GAZETTE

The 12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technologies will be fully virtual on 11-14 May 2021

12th PBP World Meeting
(see page 4)

Information Day "Functional solid oral dosage forms"
(see page12)

APGI Young Investigator Award 2021
(see page 17)

Information Day « Functional solid oral dosage forms» 1st June 2021

April 2021
N°36

www.apgi.org

APGI board

President :	Prof. Juergen Siepmann
Vice-President :	Prof. Elias Fattal
Treasurer :	Prof. Marie-Pierre Flament
Secretary :	Prof. Odile Chambin
Member :	Dr. Joël Richard
Member :	Dr. Karine Andrieux
Member:	Dr. Maria T. Peracchia

APGI council

Prof. Karine Andrieux
Prof. Philippe Arnaud
Prof. Amélie Bochot
Prof. Odile Chambin
Dr. Jean-Pierre Collaveri
Dr. Vincent Faivre
Prof. Elias Fattal
Prof. Marie-Pierre Flament
Dr. Alexandre Gil
Dr. Mounira Hamoudi-Ben Yelles
Dr. Youness Karrout
Dr. Elise Lepeltier
Dr. Simona Mura
Dr. Susanne Muschert
Prof. Anne-Marie Pensé-Lhéritier
Dr. Maria-Teresa Peracchia
Dr. Géraldine Piel
Dr. Joël Richard
Prof. Florence Siepmann
Prof. Juergen Siepmann

Secretary of the association
Mrs Laurence Houzé

Editorial

Dear Collegues,

I hope you and your families are doing fine despite the ongoing pandemic.

Due to the COVID crisis, the **12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology** had to be postponed twice and will finally be held as a fully virtual conference on May 11th-14th 2021.

We very much regret this, but a virtual conference was the only viable option under the given circumstances. A major part of this Gazette is dedicated to the practical details on how to register, attend live talks and discussions, see pre-recorded presentations, have a look at posters and chat with presenters, exhibitors and other participants.

It was not straightforward to postpone this event twice, reacting to the steadily changing pandemic situation. In the name of the APGI, I would very much like to thank our Italian and German sister societies: the ADRITELF and the APV, with whom we organize this conference.

Despite the unfavorable circumstances, close to 1000 abstracts have been submitted and 36 invited talks, 7 plenary lectures as well as 72 short talks will be presented.

Exceptionally, the meeting will start on a Tuesday afternoon and finish on Friday evening (instead of the common "Monday afternoon to Thursday evening" period). This is because of the hope we had last year (in 2020) to be able to organize a face-to-face conference in 2021 in Vienna, and the availability of the conference center was limited. Unfortunately, the COVID crisis evolved differently. Also, we regret that the 13th May, which is a holiday in many countries, is in the middle of the conference. Again, this was due to the limited availability of the Vienna conference center at the time point when we decided to postpone the meeting (for a second time). When it became clear that the conference had to be organized completely virtually, we did not want to change the conference dates for a third time. We very much hope that you will understand.

We will also be very happy to organize an **Information Day on "Functional solid oral dosage forms"**, jointly with Evonik, on 1st June 2021 (also fully online) and a **Hot Topic Day on "Colon targeting"** at the end of November 2021: hopefully onsite in Lille (but to be confirmed). Please have a look for details on these events in this Gazette.

We would be very happy to see you again (even if only online) during one of these events!

Please take care,

Prof. Juergen Siepmann
President of APGI

International Conferences and Events

12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology 11-14 May2021 fully virtual

Due to the ongoing COVID crisis, the 12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology and its accompanying exhibition ResearchPharm® will be held fully online.

Plenary and invited talks will be given live.
Short talks will be pre-recorded.

All question & answer sessions will be live (also for the short talks).

Posters can be downloaded as pdf file, as well as accompanying 2 min videos (in most cases). Furthermore, the poster presenters can be contacted via a Chat function. They are highly encouraged to be logged in during the dedicated poster presentation sessions to allow for **live** exchanges with interested participants.

In addition, all presentations (oral and poster) will be accessible for 2 months after the conference.

The pandemic forced us to postpone the conference twice: It was initially planned for March 2020 in Vienna. It was then postponed to February 2021 and subsequently to May 2021. When it became clear that the conference could still not be held as a face-to-face meeting in this period, we decided (together with our Italian and German sister societies) to organize the event fully online. And we did not want to change the dates for a third time. This is why, unfortunately, a public holiday in many countries is right in the middle of the conference. The availability of the conference center in Vienna was very limited when we postponed the meeting for the second time. We very much hope that you will understand.

International Conferences and Events

For the same reasons the conference exceptionally starts on Tuesday afternoon (and not Monday afternoon as usual) with the opening ceremony and a series of plenary lectures. On the following days (Wednesday to Friday) up to 5 parallel oral sessions will be offered:

- **2 Live sessions with invited talks:** 30 min + 10 min discussion (right after the talk), giving overviews on the current state of the art in the respective fields

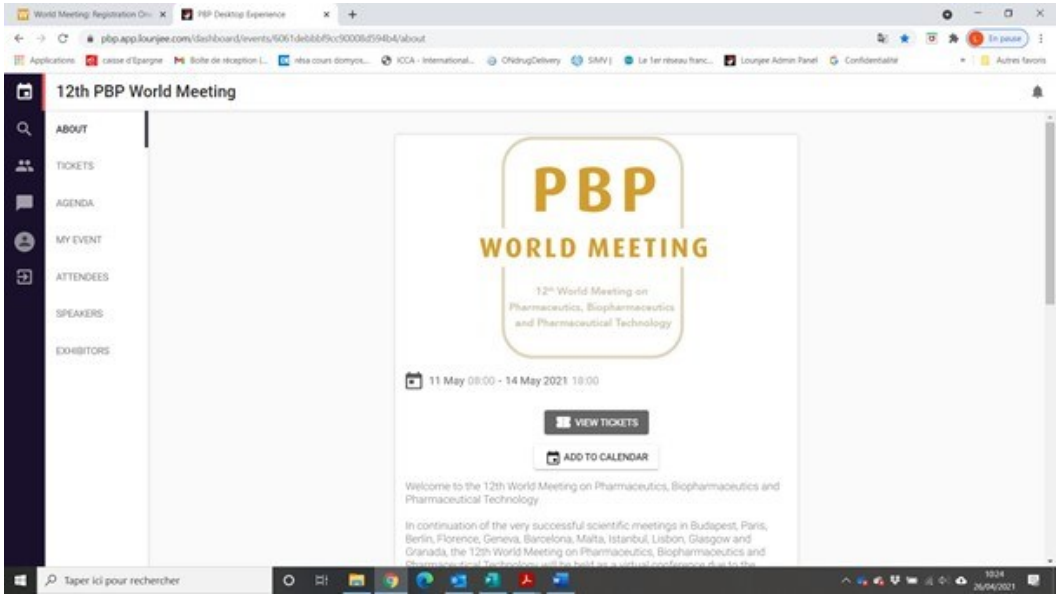
- 2 **Pre-recorded sessions with short talks**: 15 min each, on most recent research findings. After two short talks, a combined 10 min **question & answer session will be live**.

- **1 Session with pre-recorded talks from partners/exhibitors**: 20 min, directly followed by 10 min **live discussion**. Please note that these talks did not undergo any review process. This extra session (which is usually not offered) is an attempt to compensate the missing personal, face-to-face interactions during our exhibition.

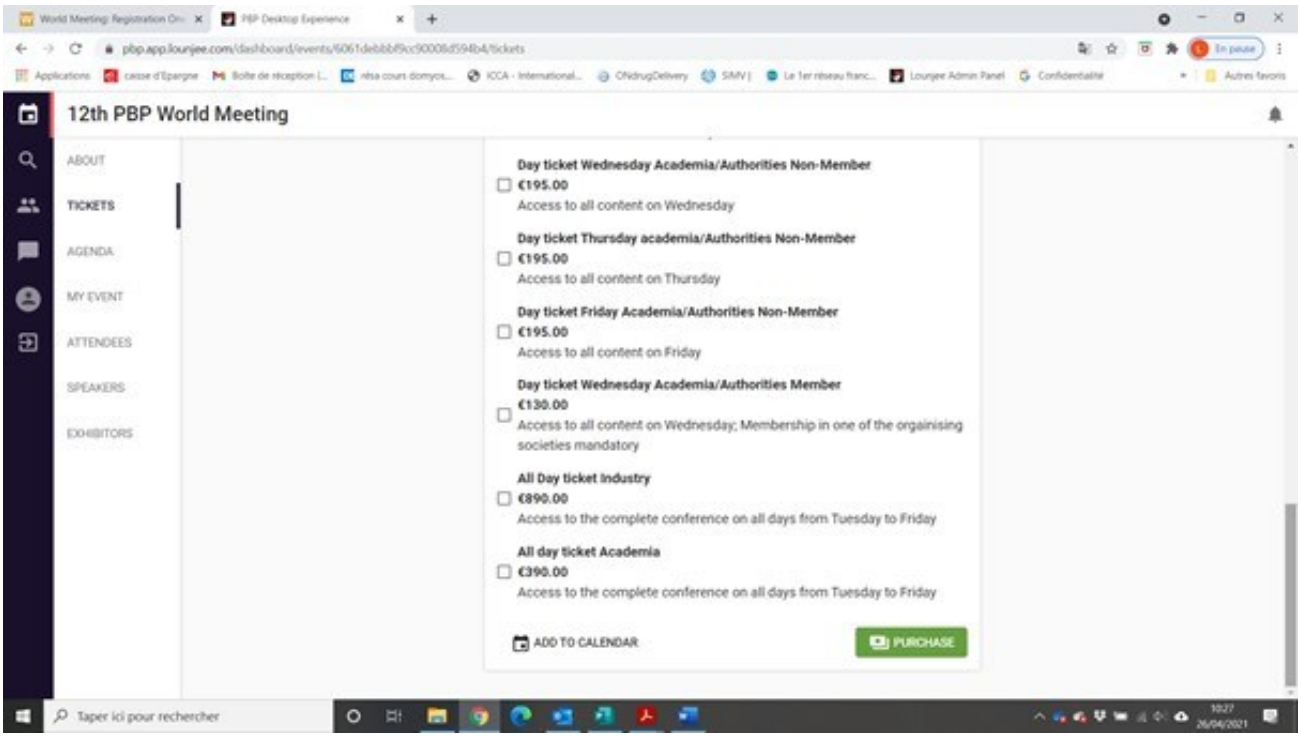
In certain cases, a drop-out of an invited talk was substituted by 2 short talks.

