingredients with poor absorption properties. Different forms of microneedles are present from the 1990's but the production cost was incredibly high due to the expensive and hardly accessible technologies. Additive manufacturing helped to step over this gap.[1] 3D Printing of Microneedle Arrays (MNA-s) in laboratory scale has become an affordable for many research groups throughout the globe. By having access to a Projet 6000 HD Stereolitographic printer (3D Sytems, Rock Hill, USA) we focused on the optimization of directly printed MNAs. Over the 4 generation of the printed MNAs the influence of printing and design parameters to the final MNA product was investigated. Conical geometry was chosen for this study due to its circle-based shape and simplicity. Our aim was to optimize 3 crucial geometrical parameters: the needle base diameter, needle height and the needle tip diameter. However, varying the printing parameters did not show significant improvement in the 3 mentioned geometrical parameters, the design parameters showed strong influence. It was observed that the real base diameter could not be set under 320 ±9 µm-s. Nominal and real needle heights showed a linear correlation. Using the equation of correlation in the 1000 – 1500 µm range, the needed nominal parameter can be set to reach the desired nominal height. The equation may be used on a broader spectrum – further measurements required. Needle tip diameters showed an inverse relationship with the needle height parameters. Altogether, by determining the correlation between the investigated setting parameters and obtained geometrical parameters MNAs with desired design can be produced and applied for further medical purpose.

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OP-27

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Determination of design space for direct pelletization using ProCepT granulator

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The high shear granulator is one of most common devices used as an alternative pelletization technique for extrusion spheronization to produce pellets with good flowability, compressibility and bulk density. It is also a rapid process with minimum cost in one step [1-3].

This study aimed to determine the process design space for pellet preparation in a single-step process by using a ProCepT granulator. Experiments were performed for formulations that contained microcrystalline cellulose, mannitol and water as granulating liquid according to many different designs of experiment (DOE) which were full factorial design and central composite design to study the effects of five process parameters. The process resulted in pellets with good yield within a narrow size range, with the required aspect ratio, acceptable hardness and friability. The process design space process was estimated by using the combination of the best process parameters, where the pellet quality parameters were within acceptable values.

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OP-28

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Preparation and optimization of hydrophobic ion pairing complex of lysozyme

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Hydrophobic ion pairing (HIP) has emerged as an approach to enhance the encapsulation and loading of water soluble peptides/proteins in their micro and nanocarriers. The hydrophobicity of these molecules is increased through a reversible electrostatic complexation with an oppositely charged amphipathic molecule at suitable pH [1,2].

This work aims to investigate different factors that affect the preparation of HIP of lysozyme (LYZ) with the surfactant sodium dodecyl sulphate (SDS). Based on the literature and previous experience, risk assessment as one of the quality by design tools has been employed to explore a variety of process parameters and material attributes that affects the formation of such complex. This initial assessment shows that the pH and molar ratio of the SDS:LYZ are the highly ranked influential factors. In this study, optimum molar ratios were determined for this complexation at selected pH values by titration using particle charge detector (PCD). The titration experiment revealed variable optimum of SDS:LYZ molar ratios at different pH environment which was confirmed by series of complexation experiments that showed high yield of the hydrophobic complex. Furthermore, the integrity of the peptide was successfully reserved as it remained biologically active after complexation and drying process.

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OP-29

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Formulation of sustained release sodium alginate beads loaded with antidiabetic drug containing polymeric micelles

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Polymeric micelles offer multiple beneficial properties such as the increase in drug release and permeability as key factors determining drug bioavailability. However certain therapies do not require all these benefits. Antidiabetic drugs are usually administered in extended-release formulations meaning that the drug release must be controlled to avoid burst-like effect. A solution to this technological requirement could be the application of sodium alginate beads which would prolong the drug release whist retaining the enhanced permeability effect of polymeric micelles.

The aim of this current study was to develop a sodium alginate bead formulation containing metformin as hydrophilic drug embedded in the biopolymeric matrix and pioglitazone which would be encapsulated inside the polymeric micellar core.

At first, Quality by Design based risk assessment procedures were performed on multiple level, regarding the polymeric micelle optimization and the sodium alginate bead formulation process. The optimization was performed at multiple levels via factorial designs corresponding to the crucial steps of the preparation method. The polymeric micelles were characterized via dynamic light scattering and the encapsulation efficiency was evaluated. The swelling and drug release profile were investigated regarding the sodium alginate beads.

