HELSINGIN YLIOPISTO
HELSINGFORS UNIVERSITET
UNIVERSITY OF HELSINKI
FARMASIAN TIEDEKUNTA
FARMACEUTISKA FAKULTETEN
FACULTY OF PHARMACY

UNGAP

NORDIC POP

Advanced spectroscopic analytical methods and new technologies in drug delivery

Combined UNGAP & NordicPOP hands-on Training School.

Helsinki, October 23-25, 2019

doctoral programme in drug research

MATRENA
Doctoral Programme in Materials Research and Nanosciences

ORION

SOCIETAS PHARMACEUTICA FINLANDIAE

Dear participant,

It is a pleasure to welcome you to the Training School, ***Advanced spectroscopic analytical methods and new technologies in drug delivery***, in Helsinki, from 23 to 25 of October 2019, organised by UNGAP COST Action, NordicPOP, and the Faculty of Pharmacy, University of Helsinki. The training school is also supported by the University of Helsinki Doctoral Programs in Drug Research (DPDR) and Materials Research and Nanosciences (MATRENA), the Finnish Pharmaceutical Society, and Orion Corporation.

At this training school we will be introducing you to selected modern and emerging techniques applied to study drug delivery, in some cases with an emphasis on drug absorption from the intestinal tract. We have combined Raman and non-linear optical imaging, X-ray diffraction analysis, surface plasmon resonance (SPR), and nuclear imaging (single photon emission computerised tomography (SPECT)), together with several nanotechnology based drug delivery platforms, with the overall aim of providing new opportunities for understanding and optimising drug delivery. These technologies are presented by experts in their fields, who will describe not only how the technologies work, but also their potential to answer important questions in the field of drug absorption and beyond. You will also gain hands on experience with instrumentation representing one of the analytical technologies, through laboratory practices specially developed for this training school. You will have the opportunity to directly ask specialists about the basis, means and scope of these technologies, as well as technical and operational details.

The training school is organised with introductory lectures on October 23, which will provide some theoretical background on the various technologies, followed by hands on laboratory exercises in Raman, SPR and SPECT on October 24. A presentation and discussion session will end the Training School on October 25.

We wish you a productive and enlightening event!

Sincerely,

The Organising Committee

Helsinki 2019

ORGANISING COMMITTEE

Doc. Arturo García-Horsman (University of Helsinki, chairperson)

Doc. Tapani Viitala (University of Helsinki)

Doc. Leena Peltonen (University of Helsinki)

Doc. Mia Siven (University of Helsinki)

Dr. Jukka Saarinen (University of Helsinki)

Prof. Clare Strachan (University of Helsinki)

Prof. Gøril Eide Flaten (University of Tromsø – The Arctic University of Norway)

Dr. Mikko Koskinen (Orion Pharma Oyj)

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PROGRAMME

Wednesday 23rd October – Lectures (room 2012, Biocentre 2)

9:00-9:10 Welcome words and opening

9:10-10:40 Advanced diffraction and imaging methods (cont.) (Chair: Assoc. Prof. Clare Strachan)

- 9:10-9:40 Small angle X-ray scattering: Theory, working principle and application for characterization of nanoparticle-based drug delivery systems (Prof. Ben Boyd)
- 9:40-10:10 Single photon computer tomography, SPECT (Dr. Arturo García-Horsman)
- 10:10-10:40 Animal nuclear imaging: Animal imaging in drug formulation development: where's the dose (gone)? (Prof. Clive Wilson)

10:40-11:00 Coffee break

11:00-12:30 Advanced spectroscopic methods (Chair: Doc. Leena Peltonen)

- 11:00-11:30 Raman spectroscopy: Theory, working principle and applications in drug delivery (Assoc. Prof. Clare Strachan)
- 11:30-12:00 Coherent anti-stokes Raman scattering (CARS) microscopy: Theory, working principle and applications in drug delivery (Dr. Jukka Saarinen)
- 12:00-12:30 Surface Plasmon resonance spectroscopy: Theory, working principle and application for characterizing drug-excipient interactions and cell uptake of nanoparticles (Doc. Tapani Viitala)

12:30-13:30 LUNCH (Unicafe, Biocentre 1)

13:30-15:00 Nanotechnology in drug delivery (Chair: Doc. Tapani Viitala)

- 13:30-14:00 Lipid based nanocarriers (Prof. Gøril Eide Flaten)
- 14:00-14:30 Drug nanocrystals (Doc. Leena Peltonen)
- 14:30-15:00 Nanomedicines for oral drug delivery applications (Assoc. Prof. Hélder Santos)

15:00-15:20 Hands-on practical work planning

15:20-18:00 Posters and pizza (2nd floor lobby, Biocentre 2)

Thursday 24th October – Practical work

8:30-12:30 Parallel sessions I

- Group 1: Surface plasmon resonance spectroscopy – Real-time label-free nanoparticle cell uptake (Viitala Group) (Room 2044b, Biocentre 2)
- Group 2: Raman spectroscopy (Strachan and Saarinen group) (Room 1078, Biocentre 2)
- Group 3: Animal nuclear imaging – Tracer preparation (Garcia-Horsman group) (Room 1019, Biocentre 3)

12:30-13:30 LUNCH (Unicafe, Biocentre 1)

13:30-17:00 Parallel sessions II

- Group 1: Surface plasmon resonance spectroscopy – Stabilizer/excipient drug interactions (Viitala group) (Room 2046, Biocentre 2)
- Group 2: Coherent anti-Stokes Raman scattering (CARS) microscopy (Strachan and Saarinen group) (Biomedicum Imaging Unit, Meilahti Campus)
- Group 3: Animal nuclear imaging (Garcia-Horsman group) (Room 1019, Biocentre 3)

19:00 Dinner (Ravintola Sipuli, Kanavaranta 7, Helsinki)

Friday 25th October – Presentations and discussion

9:00-12:00 Preparation of group presentations (rooms 1014, 2012, 3045c, 4055a, all Biocentre 2)

12:00-13:00 LUNCH (Unicafe, Biocentre 1)

13:00-14:50 Group presentations and discussion (room 2012, Biocentre 2)

14:50-15:00 Closing

doctoral programme in drug research

MATRENA Doctoral Programme in Materials Research and Nanosciences

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Societas Pharmaceutica Finlandiae

SPEAKERS

Prof. Ben Boyd, Monash University, Australia

Prof. Ben Boyd is a physical chemist with PhD from the University of Melbourne (1999). After industry experience in the explosives and pharmaceutical industries, he commenced an academic position at Monash Institute of Pharmaceutical Sciences. His group focusses on colloidal and structural aspects of lipids, lipid self-assembly and pharmaceutical systems and are active in developing new characterization approaches for lipid and solid state systems. His group has published over 200 papers receiving over 9000 citations. He is a Fellow of the Controlled Release Society and was the recipient of the AAPS Lipid-based Drug Delivery Outstanding Research Award. He is currently President of the Australian Colloid and Interface Society and is Co-editor of the Journal of Colloid and Interface Science and Editor for Asia for Drug Delivery and Translational Research.

Doc. PhD. García-Horsman, University of Helsinki.

Dr. García-Horsman received his PhD in Biochemistry in 1990 (National University of Mexico). He has obtained research experience as scientist in a number of institutions, including University of Illinois at Urbana-Champaign, USA (1990-1994); National University of Mexico (1994-1995); and University of Helsinki (1995-2000). He also served as Senior Researcher at the University of Eastern Finland (2000-2004) and was a Group Leader at the Prince Philip Research Centre in Valencia, Spain, as Ramón y Cajal fellow (2004-2007). Since 2007, Dr. García-Horsman has served as Group Leader at the Regenerative Pharmacology Unit, at the Faculty of Pharmacy, and as head of the SPECT/CT Imaging Core Unit of the same faculty, at the University of Helsinki.

Dr. García-Horsman has developed expertise in a range of disciplines including physical chemistry, biochemistry, molecular biology, chromatography and protein purification, enzymology, and spectroscopy. He also has experience in transgenic mice, and he has specifically developed two catechol O-methyl transferase gene (COMT) mutant mouse strains and one prolyl oligopeptidase (PREP) knockout strain. Currently, Dr. García-Horsman is developing further expertise in molecular imaging and computerized tomography. Indexed in the Web of Science (Clarivat Analytics), Dr. García-Horsman has 83 publication, has been cited 2,480 times (without self- citations), with an average of 32.87 citations per publication and an h-index of 26.

Research Professor Clive G Wilson, Ph.D., E.F.A.P.S., F.C.R.S., Strathclyde Institute of Pharmacy & Biomedical Sciences, Glasgow, United Kingdom

Clive Wilson is a Research Professor at Strathclyde University and was the J. P. Todd Chair in Pharmaceutics until his formal retirement. He remains an active member of staff heavily involved in global pharmaceutics projects in the USA and Europe across industry and academic groups. He is a past-president of the European Union Federation for Pharmaceutical Sciences (EUFEPS). He serves on Senate of EUFEPs with interests in European training policy and education.

Major areas of research have been the study of the behaviour of drug formulations in man. With John Hardy in Medical Physics at Queen's Medical Centre and later Professor Davis in Pharmacy at Nottingham, he pioneered applications of scintigraphy in the study of drug absorption following oral, nasal, pulmonary and ophthalmic delivery. These activities continued at Strathclyde and his research group covers projects in novel polymer chemistry, oral bioavailability, microfabrication of implants for ocular drug delivery and drug-loaded stents. This is added to his long-standing and continuing interest in gastrointestinal physiology applied to the study of oral dosage forms and too many topics in ocular physiology and ophthalmic drug delivery, especially with Queen's University Belfast. He has published more than 190 papers, seven books and over 100 reviews and book chapters and has supervised 67 Ph.D., 1 D.Eng. and 1 M.D. student. He was made a Fellow of the Controlled Release Society in June 2010 and an Eminent Fellow of the Academy of Pharmaceutical Sciences in September 2011. In November 2017, he was awarded doctor honoris causa of Semmelweis University, Budapest, Hungary.

Prof. Clare J. Strachan, University of Helsinki

Dr. Clare Strachan is Associate Professor at the University of Helsinki where she heads the Formulation and Industrial Pharmacy Unit within the Division of Pharmaceutical Chemistry and Technology, Faculty of Pharmacy. Her group's research largely focuses on the pharmaceutical application of vibrational spectroscopy and imaging, including in solid state and formulation analysis. She has a particular interest in the application of Raman, CARS and other forms of non-linear optical imaging to understand and optimise drug behaviour at different stages of the drug lifecycle (e.g. manufacturing, storage, administration and drug delivery).

