



Information day

SOTAX

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MALVERN PANALYTICAL

14 November

CNAM

Paris, France

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APGI Thesis Award

2018-2019

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JDDST Award

2018

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**2019
N°34**

GAZETTE

**12th World Meeting on Pharmaceutics,
Biopharmaceutics and Pharmaceutical
Technology**

23-26 March 2020

Vienna, Austria

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"Early bird until 15 January 2020!"



www.apgi.org



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APGI Thesis Award 2019-2020



The "APGI YOUNG INVESTIGATOR AWARD" (sponsored by Sanofi and delivered jointly by SANOFI and APGI) recognizes the most outstanding doctoral thesis in the field of Pharmaceutical Technology each year.

The winner will be announced and awarded on the 12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology in Vienna, Austria)

Editorial

Dear Colleagues,

It is my great pleasure to announce that we have a new secretary: **Mrs. Laurence Houzé**.



Laurence is based at the College of Pharmacy at the University of Lille. She will always be happy to answer any question and be of help for you. You can reach her by email (apgi.asso@u-psud.fr) or phone (06 14 27 45 01). Please do not hesitate to contact her! Our former secretary, Mrs. Catharina Kroling, retired after almost 20 years with our association.

In 2020, we will jointly organize the **12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology**, together with our Italian and German friends: the ADRITELF and the APV. We expect more than 1300 participants, close to 1000 abstracts, and will have 36 invited talks, 7 plenary lectures and 72 short talks. The meeting will be held from 23 to 26 March 2020 (Monday afternoon to Thursday evening) in the wonderful town of Vienna. The conference will be accompanied by an industrial exhibition, which is steadily growing. Please do not miss this perfect occasion to get an update on the latest developments in the various fields of drug product formulation, manufacturing, characterization and related domains, and to network with your colleagues.

We are very much looking forward to seeing you!

Prof. Juergen Siepmann

President of APGI

International Conferences and Workshops

12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology

23-26 March 2020, Vienna, Austria



In continuation of the very successful past meetings in Budapest, Paris, Berlin, Florence, Geneva, Barcelona, Malta, Istanbul, Lisbon, Glasgow and Granada, we will organize the 12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology in Vienna, Austria, on 23-26 March 2020.

As in all the even years, we will jointly organize this largest event in our field in Europe jointly with our German and Italian friends: the APV and the ADRITELF, as well as with many other European sister societies. More than 1300 participants from all over the world are expected and close to 1000 abstracts. Various hot topics in our field will be addressed, and world-wide leading researchers will present overview talks on the current state of the art in their fields. In addition, short talks selected from submitted abstract will allow learning about cutting edge research findings.

As in the past, the accompanying exhibition "ResearchPharm" will provide a cross-disciplinary platform for pharmaceutical scientists working in all fields of drug development in industry, academia and regulatory bodies.

Roughly one third of the participants are expected to come from industry, one third from academia, and one third will be young scientists (PhD students and post-docs): The next generation.

In total, 7 plenary lectures, 32 invited lectures, 64 short talks and hundreds of poster presentations will be held, covering the entire range of research and development in pharmaceutics, biopharmaceutics and pharmaceutical technology.

Please already save the date and plan to join us!
The overall program structure is as follows:

Monday, 23 March 2020

13:00 – 13:45	Opening Ceremony
13:45 – 14:45	Key note lecture
14:45 – 15:30	Coffee break
15:30 – 17:30	Hot topic lectures
17:30 – 19:00	Welcome Reception

Exhibition

Tuesday, 24 March 2020

09:00 – 11:00	Invited talks	Short talks
11:00 – 11:30	Coffee break	
11:30 – 13:00	Award session and Plenary lecture	
13:00 – 15:00	Lunch	
15:00 – 17:00	Invited talks	

Posters
Exhibition

International Conferences and Workshops

Wednesday, 25 March 2020

09:00 – 11:00	Invited talks	Short talks		
11:00 – 11:30	Coffee break			
11:30 – 12:00	Award session		Posters	
12:00 – 13:00	Plenary lecture			Exhibition
13:00 – 15:00	Lunch			
15:00 – 17:00	Invited talks	Short talks		
20:00 – 00:00	Gala dinner at the Hofburg			

Thursday, 26 March 2020

09:00 – 11:00	Invited talks	Short talks		
11:00 – 11:30	Coffee break			
11:30 – 12:00	Award session		Posters	
12:00 – 13:00	Plenary lecture			Exhibition
13:00 – 15:00	Lunch			
15:00 – 17:00	Invited talks	Short talks		

The following “hot topics” will be presented at the Vienna meeting:

- What's new in nanotechnology?
- Solid dosage forms
- Advanced therapeutic products: an industrial perspective
- 3D-printing
- Formulation issues for biotech drugs
- Oral drug delivery
- Localised drug delivery
- Amorphous drug delivery systems
- In silico simulation for manufacturing processes
- Nanofabrication technologies
- Dermal and transdermal delivery
- Continuous manufacturing

by world-wide recognized experts, including:

Twan Lammers, What's needed in nanomedicine?

Nathalie Mignet, Nanotechnologies for advanced imaging

Alexander Kabanov, Hyperloaded polymeric micelles for chemo- and immunotherapy

Michael Leane, Adoption of the MCS concept in the pharmaceutical industry

Jukka Rantanen, Process design for innovative drug delivery systems

Kevin Roberts, Crystallization of pharmaceuticals

Chris Van der Walle, Finding answers to antibody bioprocessing challenges in biophysics

James Miskin, Gene-based medicines from concept to market

Maria Luisa Nolli, Biodrugs and advanced therapy medicinal products: a revolution in medicine

Clive Roberts, 3D-printing of medicines and implants: making the formulations work

Matthew Peak, 3D-printing in a hospital setting

Timothy Tracy, 3D-printing pharmaceutical products

Stefan Schneid, Pellet freeze-drying of biopharmaceuticals

Henning Gieseler, L-arginine-based protein formulations in freeze drying: opportunities and challenges

Susanne Jorg, Biologics drug product development: challenges at the interface of formulation, primary packaging and application

Andreas Bernkop-Schnürch, Oral drug delivery: How to formulate poorly absorbed drugs

Caitriona O'Driscoll, Biological barriers to oral delivery of macromolecules

Giovanni Tosi, Jumping to the brain: Tailored nanomedicines

Amélie Bochot, Drug delivery to the eye and ear

Nathalie Wauthoz, Inhaled chemotherapy: A new modality for lung cancer treatment?