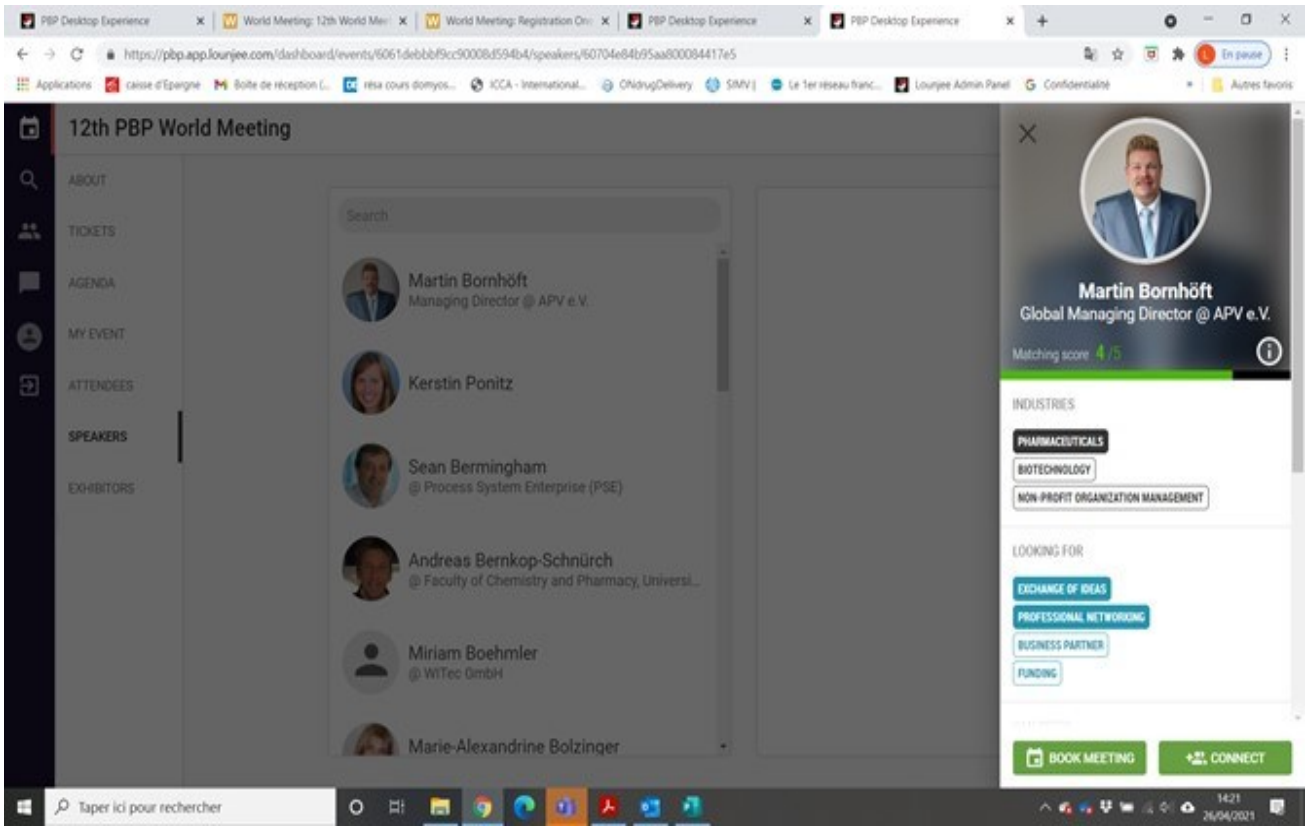
Please note that **this year, also day tickets can be booked** as the following website:
https://pbp.app.lounjee.com/

The online platform “Lounjee” has been selected to host our online conference and exhibition. Participants already registered via the website of the World Meeting will get a link to access to Lounjee.



From now, you **can also register via the Lounjee website:** https://pbp.app.lounjee.com/





We promise to do our best to organize one of our future World Meetings on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology in the wonderful city of Vienna!

Please have a look at the programme overviews on the following pages to plan your conference.

Tuesday, 11 May 2021

13:00	**OPENING CEREMONY**
13:45	Key note lecture incl. Q&A **Engineering cancer immunotherapy** David J. Mooney, Harvard School of Engineering and Applied Sciences, Cambridge, USA
14:45	Coffee break/exhibitor
	Hot Topic session incl. Q&A
15:15	**Digital assistant to support drug product development** Ferdinand Brandl, BASF, Ludwigshafen, Germany
16:05	**Advances in PLGA drug delivery system** Steven Schwendeman, University of Michigan, Ann Arbor, MI, USA
16:55	**Pfizer's "continuous" journey - Implementing continuous manufacturing into a factory for solid dosage forms** Clemens Stief, Pfizer, Freiburg, Germany
17:50	**Closing**

Wednesday, 12 May 2021

	Invited talks: Advanced therapeutic products: an industrial perspective incl. Q&A Chairs: Karine Andrieux, University Paris Sud and Andreas Zimmer, University of Graz	**Invited talks: Solid dosage forms incl. Q&A** Chairs: Iris Ziegler, Cordon Pharma and Rok Dreu, University of Lubljana		**Short talks: Controlled drug delivery** Chairs: Werner Weitschies, University of Greifswald and Julijana Kristl, University of Lubljana	**Short talks: Preformulation and bioavailability** Chairs: Catherine Herry, Nextpharma and Lea Ann Dailey, University of Vienna
8:45	**Formulation approaches for cell and gene therapies** Chris Van der Walle GlaxoSmithKline, United Kingdom	**Adoption of the MCS concept in the pharmaceutical industry** Michael Leane Bristol-Myers Squibb, New York, USA & Kendal Pitt GlaxoSmithKline, Ware, United Kingdom	8:45	**Design and control of a floating gastroretentive drug delivery system made by hot-melt tube extrusion** Paul Bebemik, University of Bonn, Germany	**In situ drug amorphization using laser irradiation** Nele-Johanna Hempel, University of Copenhagen, Denmark
			9:00	**A new calcium oral-controlled-release system based on zeolite for prevention of osteoporosis** Anna Maria Piras, University of Pisa, Italy	**Understanding the Release of ITZ:HPMCAS Amorphous Solid Dispersions** Patricia Nunes, Hovione, Portugal
			9:15	Q&A	Q&A
9:35	**Comparison of different chromatography-based purification strategies for AAV vectors** Ruth Rieser, University of Munich, Germany	**Process design for innovative drug delivery systems** Jukka Rantanen University of Copenhagen, Denmark	09:35	**Spray dried microparticulate drug delivery systems for long-term local osteoarthritis treatments** Carlota Salgado, University of Geneva, Switzerland	**Evaluation of different preprocessing methods of x-ray micro-computed tomography images** Sebastien Bollmann, University of Düsseldorf, Germany
9:50	**Formulation of cationic liposomes enhances the immunogenicity of pDNA vaccine againts SARS-COV-2** Allegra Peletta, ISPSO, University of Geneva, Switzerland		09:50	**Tuning the mechanical poreperties and release profile on an antimicrobial peptide from an injectable hydrogel using glycol chitosan** James Flynn, University of Limerick, Ireland	**Experimental and numerical studies of input parameters calibration for the simulation of the wet granulation process for pharmaceutical use** Maroua Rouabah, University Lyon 1, France
10:05	Q&A		10:05	Q&A	Q&A
10:25	**Biodrugs and advanced therapy medicinal products: a revolution in medecine** Maria Luisa Nolli NCNbio, Milan, Italy	**The importance of understanding the physical and chemical properties of APIs in the digital design of drug products** Kevin Roberts University of Leeds, United Kingdom	10:25	**Development of N-acetylcysteine-functionalized microcontainers for degradation of biofilm matrix** Stine Egebro Birk, Technical University of Denmark, Lyngby, Denmark	**Real-Time Oral Biodistribution of Fluorescent Labelled Olmesartan Medoxomil SMEDDS** Yelda Komesli, University of Altinbas, Turkey
			10:40	**SynBiosys ® long acting injectable miroparticle formulations for large proteins** Tanja Henzler, Merck, Darmstadt, Germany	**Insight into amorphous solid dispersion dissolution behaviour: laser-diffraction and Raman spectroscopy holding hands** Maria Paisana, Hovione FarmaCiencia, Lisbon, Portugal
			10:55	Q&A	Q&A
11:15	Coffee break/exhibitor/posters				
11:45	**APGI award session** Maurice Marie-Janot Award 2020: Prof. Robert Langer Young Investigator Award 2020: Dr Eline Teirlinck Young Investigator Award 2021: Dr Raul Diaz Salmeron JDDST Best Paper Award 2020				
12:15	Plenary lecture incl Q&A - Chair: Juergen Siepmann, University of Lille **Advances in nanotechnology** Patrick Couvreur, Faculty of Pharmaceutical Scienes, Paris Sud University, France				
13:15	Lunch break/exhibitor/posters				
	Invited talks: What's new in nanotechnology? Incl. Q&A Chairs: Elias Fattal, University Paris Sud and chair tbc	**Invited talks: 3D-printing incl. Q&A** Chairs: Alvaro Goyanes, FabRex and Julian Quodbach, University of Düsseldorf		**Short talks: Pulmonary, nasal and buccal delivery** Chairs: Ajit Narang, Genetech and chair tbc	**Short talks: Tablets and coated tablets** Chairs: Katrin Bartscher, NextPharma and chair tbc
14:45	**What's needed in nanomedicine?** Twan Lammers RWTH Aachen University, Germany	**3D-printing of medicines and implants: making the formulation work** Clive Roberts University of Nottingham, United Kingdom	14:45	**High potency, brittle matrix tacrolimus powders for dry powder for inhalation by thin film freezing** Sawittree Sahakijpijarn, University of Texas at Austin, USA	**Profiling the influence of process parameters on the interfacial properties of bilayer tablets** Jan Hendrik Finke, Technical University of Braunschweig, Germany
			15:00	**Delivery of beclomethasone dipropionate nanosuspensions via electronic cigarette** Luca Casula, University of Cagliari, Italy	**Evaluation of the performance of an external lubrication system implemented in a compaction simulator** Cedrine de Backere, Ghent University, Ghent, Belgium
			15:15	Q&A	Q&A
15:35	**Nanotechnologies for advanced imaging** Nathalie Mignet, Chemical and Biological Technologies for Health, University of Paris, France	**Thermoplastic copolyesters: A promising 3D-printing excipient for personalized vaginal inserts** Martin Spoerk, RCPE, Graz, Austria	15:35	**P.aeruginosa biofilm infectred bronchial epithelium as test-system for anti-infective aerosol formulations** Claus-Michael Lehr, Saarland University, Saarbrücken, Germany	**Influence of the unloading conditions on capping and lamination during tableting: numerical and experimental study** Vincent Mazel, University of Bordeaux, France
		Semi-solid Extrusion 3D-printing of Orodispersible Films for Veterinary Use Erica Sjöholm, University of Turku, Finland	15:50	**Evaluation of a novel probiotic nasal spray in human volunteers** Filip Kiekens, University of Antwerp, Belgium	**Development of Mini-Tablets with SSR-25** Valentine Elezaj, University of Düsseldorf, Germany
		Q&A	16:05	Q&A	Q&A
16:25	**Hyperloaded polymeric micelles for chemo- and immunotherapy** Alexander Kabanov, Eshelman School of Pharmacy at Chapel Hill, University of North Carolina, USA	**3D-printing in an industrial GMP setting** Jaedeok Yoo Aprecia Pharmaceuticals, Blue Ash, USA	16:25	**Nanofibers with antibiotics and probiotics for the two-stage therapy of peridontal disease** Spela Zupancic, University of Ljubljana, Slovenia	**High solids film coating systems: continuous vs. batch processing** Christian Mühlenfeld, Ashland Industries Deutschland GmbH, Düsseldorf, Germany
			16:40	**Mucoadhesive films to elicit nanoparticle buccal permeation** Javier Morales, University de Chile, Santiago, Chile	**Effect of the compaction parameters of the final structure and properties of a press-coated tablet (Tab-in-Tab): experimental and numerical study of the influence of core and shell dimensions** Léo Picart, University of Bordeaux, France
			16:55	Q&A	Q&A
17:15	**Closing**				