Dr. Strachan completed her PhD in 2005 on the spectroscopic characterisation of solid-state drugs at the School of Pharmacy and Department of Chemistry, University of Otago, New Zealand. During this time she introduced non-linear optics to the pharmaceutical field and was also based at TeraView Ltd and the Cavendish Laboratory, University of Cambridge, UK, where she employed terahertz spectroscopy for solid-state pharmaceutical analysis. She has collaborated and consulted with academic, industrial, and regulatory partners in Europe, the USA, Asia and Australasia. She has published approximately 115 articles in international scientific journals as well as several book chapters, and has supervised about 18 PhD students. She was director of the international Pharmaceutical Solid State Research Cluster (PSSRC) from 2016-2018, and is an Honorary Associate Professor at the School of Pharmacy, University of Otago.

University Lecturer (PhD Pharm) Jukka Saarinen, University of Helsinki

Jukka Saarinen is currently working as a lecturer in pharmaceutical chemistry in the Division of Pharmaceutical Chemistry and Technology at the University of Helsinki. He finished his doctoral degree in spring 2018 and his PhD thesis was entitled: “Non-linear Label-free Optical Imaging of Cells, Nanocrystal Cellular Uptake and Solid-State Analysis in Pharmaceutics”. His research is focused on non-linear optical imaging in pharmaceutical applications including cells, nanoparticle-cell interactions, dosage forms and solid-state analysis. In addition to non-linear optical imaging, his research also includes spontaneous Raman microscopy, especially in biological analysis. Such analysis include for example the studies of nanoparticle-cell interactions, cancer resistance development and visualization of diseased tissue such as in Alzheimer’s disease. One of the publications he co-authored was awarded “Most Outstanding Pharmaceutical Research Article 2017/2018” by the Finnish Pharmaceutical Society. He has also authored book chapters about spectroscopic imaging.

Doc. PhD. Tapani Viitala, University of Helsinki

Dr. Viitala has an extensive background in physico-chemical characterization of interfaces and nanoscale layers in close connection to biophysics and nanotechnology. He received his PhD in 1999 from the Department of Physical Chemistry at Åbo Akademi University in Turku, Finland. After his PhD he worked 10 years at KSV Instruments Ltd/Biolin Scientific Oy, a company providing high-tech, precision analytical instruments for nanoscale study of interfaces. He returned to academia in January 2010 as a senior researcher at University of Helsinki and held an Academy Research Fellow position until 2015. He is currently a co-group leader, together with Dr. Alex Bunker, of the Pharmaceutical Biophysics research group at the Faculty of Pharmacy at University of Helsinki. His main research focus is to utilize model surfaces, living cells, nanoscience and –technology, and various physicochemical characterization techniques (e.g. surface plasmon resonance, quartz crystal microbalance and time-resolved Raman spectroscopy) to improve the mechanistic understanding of drug and nanoparticle action and delivery. He has published 79 internationally peer-reviewed articles, 8 non-refereed scientific articles and conference proceedings, co-authored 7 invention disclosures and 2 patents, and supervised 6 PhD theses and 16 Master´s theses.

Prof. Gøril Eide Flaten, Drug Transport and Delivery research group, Department of Pharmacy, UiT The Arctic University of Norway, Tromsø, Norway

Flaten’s research is focusing on permeability of drug through different absorption barriers, both in respect of understanding the mechanisms and factors affecting the permeability of compounds and formulations, as well as means to improve the permeability through use of advanced (mainly lipid based) drug delivery systems. Her research experience spans from development of liposome based models for permeability screening, formulation of poorly

soluble drugs, characterisation of nanoparticulate delivery systems and biopharmaceutical characterisation of delivery systems, to *in vivo* biodistribution studies of liposomal formulations in mouse tumour models.

Gøril Eide Flaten is currently working as professor in pharmaceutics and biopharmaceutics and has her background as pharmacist with a PhD in pharmaceutical technology from UiT in 2007. She further did a post doc in School of Medicine, UTHSCSA, San Antonio, Texas in 2008-2009.

Flaten is the leader of work package “Products” in the NordicPOP consortium and member of the MC in the UNGAP consortium. Flaten is also member of several national scientific committees in addition to both national and institutional committees for the bachelor and master programs in pharmacy.

Doc. PhD. Leena Peltonen, University of Helsinki.

Dr. Leena Peltonen has educational background both in physical chemistry and in pharmacy. She received the doctoral degree in 2001, and the title of docent in 2004 from the area of pharmaceutical technology in the University of Helsinki, Finland. After her dissertation she initialized the nanotechnological research in the Division of Pharmaceutical Technology, University of Helsinki. Since 2003 she has been in a position of university lecturer in Division of Pharmaceutical Chemistry and Technology, Faculty of Pharmacy, University of Helsinki. Her main research areas are drug nanocrystals and related analytical techniques, dissolution and solubility testing and physical pharmacy. She has published 85 peer-reviewed scientific articles, 10 book chapters and 2 patents.

Prof. Hélder A. Santos, University of Helsinki

Dr. Santos is Associate Professor in Pharmaceutical Nanotechnology, Head of Division of Pharmaceutical Chemistry and Technology, Head of the Nanomedicines and Biomedical Engineering Group, and Director of the Doctoral Program in Drug Research at the Faculty of Pharmacy, at the University of Helsinki. He is also a Fellow Member of the recently established Helsinki Institute of Life Science (HiLIFE), and former World Portuguese Network Adviser for Science. Dr. Santos research interests include the development of nanoparticles/nanomedicines for biomedical applications. Prof. Santos is co-author of more than 270 publications (+7200 citations; h-index = 52), 25 book chapters and more than 235 conference proceedings/abstracts. He has given over 150 invited talks at prestigious conferences, universities and summer schools around the world. Dr. Santos has received a number of prestigious awards and grants, such as the "Talent Prize in Science" attributed by the Portuguese Government in 2010, the European Research Council Starting Grant in 2013 and ERC Proof-of-Concept in 2018, the Young Researcher Award in 2013 attributed by the Faculty of Pharmacy at the University of Helsinki, the Academy of Finland Award for Social Impact in 2016, and honour nomination for the USERN Prize in Biological Sciences in 2017.

PRACTICAL INFORMATION

AIRPORT – HELSINKI

Helsinki-Vantaa Airport service area map

There are several ways to transfer from the airport to Helsinki Central Railway Station.

BY TRAIN *most convenient*

The trains run very frequently (approx. every 10 min). The journey from the airport to the Central Railway Station with **I train** takes about 27 minutes, and with **P train** about 32 minutes.

All trains are modern, low-floor trains providing easy access for passenger with luggage, prams or wheelchairs.

At the airport, **I trains** leave from track 2, and **P trains** from track 1.

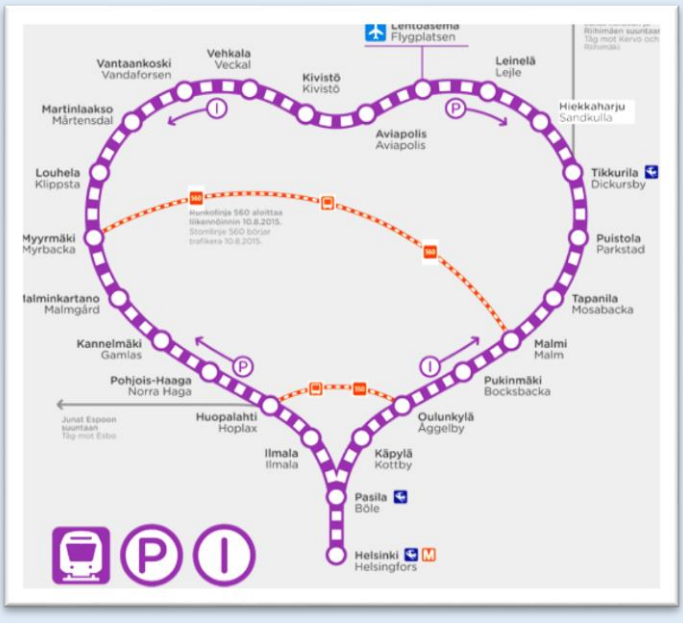
At the Helsinki Central Railway Station, **I trains** mainly leave from tracks 1-3, and **P trains** from tracks 16-18.

Trains run from around 5 am to 0.30 am (next day).

P trains run clockwise, and I trains run counter clockwise.

P train: Helsinki – 13 stops – Airport – 10 stops – Helsinki

I train: Helsinki – 10 stops – Airport – 13 stops – Helsinki



BY BUS

HSL bus 615 or 415 *(specially if traveling between ~ 1am and 4am)*: The bus trip to the Central Railway Station takes about 40 mins. The buses run every 30 minutes 24h/day. They leave, at the airport, from the station in front of the Terminal 2 (see map above). The regular bus ticket price is 4,60 € at single ticket machine (located between arrivals hall 2A and Arrivals hall 1, and at the train platform). Bus drivers also sell single tickets (6,50 €).

You can also take a branded Finnair bus that takes around 30 minutes to get to the central railway station. The bus leaves from T2 and makes only one stop before the railway sation at Hesperia Park (8 min walk to Töölö Towers). The trip with Finnair bus costs 6,80 € (from about 5 am to 12 pm, see time table here)

TICKETS *cover transfers to all HSL services – train, bus, tram, and metro – within 80 mins*
ABC regional ticket is required for journeys from Helsinki city center to the airport and vice versa.

You can purchase your ticket:
1. HSL ticket machine. There are HSL ticket machines at the train station entrance in the corridor between the T1 and T2 terminals, in the baggage claim hall in T2 and at bus stops;
2. HSL app;
3. R-kiosks all around the city;
4. Bus driver (more expensive);
Tickets are not sold on trains.

Click here **for detailed timetables of public transport between Airport ⇔ Helsinki**.
OTHER SERVICES

Taxis are always available at the airport exits and at the Helsinki Central Railway station. Phone number: 0100 0700

Taxis will take around 30-50 min from the airport to Töölö Towers. They cost is around 50 €. The price may vary depending on the taxi company.

There are also shared taxi services: Airport Taxi Helsinki-Vantaa or Airport Taxi Yellow Line, they charge around 35-45 €/person, look for the booths inside the airport terminal.