Aaro Goodwin, The impact of atomization and drying rate on the mechanical properties of spray dried amorphous solid dispersions

Lennart Fries, Hybrid mixtures: A perspective on amorphous solid dispersions in food applications

Marc Descamps, The variability of the amorphous state in relation to processing

Johannes Khinast, Digitalization in pharmaceutical product and process design: from advanced simulations to deep learning and cloud based intelligence

Sean Bermingham, Digital Process Design Process System Enterprise (PSE)

Stefan Heinrich, Modelling and simulation of fluid-bed processes

Mohan Edirisinghe, Manufacturing fibres at all scales for healthcare

Nalin de Silva, Advances in electrospinning

Josue Sznitman, Advanced microfluidic platforms for respiratory research: bridging in vivo and in vitro interfaces

Marie-Alexandrine Bolzinger, Pickering emulsions

Ryan F. Donelly, Microarray patches for high-dose drug delivery: targeting global healthcare challenges

International Conferences and Workshops

Michael Schrader, Improved vaccine immunogenicity through microneedle delivery Vaxess

Victoria Pauli, Redundant process control strategy in pharmaceutical continuous manufacturing

Stief, Pfizer, Implementing continuous manufacturing into a factory for solid dosage forms

Kendal Pitt, Continuous manufacturing of solid dosage forms; opportunities and controversies

For more detailed information, please have a look at the meeting's website :

<https://www.worldmeeting.org/>

and download the most recent announcement.

Looking forward to meeting you in Vienna!



International Conferences and Workshops

Formulation Days 2019

10-11 January 2019, Lyon, France

Les Journées de Formulation, colloque national annuel, sont généralement organisées par le Groupe Formulation de la Société Chimique de France pour réunir experts académiques, industriels et étudiants (doctorants et masters) autour d'une thématique de la formulation.

Pour le colloque Journées de Formulation 2019, le Groupe Formulation de la Société Chimique de France s'est rapproché de l'Association de Pharmacie Galénique Industrielle (APGI) via le Laboratoire d'Automatique, de Génie des Procédés et de Génie Pharmaceutique (LAGEPP, UMR 5007, Lyon). L'objectif était de proposer conjointement un congrès à envergure européenne concernant les avancées dans la formulation de molécules actives pour des applications dans les cosmétiques et les produits pharmaceutiques. C'est pourquoi l'intitulé de ce congrès est devenu *Formulation Days 2019 – Advances in Formulation of Active Ingredients* et les conférences se sont tenues en langue anglaise. Parmi les 160 conférenciers, 17% venaient de l'étranger : Grande-Bretagne, Italie, Belgique, Pays-Bas, Côte d'Ivoire, Brésil. Nous avons 18 % d'industriels, 18% d'étudiants de Master et 64% de chercheurs académiques.

Pour cette édition, le programme scientifique a couvert 4 thèmes pour lesquels le site Lyon St Etienne est reconnu et pour certains en lien avec les thèmes IDELYON :

- Matériaux, biomatériaux (session 1)
- Formulations pour l'administration cutanée ou pour les voies muqueuses (session 2)
- Nanoparticules : nanomédecine, toxicologie, réglementation (session 3)
- Procédés, caractérisation, modélisation (session 4)

Plus particulièrement, le LAGEPP via son équipe GE-PHARM possède une expertise dans le domaine de la formulation et la vectorisation de principes actifs pour des applications thérapeutiques, diagnostiques ou cosmétiques qui est reconnue au niveau national et international.

Des chercheurs académiques européens de haut niveau (Universités de Londres, de Leeds, de Ghent) ainsi que des industriels du domaine de la Santé reconnus pour leur développement et leur potentiel d'innovation (Sanofi, Ipsen, L'Oréal, BASF) ont été invités pour présenter leurs travaux. Les journées ont participé au rayonnement du site dans le domaine de la chimie appliquée à la santé, et ont sans nul doute permis des échanges entre chercheurs académiques et industriels en vue de l'établissement de projets collaboratifs. La forte participation des industriels à ces journées est à noter, ainsi que leur volonté de communiquer leurs travaux dans un contexte concurrentiel.

Par ailleurs, ces journées ont été ouvertes aux étudiants de plusieurs masters de l'Université Lyon 1 (Formulation



et Chimie industrielle, Matériaux, Conception et Optimisation des Produits de Santé) ; aux étudiants de 3ème année de Polytech filière Matériaux et aux étudiants de 5ème année de CPE Lyon majeure formulation, ainsi qu'aux doctorants (notamment du LAGEP et de l'IMP) dont certains ont ainsi pu bénéficier d'éclairages sur les sujets d'actualité dans le domaine de la formulation des produits de santé et cosmétiques.

Au cours de la 1ère session du congrès, différents intervenants ont exposé les avancées de leurs recherches dans le domaine des « Matériaux et biomatériaux ». Le **Pr Francisco M. Goycoolea de l'Université de Leeds** a présenté un sujet de recherche très actuel et considéré comme une urgence sanitaire majeure : la résistance antibiotiques (AMR). La stratégie thérapeutique présentée est basée sur l'utilisation de nanoparticules recouvertes par des biopolymères capables d'inhiber l'adhésion des bactéries Gram-négatives aux surfaces ainsi que leur capacité à développer des biofilms. Son groupe de recherche a démontré que l'adhésion et la colonisation d'*Helicobacter pylori* dans des cellules de l'estomac peuvent être inhibées par des nanoparticules recouvertes de chitosan. Ensuite, le **Pr Laurent David de l'Université de Lyon 1** a montré une autre utilisation du chitosan. Ce biopolymère très versatile peut être utilisé pour former des hydrogels capables de préserver la fertilité masculine. Son groupe de recherche a conçu un nouveau microbioréacteur à base d'hydrogel de chitosan pour la culture des spermatozoïdes. Grâce à sa structure très poruse, l'hydrogel permet la diffusion des éléments nutritifs et des cellules. De plus la structure chimique du chitosan mime en partie les glicosaminoglycans de la matrice extracellulaire et sa biocompatibilité permet des cultures cellulaires sur de longues périodes (jusqu'à 8 mois).