The polymeric micelles are in the appropriate colloidal size range in monodisperse distribution with high encapsulation efficiency above 80%. Based on the factorial design, the optimal composition regarding the sodium alginate beads were found with high swelling ratio and an extended drug release up to 24 hours.

In conclusion, the sodium alginate bead formulation loaded with polymeric micelles could be an effective and value-added alternative of currently commercialized extended-release tablets.

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OP-30

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Oregano essential oil polymeric micelles-based hydrogel as a dermal drug delivery system: *in vitro* and *in ovo* assessment

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The essential oil extracted from *Origanum vulgare* var. *vulgare* (OEO) is intensively studied for novel therapeutic dermatologic applications, such as an alternative approach for acrochordons, also known as skin tags. Innovative cutaneous formulations are developed in order to improve bioavailability and stability of essential oils. This study aims to investigate an OEO cutaneous drug delivery system - a polymeric micelle-based hydrogel (OEO-PbH). Scanning electron microscopy (SEM) analysis indicated a regular aspect after the encapsulation process, while *in vitro* release studies showed a sustained release of the essential oil from the polymeric micelle-based hydrogel. As revealed by the *in ovo* assessment, using the chick chorioallantoic membrane (CAM), OEO-PbH did not cause irritative effects on CAM and was well-tolerated. In the same time, the angiogenic process was modulated at concentrations as high as 200 µg/mL. Hence, the optimal particle characteristics and release properties of OEO-PbH, its non-irritative character and the modulatory effects on angiogenic process on CAM indicate the potential of OEO-PbH as a safe and biocompatible approach for dermatologic applications such as skin tags.

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OP-31

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Application of albumin-based nanoparticles integrated with thermo-responsive gel systems for enhanced nasal delivery of amoxicillin

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Amoxicillin is recommended as the first-line therapy for the treatment of Acute Bacterial Rhinosinusitis (ABR). However, orally administered amoxicillin is highly related to many systemic adverse effects and has poor bioavailability.
Therefore, this study aimed to prepare topical nasal formulation of amoxicillin utilizing albumin-based nanoparticle combined with thermo-responsive nanogel system to enhance the residence time in nasal cavity and prolong drug release.
Gelling temperature investigations revealed that all formulations (21 – 23% *w/w* Poloxamer 407) were suitable for nasal application (sol-gel transition at ~35°C). Particle size measurement revealed a nanosized preparation (< 200 nm) was obtained. Moreover, the mucoadhesive strength and drug release properties exhibited that the formulation with 21% *w/w* Poloxamer 407 could be considered optimal for effective nasal application. Antibacterial activity studies showed that the optimized *in situ* thermogelling nasal nanogels of amoxicillin preserved its effectiveness in terms to inhibit the growth of five common ABR pathogens in comparison to 1 mg/mL amoxicillin aqueous solution as positive control.
In conclusion, the preparation of Amoxicillin albumin-based nanoparticles incorporated into *in situ* thermo-responsive gel systems appeared as a potential candidate for local antibiotic therapy in the nasal cavity.

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Chitosan-Casein complexes as carriers for bioactive compounds

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Complexes based on the physical interactions between polyelectrolytes, and especially the ones based on biocompatible materials, have attracted the attention of the researchers in the medical and the pharmaceutical fields. Due to their biodegradability and lack of immune response in the human body, they can be applied as carriers for wide diversity of compounds with different pharmaceutical aim and purpose. By encapsulation of active pharmaceutical ingredients into polyelectrolyte complexes their solubility could be significantly improved along with their bioavailability. Another advantage of this process is the alternated kinetics of the release process, leading to more efficient therapy for shorter period of treatment and by applying lower doses of drugs. By combination of two types of bioactive compounds (e.g. polyphenol and pharmaceutical agent), a synergetic effect could be observed and this can be an approach for addressing the problem with antibiotic resistance and improving the anticancer treatments. Casein and chitosan are both weak polyelectrolytes from natural origin. Casein is a major milk protein with polyampholitic nature, which enables it to form complexes with both polyanionic and polycationic compounds. Chitosan is polycationic material with antimicrobial, mucoadhesive and blood clotting properties, making it highly preferable material for wound dressing and/or local application of pharmaceutical agents. In the present study, chitosan-casein polyelectrolyte complexes at different stoichiometric ratios are obtained and their possible application for delivery of one water soluble and one water insoluble compound is investigated.