Uber is also available in Helsinki. Download the Uber app on Google Play or App Store for more information.Helsinki public transport

ONE TICKET FOR ALL MODES OF TRANSPORT

Helsinki region has an integrated public transport ticket system. HSL's tickets are valid on public transport services in Helsinki, and in its surrounding regions.

The HSL area is divided into four zones and ticket prices are based on the distance traveled, i.e. on the distance from the center of Helsinki. Helsinki, Espoo, Vantaa and Kauniainen form zones A, B and C, while Kerava, Kirkkonummi, Sipoo and Siuntio are in zone D.

You must buy a ticket for all the zones you will be traveling through.

A few tips:

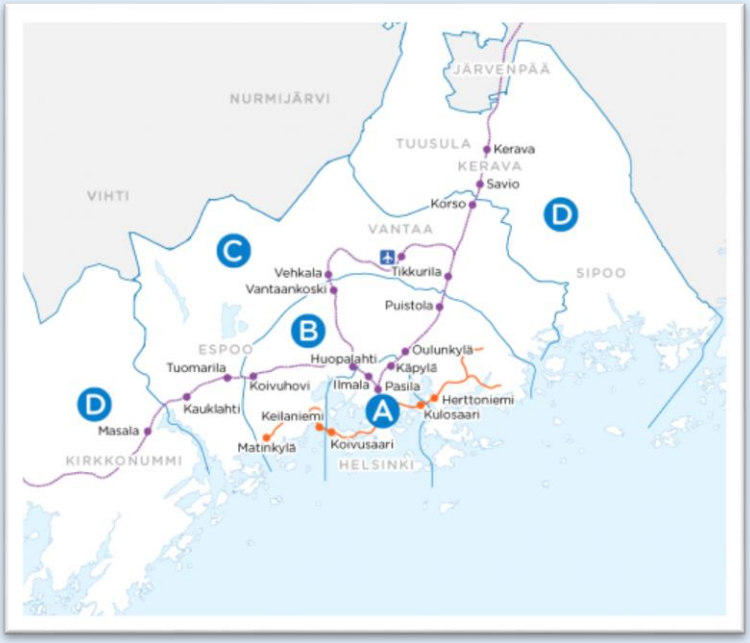
- The same tickets can be used for traveling on buses, trams, the Metro, commuter trains and the ferry to Suomenlinna.
- You can also transfer from one vehicle to another with the same ticket.
- Single tickets are available from bus drivers, ticket machines or HSL app, as well as in advance from R-kioski or several other sales points.

Discover the Helsinki region by public transport

The best sights in Helsinki are accessible by bus, tram or the Metro.

A Helsinki internal ticket takes you to the Linnanmäki amusement park, Seurasaari outdoor museum or Villa Aino Ackté. Trams are also ideal for city sightseeing. For more sightseeing attractions, please, click here.

With a Helsinki internal ticket you can travel to the Suomenlinna sea fortress by ferry from Kauppatori (Market Square) and Katajanokka. You can also reach the harbors easily by public transport.



The easiest way to purchase single use and multiday tickets, as well as to check timetables and route options, is to download the HSL app https://www.hsl.fi/en/app. Please note tickets cannot be purchased on trains, trams or the ferry, and are more expensive if purchased from bus drivers. Please see the public transport website at https://www.hsl.fi/en for more information.

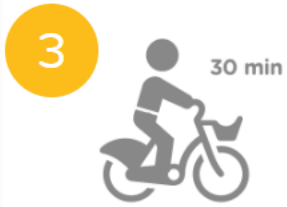
You can also refer to the site https://www.hsl.fi/en/information/how-use-public-transport/visitors for more information on routes and maps.

CITY BIKES

If you are into biking, **City Bikes** is also a good option to move around the city.
Helsinki has an excellent cycling route network.

You can purchase a daily pass for 5€ or a weekly pass for 10€.

How to do it:

	Register **Pay for a daily, weekly or annual pass here.** **You will be given a personal cyclist ID and a PIN code for collecting your bike.**
	**Collect** Find the nearest available bike. You can see the stations and bike availability on a map here. Type the personal cyclist ID and a PIN code on the display. Wait for the beep and off you go!
	**Ride** You can do as many rides as you want, up to 30 minutes each. Extra charges apply for longer journeys. Adjust the saddle height, check the brakes and get going. Keep a good attitude and follow the traffic rules.
	**Return** Return the bike to any city bike station. When the bike is secured to the rack and the bike says OK for a successful return process, your responsibility for the bike is over. You can return the bike to a station with no free space if “Return” can be chosen on the bike screen.

SOURCE: HTTPS://KAUPUNKIPYORAT.HSL.FI/EN

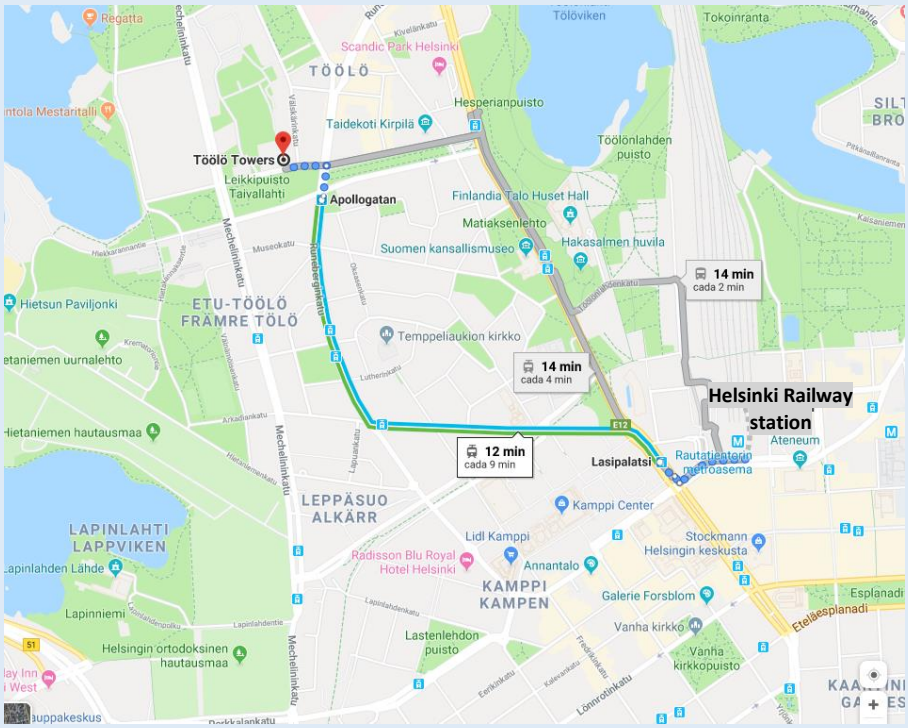
HELSINKI – VIIKKI CAMPUS

The main venue will be Biocenter 2, at the University of Helsinki Viikki Campus, Bioscience Park. Street address: Viikinkaari 5.

Viikki campus can easily be reached by public transport within the greater Helsinki area. For example, the number 78 bus regularly runs from the central railway station (platform 1) in the city centre to the teaching location Viikki Biocentre 2 (Viikinkaari 5) (bus stop name Viikin biokeskus) and the number 70 bus runs from close to Töölö Towers (bus stop name Apollonkatu at Runeberginkatu 23) to Viikki campus (bus stop name Viikki). Viikki campus is located in Zone B and the city centre (including Töölö Towers) is located in Zone A. We recommend purchasing a single AB-zone multi-day ticket (€24 or €28 for 5 or 6 days, respectively, on the HSL mobile app or from ticket machine), which allows unlimited public on transport within the A and B zones (bus, train, tram, and ferry to the island fortress, Suomenlinna).

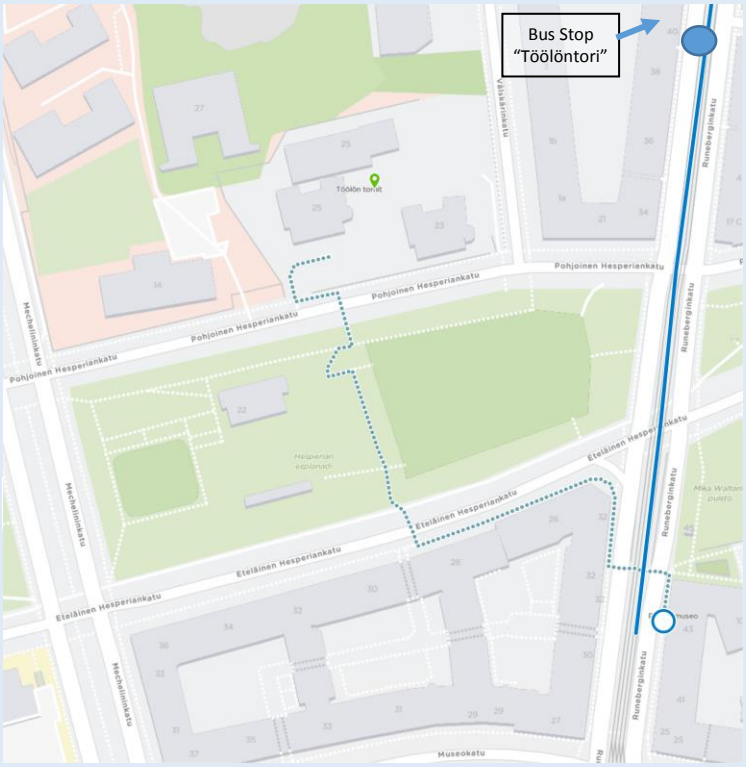
TÖÖLÖ TOWERS

Töölö Towers (you can google-map them with this name). They are relatively close to the central railway station, in Helsinki City centre. They are around 1,7 km from the railway station (25 min walk), where you can take tram 1 or 2 northwards: from the tram stop “Lasipalatsi” (one block away from the railway station), to the stop “Apollonkatu”. Töölö Towers are under 200 m ahead and to the right (see map below).