International Conferences and Workshops

Le Dr Catherine Le Visage, de l'INSERM de l'Université de Nantes a montré l'application des hydrogels d'alginat pour les thérapies cellulaires. Ces particules d'alginat ont été développées en tant que support pour des cellules mésenchymateuses humaines et ensuite administrées dans les jonctions articulaires de petits animaux en tant que nouvelle stratégie thérapeutique pour le traitement des pathologies ostéoarticulaires.

La seconde session du congrès était consacrée aux formulations pour la cosmétique et l'administration topique, cutanée ou mucosale. Elle fait l'objet d'un article à paraître dans la revue « Expression Cosmétique ». Le **Pr Majella Lane du Skin Research Group de l'University College of London** a montré l'importance du choix des excipients de formulation pour faire franchir la barrière étanche du stratum corneum par une fraction suffisante de substance active quelle que soit leur hydrophilie/lipophilie. Les formulateurs innovent et développent des stratégies pour optimiser le passage des actifs dans la peau en maintenant des propriétés sensorielles ressenties par les consommateurs. Cela peut se traduire par la formulation de formes innovantes facilement incorporées dans une formulation composée d'un véhicule hydrophile dispersé dans une phase aqueuse. Le **Dr Emilie Munnier de la Faculté de Pharmacie de l'Université de Tours** a travaillé sur l'encapsulation d'esters à activité dépigmentante et lipolytique inclus dans les nanovecteurs lipidiques recouverts d'une enveloppe hydrophile afin d'être facilement dispersés dans des gels hydrophiles. Le **Dr. Odile Sonneville-Aubrun de la société L'Oréal** a montré l'intérêt des structures particulières à base d'alcools gras et de tensioactifs anioniques organisés en phases lamellaires cristallisées fortement gonflées d'eau qui assurent une libération prolongée de l'actif tout en apportant un bénéfice sensoriel important. Le **Dr Marc Eeman de Dow** a montré l'intérêt des élastomères de silicium inclus dans des formulations O/Si pour contrôler la libération et la pénétration de certaine substance dans la peau. Le **Dr Anne-Claire Groo de l'Université de Caen** a montré que l'énergie d'adhésion à la muqueuse nasale d'inhibiteurs de la butylcholinestérase pour le traitement de la maladie d'Alzheimer était plus élevée pour une forme liposomale associée à des excipients mucoadhésifs comme la cellulose, le chitosan et des poloxamères par rapport à des solutions simples contenant ces mêmes excipients. **Malgorzata Tarnowska, doctorante au LAGEPP à l'Université Lyon1** a montré *in vitro* sur de la peau métaboliquement viable montée en cellule de Franz que les cations présents dans une eau thermale commerciale et physiologiquement importants pour la fonction barrière cutanée (Ca^{2+} et Mg^{2+}) pénètrent dans les couches cutanées profondes. L'innovation de nouvelles formes galéniques n'entraîne pas obligatoirement plus de complexité. Les émulsions de Pickering en sont un exemple. C'est ainsi que le **Dr Yves Chevalier et le Pr Marie-Alexandrine Bolzinger du LAGEPP** ont inauguré la session par une présentation physicochimique des

émulsions de Pickering et par un aperçu des propriétés biopharmaceutiques de ces émulsions particulières pour délivrer de la caféine ou du rétinol dans la peau.

Au cours de la troisième session la thématique de la **Nanomédecine** a été abordée. Le **Pr Elias Fattal de l'Institut Galien Paris-Sud** à Châtenay-Malabry a montré l'importance d'intégrer l'évaluation toxicologique dans les études physico-chimiques et biologiques des nouveaux nanomédicaments pour favoriser leur développement sur le marché. Ensuite **le Dr Katrien Remaut du Laboratoire General Biochemistry and Physic Pharmacy de Ghent** en Belgique a présenté le développement et la caractérisation de nanosystèmes pour la délivrance oculaire de l'ARN afin de moduler l'expression protéique dans la rétine. **Joëlle Balegamire, doctorante au LAGEPP, à l'Université Lyon1**, a montré le développement de nouveaux nanosystèmes à base d'un polymère iodé comme agent de contraste pour la tomographie (Computed tomography). D'autres doctorants, **L. Segui de l'Université de Caen**, et **K. Matha de l'Université d'Angers**, ont discuté des applications des nanosystèmes pour formuler de nouvelles nanoémulsions et des nanocapsules lipidiques. Pendant cette session, différents intervenants industriels ont aussi participé. Le **Dr François Dalençon de SANOFI** a présenté le développement de nouveaux adjuvants pour formuler des vaccins. Quant au **Dr S. Acker de BASF**, elle a présenté l'utilisation de nanoparticules comme agent de vectorisation pour des molécules ayant une activité de protection solaire. La session s'est terminée avec la présentation du **Dr J Richard de IPSEN** qui a exposé les applications des nanomédecines pour la délivrance de peptides.

La dernière session du congrès a été consacrée aux procédés, à la caractérisation et la modélisation. Le **Dr Christophe Marquette, de la plateforme 3d.FAB de l'Université de Lyon 1** a présenté l'utilisation des imprimantes 3D pour développer de nouvelles formulations. L'objectif de sa recherche est de rendre "imprimables" des matériaux et de découvrir de nouvelles applications des polymères. Le **Dr Vincent Faivre, de l'Institut Galien Paris-Sud, Châtenay-Malabry**, a exposé des exemples de formulation pour améliorer la solubilité des principes actifs lipophiles en utilisant des techniques très innovantes comme les microsphères et les particules Janus produites par prilling et homogénéisation à haute pression.