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Abstracts

Flash presentations

FP-01

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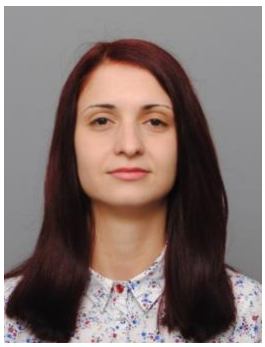
Development of poly-ε-caprolactone nanocarriers for nasal administration of idebenone



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Idebenone (IDE) is a synthetic analogue of coenzyme Q10 developed for the treatment of neurodegenerative disorders. After oral administration, IDE undergoes excessive first-pass metabolism, so that less than 1% reaches the circulation. To overcome this, IDE could be incorporated into a suitable delivery system for an alternative route of administration. The aim of the present work was to develop an optimal model of poly-ε-caprolactone nanoparticles as potential carriers for nasal administration of IDE. Nine models of placebo nanoparticles were prepared by solvent evaporation method under different process parameters. Polymer with different molecular weight (14,000, 80,000 and 145,000 g/mol) was used. Polysorbate 20 and Poloxamer 407, alone and in combination, were used as emulsifiers at different concentrations to obtain a stable emulsion. Particle shape, size, and polydispersity index were determined by laser diffraction and transmission electron microscopy. The resulting structures were spherical in shape and their size distribution depended on the type of emulsifier. The average particle size ranged from 188 to 628 nm. The effect of both studied variables was established. Optimal models of appropriate size for nasal administration were selected for inclusion with IDE. Three models of IDE-loaded nanoparticles were developed and the effect of molecular weight on the entrapment efficiency was investigated. Increased entrapment efficiency was found when higher molecular weight poly-ε-caprolactone was used.

FP-02

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Formulation and investigation of buccal mucoadhesive films for improving buccal absorption

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Oral mucosa is simply accessible and highly vascularized, which means direct access to the systemic circulation, bypassing the liver first-pass effect, in addition to further advantages. Therefore, mucoadhesive dosage forms – especially films – are a promising delivery alternative to various drugs [1]. Among the mucoadhesive film-forming polymers, chitosan is a good candidate with several advantages. Chitosan is a safe, biocompatible, and biodegradable polymer with adequate mucoadhesive properties, in addition to permeation enhancer properties, which could be improved by polymer salification with ascorbic acid [2, 3].

The main aim of our research is to investigate the permeation of different active pharmaceutical ingredients with different log P through the buccal mucosa using chitosan ascorbate-based mucoadhesive films. Films will be prepared by the solvent casting method. In vitro mucoadhesion, tensile strength, film thickness, drug content uniformity, and other film properties will be evaluated.

Another aim of this work is to get to know the process parameters and material attributes influencing the studied parameters, and to optimize the composition of the films based on the results by factorial design. Ideal buccoadhesive films should be safe, nontoxic, with good mechanical strength, immediate adherence to the buccal mucosa, and should achieve controlled drug release in addition to adequate patient compliance [4].

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FP-03

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Extraction of Pistacia lentiscus seeds growing in Algeria and determination of the fatty acid composition

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In Algeria, the fruits oil of Pistacia Lentiscus is used by the population in traditional medicine in many ways, as an anti-burn, antidiarrheal, antifungal, antimicrobial, and antioxidant.
The aim of this work is to learn more about the fatty acid composition of fruits oils of P. lentiscus in order to confirm results of previous works in other countries, and to compare them with ours. This study was performed on oil extracted from mature fruits of Pistacia lentiscus harvested from Northeast Algeria. Extraction was done by the semi-artisanal (pressing) method [1], that was proposed to improve the yield and the quality of oil. The black fruits of P. lentiscus has the yield of 19.38%. Fatty acid composition was determined by gas chromatography-mass spectrometry (GC/MS); It revealed that the three dominant fatty acids found are: Oleic acid C18:1 (44.11%), linoleic C18:2 (22.61%) and palmitic C16:0 (22.13%). Various studies reported that linoleic and oleic acids, which are important constituents of P. lentiscus fixed oil, have potential antibacterial properties and are attributable to its unsaturated long-chain [2].
Further studies are needed for the valorization of unsaponifiable matters in the oil and also to determine composition of the carotenoids, tocopherols and phenolic compounds.