Travelling between Viikki and Töölö Towers

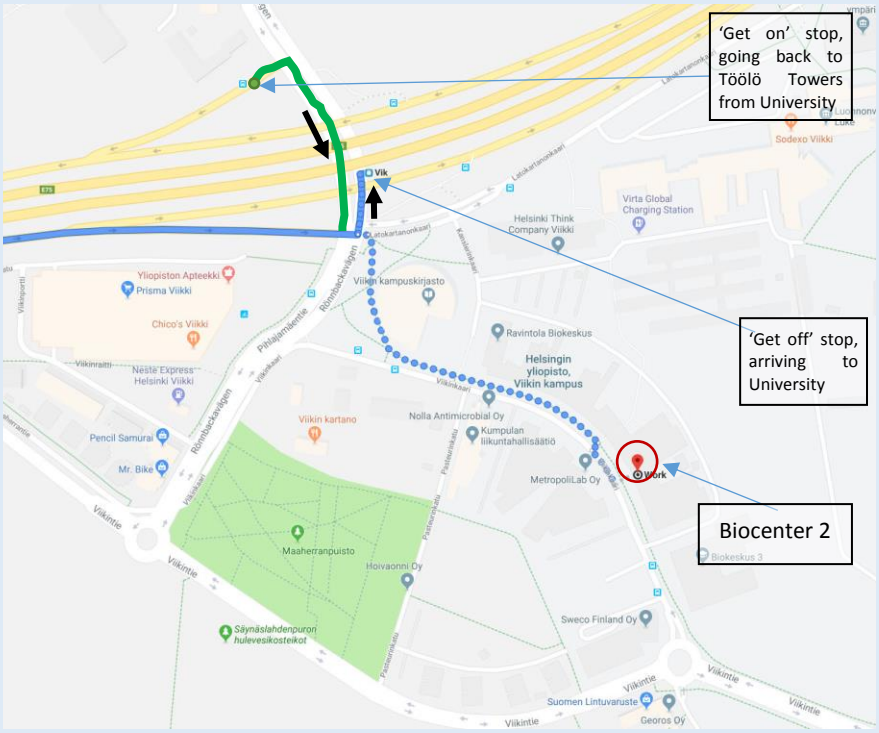
Walk from Töölö Towers to Bus 70 stop “Apollonkatu”



Bus 70 Malmi (Malm) Northbound,
Stop: (H1307) Apollonkatu
Monday –Friday time table
(times are estimates)

Hour	min
05:	44,
06:	8, 22, 42, 57,
07:	9, 19, 29, 39, 49, 58
08:	08, 18, 28, 38, 41, 56,
09:	11, 26, 41,
10:	01, 21, 41,
11:	01, 21, 41,
12:	01, 21, 41,
13:	00, 19, 34, 49, 59
14:	09, 19, 29, 39, 48, 57,
15:	06, 15, 25, 35, 45, 55,
16:	05, 16, 27, 38, 49,
17:	00, 10, 20, 30, 45,
18:	00, 20, 41,
19:	00, 20, 43,
20:	06, 36, 52,
21:	17, 46,
22:	16

Walk between Bus 70 stops and Biocenter 2



Bus 70 Malmi (Malm) Southbound,
Stop: (H1307) Apollonkatu
Monday –Friday time table
(Times are estimates)

Hour	min
05:	09, 29, 58,
06:	15, 30, 45, 57,
07:	2, 12, 22, 31, 41, 50
08:	08, 18, 28, 38, 41, 56,
09:	01, 11, 21, 31, 50
10:	10, 30, 50,
11:	10, 30, 50,
12:	10, 30, 50,
13:	10, 30, 50,
14:	10, 30, 45, 59,
15:	10, 20, 31, 42, 52
16:	02, 12, 22, 32, 46,
17:	01, 16, 31, 51,
18:	11, 30, 50,
19:	10, 30, 50,
20:	09, 29, 49,
21:	10, 40,

On the way back to Töölö Towers, you can also get off on the Bus stop Töölöntori.

AROUND TOWN - HELSINKI

Helsinki is both historic and modern. But what is like to live in this city?

Here are some suggestions on where to eat, to drink and party, and where to have a cup of coffee.
If you feel like exploring Helsinki, check also what to visit below!

Where to eat

Momotoko
Pizzeria Via Tribunali
NAUGHTY BRGR
Café Bar No 9
Döner Harju City
Eat Poke HKI
Itsudemo
Social Burgerjoint Citycenter
Bangkok9
Zetor
Vapiano
Fafa's Mikonkatu
Ravintola Base Camp
Bites Burgers Kamppi

Where to drink and party

Corona bar & billiard
Café Mascot
Katmando Bar
Siltanen
Los Cojones
Ravintola Kaarle XII
Bar Chaplin
Bryggeri Helsinki
Oluthuone Kaisla
Navy Jerry's
Black door
DTM
Thirsty Scholar
Bar Llamas

Where to have coffee

Sinisen Huvilan Kahvila
Regatta
Roasberg
Karl Fazer Café
Hav a Java

What to visit

Helsinki Winter Garden
Kaisaniemi botanic garden
Linnanmäki
Ateneum
Amos Rex
Helsinki Art Museum
Finnish Museum of Natural History
Museum of Contemporary Art Kiasma
Suomenlinna
Kaivopuisto observatory
Seurasaari Open-Air Museum
The National Museum of Finland
Central Library Oodi
Ateljee Bar

WIRELESS NETWORK AT THE UNIVERSITY OF HELSINKI

A joint guest user account has been created for the UNGAP Training School participants to access the University of Helsinki network. The account is valid for one week from the first use within the group.

- Find and connect to the Wi-Fi network, **Univ of Helsinki HUPnet**.
- Launch your Web browser. If the browser does not automatically redirect you to the HUPnet login page, try the address https://login.hupnet.helsinki.fi.
- Enter the username and password provided during the training school.

NICE TO KNOW

Weather in Helsinki
Fall in Helsinki is rather rainy and cool. There is an average of 18 rainfall days/month in September or October and temperatures range, during the day, from 6 - 14 °C in September and from 2 – 7 in October.

Bank/Credit card
You can pay with debit or credit cards in almost all the shops, restaurants and taxis. Cash withdrawal machines "OTTO" accept all major bank and credit cards. Banks are normally open Mon–Fri 10–16.30.

Emergencies
Dial 112 for ambulance, rescue services, fire department and police.

Health care services
All visitors are recommended to have their own travel insurance in case health care services are needed. Usually insurance is provided by the sending organization. If this is not the case, you should consider taking a personal travel insurance.

If you are not a citizen of an EU or EEA country and you need a Finnish doctor or medical care using travel insurance or payment, you should contact a private healthcare provider mentioned below. Travelers from EU or EEA countries holding a European Health Insurance Card are entitled to use Finnish public healthcare.

You can find more information on private health care in Finland here:
https://www.expat-finland.com/living_in_finland/private_healthcare.html.

FACTS AND FIGURES

Finland
Area: 338 000 km2 of which 10% water.
Population: 5,3 million.
Population density: 17 inhabitants / km2
Languages: Finland has two official languages: 92,3% speak Finnish and 5,6% Swedish. About 1 600 inhabitants in Lapland speak Sámi. Most of the people, especially in metropolitan areas speak English.
Religion: 84,9% Lutheran, 1,1% Orthodox, 1,1% other denominations, 12,9% unaffiliated. Freedom of religion is guaranteed by the Finnish constitution.
Form of government: republic, headed by President Mr. Sauli Niinistö, elected by direct popular vote for a six-year term (from March 2012). The Parliament consists of one chamber of 200 members elected for a four-year term.
Security policy: Finland observes a policy of neutrality and is not a member of any military alliance. Member of the European Union since 1995.
National epic: The Kalevala (Kalevala Day on February 28)
Capital: Helsinki (the centre of government, business, culture and science)
Metropolitan area: Helsinki, Espoo, Kauniainen and Vantaa

Helsinki
Founded in 1550
Capital of Finland since 1812
Area: 214 km2
Inhabitants: 595 000
Population density: 2 752 inhabitants / km2
Coastline 98 km, islands 315
Finnish-speakers 83,7%, Swedish-speakers 6%
Other language groups 10,2%
Foreign nationals 5,5 %
Evangelical Lutherans 72%, Orthodox 2%
Municipal tax rate 17,5 %
Mobile phones per 100 inhabitants 96
Mayor of Helsinki: Mr Jan Vapaavuori

Metropolitan area
Consists of the following cities: Helsinki, Espoo, Kauniainen and Vantaa.
Area: 770 km2
Inhabitants: 1,3 million
Population density: 1,688 inhabitants / km2

ABSTRACTS

P1

Raman surface mapping as an effective tool in drug product formulation development

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Abstract: Raman surface mapping is a versatile tool applied in multiple stages of drug product development process. Technique provides unique insight in the chemical surface structure and therefore is readily used as a way for assessment of the formulation process and correlation of drug product properties e.g. active substance and excipients distribution with obtained in vitro dissolution characteristics. This type of correlation is a must in the generic drug product industry where retention of qualitative and quantitative product features is often a key point in conducting successful bioequivalence trial. Raman surface map of a drug product contains varied indicators of manufacturing process steps utilized during formulation stages. Application of this comprehensive approach is a suitable way of characterizing both reference product and generic prototypes on various development stages. Consequently, employment of a tailored strategy supports design of a high-quality bioequivalent formulation.

Presented studies were conducted as a part of broad preformulation approach to generic formulation design. Discussed example of a model drug compound's immediate release formulation development illustrates how application of Raman surface mapping can be utilized to investigate influence of the manufacturing process on distribution of an active substance and excipients in the dosage form and subsequently on its performance in vitro and in vivo.

P2

Characterization of Modified Biotherapeutics by FTIR and Raman Spectroscopy

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Abstract: Vibrational spectroscopic techniques provide the foundation to investigate the structures, hydrogen-bonding, orientation, and interactions of side chains (as aromatics, free sulfhydryl, and disulfide bonds) in proteins that play key role to their biostability and bioactivity. These techniques are used for characterization of protein pharmaceuticals in native and/or denatured states, to assess conformation changes, protein–protein interactions, aggregation, fragmentation, and also for protein drug product characterization.

In our study, we used FTIR and Raman spectroscopy to characterize chemically modified monoclonal antibody preparations, specifically antibodies conjugated with different bifunctional chelating agents that were prepared in order to be subsequently labeled with radioisotopes, in solution, in freeze-dried state and after reconstitution.

Based on the frequencies assigned for amide bands, the investigated formulations contain the highest percentage of β-sheet conformation (antiparallel and parallel), followed by α-helices in the structure. Significant changes in comparison with FTIR and Raman spectra of native antibody upon applied processes of conjugation and freeze-drying were not observed. In the experimental IR (in the region 2000-500 cm^{-1}) and Raman spectra (2000–400 cm^{-1} region) we observed retaining of native structure of the antibody and modified antibody and no obvious aggregation.