Le **Dr Flavio Dormont, de l'Institut Galien UMR CNRS 8612 de l'Université de Châtenay-Malabry** a décrit la problématique de transposition d'échelle des procédés de production des nanoparticules et a exposé le cas concret des nanoparticules à base de squalène.

L'influence des analogues du squalène dans le développement à large échelle industrielle a été examiné. Ces analogues, considérés comme impuretés peuvent avoir un impact élevé sur la reproductibilité et les propriétés des lots des nanoparticules.

International Conferences and Workshops

Pour la transition vers une utilisation clinique de ces nanomédecines, les problématiques concernant la pureté des excipients, la détection analytique et la caractérisation des nanomédecines ont été exposées pendant sa présentation. Finalement, le **Pr Christian Jallut** et le **Dr Isabelle Pitault (LAGEPP)** clôturaient ces journées par une présentation concernant les méthodes de prédiction du transfert des actifs dans la peau. Ces deux chercheurs ont démontré l'intérêt de la prise en compte des approches de Génie des Procédés pour mieux appréhender ces phénomènes de transfert dans la peau et ont ouvert un large champ de perspectives de recherche tant du point de vue de la modélisation que de celui de l'acquisition des données expérimentales.



International Conferences and Workshops

3rd European Conference on Pharmaceutics 25-26 March 2019, Bologna, Italy

The 3rd European Conference on Pharmaceutics was held this year in the lovely town of Bologna, in Italy.

The conference was jointly organized by the APV (German "International Association for Pharmaceutical Technology"), A.D.R.I.T.E.L.F. (Italian "Associazione Docenti Ricercatori Italiani di Tecnologie e Legislazione farmaceutiche") and APGI (French "International Society of Drug Delivery Sciences and Technology). In the following a brief summary of the 2 days conference is given:

Monday

The opening ceremony started in the morning with the participation of Prof. Joerg Breitkreutz (President of APV), Prof. Anna Maria Fadda (President of A.D.R.I.T.E.L.F.), Prof. Juergen Siepmann (President of APGI) and Prof. Nadia Passerini from the University of Bologna, who welcomed the participants. The first plenary lecture on "Cytosolic delivery of bio-therapeutics: the struggle with biological barriers goes on" followed. This very interesting talk was given by Prof. Stefaan de Smedt, University of Ghent, Belgium. After the coffee break, invited talks were presented on the theme of "Manufacturing equipment and technologies". Dr. Giustino di Pretoro (Johnson & Johnson, Belgium) gave a comprehensive up-to date presentation on "Continuous drug product manufacturing - what does the future of pharmaceutical manufacturing looks like?", Dr. Iris Ziegler (Corden Pharma, Germany) talked about "Containment of highly potent compounds during manufacturing of solid dosage forms: in the past, at present and where will this all go to?" and the morning session ended with a presentation given by Dr. Odra Pinato and Annalisa Delnevo from the Stevanato Group in Italy about "The role of primary packaging in biotech drug stability: innovative solutions".

A lunch break (included in the registration fees) took place in different areas of the site allowing for networking between all the participants.

The afternoon session included the following invited talks on nanomedicines: Dr. Julien Nicolas from the University of Paris-Sud, France, started the session with a presentation about "New polymer-based drug delivery systems for cancer therapy", followed by Dr. Paolo Gatti (Aptuit, Italy) who gave a presentation about "Drug product nanotechnologies: formulation and process aspects from laboratory to production plant". The final presentation in that session was given by Prof. Maria José Blanco-Prieto (University of Navarra, Spain) on "Neurotrophic factor brain delivery for Parkinson's disease therapy".

In parallel, short talks were given on the topic "Controlled Drug Delivery", including: "Enhancement of skin penetration of lipid-based nanocarriers" by Coralie Bellefroid (University of Liege, Belgium), "Glycosaminoglycans



based scaffolds for wound healing" given by Giuseppina Sandri (University of Pavia, Italy) and "Development of dissolving microneedles for delivery of vancomycin hydrochloride" by Delly Ramadon from Queens University of Belfast in the United Kingdom. Dina Kottke from the University of Düsseldorf in Germany gave a talk about "Established and innovative buccal dosage forms controlling oromucosal lidocaine permeation". Adriana Santos (University of Beira Interior, Portugal) gave a presentation entitled "Oral self-emulsifying drug delivery system and intranasal nanoemulsions of phenytoin", and last but not least, Prof. Paolo Colombo from the University of Parma in Italy talked about "High dose tobramycin dry powder inhaler: in vivo-in vitro dose emission".

In the afternoon session, short talks and invited talks on "Bioavailability and IVIVC", "Pharmaceutical manufacturing and engineering included": "In vitro and in vivo assessment of different enabling approaches for oral delivery of fenofibrate" by Ana Caldúch-Arques/Anette Müllertz (University of Copenhagen, Denmark), "Improved vitamin K uptake from orally administered mixed micelles under bile deficient conditions" presented by Thijs Rooimans (University of Utrecht, Netherlands), "A novel predictive dissolution method for establishing an IVIVC for contraceptive intravaginal rings" by Katharina Tietz (University of Greifswald, Germany), "The Manufacturing Classification System: factors influencing process choices" by Dr. Neil Dawson from Pfizer Worldwide Research & Development in the United Kingdom, followed by "Lean and efficient development of a pseudoephedrine formulation resistant to conversion into meth" given by Dr. Isabella Immohr (Grünenthal GmbH, Germany) and finally, "Solvent-induced phase separation during ASD preparation" presented by Prof. Gabriele Sadowski from University of Dortmund in Germany.