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FP-04

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y-F_2O_3 nanoparticles as a mediator for photothermal therapy – preparation, characterization and heating ability in muscle tissue phantom

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Photothermia is an experimental antitumor therapy in which nanoparticles convert infrared laser irradiation into heat to produce local hyperthermia. Nanoparticles that mediate this therapy must have biocompatibility, acceptable conversion efficiency, and good accumulation and distribution in tumor tissue. Iron oxide superparamagnetic nanoparticles (SPIONs) are a good candidate that also have various medical applications. The magnetic properties determine their potential as a theranostic agent and as a tool for hybrid therapy (such as combining magnetic hyperthermia with photothermia).

The aim of the present work was to develop SPIONs as a conversion agent for photothermal therapy, and to investigate their heating ability. Co-precipitation method was used to prepare y-F2O3 and casein was selected as the stabilizing polymer. The process parameters were varied in order to produce particles of suitable size and lower tendency to agglomerate. Particle size was determined by scanning electron microscopy, transmission electron microscopy and dynamic light scattering. Mössbauer spectroscopy was used to study the crystal structure and magnetic properties. The heating profile of the nanoparticles under laser irradiation was observed trough aqueous suspensions of y-F_2O_3 nanoparticles in distilled water as well as trough phantom muscle tissue . A thermal camera was used to monitor the temperature changes and temperature gradient in the samples. The increase in temperature was considered sufficient for mild hyperthermia and showed a concentration dependence.

FP-05

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Polymorphic behavior of hemisynthetic triglyceride-based ingredients intended for pharmaceutical products.

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Triglycerides are lipid molecules widely used in the pharmaceutical industry [1], especially in the production of vaginal and rectal dosage forms [2]. Vaginal formulations have a great interest in drug delivery for both local and systemic therapies. Since the vagina allows the release of higher concentrations, minimize the systemic side effects when aiming at a local treatment, and avoid the first hepatic passage and the gastrointestinal side effects [3].
Hemi-synthetic glycerides, principally triglycerides constitute the lipidic matrix used for the formulation of pessaries nowadays. These triglycerides are generally mixtures of three fatty acid molecules with an even number of carbon atoms and one glycerol molecule. In the solid state, they are organized in different crystalline or polymorphic forms (three crystalline varieties α, β and β' in order of increasing stability) hence their very complex thermal behavior [4].
This study focuses on the thermal and structural study of triglycerides pharmaceutical excipients in order to determine their crystalline forms using two techniques (X-ray diffraction "DRX" and differential scanning calorimetry "DSC").
The findings showed the presence of three polymorphs for the samples studied, with a predominance of the β' polymorphic form.

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FP-06

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Laser applications in pharmaceutical industry

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Laser technology has made rapid progress over the last decade in many different fields, and its applications in the pharmaceutical industry are increasing day by day. The most common applications that can be mentioned currently in this context is the encoding information on conventional dosage forms for anti-counterfeiting or personalization purposes and the use of laser in three-dimensional (3D) printing, especially Selective Laser Sintering (SLS), and this technique relies briefly on directing laser towards powder bed and drawing a 3D model by sintering the powder particles on the surface layer by layer. SLS is superior to other techniques in some features, the most important of which are: a solvent-free process and it does not require pre-production of the filaments as with Fused Deposition Modelling (FDM). On the other hand, this technology suffers from a major drawback, which is the concern about the degradation of drugs by the used laser.

From the foregoing, this research aimed to study the effect of various lasers on different active pharmaceutical ingredients and polymers to determine the suitable and stable materials and settings for SLS 3DP technology, and furthermore to reveal the applicability of sintering in the tailoring of the drug release of conventional solid dosage forms.

FP-07

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Clinical validation of video-otoscopy based medical device for remote diagnosis of ear complains

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Telemedicine refers to delivering remote clinical services over a distance, which offers increased access to health care, improved health care outcomes, reduced costs, and it is an emerging trend in many fields of health care specially, during or after a pandemic era. Sharing data, photos etc. can be useful among doctors (specialist – GP), between doctor and patient or for quick communication among other health care providers and all these aids fall under the regulation of medical devices [1].

Otoscopy is a routine methodology, and it is an essential step in clinical examination for ear complaints as the key step in diagnosis; while video-otoscopy shows potential as a safe and effective method for detecting the presence of ear disease in a wide range of healthcare settings [2,3].

Performance of video-otoscopy telemedicine application (software; classification based on the MDR is Class IIa) is evaluated in an opened randomized clinical trial; differences and similarities of the diagnosis and the treatment variables were studied depending on the type of diagnosis (remote or present).

Clinical evaluation is a central concept in Medical Device Regulation, in order to ensure that the medical device performs within its intended purpose and that it is safe and effective.