Thursday, 13 May 2021

	Invited talks: Formulation issues for biotech drugs - incl. Q&A Chairs: Chris van der Wall, GSK and Karoline Bechtold-Peters, Novartis	**Invited talks: Localised drug delivery incl. Q&A** Chairs: Carmen Alvarez Lorenzo, University Of Santiago de Compostella and chair tbc		**Short talks: Nanotechnology** Chairs: Giuseppe de Rosa, University of Naples and chair tbc	**Short talks: Continuous manufacturing / Modeling and simulation** Chairs: Joao Pinto, University of Lisbon and Martin Bornhöft, APV
8:45	**Pellet freeze-drying of biopharmaceuticals** Stefan Schneid, Bayer,Wuppertal, Germany	**Jumping to the brain: Tailored nanomedicines** Giovanni Tosi, University of Modena and Reggio Emilia, Italy	8:45	**Heterotelechelic polymer prodrug nanoparticles for imaging and combination therapy** Julien Nicolas, University Paris Sud, France	**Characterization of a Continuous Small-Scale-Solid Liquid Separator for Filtration, Washing, and Drying of Pharmaceutical Suspensions** Claas Steenweg, University of Dortmund, Germany
			9:00	**Comparison of Exosome Loading Methodologies - Development of Blood-Brain Barrier-Targeting Exosomes via Dual Asymetric Centrifugation** Anne Mahringer, University of Heidelberg, Germany	**Continuous production of cyclodextrin-based reconstitution powder from aqueous solution using scaled-up electrospinning** Panna Vass, Budapest University of Techcnology and Economics, Hungary
			9:15	Q&A	Q&A
9:35	**Please stay my dear: Interfacial adsorption as driving force for protein particle formation during peristaltic pumping** Natalie Deiringer,University of Munich, Germany	**Development of a dissolution method for dosage forms administered into subtenon space** Tobias Auel, University of Greifswald, Germany	09:35	**Antiangiogenic folate-targeted nanoparticles for docetaxel delivery in ovarian cancer** Claudia Conte, University of Naples Federico II, Italy	**An in-silico workflow for designing a continuous mixing process with DEM simulations** Peter Toson, RCPE, Graz, Austria
9:50	**Creating Highest Quality Lyophilisates with Low Oxygen and Water Content by Smart Polymer Packaging** Nicole Härdter, University of Munich, Germany	**Impact of the vitro release set-up on drug release from PLGA implants** Céline Bassand, University of Lille, France	09:50	**Cellular and subcellular targeting of TRAP1 as a new therapeutic approach for cancer treatment** Clelia Mathieu, Institut Galien - Paris Sud, France	**Visualization of solvent effects on crystal surfaces by chemical force mapping - a combined experimental and simulation approach** Mikkel Herzberg, University of Copenhagen, Denmark
10:05	Q&A	Q&A	10:05	Q&A	Q&A
10:25	**Biologics drug product development: challenges at the interface formulation, primary packaging and application** Susanne Jörg, Lonza AG, Basel, Switzerland	**Inhaled chemotherapy: a new modality for lung cancer treatment?** Nathalie Wauthoz, Université Libre de Bruxelles, Belgium	10:25	**Effects of cytokines release in tissue regeneration and cancer treatments** Slivia Pisani, University of Pavia, Italy	**Predicting crystal breakage in pharmaceutical agitated dryers** François Hallac, University of Leeds, United Kingdom
			10:40	**Bacterial membrane vesicles as novel treatment avenue for intracellular infections** Gregor Fuhmann, HIPS, Saarbrücken, Germany	**Dissolution and re-crystallization of supersaturated indomethacin solutions** Andreas Danzer, University of Dortmund, Germany
			10:55	Q&A	Q&A
11:15	Coffee break/exhibitor/posters				
11:45	**APV Award session** APV Research Award 2019/2020: Professor Olivia Merkel APV Best Thesis Award 2019/2020: Flavia Fontana EJBP Best Paper Award 2020				
12:15	Plenary lecture incl. Q&A - Chair: Joerg Breitkreutz, University of Düsseldorf **Pharmacomicrobiomics: drugs meet the human microbiome** Christine Moissl-Eichinger, Medical University of Graz, Austria				
13:15	Lunch break/exhibitor/posters				
	Invited talks: Oral drug delivery incl. Q&A Chairs: Robert O.Williams, University of Texas and chair tbc	**Invited talks: Amorphous drug delivery systems incl. Q&A** Chairs: Susanne Page, Roche and Thomas Rades, University of Copenhagen		**Short talks: 2D- and 3D-printing** Chairs: Milen Dimitrov, University of Sofia and Natalja Genina, University of Copenhagen	**Short talks: Skin delivery and protein formulations** Chairs: Nina Dragicevic, University of Beograd and chair tbc
14:45	**Hydrophobic ion pairs: A game-changing approach for delivery of BCS class 3 drugs** Andreas Bernkop-Schnürch, Faculty of Chemistry and Pharmacy, University of Innsbruck, Autria	**Hybrid mixtures: A perspective on amorphous solid dispersions in food applications** Lennart Fries, Nestlé Research Center, Vevey, Switzerland	14:45	**Direct powder extrusion 3D-printing: novel technology for manufacturing amorphous solid dispersions** Alvaro Goyanes, FabRx, London, United Kingdom	**A new approach to predict in vitro-in vivo correlation for transdermal therapeutics systems** René Rietscher, LTS Lohmann Therapie-Systeme, Andernach, Germany
			15:00	**Semi-solid extrusion and alginate ionotropic gelation: a successful duo for the production of personalized gastro-retentive formulations** Paola Russo, University of Salerno, Fisciano, Italy	**Proliposomes for the production of deformable liposomes containing drug micelles** Silvia Franze, University of Milan, Italy
			15:15	Q&A	Q&A
15:35	**Biological barriers to oral delivery of macromolecules** Caitriona O'Driscoll, School of Pharmacy, University of Cork, Ireland	**Rational selection of Amorphous Solid Dispersion (ASD) Compositions for Improving Drug Candidate Bio-performance** David Lyon, Lonza, USA	15:35	**Selective laser sintering of Solid Oral Dosage Forms with Copovidone and Paracetamol Using a CO2 Laser** Yanis Abdelhamid Gueche, University of Montpellier, France	**EPR study of effect of ascorbic acid on hair and feather samples in relation to eumelanins and pheomelanins** Michael Lawson, University of Bratislava, Slovakia
			15:50	**Direct-ink writing of implantable hybrid PCL/PEO drug delivery systems** Se Hun Chung, University College of London, United Kingdom	**α-relaxation studies to improve long term stability of lyophilized products from a thermodynamical point of view** Sebastial Groel, University of Munich, Germany
			16:05	Q&A	Q&A
16:25	**The virtual patient and the in-silico design of solid oral dosage forms** Hans Leuenberger, College of Pharmacy, University of Florida, Lake Nona Medical Campus, Orlando, Florida, USA	**The variability of the amorphous state in relation to processing** Marc Descamps, University of Lille, France	16:25	**Investigations on inkjet printed metoprolol tartrate orodispersible films for paediatric application** Olga Kiefer, University of Düsseldorf, Germany	**Continuous alternative to freeze-drying: solid formulation of a monoclonal antibody using high-speed electrospinning** Julia Domjan, Budapest University of Technology and Economics, Hungary
			16:40	**Traceable personalized oral dosage forms containing cannabinoids** Natalia Genina, Abo Akademi University, Finland	**A holistic approach to develop a spray-drying method for CXCL8** Sonja Hartl, RCPE, Graz, Austria
			16:55	Q&A	Q&A
17:15	**Closing**				