Our investigation has provided characterization of the formulations using FTIR and Raman spectroscopy, thus enabling insight in the structural changes of conformation and the stability of preparation in dissolved and solid (freeze-dried) state. In addition, these techniques were suitable for conformation assessment of the protein in solid state and in reconstituted solution. These results create good foundation for further studies of this kind in order to characterize protein-based biotherapeutics that have similar structure properties.

A redispersible dry emulsion system with simvastatin prepared via fluid bed layering as a means of dissolution enhancement of a lipophilic drug

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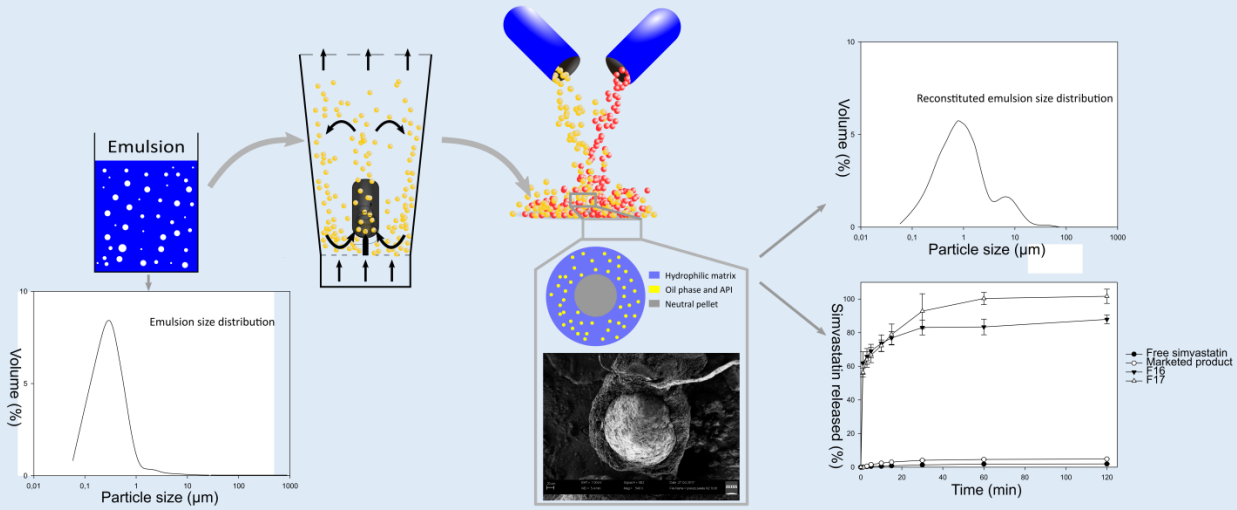
Abstract: The purpose of the study was to develop a redispersible dry emulsion, containing a lipophilic, poorly water soluble model drug simvastatin, by employing fluid bed coating technology. The presented dry emulsion manufacturing approach produces pellets in a way, where a layer of the dry emulsion is applied to a neutral core. In the preliminary formulation development phase 1-oleoyl-rac-glycerol was chosen as the oily lipid phase, based on the high drug solubility and potential bioavailability enhancement capability. Mannitol, HPMC and Tween 20 were selected as the solid carriers and surfactant, respectively. The design of experiments, specifically the mixture design approach, was used to obtain the optimal formulation composition. The emulsion reconstitution ability and stability were the main responses, used as the decisive parameters for formulation optimisation. Optimised formulations showed narrow droplet size distribution upon reconstitution, high stability, suitable drug loading and enhanced dissolution profile, compared to a non-lipid based tablet and the pure drug. The scanning electron microscopy, Raman spectroscopy and image analysis disclosed a uniform morphology of the applied layer with separated droplets with simvastatin and uniform size distribution and a circular shape of coated pellets. The study represents the proof of concept of designing redispersible dry emulsions using a fluid bed layering approach.



Funding and disclosures: The authors thank the Faculty of Pharmacy, University of Ljubljana, Slovenia for supporting this study. The world federation of scientist (WFS) is acknowledged for providing financial support for the PhD student. Financial support for the research project was provided by the Slovenian Research Agency under contract number P1-0189.

P4

Effect of Hydrophilic Polymer on Complexation and Solubilization of Cyclodextrin/ Kinase inhibitors Nanoparticles

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Abstract:

Cyclodextrins (CDs) can solubilize various hydrophobic drugs through nanoparticles complexation. Many protein kinase inhibitors (KIs) are practically insoluble in aqueous media with intrinsic drug solubility (S_0) in low microgram/ml range thus, CDs will still result in limited solubility enhancement. Addition of hydrophilic polymer has been shown to improve the complexation and solubilizing efficiencies of CDs. The aim of present study was to enhance aqueous solubility of different KIs through formation of drug/γ-cyclodextrin (γCD)/polymer complexes.The complexes were prepared by heating technique, then evaluated both in solution and in solid state.The phase-solubility profiles showed formation of binary KI/γCD complexes that have limited solubility in water or B_S-type. γCD only had significant solubilizing effect on motesanib and axitinib. The aqueous solubility of the binary KI/γCD complexes was pH-dependent. Cediranib/γCD complex had the highest solubility, followed by motesanib, while axitinib, pazopanib and regorafenib were much less soluble. Upon formation of ternary complexes, the solubility of five KIs was changed. Interestingly, the solubility of motesanib/γCD complex and axitinib/γCD complex were mainly increased due to synergistic effects of γCD and hydrophilic polymers. Hexadimethrine bromide (HDMBr) was the most effective polymer. The ternary complexes formed nano-sized aggregates between 250 and 350 nm. Osmolarity and pH were monitored. The solid ternary motesanib/γCD/HDMBr complex and axitnib/γCD/HDMBr complex were analyzed by FTIR and DSC, and shown to be a true complex as well as by NMR study in liquid state. Of the binary and ternary complexes tested, the ternary motesanib/γCD/HDMBr complex and axitnib/γCD/HDMBr complex had higher increase of aqueous solubility.

Funding and disclosures:

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Pharmaceutical Excipients are not Inert: Polyoxyethylated Solubilising Excipients Increase Oral Drug Bioavailability in Male but not Female Rats

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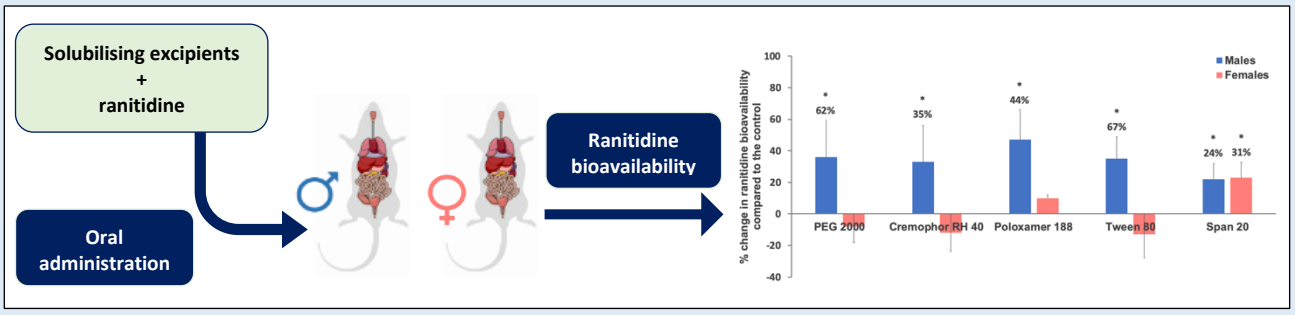
Abstract: Although it is widely appreciated that variability in drug performance is governed by a multitude of factors, the impact of sex has traditionally been under-evaluated. Adding further to complication, pharmaceutical excipients are listed as inactive ingredients that are intentionally co-formulated in drug delivery systems. A growing body of evidence, however, has challenged the inert nature of these agents. In this work, the influence of pharmaceutical excipients on drug bioavailability in males and females were examined. Using a Wistar rat model, a portfolio of polyoxyethylated solubilising excipients (polyethylene glycol 2000, Cremophor RH 40, Poloxamer 188 and Tween 80) increase ranitidine bioavailability in males but not in females. The *in vivo* sex and excipient effects were reflected *ex vivo* in intestinal permeability using an Ussing chamber system. The mechanism of such effect on drug bioavailability is suggested to be via the interaction between the excipients and the efflux membrane transporter P-glycoprotein (P-gp), whose gene and protein expression were inhibited by the solubilising agents in male but not female rats. In contrast, the non-polyoxyethylated excipient, Span 20, significantly increased ranitidine bioavailability in both males and females in a non-sex-dependent manner. These findings have significant implications for the use of polyoxyethylated solubilising excipients in drug formulations in light of their sex-specific modulation on the bioavailability of a P-gp drug substrate. As such, pharmaceutical research is required to retract from a 'one size fits all' approach and to, instead, evaluate the potential interplay between excipients and sex on drug effect to ensure effective pharmacotherapy.



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P6

Lipid nanoparticles as novel systems to eradicate bacterial biofilms

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Abstract:

Bacterial biofilm implant-associated infections are an increasing concern at a worldwide level due to the high demand for implants and the escalating rates of antibiotic resistance. Consequently, these infections represent an economical burden for Healthcare Systems. Thus, novel nanosystems for an efficient delivery of antimicrobial agents are urgently needed to eradicate bacterial biofilms and fight antibiotic resistance phenomena.

Lipid nanoparticles are useful for delivery purposes, since they protect the encapsulated compounds against *in vivo* degradation. Furthermore, these nanoparticles exhibit a controlled drug release at the target site, reducing systemic side effects and simultaneously increasing therapeutic compliance and efficiency.

N-acetyl-cysteine (NAC) is a mucolytic agent with antibacterial activity against a variety of bacteria, both in planktonic and biofilm forms. In this work, NAC-loaded lipid nanoparticles were prepared by double emulsion technique to enhance its antibiofilm efficiency. The nanoparticles were optimized by a response surface design and the optimal formulation was characterized according to size, polydispersity index, zeta potential, encapsulation efficiency, release profile and morphology. The *in vitro* antibiofilm efficiency of the developed nanoparticles were tested against *Staphylococcus epidermidis* and *Pseudomonas aeruginosa*. At the tested concentrations, no cytotoxic effects were observed in L929 fibroblasts cell line.