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FP-08

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Design of *in situ* gelling systems containing natural ingredients for treatment of periodontitis

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Periodontitis is an infectious and inflammatory disease resulting in destruction of periodontal tissues and ultimate bone loss. Anaerobic gram-negative and gram positive bacteria are responsible for progression of this disease. A number of antibiotics are currently used as first line therapy in dentistry. Essential oils are also reported as effective anti-inflammatory and analgesic agents against bacteria residing in oral cavity. Long term oral administration and side effects associated with high dose of antibiotics are the main hurdles to treat periodontal disease effectively. Hence, this study aims to formulate antibiotics and essential oils containing nanostructured lipid carriers (NLC) loaded in an in situ gelling system carrying hydrophilic antibiotics for periodontal cavity administration. The system is based on sodium alginate as the gelling agent and hyaluronic acid as a co-polymer. NLC will be prepared by homogenization method and then optimized formulation will be loaded in an ion activated *in situ* gelling system. The formulation will be investigated for particle size, poly dispersity index, zeta potential and entrapment efficiency of NLC. Characterization of the formulation such as drug content, solubility, pH, gelling characteristics, injectability, bioadhesiveness will be performed. Antimicrobial efficacy studies will provide a clear picture of effectivity of natural extracts against bacteria. In vitro release studies will depict the sustain release of active content from NLC and NLC loaded formulation. FTIR, DSC of gelling system will ensure the stability of system and compatibility of formulation contents. Conclusively, an in situ gel system with enhanced, prolonged, and sustained antibacterial activity will be obtained for the management of periodontitis.

FP-09

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Goat whey as a coating/protective material in the spray drying process of grape pomace extract

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Goat whey, the former "unusable" by-product of the dairy industry, today finds its application in a variety of industries and processes, including the spray drying process, all while promoting the concept of a circular bioeconomy. Grape pomace is a byproduct of the wine industry, that contains a significant amount of polyphenolic compounds, which have already been proven to have numerous beneficial effects on human health. In our study, liquid grape pomace extract was spray-dried using goat whey powder as a coating material. The effects of goat whey on the preservation of polyphenolic compounds from grape pomace extract after spray drying and during different phases of the simulated enzyme-free digestion process *in vitro* were studied.

The encapsulation efficiency of polyphenolic compounds from grape pomace extract during the spray drying process varied from 61.89 % up to 97.34 % depending on the drying temperature, feed flow, and the proportion of coating material. Up to 76.52 % (127.54 mg $_{\text{TOTAL POLYPHENOLIC COMPOUNDS}}$/g dry matter $_{\text{POWDER}}$) of the total amount of polyphenols in spray-dried powder, was released in the small intestine throughout the process of *in vitro* simulated digestion without enzymes.

FP-10

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Optimization of SMEDDS orodispersible tablet formulation

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Self-microemulsifying drug delivery systems (SMEDDS) have numerous advantages, as formulations developed for solubility enhancement of poorly water-soluble drugs, though their solidification is still challenging the field of pharmaceutical technology. Lately, large progress was made by improving the flow properties of self-microemulsifying powders by wet granulation, using high-shear and fluid-bed equipment [1, 2]. Obtained granules exhibited the flow characteristics suitable for further tableting, yet low hardness and large mass of single dose SMEDDS tablet proved to be a major drawbacks. Thus, the aim of the present study was to optimize the amount of SMEDDS in tablets, while obtaining appropriate mechanical properties. Additionally, produced SMEDDS tablets were characterised regarding disintegration time, friability, self-microemulsifying and *in vitro* dissolution properties.

Within this research, different tableting mixtures were prepared, containing 25-50 % of SMEDDS granules. Increasing granule amount found to have a negative influence on SMEDDS tablet hardness, which was in agreement with our expectations, given the granules' high liquid SMEDDS content. An adequate hardness ≈100 N was achieved only with the tablet formulation containing 25 % of granules, in addition to lamination occurring with other tableting mixtures, due to use of high compression forces. Produced tablets preserved self-microemulsifying properties of liquid SMEDDS, as upon dispersion in water media the average droplet diameter was <100 nm. Due to short disintegration time (<2 minutes), prepared orodispersible SMEDDS tablets exhibited similar *in vitro* dissolution profile as corresponding SMEDDS granules, with complete drug release achieved within tested time interval.