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Tuesday

The conference started with an invited talks session on "Arising new manufacturing technologies". Invited talks included: "Electrospinning and its applications in pharmaceuticals" presented by Prof. Romána Zelkó (Semmelweis University, Hungary), a presentation on "Electrospraying in drug formulation" by Prof. Guy van den Mooter from University of Leuven in Belgium and another talk given by Dr. Alice Melocchi (University of Milan, Italy) entitled: "From 3D- to 4D-printing in the development of drug delivery systems". In parallel to this session, short talks were given on "Oral drug delivery", including: "Mathematical modelling of antibacterial release from a biphasic gel system" by Prof. Mario Grassi (University of Trieste, Italy), "Prilling of API/FA suspensions: Screening of additives for drug release modification" presented by Elien De Coninck from University of Ghent in Belgium, "Adipic acid/Saccharin based celecoxib eutectic mixtures for improvement of wettability and dissolution rate" given by Sharif Md Abuzar from University of Yonsei in Republic of Korea, "Comparison of different dosage forms to deliver extremely oxygen-sensitive probiotics" by Prof. Odile Chambin (University of Bourgogne Franche-Comté, France), "Scaled up solid formulation of living anaerobic bacteria for oral delivery using electrospinning" by Panna Vass (University of Budapest, Hungary) and last but not least Hend Abdelhakim from College of London in the United Kingdom talked about "Utilising co-axial electrospinning as a taste-masking technology for paediatric drug delivery".

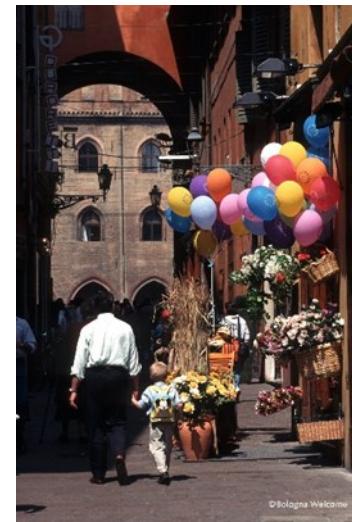
After the coffee break, the winners of the « APGI Young Investigator Award 2018» (sponsored by Sanofi) as well as the "JDDST Best Paper Award 2018" were announced. This was followed by a plenary lecture given by Prof. Paola Minghetti from the University of Milan in Italy on "From the idea to the bedside: is the regulatory path coherent with patients' expectations?"

After lunch break, the invited talks afternoon session started with a very interesting presentation on "Novel in vitro test methods for predicting the performance of oral dosage forms in the gastrointestinal tract" given by Prof. Werner Weitschies from the University of Greifswald in Germany, followed by a presentation on "New insights into tablet porosity and its critical role in oral drug delivery" by Prof. Axel Zeitler (University of Cambridge, United Kingdom) and a talk by Dr. Marc Schiller (Grünenthal GmbH, Germany) on "Innovation in solid oral dosage forms - an industrial view".

In the parallel session, short talks were given on "Nanoformulations", including: "Chemical reaction-free coating of biodegradable nanoparticles with hyaluronic acid: Cell uptake experiments and mathematical modeling" by Marco Biondi (University of Napoli, Italy), "Multicellular spheroid based on a triple co-culture: a novel 3D model to mimic pancreatic tumor complexity" given by Simona Mura from University of Paris-Sud in France,

"The effect of PEG geometry on the circulation properties of polymeric micelles" was presented by Marzieh Najafi (University of Utrecht, Netherlands), "A new theranostic system for the treatment of inflammatory diseases" by Sara Baldassari from University of Genova in Italy, "Theranostic nanocarriers loaded with nerve growth factor enable enhanced brain recovery after stroke" by Matthias G. Wacker (Fraunhofer IME, Germany) and finally, "Evaluation of liposomes as antisense therapy vectors for the treatment of preeclampsia" was presented by Prof. Karine Andrieux from the University of Paris Descartes in France.

Furthermore, poster presentations exhibited during the entire conference gave the opportunity to get an update on the most recent research in Pharmaceutics and to personally exchange with the authors. Also, an industrial exhibition accompanied the Conference and allowed the participants learning about the latest trends and newest products in the area of pharmaceutical ingredients, developing & processing equipment, analytical technologies, medicinal products & devices and many other fields.



International Conferences and Workshops



Skin Forum
international skin science network

Skin and Formulation
5th Symposium & 17th Skin Forum
Reims, France
23-24 September, 2019



Skin and Formulation, 5th Symposium & 17th Skin Forum, Reims, 23-24 September 2019

This two-days meeting was co-organized by Skin Forum (International Skin Science Network) and APGI (French “International Society of Drug Delivery Sciences and Technology”) in Reims (France). After registration accompanied by coffee and pastries, the welcome introduction started on Monday morning with the participation of Dr. Majella Lane (Skin Forum) and Dr. Vincent Faivre (APGI), co-chairs of the symposium. They thanked sponsors and supports, the organizers and welcomed the attendees. There were about 160 participants from 5 continents and representing more than 25 countries. Around 100 posters were presented during the coffee and lunch breaks and champagne evening, included in the registration fees, and organized in the exhibition area. Discussions between young scientists, confirmed academic researchers and industrials were numerous.

The scientific sessions started with an opening talk by Dr. Anne-Marie Pensé-Lhéritier (EBI, France) on “Sensory and sustainable challenges” describing notably how methods using experimental design strategy are useful to reach all the specifications including sensory characteristics. Then, Dr. Cécile Clavaud (L’Oréal, France) described the deep interactions between human skin and bacteria in an impressive talk on “Skin microbiome signatures in healthy skin across daily life: perspectives for cosmetics”. After that, Pr. Jonathan Hadgraft (University of London, UK) gave a talk entitled “Formulation science - a half century of progress?” and expressing a very well documented point of view on skin formulation development. Then came the coffee break and poster session time before resuming the presentations with an interesting talk by Dr. Dominik Imfeld (DSM Ltd, Switzerland) on “Novel anti-aging approaches with bioactive lipids”. Following these invited speakers, two short communications were done by Dr. Emilie Munnier (University of Tours, France) and Marcella Sessa-Rivera (University of Barcelona, Spain) on “Shielding the skin from biofilm: Spirulina platensis sustainable lipid extracts and their formulation” and “Release and permeation study of meglumine antimoniate semisolid dosage form for the treatment of cutaneous leishmaniasis” respectively. Selected on abstracts, these two dynamic communications perfectly closed the morning session. The lunch break, around exquisite food from the “Maison Schosseler” (Reims), allowed sweet networking between participants.