Friday, 14 May 2021

	Invited talks: In silico simulation for manufacturing processes - incl. Q&A Chairs: Pierre Tchoreloff, University of Bordeaux and Peter Kleinebudde, University of Düsseldorf	Invited talks: Nanofabrication technologies incl. Q&A Chairs: Claus-Michael Lehr, University of Saarbrücken and Maria Carafia, University of Rome		Short talks: Gene delivery and ATM Chairs: Nathalie Mignet, University of Paris and Juan M. Irache, University of Navarra	Short talks: Advanced drug delivery Chairs: Olivia Merkel, University of Munich and chair tbc
8:45	**Digitalization in pharmaceutical product and process design: from advanced simulations to virtual drug product development** Johannes Khinast Graz University of Technology, Austria	**Novel manufacturing for healthcare: microbubbles, particles, capsules and fibres** Mohan Edirisinghe,Biomaterials Processing Laboratory, Dept Mechanical Engineering, University College of London, United Kingdom	8:45	**Formulation development of stabilize viral vectors** Julia Rabas, Leukocare, Munich, Germany	**Repurposing of cationic apphiphiles to promote cytosolic RNA delivery** Koen Raemdonck, Ghent University, Belgium
			9:00	**Tablets of siRNA lipoplexes: impact of processes on structure and gene-silencing efficacy** Virginie Busignies, University of Bordeaux, France	**Alginate-spermidine microgels as filling matrix of multi-channel PLGA scaffolds for the treatment of peripheral nerve injuries** Caterina Valentino, University of Pavia, Italy
			9:15	Q&A	Q&A
9:35	**Digital Process Design** Sean Bermingham Process System Enterprise (PSE), London, United Kingdom	**Advances in electrospinning** Nalin de Silva, Dept of Chemistry, University of Colombo, Sri Lanka	09:35	**Anti-EGFR nanovector of siNRA - a theranostic tool for triple negative breast cancer active targeting** Phuoc Vinh Nguyen, Tours University, France	**Preparation and evaluation of anticancer agent nanocrystals** Yohann Corvis, University of Paris, France
			09:50	**siRNA in lung slices: knocking down fibrosis?** Mitchel Ruigrok, University of Groningen, The Netherlands	**Evaluation of in vivo efficacy of ferrocifen loaded lipid nanocapsules on ovarian cancer** Elise Lepeltier, University of Angers, France
			10:05	Q&A	Q&A
10:25	**Study of the drying process in simulated pharmaceutical coatings: Model and experiment** Onjdrej Navratil, University of Prague, Czech Republic	**Advanced in vitro lung-on-chip platforms for inhalation assays** Josue Sznitman, Dept of Biomedical Engineering, Israel Institute of Technology, Haifa, Israel	10:25	**mRNA based Skin Vaccination by intradermal application of lipid coated polymeric nanoparticles** Lena Kliesch, Helmholtz-Institute for Pharmaceutical Research Saarland, Germany	**A novel polyethlyene glycol-based linker platform for the development of hydrophilic antibody-drug conjugates** Tommaso Tedeschini, University of Padova, Italy
10:40	**In silico design of tablet microstructure by evolutionary algorithm** Frantisek Stepanek, University of Prague, Czech Republik		10:40	**MSC extracellular vesicles for treatment of alpha-1-antitryspin deficiency pulmonary diseases** Elia Bari, University of Pavia, Italy	**Dithiolane-crosslinked polymer micelles: reduction responsive drug release** Cornelus van Nostrum, University of Utrecht, The Netherlands
10:55	Q&A		10:55	Q&A	Q&A
11:15	Coffee break/exhibitor/posters				
11:45	**International ADRITELF Award 2020** Giuseppe De Rosa, University of Naples Federico II, Italy				
12:15	Plenary lecture incl. Q&A - Chair: Anna-Maria Fadda, University of Cagliari **Oral drug delivery systems: from irrelevance to top-selling products and ongoing challenges** Andrea Gazzaniga, Biopharmaceuticals and Pharmaceutical Technology Laboratory, University of Milan, Italy				
13:15	Lunch break/exhibitor/posters				
	Invited talks: Dermal and transdermal delivery incl. Q&A Chairs: Paola Minghetti, University of Milan and chair tbc	**Invited talks: Continuous Manufacturing incl. Q&A** Chairs: Ali Rajabi-Siahboomi, Colorcon and Michael Repka, University of Mississipi		**Short talks: Oral drug delivery/Pediatric formulations** Chair: Sandra Klein, University of Greifswald and Luigi Boltri, Adare	**Short talks: Processing and PAT** Chairs: Javier O.Morales, University of Chile and Fransisco Otero Espinar, University of Santiago de Compostelle
14:45	**Skin permeation from Pickering emulsions** Marie-Alexandrine Bolzinger Claude Bernard University Lyon, France	**Process development of the future: fully automated DoE process analysis in an integrated continuous manufacturing plant for solid oral dosage forms** Victoria Pauli Novartis, Basel, Switzerland	14:45	**The Use of Partially Hydrolysed Polyvinyl Alcohol for The Production of High-Drug-Loaded Sustained Release Pellets via Extrusion-Spheronization and coating: In Vitro and In Vivo Evaluation** Valerie Vanhomme, University of Ghent, Belgium	**Improving flowability and reducing storage agglomeration of metformin hydrochloride through QESD crystallization** Jerome Hansen, University of Düsseldorf, Germany
			15:00	**X-Ray imaging of micorcontainers used for oral drug delivery** Rolf B. Kjeldsen, Technical University of Denmark, Lyngby, Denmark	**Production and downstream-processing of API-nanosuspensions** Arno Kwade, Technical University of Braunschweig, Germany
			15:15	Q&A	Q&A
15:35	**Microarray patches from high-dose delivery: targeting global healthcare challenges** Ryan F. Donnelly School of Pharmacy, Queen's University Belfast, United Kingdom	**Residence Time Distribution (RTD) concept as element in drug product quality control strategies for continuous manufacturing** Bart Nitert Janssen Pharmaceuticals, Beerse, Belgium	15:35	**Controlled permeability enhancement with short peptide inhibitors of protein kinase C zeta** Joel Brunner, University of Geneva, Switzerland	**Improving particle size distributions in a conical mill through new impeller air flow optimization comparisons utilizing computational fluid dynamics (CFD) analysis and empirical DoE** Wilf Sanguesa, Quadro Engineering, Ontario, Canada
			15:50	**A toolbox for mimicking gastrointestinal conditions in children: S(imulated) P(aediatric) B(reakfast) M(edia) for addressing the variability of gastric contents after typical paediatric breakfasts** Lisa Freerks, University of Greifswald, Germany	**Innovative preparation of API salt coated on particles using fluidised bed** Jakub Muzik, University of Prague, Czech Republic
			16:05	Q&A	Q&A
16:25	**Improved vaccine immunogenicity through microneedle delivery** Michael Schrader Vaxess, Boston, MA, USA	**Continuous manufacturing of solid oral dosage forms: opportunities and controversies** Kendal Pitt GlaxoSmithKline, Ware, United Kingdom	16:25	**Design and evaluation of self-emulsifying drug delivery system for pediatric use** Xiona Liu, University of Copenhagen, Denmark	**Insight into the impact of compaction process variations on tablet disintegration by non-destructive at-line terahertz porosity sensing** Prince Bawuah, University of Cambridge, United Kingdom
			16:40	**Acceptability of antibiotics in pediatrics: findings from an international observational study** Thibault Vallet, Clinsearch, Malakoff, France	**NIR as in-line PAT tool to study desorption kinetics in spin freeze-dried formulations** Laurens Leys, Ghent University, Belgium
			16:55	Q&A	Q&A
17:15	**END OF THE CONFERENCE**				

International Conferences and Events

	Partner talks recorded, followed by live discussions		
	Wednesday 12 May, 2021	**Thrusday 13 May, 2021**	**Friday 14 May, 2021**
08:45	**Surface modified HPMC for continuous manufacturing of modified release formulations** Daniel Sieber, Ashland	**Grace mesoporous silica gels for today´s formulation challenges** Joachim Quadflieg, Grace	**EDEM -Particle Based Simulation of Pharmaceutical Production Processes** Jens Dornieden, EnginSoft GmbH
09:05	Q&A	Q&A	Q&A
09:15	**How to develop continuous granulation process?** Margarethe Richter, Thermo Fisher	**ASD and Implant Development made easy** Daniel Treffer, MeltPrep GmbH	**Linkam temperature and environmental control stages** Shrey Sharma/Duncan Stacey, Linkam
09:35	Q&A	Q&A	Q&A
09:45	**Engineering Drug Release in EVA based Implants: platform tools & predictive modeling** Christian Schneider, Celanese	**Interreg project "Site-Specific Drug Delivery"** Juergen Siepmann, University of Lille,	**Dissolvable Microarray Patch Systems - Microneedles that are able to meet the content uniformity requirements** Stefan Erlhofer, LTS
10:05	Q&A	Q&A	Q&A
10:15	**Unique Nanoforming Technology for Poorly Soluble APIs by Nanoform** Niklas Sandler, Nanoform	**How to make injectable implants for drug delivery?** Valerie Louise Pietsch, Thermo Fisher	**Smart robotic solutions in aseptic fill/finish environments** Rudolf Michael Weiss, Stäubli Robotics
10:35	Q&A	Q&A	Q&A
10:45	**Data-driven formulation development on STYL'One Nano** Bruno Leclercq/Quentin Boulay, Medelpharm		**Understanding Compaction with USP <1062> and Gamlen Instruments** Rebecca McVicker, Gamlen
11:05	Q&A		Q&A
13:15	Lunch Break/Exhibitor/Posters		
14:45	**From meter to nanometer** Roy Housh, Frewitt	**Dissolution Testing of Nanoparticles with the NanoDis System** Dr. Karen Krauel-Göllner, Agilent	**Raman and IR QCL Imaging Solutions in Formulation Development and Quality Control of Pharmaceuticals** Andreas Kerstan, Agilent
15:05	Q&A	Q&A	Q&A
15:15	**Viscosity Reducing Excipients for Protein Therapeutics** Tobias Rosenkranz, Merck	**The Analytical Power of Raman Imaging for Life Sciences & Pharmaceutics** Miriam Boehmler, WITec	
15:35	Q&A	Q&A	
15:45	**Development and Evaluation of Ready-to-Use Hot Melt Coating Formulations for Taste Masking** Raphael Janousek, Biogrund		
16:05	Q&A		
16:15	**Nextpharma new platform for lipid based formulation** Catherine Cornille, Nextpharma	**tbd** Beckman Coulter Life Sciences	
16:35	Q&A	Q&A	
16:45	**In Vitro Test Methodologies for Characterizing Bioavailability Enhancing Formulations** David Lyon, Lonza	**Origin and Future of HPMCAS - A Success Story in amorphous Solid Dispersion** Andreas Sauer, Shin-Etsu	
17:05	Q&A	Q&A	
17:15	Closing		

Information Day

Information Day APGI/EVONIK
"Functional solid oral dosage forms"
1st June 2021 – online

The APGI and EVONIK Health Care are jointly organizing their next Information Day, which will take place on the 1st of June 2021, ONLINE. This one-day event, entitled "Functional solid oral dosage forms – Superior formulation approaches & novel manufacturing technologies to meet industrial needs" will be an excellent opportunity to learn about enabling formulation approaches and advantageous manufacturing setups.