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FP-11

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Modeling of film coating thickness with use of artificial neural networks

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The thickness of the coating uniformity depends on the properties of the coating solution (e.g., solid content, viscosity, and surface tension), and a multitude of process parameters (e.g., spraying rate, air temperature, pan speed, atomization and air pressure pattern, nozzle orientation, and distance from the gun to the tablets) [1,2].

Our study decided to use the new and revolutionary approach in the field of pharmaceutical coating processes called the artificial neural network (ANN) by using the neural networks toolbox derived from the Matlab software. The experiments were performed using tablets of Alfuzosin Chlorhydrate as a model filler and an aqueous solution of Surelease as a polymer with different contents. The various parameters that can affect coating thickness, such as spray rate, air pressure, solid content, speed of the drum, pan loading, and time of coating, were studied. The properties of the coated tablets were evaluated using the ANN, and both the parameters of the coating process and the properties of the coated tablets were used as the basis for optimization, as well as the choice of the optimal structure of the ANN model. It was found that the best neural network architecture had 18 neurons in the hidden layer with a mean square error of 6.131 $*10^{-3}$ and a determination coefficient of nearly 1. The relative importance of each independent variable was quantified using the Garson equation. In this study, the spray rate was found to have the highest impact on the properties of tablets.

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FP-12

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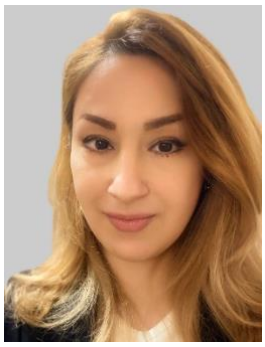
3D printing microneedle patch as drug delivery system on the skin



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To enhance drug delivery through the skin barrier, the design, and fabrication of 3D printing microneedle arrays, are considered an innovative drug administration technology to deliver APIs. There are more types of microneedles such as solid, hollow, dissolving, or coated [1-2].
In my Ph.D. work, by means of additive manufacturing technique, stereolithography [3], we plan to design and fabricate solid microneedles with different parameters and combine them with *in situ* film forming system. This is a 2 steps application system when first the solid microneedle creates channels through the epidermis which increases the API permeation from the film-forming system.
Another goal of my work is to coat microneedle arrays with film forming solution and investigate the API penetration into the skin in this way.
The investigation methods for the characterization of 3D microneedles are tests of mechanical behavior by Texture Analyzer, piercing test, investigation of coating integrity and thickness, *in vitro* release and permeation studies using Franz diffusion cell, and investigation of API permeation depth by Raman spectroscopy.
The final aim of my work is to use a semi-synthetic flavonoid as API with a strong inhibiting effect on melanoma cancerous cells [4] and investigate this drug delivery system *in vitro* and *in vivo*.

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FP-13

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The influence of bioprocessing of grape pomace by *Rhizopus oryzae* on the chemical composition and extractability of phenolic compounds

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Biological treatment of grape pomace (variety Frankovka) by *R. oryzae* was carried out in laboratory jars and a tray bioreactor under solid-state fermentation (SSF) conditions. The aim of the work was to investigate the influence of SSF on chemical composition with the special focus on the recovery of phenolic compounds from grape pomace. *R. oryzae* transformed grape pomace causing the weight loss by 17.58 % after 15 days-treatment in laboratory jars. The content of ash, protein, sugars, and certain elements (P, K, Fe, Pb, As) decreased, while the content of lignocellulosic components (cellulose, hemicellulose, lignin) and fats increased during the 15-days treatment in laboratory jars and a tray bioreactor.

The content of total phenolic compounds, total flavonoids and total extractable proanthocyanidins decreased by 47 %, 43 % and 62 % in the laboratory jars and 34 %, 21 % and 42 % in the tray bioreactor after 15 days of fermentation. Biological treatment with *R. oryzae* had a positive effect on the extractability of 10 of the 21 individual phenolic compounds quantified by the UHPLC method. The content of gallic acid, ellagic acid, *p*-hydroxybenzoic acid, syringic acid, vanillic acid, 3,4-dihydroxybenzoic acid, *p*-coumaric acid, epicatechin gallate, quercetin, and resveratrol increased 1.1- to 2.5-fold.

FP-14

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Application of pharmacopeia tests on an Algerian Bentonite to assess its potential suitability as a pharmaceutical substance

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The purpose of this study is to explain the phenomena that occur at the level of the raw structure of Ca-Bentonite from the Hammam Boughrara deposit in the region of Maghnia (northwest Algeria) by applying pharmaceutical tests to assess their potential suitability as materials in pharmaceutical applications.