From concept to final product, skin product development significantly depends on the context. New active ingredi-

ents or reformulation? Pharmaceutical application or cosmetic product? Through case studies, the Monday afternoon session illustrated some innovative and key-concepts of such developments. Fruitful complementarities between engineering and pharmaceutical / cosmetical approaches clearly emerged during this session. The afternoon started with a presentation from Pr. Guoping Lian (University of Surrey, UK) on “Multi-scale modelling of solute partition in complex topical products and impact on transdermal permeation” which is an important non-animal alternative to support innovation on skin delivery. Then, Dr. Milica Lukic (University of Belgrade, Serbia) gave an extensive presentation, entitled “From emulsions' stability concerns to sensory properties: tools that we use”, in which she explained, among others, correlations between instrumental parameters and consumer percept attributes. Before coffee break, Mohamed Amine Beladjine (Paris-Sud University, France) delivered a valued short communication on the “co-encapsulation of immunosuppressant and anti-inflammatory agents in a Pickering emulsion for the treatment of skin disease”. He received an award from Skin Forum for this very nice work. The last part of this afternoon session began with a duet composed of Pr. Vincent Boly and Dr. Javier Arrieta Escobar (University of Lorraine, France) who shared with the audience their innovative *in-silico* methodology to develop complex formulated products in a talk entitled “Integration of Heuristic Knowledge in the Design of a Skin Moisturizer”. To conclude the scientific programme of this first day, Julie Quartier (University of Geneva, Switzerland) and Dr. Cristina Padula (University of Parma, Italy) presented their results on “Polymeric micelle formulations for the cutaneous delivery of sirolimus: a new approach for the treatment of facial angiofibromas in tuberous sclerosis” and “New strategies for improving budesonide skin retention” respectively.



International Conferences and Workshops

Julie Quartier also received an award from the jury that really appreciated her work and her answers to questions. After this intense day, the organizers allowed a small outing to participants in the park adjacent to the congress center!. Fortunately, most of the participants (all of them?) came back to the center and participate the sparkling champagne evening included in the registration fees. Attendees continued scientific exchanges between tastings and discussion with winemakers during a pleasant party. Fine tools are needed to investigate skin and its interaction with topical formulations. Description of recent progress in imaging and characterization techniques was the main topic of the morning session of the second day. To open this session, Dr. Christoph Riethmüller (Centre for Nanotechnology, Germany) made a fine focus on "AFM of the skin barrier" and more precisely how AFM recordings is employed to quantify topographical elements, resulting in a dermal texture index linked to the degree of biological stress of skin cells. Then, Pr. Malcom R. Clench (Sheffield Hallam University, UK) detailed the uses of MALDI-MSI to study drug penetration and metabolism in skin and wound healing during a talk titled "MALDI-MSI for skin investigations". Spectroscopic methods were the core of the short communication presented just before the poster session by Claudia Vater (University of Vienna, Austria) on the "Cytotoxicity of lecithin-based nanoemulsions on primary skin cell types and penetration monitoring by ATR-FTIR spectroscopy". After the break, Dr. Jean Doucet (Novitom, France) showed, in a talk on "x-ray based methods for skin delivery", the recent spectacular technological developments of "old" techniques" thank to the use of synchrotron light sources. Nowdays, computational methods and integrated analysis of metabolites and transcripts are necessary to obtain a comprehensive landscape of the "Metabolic drivers of skin function" as it was brilliantly demonstrated by the following speaker, Pr. Nicola Zamboni (ETH Zurich, Switzerland). At last, Dr. Gerwin Puppels (RiverD, Netherlands) concluded this morning session with a very pedagogic presentation on "Quantitative analysis of *in vivo* skin penetration of topically applied materials" with non-invasive confocal Raman spectroscopy.

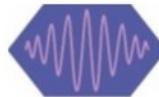
Rheology of skin products is an important part of the applied physics for the scientists, crucial process parameters for industrial, textures for the consumers. Rheology is a complex area which has been addressed during the last afternoon of the symposium. Pr. Florence Agnely (Paris-Sud University, France) opened this session with a con-

ference on "Contribution of interfacial rheology for the study of topical emulsions" and innovative examples with emulsions stabilized by nanoparticles or proteins. Then, Dr. Pascal Brochette (Atellane, France), with a talk entitled "Rheology of skin products: industrial point of view" gave a percussive opinion on the multiple industrial issues around rheology, from ideal profile for consumers to consequences on processes or quality control. After that, Sylvia Imbart (EBI, France) described the "Relationship between sensory assessment and rheological properties of a sensorial referential" during her short communication. To complete these scientific talks, and after a coffee break, Dr. Valentine Ibekwe (MHRA, UK) presented a "Regulation point of view" thank to an overview of current regulatory requirements regarding characterisation and control of rheological properties of skin products. Coralie Bellefroid (University of Liège, Belgium) concluded the scientific program with a sharp short communication on "Nucleic acids skin penetration enhancement: a combined approach of deformable liposomes and microneedles".



The organizers of the symposium really enjoyed the scientific quality of the different communications, from invited talks to poster presentations by young researchers. For that reason, beside awards for oral presentations attributed to Mohamed Amine Beladjine and Julie Quartier, three poster awards were attributed to Anna Novackova (Charles University, Czech Republic), Ecaterina Gore (Le Havre, University, France) and Sabrina Valetti (Malmo University, Sweden).

International Conferences and Workshops



Skin Forum
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We are pleased to thank our sponsors during our congress
“Skin and Formulation, 5th Symposium & 17th Skin Forum”



We Invest in Quality.