Programme

ADVANCED DRUG DELIVERY

- Taste masking of bitter actives, *Evonik Healthcare, Germany*
- GI-targetting with EUDRAGIT ® polymers – from conventional coatings to specific technologies, *Evonik Healthcare, Germany*
- Compression of matrix tablets and coated multiparticulates, *Evonik Healthcare, Germany*
- Poorly soluble formulations – highly efficient cleaning of production equipment, *Priya Poduval – Dober, Germany*

NOVEL & CHALLENGING TECHNOLOGIES

- Drug Delivery for Microbiome Therapeutics, *Evonik Healthcare, Germany*
- Self-microemulsifying drug delivery system (SMEDDS) for solubility enhancement – adsorption to a solid carrier, *Prof Sandra Klein – University of Greifswald, Germany*, *Fabian-Pascal Schmied – Evonik Health Care, Germany*
- Additive manufacturing of dosage forms: How 3D Printing drives formulations, *Dr Julian Quodbach – University of Düsseldorf, Germany*
- Continuous processing: An attractive option for higher production efficiency, *Bill Nicholson – GEA, United Kingdom*

Information Day

Participation fee

APGI members: Free of charge

Non-members: Industry 195€ (+20% French VAT)
Academia 80€ (+ 20% French VAT)
Students 25€ (+ 20% French VAT)
+ free & non-recurring APGI membership for 2021

Registration

Registration is possible on our website

Hot Topic Day

Hot Topic Day « 3D printing in Pharmaceutics »
27 November 2020 – fully virtual

Last year we introduced a new type of APGI events:

"Hot Topic Days", which are 1-day events dedicated to a rapidly evolving topic of key interest in our field. The aim is that pioneers and opinion leaders in the field give a comprehensive overview on the current state of the art, present most recent results and provide an outlook on future developments.
Due to the COVID crisis, we had to organize the event fully virtually.
171 participants joined the presentations and discussions by world-wide leading experts, explaining the underlying basics, the most recent technical achievements & practical applications and addressing crucial bottlenecks to be overcome.

- Prof. Abdul Basit, University College London, UK
  3D Printing in Pharmaceutics: Where are we?
- Dr. Atheer Awad, University College London, UK
  Clinical Applications of 3D Printed Medicines
- Dr. Mohammad J. Mirzaali, University of Delft, The Netherlands
  3D Printing from an engineering point of view: What is feasible today?
- Dr. Jonathan Goole, University of Brussels, Belgium
  3D Printing with biodegradable polymers
- Prof. Andrea Gazzaniga, University of Milano, Italy
  Towards 4D printing
- Dr. Alvaro Goyanes, FabRx, Ashford, UK
  Novel 3D Printing Technologies in Pharmaceutics
- Prof. Jukka Rantanen, University of Copenhagen, Denmark
  Analytical aspects of printed oral dosage forms
- Dr. Korinde van den Heuvel, Senior product developer, DFE Pharma, The Netherlands
  3D Powder bed printing with lactose: a showcase
- Dr. Camille Dumont, Formulation Scientist-Pharma, Gattefossé, France
  3D Printing of pharmaceutical solid lipid-based formulations

3D Printing is a real "Hot Topic" in Pharmaceutics: The versatility of this novel production technique offers a large range of advantages and will likely enable substantially improved medications in the future. Personalized medicine with individualized dosing adapted to the specific needs of each patient is just one of the many possible breakthroughs that might become reality. It is telling that in our societies we are used to have a broad choice of standard sizes and shapes for our clothes, but generally only a very limited choice of dose strengths of medicines.
However, there are numerous hurdles that are still to be overcome for 3D printing in pharmaceutics, and we are only at the very beginning of the discovery of the real potential of this revolutionizing technique.

APGI members have access to the slides of the presentations once logged in their personal account on our website: https://www.apgi.org/connection

Hot Topic Day

Hot Topic Day « Colon targeting »
End of November 2021, Lille, France

The second "Hot Topic Day" of the APGI will be dedicated to a particularly challenging aim in pharmaceutical formulation:

Site-specific drug delivery to the colon

The idea is to minimize drug release in the upper part of the gastro intestinal tract (stomach and small intestine), and to delivery the drug specifically to the colon. This type of systems can be very helpful to improve the efficacy of local drug treatments of the colon, such as chronic inflammatory bowel diseases (e.g. Crohn's disease and ulcerative colitis). Also, the way could be paved for a holy grail in our field: The oral delivery of biopharmaceuticals for systemic action.

A variety of strategies has been proposed to allow for colon targeting, including dosage forms with polymeric coatings exhibiting pH dependent solubility, systems which are preferentially degraded by enzymes secreted by bacteria present in the colon, and/or "time-controlled" devices, which release the drug after a pre-programmed lag-time (e.g., due to the rupturing of an outer film coating). A large spectrum of excipients and manufacturing techniques has been suggested with more or less promising results in vitro and in vivo.

Yet, the variability of drug release at the target site remains high, and numerous technical and biological challenges remain to be addressed and overcome. The role of the human microbiome is still not fully understood and premature drug release in the upper gastro intestinal tract is often not sufficiently controlled.

Hot Topic Day

This “Hot Topic Day” will allow getting familiar with the current state of the art in this rapidly evolving field, including the latest clinical trials and novel delivery strategies with promising in vitro results and data obtained in animal studies. The academic and industrial speakers will also present most recent research findings, discuss current bottlenecks and give future outlooks.

We very much hope that it will be possible to hold this 1-day event onsite in Lille, France, as a face-to-face meeting. In case the COVID crisis will still not allow this, all presentations and discussions will be *live* online. In the case of an *onsite* event, also poster presentations and an industrial exhibition will accompany the scientific talks.

The exact date of the “Hot Topic Day” will be announced shortly, as well as the details of the scientific programme.

We very much hope that we will be able to welcome you in person in Lille!

The organizing committee

Participation fee

APGI members: Free of charge

Non-members: Industry 195€ (+20% French VAT)
Academia 80€ (+ 20% French VAT)
Students 25€ (+ 20% French VAT)
+ free & non-recurring APGI membership for 2021

Registration

Registration will start in September

APGI Young Investigator Award 2021

The “Young Investigator Award” recognizes the most outstanding doctoral thesis in the field of Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology every year.

It is our great pleasure to announce the laureate of the APGI Young Investigator Award 2021:

Raul Diaz Salmeron, University Paris-Saclay, France

The composition of the jury was as follows:

Prof. Géraldine Piel, University of Liège (president)
Dr Susanne Muschert, University of Lille
Dr Joël Richard, Medincell
Dr Gaëlle Vacher, University of Bordeaux

APGI Award

Title of thesis: "Directed-mobility and enhanced-adhesion nano-platelets for local drug delivery: towards a new treatment of bladder diseases."

Supervisors: Prof. Gilles Ponchel and Prof. Kawthar Bouchemal (University of Paris-Saclay)

Abstract: Local drug delivery allows to bring large amounts of drugs with reduced side effects, in comparison with systemic administration. Despite the advantages provided by the local drug delivery, intravesical drug delivery is still challenging because it exhibited several issues which are decreasing the therapeutic efficacy and the patient compliance to the treatment. Most therapies for the treatment of bladder diseases are simple drug solutions or suspensions administered intravesically by using a catheter through the urethra in order to easily reach the bladder and, consequently, the urothelium. Since the drug is administered into the bladder, drug dilution is occurring because of the continuous production of urine. Furthermore, active substances are being eliminated during washout when bladder urine voiding is happening. These two processes lead to the decrease of local drug concentration close to the urothelium. Patients need repeated catheterization, performed by health care practitioners, to reach the therapeutic dose of the drug.

The main goal of this PhD thesis was to create and design a new nanoparticulate system with non-spherical shape susceptible to move in a different manner compared to spherical nanoparticles. These systems may exhibit an amplified mucoadhesion allowing to bring more important amounts of drug than classical and nanoparticle administration. These nanoparticles, called now nano-platelets have shown different movement behavior than the spherical ones. Indeed, they diffuse more rapidly in a straight-line way. Thanks to their oriented and directed motion and to their intrinsic properties, due to the shape, these systems have shown a better mucoadhesion on the bladder tissue, a better uptake in different cell lines and they were far less rapidly eliminated from the urothelium mucosa.

An *in vivo* model of Bladder Painful Syndrome / Interstitial Cystitis in rats demonstrated the therapeutic efficacy of nano-platelets, especially for hyaluronic acid nanoparticles. Indeed, they demonstrated a better bioaccumulation into the bladder and a better therapeutic efficacy as anti-inflammatory and urothelium regenerating agents.

These nanoparticulate systems represent a new innovative, rational and effective approach allowing to open new research pathways for the treatment of bladder diseases.

APGI Award

List of former awardees

2014: Amrit Paudel, University of Leuven
2015: Anne-Laure Laine, University of Angers
2016: Alice Gaudin, University Paris-Sud
2017: Stephan Stremersch, Ghent University
2018: Ranhua Xiong, Ghent University
2019: Karen Peynshaert, Ghent University
2020: Eline Teirlinck, Ghent University

Sponsor

The “APGI Young Investigator Award” is kindly sponsored by Sanofi.

SANOFI

Hydroxypropyl-β-cyclodextrin as Promising Functional Alternative to Surfactants in Biologics

S. Hong[1], T. Peng[1], O. Häusler[2]

1 Roquette Asia Pacific PTE Ltd., Singapore2 Roquette Frères, 62080-Lestrem, France

olaf.haeusler@roquette.com, corresponding address

Introduction

Therapeutic proteins undergo various stresses during upstream, downstream, formulation fill-finish processes, transportation and storage.[1] As proteins are inherently unstable, they tend to formaggregates during these processes. As such, protein aggregation is recognized as a key qualityattribute of biotherapeutics. Formulation development is critical in identifying optimal pH and excipients to limit the progression of aggregation pathways. In formulating a therapeutic protein for parenteral administration, non-ionic surfactants like polysorbates are commonly employed to stabilize proteins against interfaced-induced aggregation. However, polysorbates are not without problems because there are concerns over their composition and stability. Cyclodextrins and their derivatives such as hydroxylpropyl ß-Cyclodextrin (HPβCD) are well-established enabling excipients for small molecule drugs. Recent research has highlighted HPβCD as promising alternative to surfactants for biologics. In addition to its role in mitigating aggregation in therapeutic proteins, HPβCD is also an approved excipient for use in parenteral applications.