The pharmaceutical industry is increasingly interested in bentonite for its high cation exchange capacity as well as for its exceptional swelling rate. These are naturally hydrated phyllosilicates containing clayey minerals of the smectite group (Montmorillonite).

The structure of the Montmorillonite consists of a stack of sheets (composed of two tetrahedral layers and between them an octahedral layer), each of which is separated by an interfoliar space. The Montmorillonite network is negatively charged, mainly due to isomorphic substitutions within the structure that create a permanent load deficit offset on the outside of the sheet by compensating cations [1].

Before use in the pharmaceutical industry, raw bentonite samples must be conform to recommendations and directives of pharmacopeia. A set of technological tests were investigated with the samples, such as pH, sedimentation volume and swelling capacity.

The pH test reveals the type of stacking of the sheets following the hydration of the montmorillonite. The sedimentation test evokes the interactions that occur during hydration without any external action. The swelling capacity indicates the type of network formed as a result of thermal activation of cation exchange.

In view of the results obtained, Montmorillonite could be applied to formulate various drug delivery systems to control and/or improve the pharmaceutical properties of drugs, including solubility, dissolution speed, and absorption.

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FP-15

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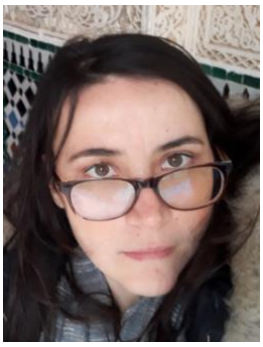

Solid lipid particles as carriers for sustained drug release

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Solid lipid particles (SLP) are carrier systems based on a high melting point lipid as a solid core. They are derived from an oil-in-water emulsion by exchanging the liquid lipid (oil) with a solid lipid. SLP has emerged as an alternative colloidal carrier among all colloidal carriers due to its advantages. Recently, SLP has been widely used for skin delivery due to their safe interaction with skin layers, and improved skin permeation. However, encapsulation of hydrophilic drugs into the hydrophobic lipid of SLP is a major problem because during the production process the drug tends to partition towards the aqueous phase.

The aim of the present study was to enhance the skin delivery of metformin by making SLP containing metformin using the rotor-stator homogenization method. To achieve the optimum skin delivery for metformin, the effects of the ratio of two surfactants (soy lecithin: tween 60) on particle properties and their performance were investigated. *In vitro* drug release test was performed under skin conditions on phosphate buffer saline pH 7.4.

Results showed that the highest entrapment efficiency of 86.70% was obtained for formulation with a low concentration of soy lecithin and high concentration of tween 60 whereas the smallest particle size (0.3µm) was obtained for the formulation with the highest soy lecithin concentration and low concentration of tween 60. The drug release profiles show that the percentage of free metformin that passes through the membrane reached 100% in the first hour. The release profile of the SLP exhibited a rapid release in the first hour of around 30% of the encapsulated metformin. The release then slowed, to plateau at around 35% by the 2 hours. The drug release from lipid formulations was prolonged remarkably in comparison with the drug solution.

FP-16

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Formulations for subcutaneous administration: Exploring the influence of monoclonal antibody concentration and addition of excipients on their viscosity

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In the field of biopharmaceuticals, the current trend is oriented towards subcutaneous (SC) administration, which is faster, more convenient and comfortable for the patient thus, leading to increased compliance and cost-effectiveness. In contrast, the most limiting factor in SC application is the relatively small injection volume (≤2 mL) that requires highly concentrated protein formulations (above 100 mg/mL). The development of such formulations is associated with many challenges, such as ensuring protein stability and formulation injectability, where the latter is an obstacle resulting from increased viscosity of formulations for SC application [1].

The objectives of the study were: (i) to investigate the effect of monoclonal antibody (mAb) concentrations on sample viscosity; and (ii) to explore the potential of arginine as viscosity reducer agent in water-based mAb solutions.

First, the calibration curve of viscosity (m-VROC®, RheoSense, USA) as a function of mAb concentration was constructed and an exponential increasing trend was demonstrated. The lowest mAb concentration that exceeded the viscosity threshold for SC administration (i.e. 20 mPa·s) was 150 mg/mL. At this concentration potential viscosity reducing agent arginine (25mM) was tested and resulted in effective viscosity reduction for 0.46 factor. Then viscosity reducing effect of arginine was evaluated at different mAb concentrations where a relation was demonstrated. Namely, arginine lowered the viscosity more effectively with increasing protein concentration.