Miscellaneous

Young investigator award

APGI Thesis award 2018/2019

Dr Karen Peynshaert

Faculty of Pharmaceutical Sciences, Ghent University

Promotors: Prof. Katrien Remaut and Prof. Stefaan De

Smedt

Titre: What you seen is what you get: The physicochemistry of nanoparticles dictates how they cross ocular delivery barriers and alter autophagy

Summary and conclusions

Thanks to worldwide research nanotechnology is one of the key drivers of the current scientific advancements in the 21st century. The field has expanded astonishingly over the last decade, where it is estimated that nearly 10 % of all publications indexed in Web of Science in 2016 involved nanotechnology. Nonetheless, despite this extensive research the translation of these widely investigated nanoparticles (NPs) toward the clinic is rather limited. For organic particles such as liposomes and polymeric particles this is mainly owing to their lack of efficacy evoked by the many intra-and extracellular barriers they encounter. The translation of inorganic particles is primarily restricted by safety concerns, since many of them, including Quantum Dots (QDs), are made up of heavy metals that are known to be toxic. As confirmed in this thesis, it is established that the physicochemical features define how the cell 'sees' the particle and thus dictates the NP's efficacy and toxicity – what you see is what you get! While this perception is fully acknowledged by the nanotechnology community it remains challenging to connect certain physicochemical properties to specific biological effects, making it hard to predict the therapeutic power or potential toxicity of a NP. This is primarily due to faulty project design, the lack of representative models and the inherent complexities associated to working in the nano-range. The difficulty to link NP physicochemistry to desired or unwanted effects is an issue that affects nearly every research field that aims to take advantage of the unique and powerful properties of NPs, yet in this thesis we aimed to aid in overcoming this issue in context of retinal gene delivery (Part I, Chapter 1-4) and autophagy (Part II, Chapter 5 and 6). In Chapter 1 we provided an overview of the most prevalent acquired diseases and most well-documented inherited retinal diseases that could be treated with retinal gene therapy. We furthermore described the morphology and functions of the Müller cell, the target cell type for our non-viral approach. Based on the overview of publications linking physicochemical properties of therapeutics and their carriers presented in Chapter 2, we concluded that the ideal physicochemical characteristics of a therapeutic (carrier) highly depends on the barrier it



needs to overcome and therefore also on the preferred administration route. We further found that nearly each barrier undergoes changes in function of age and disease, an important notion when evaluating the potential of carriers to cross delivery barriers. We found many useful in vitro and ex vivo approaches to study Summary and conclusions | 203 drug delivery barriers in the posterior segment of the eye, though argue that there is still a great need for more straightforward and representative models. Convinced of the latter argument, we presented the so-called 'vitreoretinal explant' in Chapter 3, an novel ex vivo model especially developed to look into the interaction of nanomedicines with the vitreoretinal (VR) interface. This interface comprises the vitreous and the inner limiting membrane (ILM), both well-recognized drug delivery barriers. We confirmed the viability of this explant model and validated its value by means of polystyrene beads. Since 40 nm beads more efficiently crossed the VR interface than 100 or 200 nm particles we concluded that the entry of NPs into the retina is size-dependent. Moreover, we found that removing the vitreous, as commonly done for culture of conventional explants, led to an overestimation of NP uptake, and concluded that the principal barrier to overcome for retinal entry is unquestionably the ILM.

This VR explant is currently the most representative ex vivo model available that is alive for a sufficiently long time to study NP uptake in the retina. In Chapter 4 we applied an elementary set-up to examine if Müller cells, which we regard as an ideal target for neuroprotective strategies, are able of efficiently processing lipoplexes and expressing their pDNA or mRNA cargo.

Miscellaneous

Here, we found that mRNA lipoplexes outperformed the DNA lipoplexes in transfection of healthy Müller cells since both the number of transfected cells as well as the level of GFP expression was higher for mRNA lipoplexes. In Müller cells that were exposed to hyperglycemia, oxidative stress or hypoxia no changes in mRNA-induced expression was observed when compared to healthy Müller cells. On the other hand, we did find that Müller cells treated with oxidative stress or hypoxia were more sensitive to lipoplex-induced toxicity while hyperglycemia had a protective effect. Although preliminary, this study indicates that, despite a stressful environment, Müller cells are capable of taking up lipoplexes and expressing their nucleic acid cargo. Chapter 5 presented an overview of the most relevant reports on NP-mediated autophagy alterations and intended to investigate the interplay between NP physicochemistry and autophagic changes. Hence, several NP properties were put forth as probable influencing factors of NP-induced autophagy disruption or upregulation such as size, charge and chemical composition. However, owing to the shortcomings of some studies and the contradicting claims made in literature it was virtually impossible to draw general conclusions. We thus judged that systematic studies which include sufficient characterization data could greatly support us to truly elucidate the impact of NP physicochemistry on NP-associated autophagy changes. 204 | Summary and conclusions In view of this understanding we performed a study in Chapter 6 with as goal to carefully define the influence of QD coating on lysosomal health and autophagy. Our study showed that the cellular effects induced by QDs on HeLa cells were strongly dictated by the surface coat (i.e. MPA or PEG) of the otherwise identical particles. MPA-coated QDs proved to be highly compatible as a result of lysosomal activation and ROS reduction, two cellular responses that help the cell to cope with NP-induced stress. In contrast, PEG-coated QDs were substantially more toxic owing to a rise in ROS production and lysosomal impairment. This impairment next resulted in autophagy dysfunction which likely added to their toxic effects. Taken together, our study showed that coating

QDs with MPA is a better strategy than PEGylation for imaging applications. In Chapter 7, we summarized the advances in retinal gene therapy and nanotoxicology and discussed potential challenges that hinder NPs to advance further into clinical stages. We brought forward several guidelines that we believe could aid the nano field to progress and reconstructed them into a general approach that could aid researchers in overcoming the NP delivery barriers after intravitreal injection.



Miscellaneous

JDDST Best Paper Award 2018

The Journal of Drug Delivery Science and Technology (JDDST) Best Paper Award recognizes every year the most outstanding original research article published in the year before. The winner is selected by all the members of the editorial board. It is a two stage selection process. In the first round, each member nominates her/his top-5 favorites. The 3 top-nominated articles are selected for the 2nd round, where again all jury members indicate their favorites.

We are very happy to announce that the laureates of this highly prestigious recognition are:

Yoshiyuki Hattori, Nozomi Takeuchi, Mari Nakamura, Yuki Yoshiike, Masamitsu Taguchi, Hiroaki Ohno, Kei-ichi Ozaki, and Hiraku Onishi,

being the authors of the article:

Effect of cationic lipid type in cationic liposomes for siRNA delivery into the liver by sequential injection of chondroitin sulfate and cationic lipoplex

*Journal of Drug Delivery Science and Technology
Volume 48, 2018, Pages 235-244.*

<https://doi.org/10.1016/j.jddst.2018.09.022>



Dr. Yoshiyuki Hattori, Hoshi University

The winners were recognized during the 3rd European Conference on Pharmaceutics in Bologna this year.