Protein Formulation Issues

Due to the structural complexity of therapeutic proteins, formulation development of these molecules to achieve adequate stability is challenging. Proteins are sensitive to temperature changes, shearing, shaking, solvents, ionic strength, purity, protein concentration, pressure, and freeze/thaw-drying cycles; they only remain stable within a narrow pH range and are susceptible to surface adsorption.

Other challenges include viscosity and solubility limitations especially for high protein concentrations. Excipients with different functions are used in formulation to achieve the desired product profiles. Six categories of excipients are commonly used to stabilize proteins. They are buffers, amino acids, polyols/sugars, salt, surfactants, and antioxidants. Currently, polysorbates are the most widely used non-ionic surfactants. About 70 % of marketed monoclonal antibody formulations contain either polysorbate 20 or polysorbate 80. Owning to theirs strong surface activity, polysorbates are effectivein protecting proteins against interface-induced aggregation and surface adsorption.

Exploring Cyclodextrins

Cyclodextrins and their derivatives are wide spread excipients for small- drug molecule applications, used to enhance solubility and bioavailability, improve drug chemical and physical stability and deliver taste-masking property. Cyclodextrins are cyclic oligosaccharides obtained from starch by enzymatic cyclisation. Their unique bucket-like structure, which include a hydrophilic exterior and a hydrophobic cavity, enables the formation of inclusion complexes with small hydrophobic drugs. This complexation enables increased drug solubility and therefore higher bioavailability of poorly water-soluble drugs. When formulating for parenteral delivery, it is necessary to use a modified cyclodextrin in order to achieve the required water solubility. HPβCD is a well-established excipient in parenteral drug delivery.

However, there are two main concerns when formulating therapeutic proteins by using polysorbates.Firstly, polysorbate 20 and 80 are chemically complex mixtures, containing different types of polyoxyethylene esters of fatty acids.[2] This can potentially lead to significant lot-to-lot variabilities. Secondly, polysorbates are prone to degradation by auto-oxidation and hydrolysis. [2] Presence of residual peroxides in bulk polysorbates are often detected, which can lead to protein oxidation and aggregation.[3] These are major concerns, as polysorbates degradation not only lowered the ability of the surfactant to protect the formulation against interfacial stresses, the degradation products can also impact the stability of the protein.

Exploring Cyclodextrins

Cyclodextrins and their derivatives are wide spread excipients for small- drug molecule applications, used to enhance solubility and bioavailability, improve drug chemical and physical stability and deliver taste-masking property. Cyclodextrins are cyclic oligosaccharides obtained from starch by enzymatic cyclisation. Their unique bucket-like structure, which include a hydrophilic exterior and a hydrophobiccavity, enables the formation of inclusion complexes with small hydrophobic drugs. This complexation enables increased drug solubility and therefore higher bioavailability of poorly water-soluble drugs. When formulating for parenteral delivery, it is necessary to use a modified cyclodextrin in order to achieve the required water solubility. HPβCD is a well-established excipient in parenteral drug delivery.

Extensive toxicological and pharmacological studies have shown that HPßCD is safe for parenteral application. It is currently used in numerous approved products with low molecular weightdrug substances, for example as Iitraconazole or mitomycin.

Previous work on HPβCD in liquid protein formulations have suggested two main stabilization mechanisms.[4] It is postulated that the cavity of HPβCD can bind or interact with the exposedhydrophobic resides on the proteins. Since the exterior of HPßCD is hydrophilic, this effectively shieldshydrophobic interactions and blocks protein-protein interactions that lead to aggregation. Due to thesurface activity of HPβCD, it is also postulated that HPβCD can behave similar to non-ionic surfactants. HPβCD can displace protein from air-water interface and thereby inhibiting protein aggregation induced by exposure to the air-water interface.

Assessing HPßCD for Protein Applications

Roquette scientists continued experimental work for exploring the properties of HPßCD and its utilityfor real-world protein formulations. Two biopharmaceutical grade products from Roquette Freres, Lestrem, France were used in these studies: KLEPTOSE® biopharma HP (molecular substitution (MS)

0.88) and KLEPTOSE® biopharma HPB (MS 0.62). Both products own adapted osmolalities and viscosities (see **Figure 1)** for parenteral formulations. Its low viscosity over a broad concentration range, allows high flexibility during formulation development. The use concentration might go up to 200mM, respecting the subcutaneous injection recommended limits of 600 mOsmol/g and 20 mPas for osmolality and viscosity, respectively.

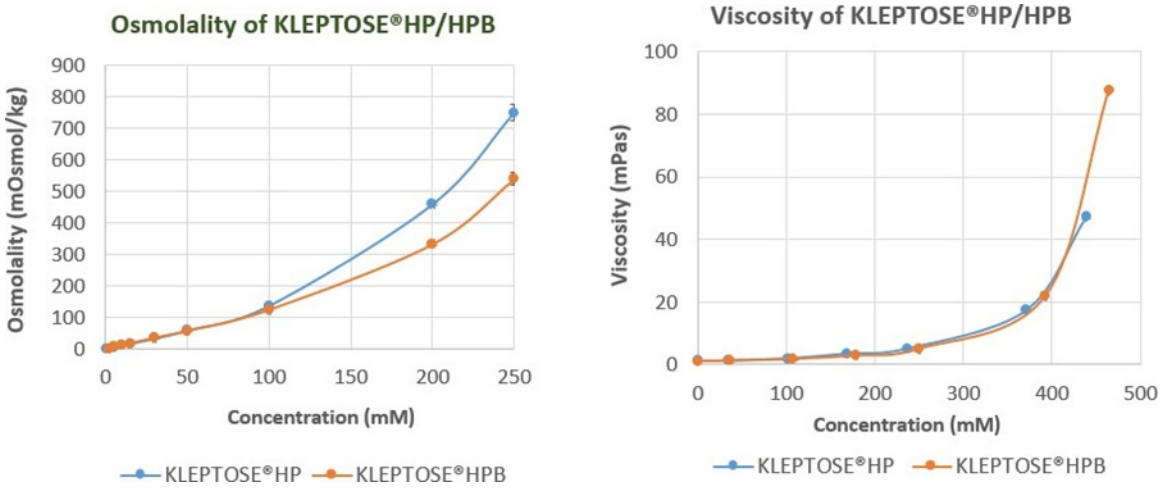


Figure 1: Physical properties of KLEPTOSE®HP and KLEPTOSE®HPB

For better understanding the potential of HPßCD as alternative for surfactants in biologics formulations, its surface activity in solution were studied in detail, using methods for static and for dynamic surface activity. The static surface activity represents the surface tension at equilibrium while dynamic surface tension represents the surface tension over a surface lifetime after surface formation. Both KLEPETOSE® HP and HB exhibit surface tension reduction properties as seen from the drop in surface tension (see **Figure 2A**). However, they present much weaker surface activity compared to polysorbate 20 and 80. Notably, KLEPTOSE® HP and HPB do not exhibit a sharp critical micellar concentration (CMC), unlike polysorbates. Their surface tension continues decreasing with increasingconcentrations, when plotted against the log of concentration.

During manufacturing, transportation or storage, proteins are subjected to different shaking stresses, where a constant "renewal" of the air-water interface takes place. As such, dynamic surface tension which measures the rate at which molecules migrate to the interfaces, is relevant in such scenarios. The maximum bubble pressure method (Krüss BP100) was used to measure the surface tension of HPßCD and polysorbates over a surface lifetime ranging from few milliseconds to several seconds (see **Figure 2B**). Despite the lower surface activity HPβCD, both grades (in 100 mM solution) migrates rapidly to the newly formed air-water interfaces, as indicated by the immediate drop in surface tension. In comparison, both polysorbate 20 and 80 at 0.05%, showed slower kinetics, possibly due tomass transfer limitations.

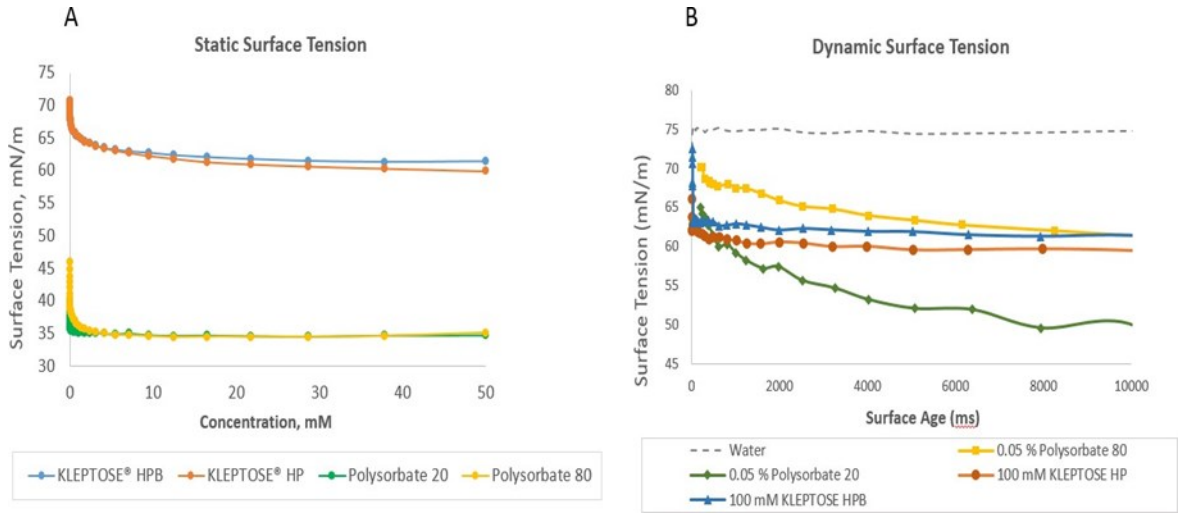


Figure 2: (A) Static and (B) dynamic surface activity of KLEPTOSE®HP and KLEPTOSE®HPB

Two application studies were performed for understanding the effects of HPßCD on therapeutic proteins under stressed conditions, including agitation and thermal stress.