The main conclusion is that arginine is a promising candidate that enables viscosity reduction in mAb SC formulations, whereas further strategies to overcome this challenge of highly concentrated mAb formulations should be discovered.

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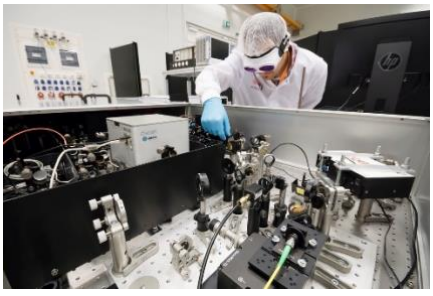
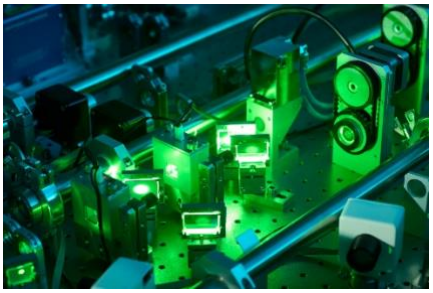


- Energy research – from solar panels to artificial photosynthesis
- High energy photonics
- Information technology, materials science and nanoscience
- THz technologies and applications



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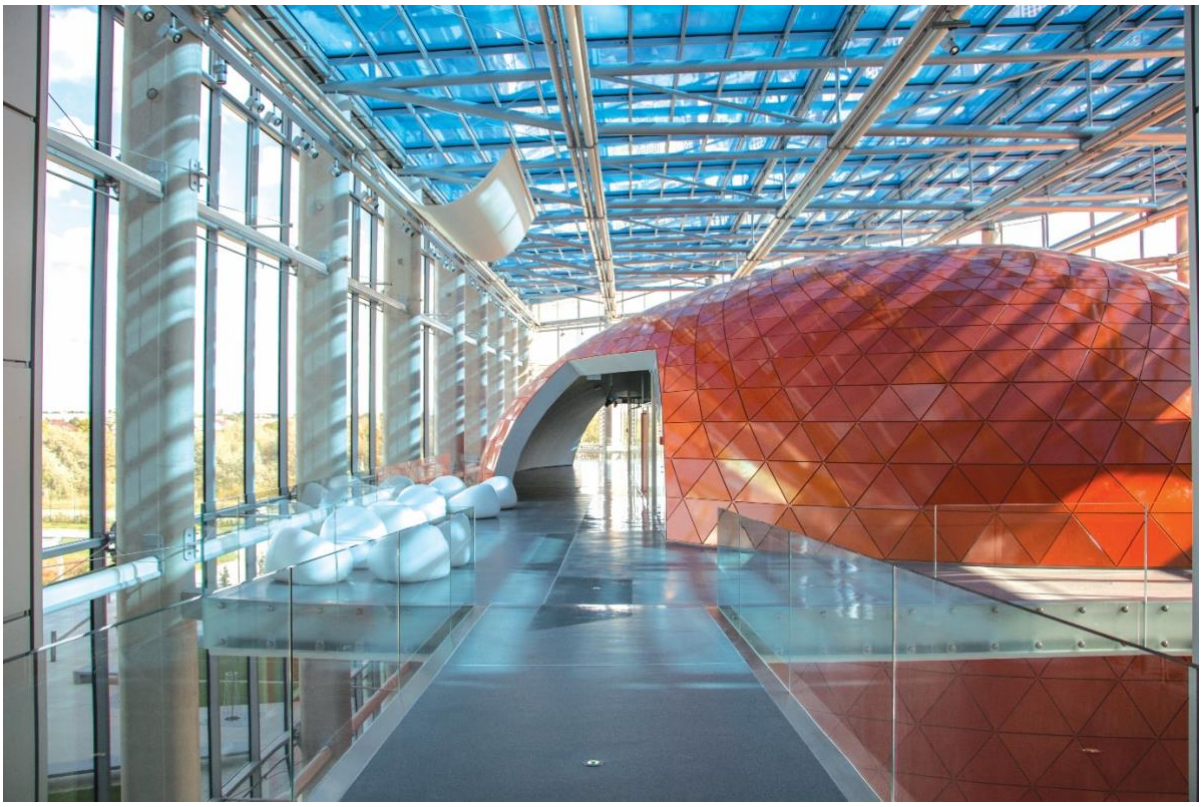

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