Funding and disclosures: RMP, DLC and CN are thankful to Fundação para a Ciência e Tecnologia (FCT) for the PhD Grant [SFRH/BD/130319/2017], the PhD Grant [PD/BD/105957/2014] and the investigator Grant [IF/00293/2015], respectively. This work was supported by FCT through the FCT PhD Programmes and by Programa Operacional Capital Humano (POCH), specifically by the BiotechHealth Programe (Doctoral Programme on Cellular and Molecular Biotechnology Applied to Health Sciences). The work was supported by UID/QUI/50006/2019 with funding from FCT/MCTES through national fund as well as from the Fund for Scientific Research Flanders (FWO grant WO.009.16N) to PVD. This work is under the framework of the project POCI-01-0145-FEDER-31444, financed by Fundo Europeu de Desenvolvimento Regional (FEDER) - through the COMPETE 2020 - Operacional Programme for Competitiveness and Internationalisation (POCI) - and by national funds through Fundação para a Ciência e a Tecnologia (FCT).

P7

At-line Quality Control of a 3D Printed Antihypertensive Polyprintlet using NIR Spectroscopy

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Abstract:

PURPOSE

Three-dimensional printing (3DP) is forecast to transition the manufacture of medicines away from a 'one-size-fits-all' approach towards personalisation. To facilitate integration of 3DP into clinical practice, the use of non-destructive quality control techniques are required to ensure final product quality[1]. For the first time, this research evaluates the use of near infrared (NIR) spectroscopy as a dose verification method for 3D printed polypills containing two drugs (amlodipine and lisinopril) as a novel treatment pathway for hypertension.

METHODS

A portable NIR spectrometer for dose predictions was evaluated on drug-loaded oral films and cylindrical polyprintlets printed using selective laser sintering (SLS). Calibration models containing therapeutically relevant dosages of amlodipine (1-5%) and lisinopril dihydrate (2-10%) were developed using partial least squares (PLS) regression and the predictive performances were compared with conventional HPLC analysis. Polyprintlets were characterised for mechanical properties and thermal analysis was performed using x-ray powder diffraction (XRPD) and thermogravimetric analysis (TGA) to evaluate solid-state characteristics post printing.

RESULTS

For the first time, we report the development of a novel method enabling a real-time quantification of two drugs in anti-hypertensive polyprintlets. Therapeutic dosages of amlodipine and lisinopril, across the concentration ranges of 1-5 %w/w and 2-10% respectively, were successfully printed using SLS. The developed PLS models were validated according to international guidance, and showed excellent linearity, accuracy and specificity. The 3D printed polypills demonstrated excellent mechanical properties (friability <1%, hardness >400N). XRPD and DSC analysis showed that the sintering process transformed the phase of both drugs from the crystalline to the amorphous forms.

CONCLUSION

This study is the first to report the fabrication and prediction of two active ingredients within 3D printed polypills using a non-destructive QC method for real-time release, supporting the integration of 3DP for personalised medicine production into clinical practice.

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P8

Oral delivery of oligonucleotides for local treatment of inflammatory bowel disease

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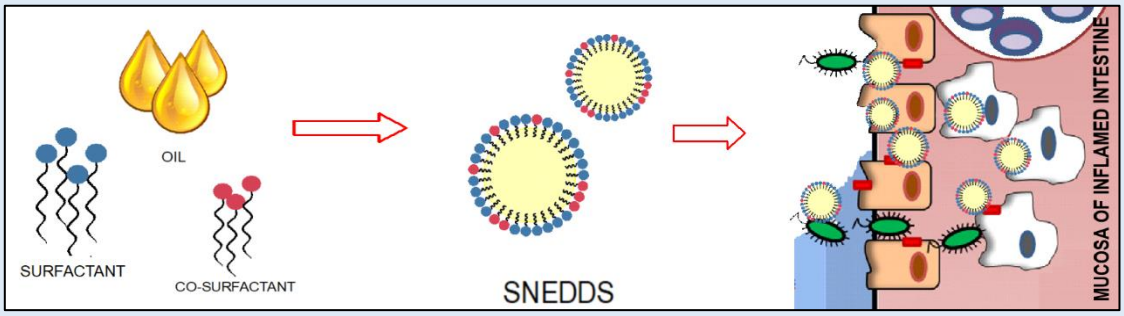
Abstract: Inflammatory bowel disease (IBD) describes pathological conditions characterised by inappropriate and sustained activation of the mucosal immune system of the small intestine and/or colon. Local treatment is preferred over systemic delivery, which is often accompanied by undesired side effects. In IBD, cationic peptides are overexpressed in the area and phagocytic immune cells infiltrate the site of inflammation. By delivery of an anti-inflammatory acting miRNA oligonucleotide, production of pro-inflammatory cytokines by macrophages within inflamed tissue decreases, and the inflammatory process itself is suppressed. However, delivery of instable negatively charged macromolecular oligonucleotides represents a challenge. Self-nanoemulsifying drug delivery system (SNEDDS) has been utilised to deliver a hydrophobic complex of oligonucleotides orally.

The complexes were prepared from a model 20-nucleotide-long oligomer and a cationic lipid dimethyldioctadecylammonium bromide (DDAB) or 1,2-dioleoyl-3-trimethylammonium-propane (DOTAP) with yields over 95% for molar ratio 1:60. The size of the complexes was estimated by atomic force microscopy to be 75-127 nm and 33- 62 nm, for DOTAP and DDAB complex respectively. The size of dispersed loaded SNEDDSs, ~200 nm, and negative surface charge enabling passive targeting to the inflamed tissue, make the formulation suitable for the intended purpose.



Funding and disclosures: The study was supported by SVV 260 401, Czech science foundation 270/53/75302 and Erasmus+.

P9

Lipid nanoparticles as drug delivery vehicles for breast cancer therapy

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Abstract:

Breast cancer is the second leading cause of cancer deaths worldwide [1]. Most of the anti-cancer drugs currently used in clinics have several limitations such as poor bioavailability, toxic side-effects, low accumulation in tumors and need for administration of large multiple doses [2]. This highlights the demand for safer and more effective treatment options. Nanotechnology may have an important role in minimizing these limitations and improving the therapeutic effect of the conventional anti-cancer drugs. Lipid nanoparticles are particularly promising delivery vehicles due to their biocompatibility, low-cost production and stability [3]. Hyperthermia is also a promising strategy for the management of breast cancer. Strong near-infrared (NIR) absorbers such as gold-based nanostructures can be used in NIR hyperthermia therapy. The local heating can cause cell death, and when combined with drugs increase their local drug release [4]. The aim of this work is to develop multifunctional lipid nanoparticles to improve the current treatment of breast cancer. Two main methodologies have been developed: the encapsulation of anti-cancer drugs into lipid nanocarriers and the development of hyperthermia therapies based on gold nanostructures. The final aim of the project is to combine these two strategies into one multifunctional therapeutic approach.

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Antioxidant capacity of trans- and cis-resveratrol in microemulsions following ultraviolet irradiation

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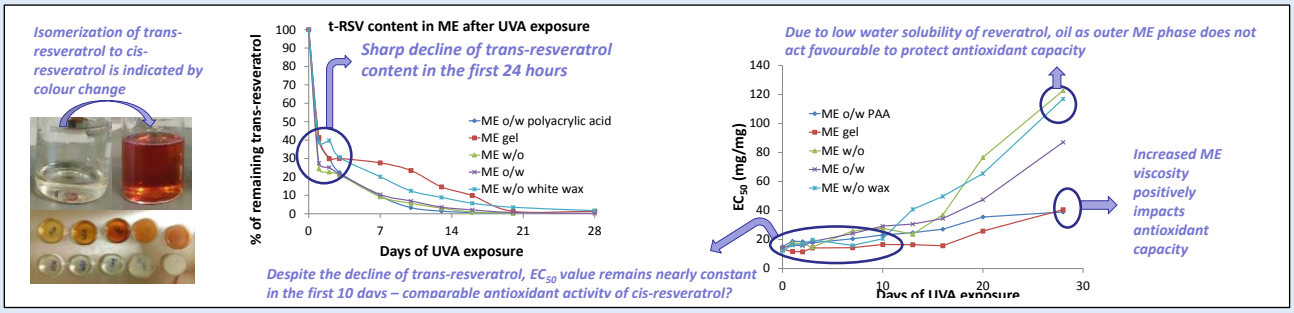
Abstract: Resveratrol has been scientifically proven to penetrate the skin barrier and exhibit antiaging activity. This poorly soluble natural antioxidant can mitigate the photoaging through the expression of AP-1 and NF-kB factors; supporting the production of collagen type I and II and decreasing hyperpigmentation. Unsurprisingly, topical use of resveratrol is on the rise. However, the majority of its proven benefits are ascribed to the *trans* analogue, susceptible to photoisomerization, presenting a great challenge in the development of topical formulations.

Microemulsions (ME) are recognized for their ability to improve solubility and skin penetration of active ingredients. Five different ME were developed (water in oil (W/O), oil in water (O/W), W/O with white wax, W/O with polyacrylic acid and ME gel) and loaded with equal amount of trans-resveratrol (0.1 %). Prepared ME were exposed to aging under stress conditions (irradiation with UVA-light (373 nm) or temperature of 40°C). During the process of aging, *trans*-resveratrol content in ME was assayed with HPLC, and antioxidant capacity was assessed with the 1,1-diphenyl-2-picrylhydrazyl reduction method.

Shielding from light retarded degradation of trans-RSV and its isomerization in ME for at least 90 days at 21°C. ME preserved > 80 % *trans*-resveratrol content and antioxidant capacity even after 4 weeks at 40°C, if kept in dark. Exposure to UVA light diminished trans-RSV content to under 40 % within 24 h while EC_{50} values remain low for several days, indicating comparable antioxidant activity of *cis*-resveratrol. ME with higher viscosity and higher water content act favourably on photostability of *trans*-resveratrol.



Funding and disclosures: The authors acknowledge financial support from the Slovenian Research Agency (research core funding, No. P1-0189).