Case Study 1: HPβCD as Functional Alternative to Surfactant in Protein Formulations

In this study, human-plasma high-purity Immunoglobulin (IgG) was chosen as model protein. Lyophilized IgG was reconstituted into 25 mM phosphate buffer at pH 6.8 before formulation with different excipients. It was formulated with HPßCD (either KLEPTOSE® biopharma HP or HPB) at 20 and at 100 mM concentration. Two controls were IgG in buffer (i) with no other excipients and (ii) withthe addition of 0.05% polysorbate 80. The concentration of IgG was 5 mg/ml in all samples.

Samples were subjected to agitation on an orbital shaker (Eppendorf Thermomixer® C) at 1400 rpm at room temperature and were analysed after 24, 48, and 96 hours of shaking. Subsequent analysis was performed using size exclusion chromatography–high-performance liquid chromatography (SEC–HPLC) on a Waters ACQUITY Arc HPLC System equipped with a UV-Vis detector at 218 nm. The percentage of soluble aggregates, monomer and fragments was calculated from the peak areas of compared with the total protein peak area at the specific time-point.

Effects of agitation. Evaluation by SEC–HPLC showed that formulations containing HPβCD maintained a higher level of monomer with a negligible decrease in monomer percentage. High concentrations (100 mM) of both the commercial HPßCD products was able to reduce aggregation rates compared to controls (see **Figure 3A**). Protein fragmentation was observed in control samples after 96 hours of agitation (see **Figure 3B**). Interestingly, this fragmentation was not replicated in any of the formulations containing HPßCD, suggesting the ability of HPβCD in preventing agitation-induced fragmentation, even at low concentrations.

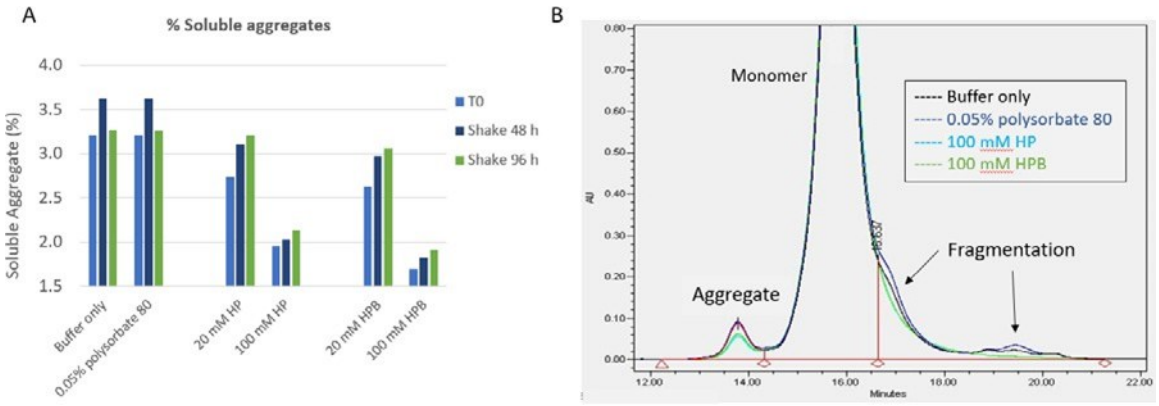


Figure 3: Effects of KLEPTOSE® HP or HPB on agitation-induced (A) aggregation and (B) Fragmentation

IgG formulations (same concentrations as used in the shaking studies) were measured with the dynamic surface tension method. Results (see Figure 4) show the displacement of IgG by HPβCD or by polysorbate 80 from the air-water interface. At newly formed air-water interfaces, as seen from the initial part of the graph, IgG-HPβCD (100 mM) formulations showed lower surface tension than IgG- polysorbate 80 (0.05%) formulation. This indicates that HPβCD occupied the interface more rapidly than polysorbate, demonstrating the effectiveness of HPβCD in protecting proteins against surface- induced aggregation or fragmentation. Nonetheless, the stronger surface activity of polysorbate 80 resulted in a substantially lower surface tension at longer timescales, when approaching equilibrium.

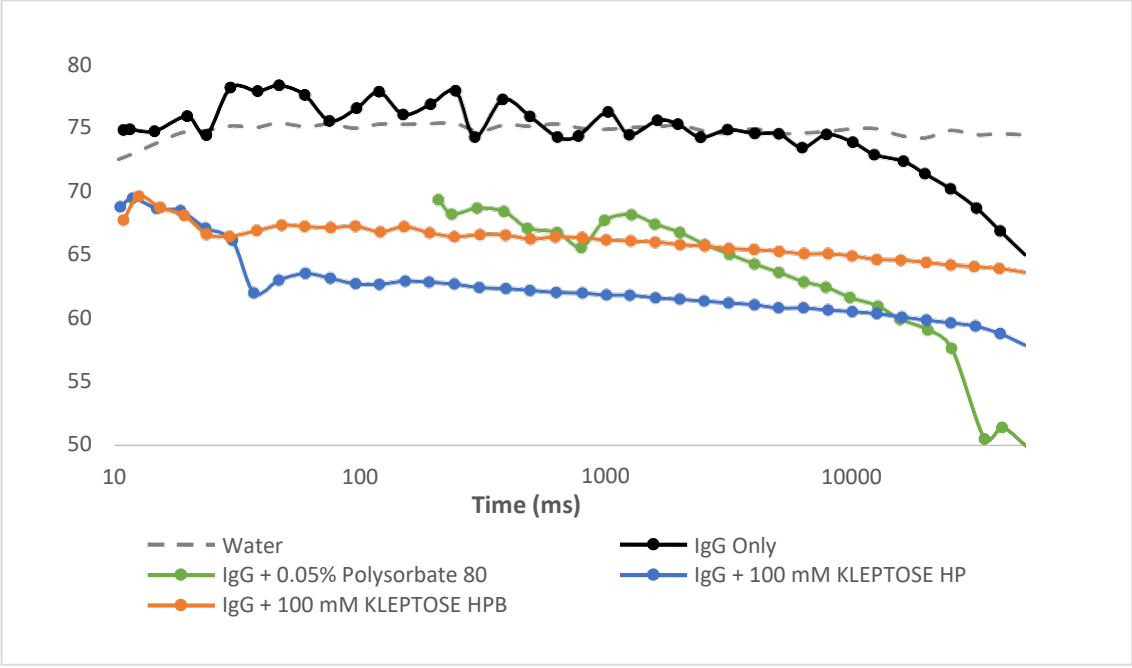


Figure 4: Dynamic surface activity of KLEPTOSE®HP and HPB and Polysorbate 80 in the presence of IgG

Conclusion: In this case study, the investigation of two commercially available HPßCD excipients confirmed their activities as surfactants in protein formulations. The anti-aggregation properties[5] of HPβCD were confirmed as well .Using Hydroxypropylated beta cyclodextrins as biopharmaceutical excipients as shown to:

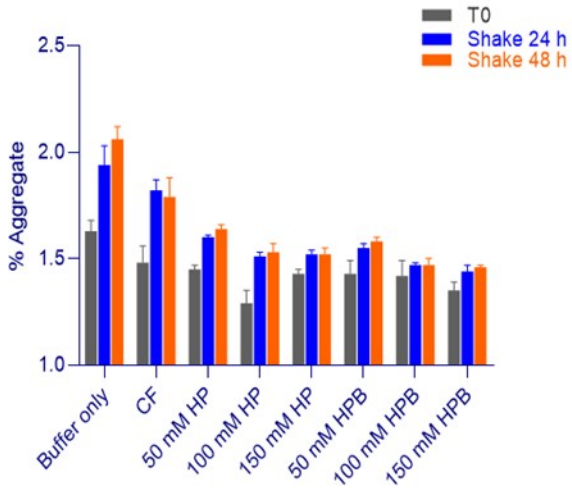
- Effectively reduce agitation -induced protein aggregation
- Prevent fragmentation during agitation
- Help displacing protein from air-water interface due its surface activity

Case Study 2: Arresting Rate of Aggregation in Bevacizumab during Agitation and Thermal Stress

Bevacizumab (Avastin®), a monoclonal IgG1 antibody, was chosen as model protein. The commercial drug formulation in 50 mM phosphate buffer (pH 6.2) contains 60 mg/ml trehalose and 0.04% polysorbate 20 as excipients. The experimental objective was to evaluate the effects of both commercial HPßCD products on the bevacizumab aggregation and stability under stress conditions.

In this study, bevacizumab was formulated at a protein concentration of 25 mg/mL (the therapeutic-use level) in 50 mM sodium phosphate buffer pH 6.2, with different HPßCD concentrations (50, 100, and 200 mM) instead of trehalose and polysorbate in the commercial formulation. These formulations were compared with control formulations of: i) buffer only and ii) commercial formulation (CF). All formulations were prepared in triplicate. All formulations were exposed to either a shaking stress at 1000 rpm, using an orbital shaker or thermal stress at 40 °C in an oven. The samples were then analysed at specific time-points using SEC-HPLC.

Effect of agitation stress: In the agitation studies, aggregate levels were analysed at 0, 24, and 48 hours, showed an progressive increase for all samples. (see **Figure 5**). The aggregation rates were calculated from using the absolute increments of aggregate percentage divided by the number of stress days. HPßCD-supplemented formulations displayed either comparable or significant slower aggregation rates compared with the commercial formulation containing polysorbate 20. While the differences of the aggregation rates appear low, they are likely to be significant in long-term storage and affect the overall shelf life of the protein. Potentially, HPßCD could also be used to reduce aggregation related to other interfacial stresses, such as solid-liquid and liquid-liquid surfaces during drug development.



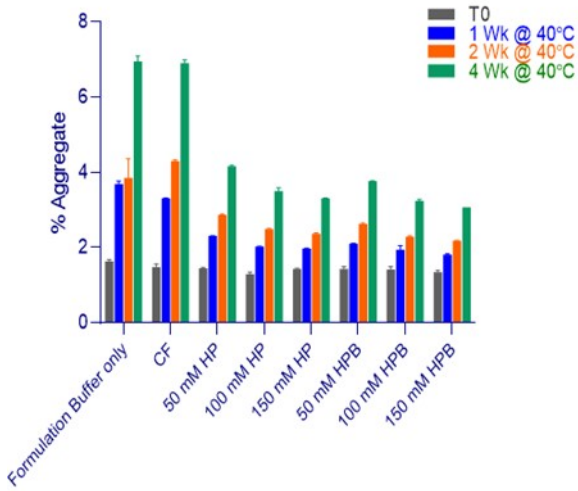
Formulation	Rate of aggregation (%) per day^
	24 h (1 day)
Formulation buffer only	0.31
CF	**0.35**
50 mM HP	0.16
100 mM HP	0.23
150 mM HP	0.09*
50 mM HPB	0.12*
100 mM HPB	0.05*
150 mM HPB	0.10*

^ Rate of aggregation per day = (% aggregate at specific day - % aggregate at T0) / # of days

A t-test was performed with CF formulation. * for $p \leq 0.05$

Figure 5: Aggregation of bevacizumab after agitation

Effect of thermal stress: The protective effects of HPßCD were also noted when samples were exposed to thermal stress at temperatures hold at 40 °C and analysed at 0, 1, 2 and 4 weeks (see **Figure 6**). Formulations containing HPßCD exhibited significantly lower aggregation rates compared with the commercial formulation containing trehalose. By summarizing all data as aggregation rate per week, HPßCD demonstrated a reduction of the aggregation rate of bevacizumab by half or more, compared with the commercial formulation. The reduction of the aggregation rate was also be found to be concentration-dependent. The capacity of HPßCD to reduce the protein aggregation will potentially help to extend the shelf-life of the bevacizumab.



Formulation	Rate of aggregation (%) per week @ 40°C^		
	1 Wk	2 Wk	4 Wk
Formulation buffer only	2.1	1.1	1.3
CF	**1.8**	**1.4**	**1.4**
50 mM HP	0.9*	0.7*	0.7*
100 mM HP	0.8*	0.6**	0.6**
150 mM HP	0.6**	0.5**	0.5**
50 mM HPB	0.7*	0.6**	0.6**
100 mM HPB	0.5**	0.4**	0.5**
150 mM HPB	0.5**	0.4**	0.4**

^ Rate of aggregation per week = (% aggregate at specific week - % aggregate at T0) / # of weeks

A t-test was performed with CF formulation. * for $p \leq 0.05$, ** $p \leq 0.01$

Figure 6: Aggregation of bevacizumab after thermal stress

Conclusion:

Both studied HPßCD grades reduced the bevacizumab aggregation, induced either by agitation or by thermal stress. This dual function stabilization property makes HPßCD a promising excipient, for extending the shelf life of therapeutic proteins.

In Summary

HPβCD are potential alternative for polysorbates as in liquid formulation of biologics, having potential for protein stabilization. The shown studies with two model proteins demonstrate the effectiveness of HPβCD to reduce protein aggregation induced either by agitation or by heat. When tested with bevacizumab, HPßCD reduced the aggregation rate of the monoclonal antibody by half or more, compared to commercial formulation. Since HPßCD is already approved for parenteral small-molecule applications, it holds considerable promise for the future of biologics formulation.

REFERENCES

1. Steinmeyer, D.E. and E.L. McCormick, The art of antibody process development. Drug Discov Today, 2008. 13(13-14): p. 613-8.
2. Ayorinde FO, Gelain SV, Johnson JH Jr, Wan LW. Analysis of some commercial polysorbate formulations using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry. Rapid Commun Mass Spectrom. 2000;14(22):2116-24.
3. Ha E, Wang W, Wang YJ. Peroxide formation in polysorbate 80 and protein stability. J Pharm Sci. 2002;91:2252–64.
4. Serno, T., Geidobler, R & Winter, G. Protein stabilization by cyclodextrins in the liquid and dried state. Adv Drug Deliv Rev, 2011. 63(13): p1086-106
5. Serno T, Carpenter JF, Randolph TW, Winter G. Inhibition of agitation-induced aggregation of an IgG-antibody by hydroxypropyl-beta-cyclodextrin. J Pharm Sci. 2010;99(3):1193-1206.

Please note that this article did not undergo a scientific review process. The authors are responsible for its contents.

Master "Industrial Pharmaceutical Technology" in Lille now also offers the "alternance" modus

For the first time, the Master "Industrial Pharmaceutical Technology" ("M2 Pharmacie Galénique Industrielle") at the University of Lille, College of Pharmacy, will also open in the "alternance" modus. This means that students can already work in the industry during the 1-year training programme.

In 2021, the master starts on 13th September with 5 weeks training (theoretical and practical classes) at the College of Pharmacy in Lille. Afterwards, the students mainly work in the company they are hired at. Roughly, once a month, theoretical or practical classes are given during one week (except for February, April and August) (but please note that the exact periods are susceptible to change). Also, part of the classes in 2022 will be offered online, to minimize traveling.
The aim is to facilitate the transition of the students from University to industry and boost a successful start of their professional career.

The French government supports this initiative, which can be attractive also for many companies.

In addition, the master will also open in the classical modus "formation initiale". This means that the students have theoretical and practical classes from mid-September until late January, followed by a 6 months full-time internship in an industry.

In both cases ("alternance" and "formation initiale"), the classes will be in French. Lectures are held by academics and industrials, coming for instance from the pharmaceutical industry, excipient suppliers and equipment manufacturers.

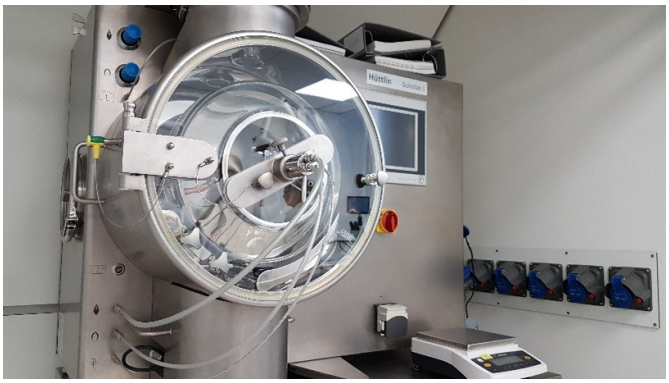
The main focus of this master is placed on the formulation, preparation and characterization of **solid oral dosage forms** (tablets, capsules, pellets). But the **entire spectrum of drug delivery systems** is covered. This encompasses for instance parenteral administration (injections, infusions, implants), pulmonary and nasal drug delivery, dermal & transdermal dosage forms as well as local drug delivery systems (e.g. to the eye, brain and inner ear). The key aspects of pre-formulation, formulation development, quality assurance, clinical supply, scale-up and production at the industrial scale are treated. The bases in physics & chemistry (including analytical techniques), mathematics (e.g. statistics) and engineering are addressed and applied to a large variety of practical examples.

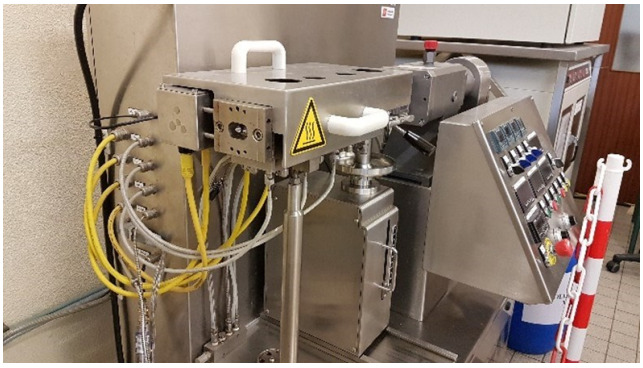
Miscellaneous

Particular emphases are placed on **controlled release** formulations as well as **"enabling strategies"** for poorly water-soluble drugs. The aim is to get prepared for working in the pharmaceutical industry ("master professionnalisant") in the field of Pharmaceutical Technology, especially in research & development, production and related domains.

Specific courses include:

- Pre-formulation: Physico-chemical characterization and biopharmaceutical aspects (characterization of powders, crystalline and amorphous states, solubility, stability, biopharmaceutics)
- Formulation strategies in Pharmaceutical Technology (solid, semi-solid and liquid dosage forms, immediate and controlled release, poorly soluble drugs, biopharmaceuticals, peptide & protein drugs)
- Manufacturing techniques (equipment, processing, engineering, scale-up, quality by design, process analytical technology).
- Quality assurance and project management (regulatory aspects, GMP, ICH, ISO, lean manufacturing, risk analysis, design of experiments, data integrity)





Laboratory courses play a key role in this master: To allow getting familiar with the equipment used for the preparation and characterization of pharmaceutical dosage forms, such as single punch & rotary tableting machines, a variety of granulators, fluid bed and drum coaters, UV spectrophotometer, laser diffractometer, pycnometer, friability, disintegration & hardness tester, as well as basket & paddle dissolution tester, to mention just a few.
It has to be pointed out that the equipment is not only demonstrated and explained: The **master students use it under conditions simulating "real life situations"**. For example, teams of 2 students develop tablet formulations on their own for given drugs and dosages during several weeks.

Graduates of this master can apply for positions as **formulators in research & development, scale-up, production, quality assurance and related areas** in the pharmaceutical industry, at excipient suppliers and equipment manufacturers or regulatory authorities.

Applications can be submitted online until 15th May 2021 online: https://ecandidat.univ-lille.fr.

If you are interested in this master, or want to offer a traineeship in your company for students of this master, please do not hesitate to contact florence.siepmann@univ-lille.fr.

Agenda

APGI events

- **12th Word Meeting on Pharmaceutics, Biopharmaceutics, and Pharmaceutical Technology**
  11-14 May 2021, virtual

- **Information Day "Functional solid oral dosage forms: Superior formulation approaches & novel manufacturing technologies to meet industrial needs" jointly organized with Evonik**
  1st June 2021, virtual

- **Hot Topic Day "Colon targeting"**
  November 2021, Lille, France

Miscellaneous

Become member!

Start your membership today and benefit from free Information Days, significant discounts on scientific congresses and symposia, and networking with individuals sharing the same passion about Pharmaceutical Technologies.

The indicated prices are for one civil year (from 1st January till 31st December)

- student: 25 € + VAT 20% = 30 €
- academic: 80 € + VAT 20% = 96 €
- industrial: 195 € + VAT 20% = 234 €

APGI
College of Pharmacy
University of Lille
3 rue du Professeur Laguesse
59000 LILLE
Phone: +33-6-14-27-45-01
E-mail: apgi@apgi.org