P11

The use of fiber optic dip probe in the determination of drug concentration in supersaturation experiments

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Abstract: One of the most common methods for the determination of the dissolved drug concentration is UV-Vis spectroscopy. The purpose of our work was to use fiber optic dip probe for *in situ* determination of the dissolved dipyridamole concentration during precipitation from supersaturated solution, triggered by medium pH change. Using the fiber optic dip probe, measurements took place directly in the working vessel and spectra from 200 to 800 nm were scanned at predetermined time points. To eliminate disturbances due to precipitated particles, different approaches were also tested in our experiments, namely subtraction of absorbances at higher wavelengths where dipyridamole does not absorb (i.e. 600 or 800 nm) and calculation of the second derivative of the absorption spectra. The obtained concentration profiles calculated from absorbances using both approaches differed from each other at early time points of the experiments, whereas nearing the end time points the calculated profiles started to overlap. Additionally, at earlier time points the measured absorbances in the range from 500 to 800 nm, where dipyridamole does not absorb, gradually decreased from lower towards higher wavelengths. One of the possible reasons for the results, described above, is the occurrence of precipitated nano-sized particles which we have shown to be present at early time points of the dipyridamole precipitation experiments using laser diffraction method. The results imply that nanoparticles do not only scatter light but could also cause wavelength-dependent light absorption. This reflects also in concentration profiles which should be considered when performing dissolution/ precipitation experiments.

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P12

Application of intelligent decision support systems in the optimization of pellets manufacturing process

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Abstract: Pharmaceutical pellets are spherical agglomerates manufactured in extrusion/spheronization process. The composition of the pellets, the amount of active pharmaceutical ingredient (API) and the type of used excipients have an influence on the shape and quality of dosage form. A proper quality of the pellets can also be achieved by identifying the most important technological process parameters. In this paper, a knowledge discovery method, called dominance-based rough set approach (DRSA) has been applied to evaluate critical process parameters in pellets manufacturing. For this purpose, a set of condition attributes (amount of API; type and amount of excipient used; process parameters such as screw and rotation speed, time and temperature of spheronization) and a decision attribute (quality of the pellets defined by the aspect ratio) were used to set up an information system. Similar analysis was also performed to discover dependences occurring between technological data describing the composition, properties and process of formulation of tablets with pellets. The DRSA analysis allowed to induce decision rules containing information about process parameters which have a significant impact on the quality of manufactured pellets. Those rules can be used to optimize the process of pellets manufacturing.

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P13

The impact of gastrointestinal transfer on luminal performance of Norvir tablets: comparison of data in human aspirates and BioGIT data

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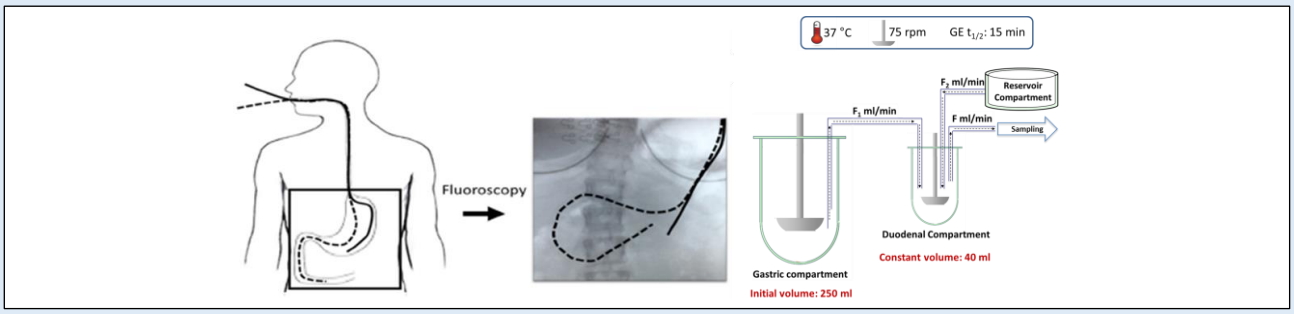
Abstract:

The purpose of this study was to evaluate the ability of the biorelevant gastrointestinal transfer (BioGIT) system to predict luminal performance of marketed ritonavir amorphous solid dispersion formulation (Norvir® tablets) by comparing concentrations in the duodenal compartment of BioGIT with data collected from the upper small intestine of healthy adults under normal and under reduced gastric acid secretion in the fasted state.

Assuming normal gastric acid secretions, in vitro drug concentrations were within the concentration range observed in vivo. Similar observations were made when simulating hypochlorhydric conditions in the stomach. While for most human volunteers duodenal concentrations in vivo were low during the first 20 minutes after oral drug intake, the BioGIT system predicted higher on average duodenal concentrations within 15 minutes after the start of the experiment. Thereafter, predicted drug concentrations corresponded to the median drug concentrations observed in vivo. Comparing both normal and hypochlorhydric conditions, the BioGIT system predicted similar duodenal concentrations between both test conditions, in line with the in vivo observations. Similar as for the in vivo situation, supersaturated concentrations of ritonavir were detected in samples collected in the BioGIT system for both test conditions. Drug supersaturation was found to be stable in both test conditions as well as similar between both test conditions, in line with the intraluminal data. However, in vitro results over-estimated the extent of supersaturation compared to the in vivo situation, especially under simulated hypochlorhydric conditions.

The present study demonstrated that the BioGIT system was useful for the prediction of the luminal performance of Norvir® tablets under both normal and reduced gastric acid secretions in stomach.



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P14

Glucose-responsive nanoparticles embedded in a 3D-engineered pancreas

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Abstract: Type 1 Diabetes mellitus (T1DM) is an auto-immune disease characterized by the lack of insulin secretion due to the destruction of insulin-producing pancreatic β-cells. Currently, there are 422 million individuals suffering from DM worldwide and this number is expected to rise to 642 million by 2040. Among those, 10% of the cases are of T1DM, making DM one of the biggest health problems in the world with very high socio-economic impact. T1DM is not a preventable disorder and most of the cases are lately diagnosed, already after a massive destruction of the pancreatic beta-cells. The only definitive cure for T1DM consists in replacing the destroyed pancreas, capable of sensing blood glucose levels and secreting appropriate amounts of insulin in a glucose-dependent manner. So far, the only available clinical approach able to restore pancreatic functions is the whole pancreas or pancreatic islet transplantation. However, the number of available pancreas or islets is limited, in addition to the need of a lifelong immunosuppression therapy. In this project, we propose an innovative approach, combining cell therapies and smart nanomedicines in order to develop a pancreas surrogate able to mimic the pancreatic closed loop and regulate insulin secretion. Induced pluripotent stem cells (iPSC), differentiated into β and α-cells, will be immobilized in a biofunctional 3D matrix as well as pH-responsive nanoparticles encapsulating exenatide and sensitive to glucose, in order to stimulate insulin production. So far, glucose-pH-sensitive NPs formulations are being optimized using different ratios of PLGA and polymethacrylates polymers.

Funding and disclosures: This work is funded by the project NORTE-01-0145-FEDER-000012, supported by Norte Portugal Regional Operational Programme (NORTE 2020), under the PORTUGAL 2020 Partnership Agreement, through the European Regional Development Fund (ERDF) through the COMPETE 2020 - Operational Programme for Competitiveness and Internationalization (POCI) and by Portuguese funds through FCT - Fundação para a Ciência e a Tecnologia/ Ministério da Ciência, Tecnologia e Ensino Superior in the framework of the project "Institute for Research and Innovation in Health Sciences" (POCI-01-0145-FEDER-007274 and POCI-01-0145-FEDER-030466). Joana Marques gratefully acknowledges Fundação para a Ciência e a Tecnologia (FCT), Portugal for financial support (fellowship PD/BD/145149/2019).

Design and evaluation of self-nanoemulsifying drug delivery systems (SNEDDS) for senicapoc

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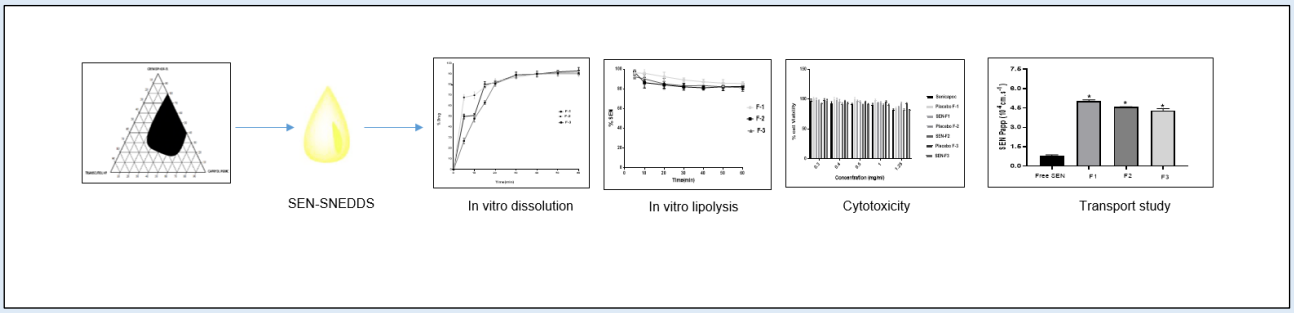
Abstract: Despite various pharmacological effects, senicapoc (SEN) a potential anti-sickling agent shows poor water solubility and oral bioavailability.To address this problem, self-nanoemulsifying drug delivery systems (SNEDDS) were prepared and evaluated for their solubilization capacity and oral bioavailability improvement.Capryol PGMC showing highest solubilization capacity was selected as oil. Self-emulsification ability of two surfactants viz. Cremophor-EL and Tween-80 were compared for the selected oil. Based on a solubility study and pseudo ternary phase diagrams, optimized nanoemulsion with droplet sizes less than 200 nm were prepared. In vitro dissolution study demonstrated superior performance of SNEDDS over free drug. During in vitro lipolysis, 80% of SEN remained solubilized. In vitro cytotoxicity study using MTT dye on Caco-2 cell line indicated safety of formulations and the transport of SEN-SNEDDS across Caco-2 monolayers was enhanced compared with the transport of free drug.



Funding and disclosures: Université Catholique de Louvain (Bourse de la coopération au développement).

Polymeric particles: a tool for site specific inflammation management

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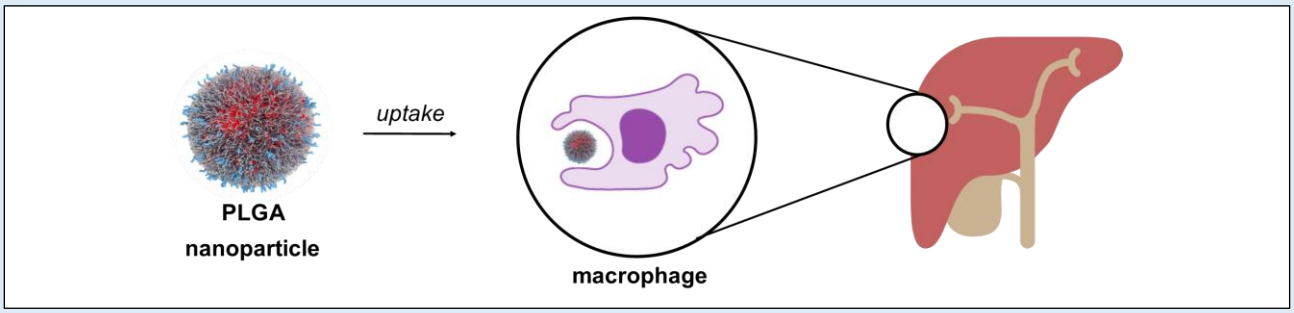
Abstract: The aim of this work was to prepare biodegradable polymeric nanoparticles with encapsulated anti-inflammatory substance (e.g. corticosteroids). Polymeric particles are actively scavenged from systemic circulation by phagocytic cells of the reticuloendothelial system (RES). Macrophages such as Kupffer cells play an important modulatory role in the development of inflammation. Therefore, such particles could be suitable for a therapy of inflammatory diseases such as non-alcoholic steatohepatitis or inflammatory bowel diseases. The encapsulation of the active substance into nanoparticles has undeniable advantages, such as reducing side effects, accurate targeting into a site of action or lower dose of an active substance.

Three different variants of poly (lactic-co-glycolic) acid (PLGA) (two linear variants with different glycolic and lactic acid ratio - 1:1 and 7:3 and a branched PLGA with polyacrylic acid - A2) were assessed for preparation of nanoparticles. These co-polymers are sufficiently stable, biodegradable and do not induce unwanted stimulation of the immune system.

We prepared polymeric nanoparticles of desired size (100 – 300 nm) with low polydispersity index (< 0,2). Formulations of these parameters are attractive for cells RES, non-toxic and also with high degree of cell entry (more than 50 %). Smaller particles (under 100 nm) were prepared by emulsification solvent evaporation method. Nanoparticles with size ranging between 150 and 200 nm were prepared by nanoprecipitation. Encapsulation efficiency for model fluorescent dye was higher for branched PLGA compared to linear PLGA co-polymers.



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P17

Functional foods: The perspective of drug interactions

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Abstract: Oral drug administration is simple and frequently chosen by patients because it gives opportunity to continue the pharmacotherapy at home, but pharmacokinetic or pharmacodynamic activities of drugs may be changed by foods consumed concomitantly as food matrix is complex and bioactive components in the foods might interact with the drug at any stages of pharmacokinetic process. Food-drug interactions are more important for elderly patients as 30% of prescribed drugs are taken by this population. Recently, the popularity of functional foods and beverages is increasing markedly because these foods are considered to promote health status or reduce the risk of some diseases. However, consumption of functional foods may lead some adverse reactions when consumed simultaneously with certain drugs. Some foods and/or beverages considered as functional such as green tea, wine, grapefruit, yogurt, garlic etc. can lead to food-drug interactions. Although intake of every food/beverage alters the physiological conditions of human intestinal tract, more attention should be paid on functional foods and drugs as their interactions are less investigated and also patients are more tend to consume functional foods during the pharmacotherapy. In this study, the pharmacological interactions between functional foods and drugs are summarized by giving some examples to these reactions.

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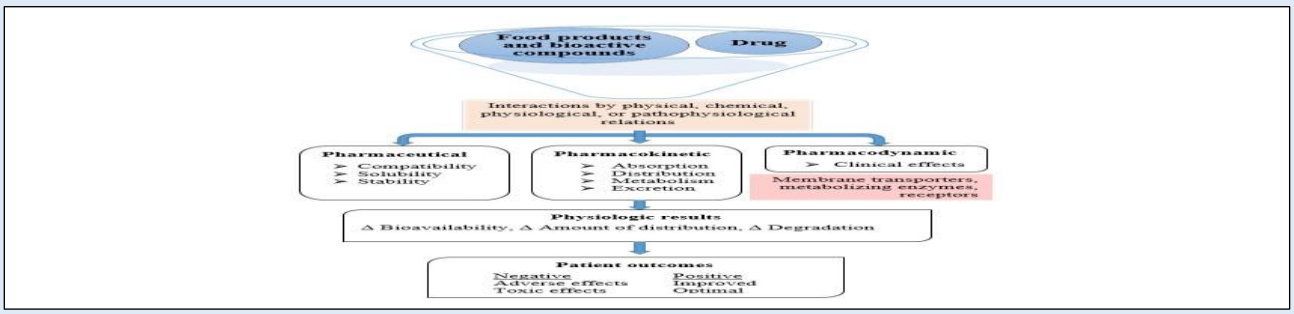

Biocidal action of Ag and soap against *Staphylococcus aureus*

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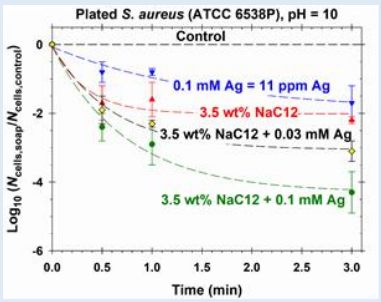
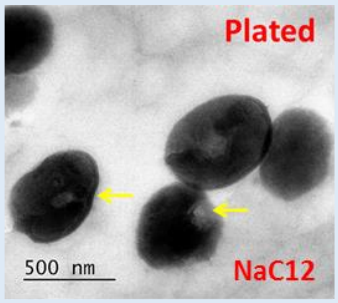
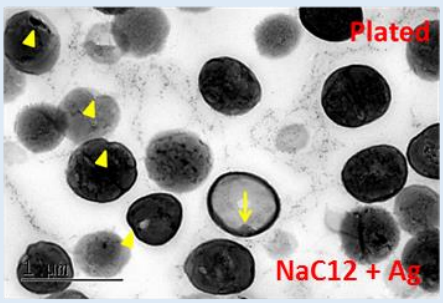
Abstract: Microbial pathogens (bacteria, viruses, and fungi), which can cause infections and diseases in humans, are one of the leading causes of death worldwide, namely one-fourth of global deaths annually (*Int. J. Mol. Sci.* **2015**, *16* (2), 3626–3655). Therefore, the control and prevention of microbial infections are of utmost importance. To fight with pathogens, many antimicrobial agents have been developed, such as antibiotics, disinfectants, and antiseptics. However, due to mutations, new strains of antimicrobial-resistant microorganisms are emerging, thus making the search of new biocides a substantial challenge.

In our study, we have tested the biocidal action of soaps and silver (Ag^+) against planktonic and adherent *S. aureus*. Soaps are commonly used in hand-wash formulations and should be able to kill most bacteria within 30-60 s without damaging the skin, however, in many cases they are not very effective alone. We found that the antibacterial properties of soaps improve when their hydrophobicity increases up to 12 carbon atoms. Moreover, when soaps are combined with Ag^+, we observed a synergistic effect: increased cell permeability due to soap, resulting into higher silver uptake and enhanced biocidal action. Furthermore, using SEM and TEM, we detected the external and internal morphological defects due to the treatment, thus elucidating the mechanism of biocidal action.







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Assessment of acetaminophen biotransformations variability in patients with selective hypersensitivity to this drug, using HPLC-MS/MS

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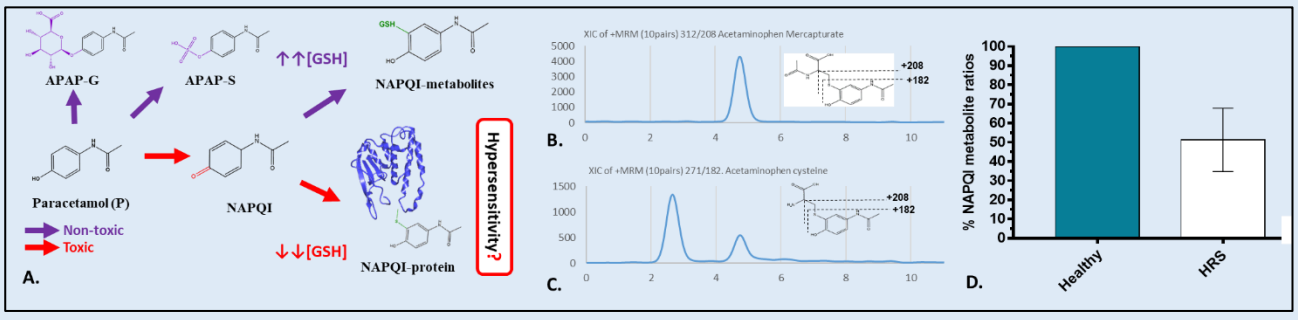
Abstract: Acetaminophen is a safe drug used for pain and fever relief, however adverse reactions to acetaminophen are common, including selective hypersensitivity reactions (HSR). The mechanisms that trigger HRS are not well understood, and it has been proposed that the interaction of the parent drug, or metabolites, with proteins could be involved in the development of hypersensitivity. Acetaminophen is mainly conjugated to acetaminophen glucuronide and acetaminophen sulfate. Around 5 to 10% of acetaminophen is oxidized to the toxic metabolite, N-acetyl-benzoquinonine imine (NAPQI); that is neutralized by GSH to giving rise to NAPQI metabolites like acetaminophen glutathione, acetaminophen cysteine and, acetaminophen mercapturate. When NAPQI levels exceed the GSH levels, free NAPQI binds to cysteine groups of cell proteins. In this work we performed a UHPLC-MS/MS analysis to quantify acetaminophen metabolites in two groups; healthy individuals tolerant to acetaminophen, and patient with acetaminophen selective hypersensitivity. NAPQI metabolites are structurally and chemically similar, so some fragment ions are common for some metabolites, making it necessary to optimize UHPC separation. Our data show that patients with hypersensitivity to acetaminophen have less neutralized NAPQI metabolites than healthy subjects, thus suggesting that in hypersensitivity patients the bioavailability of the free toxic metabolite is higher, thus facilitating protein binding and triggering the hypersensitivity reaction.



A. Acetaminophen metabolism: toxic and non-toxic pathways. **B.** +MRM Chromatogram of APAP-Merc. **C.** +MRM Chromatogram of APAP-Cys. **D.** Neutralized NAPQI production ratio in acetaminophen tolerant subjects vs patients with acetaminophen HRS.

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