JDDST is the official journal of the APGI, A.D.R.I.T.E.L.F. (Associazione Docenti e Ricercatori Italiani di Tecnologie e Legislazione Farmaceutiche) and APSTJ (Academy of Pharmaceutical Science and Technology, Japan).

Miscellaneous

Master "Industrial Pharmaceutical Technology" in Lille

The Master "Industrial Pharmaceutical Technology" ("M2 Pharmacie Galénique Industrielle") at the University of Lille, College of Pharmacy, has a long tradition (of several decades). Next year (in September 2020), it will be taken over by Prof. Florence and Juergen Siepmann, following the retirement of Prof. Anne Gayot.

The main focus of this master will remain the formulation, preparation and characterization of **solid oral dosage forms** (tablets, capsules, pellets). This includes immediate and sustained 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 professionnaliser") in the field of Pharmaceutical Technology, especially in research & development, production and related domains.

The emphasis of this master is on solid oral dosage forms, 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.

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, biopharmaceutics, 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)



The classes are in French, going from mid-September until the end of January. Lectures are held by academics and industrials, coming for instance from the pharmaceutical industry, excipient suppliers and equipment manufacturers.

Lab 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.

The master is completed by a 6 month practical training in the industry. 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 from 1st April to 15th May 2020 (period to be confirmed).

If you are interested in this master or if you have any question, please contact florence.siepmann@univ-lille.fr.

In case you want to offer a traineeship in your company for students of this master, please also write to florence.siepmann@univ-lille.fr.

Information days

Oral Solid Dosage Forms, 27 November 2018, CNAM, Paris, France

APGI Information Day:

ORAL SOLID DOSAGE FORMS

Formulation Strategies and Manufacturing Approaches for Challenging Drugs



Drug products continue to become more specialized and personalized, with advanced functional excipients and formulation technologies being increasingly utilized to address complex drug delivery challenges. For complex oral formulations, such as those for drugs with poor aqueous solubility, poor permeability, short half-lives or narrow therapeutic windows, the right drug delivery approach can maximize bioavailability and efficacy. For drugs with poor water solubility, techniques such as amorphous solid dispersions are now commonly used to improve oral bioavailability. Modified release formulations are also now widely used to improve patient compliance and reduce side effects. Furthermore, formulators are seeking to improve rates of patient compliance and brand preference with immediate release dosage forms that can better protect sensitive APIs, improve swallowability, or mask unpleasant tastes or odors.

In parallel with these formulation development trends, pharmaceutical companies are seeking to optimize the processing and production of dosage forms including controlled release multiparticulates. To enable faster commercialization times, lower development cost and reduce regulatory risk, it is now increasingly common to apply Quality by Design (QBD) principles and smart scale-up strategies. Furthermore, continuous manufacturing strategies are helping to reduce manufacturing footprints, improve batch size flexibility and enhance quality control.

Given such complex drug delivery challenges for oral solid dosage forms, it is becoming increasingly common for pharmaceutical companies to establish long-term collaborations with industry associations, research groups and CDMOs that have specialized excipient, formulation and manufacturing capabilities.

In this collaborative spirit, APGI and Evonik invited formulation scientists, lab heads, process engineers, scale-up experts and production managers to join the APGI Information Day in November last year at the historical facilities of CNAM in Paris, France. Entitled "Oral Dosage Solid Forms: Formulation Strategies and Manufacturing Approaches for Challenging Drugs", the one-day event brought together a range of expert speakers from APGI and Evonik as well as other industry leaders including Dober, GEA, Glatt and ULB (Université Libre de Bruxelles).



Information days

More than 80 scientists, students and engineers from various countries attended the event to gain new insights that could be directly applied in their daily work. All of the aspects mentioned above were discussed through extensive presentations on topics including solubility enhancement, the oral delivery of biopharmaceuticals, multiparticulate film coatings, and continuous processing.

Overall the event received a very positive feedback. Participants praised the compilation of interesting topics and expertise of the speakers.

Presentations on the below topics from the event are available on request – for details please contact healthcare@evonik.com.

- EUDRAGIT® - functional polymers for targeted drug delivery
- Poorly soluble drugs - chances and limitations of solubility enhancement
- Biopharmaceuticals - how to meet their requirements by oral formulations
- Drug delivery technologies for transcellular and paracellular bioavailability enhancement
- High precision release - tailored gastro-intestinal targeting
- Multiparticulate film coating – implementation constraints
- Scale-up of particle coating in the fluid bed - following the QbD principles
- Continuous processing: An attractive option for higher production efficiency
- Poorly soluble formulations - high efficient cleaning of production equipment



Information days

"Accelerate your developments, from powder to tablets"

Sotax- Medelpharm- Malvern Panalytical

14 November 2019, CNAM, Paris, France

The Information Day organized by the APGI was held the 14th November at the "Conseil National des Arts et des Métiers" (CNAM) in Paris.

The industrial sponsors Malvern Panalytical, Sotax and Medelpharm arranged a highly versatile program appreciated by the academic and industrial audience.

"During this seminar Medelpharm joined the companies Sotax and Malvern Panalytical to participate in a day on the theme "Accelerate your developments, from powder to tablet".

Medelpharm is a French company specializing in the development and manufacture of fully instrumented tablet presses for R & D, industrialization and production support.

Medelpharm was represented by Adrien Pelloux and Bruno Leclercq. Adrien is responsible for the application laboratory and presented the fundamentals on powder compression. Bruno Leclercq, Business Development Manager, discussed how tablet presses can improve the robustness of your formulations." Bruno Leclercq, (Business Development Pharmacist at Medelpharm), Ingrid Coyle (Director Corporate Business Development & Communication) & Gabrielle Dupont (Marketing & Communication Assistant).

"The company, Malvern Panalytical had been delighted by this collaboration with the companies Sotax and Medelpharm, which had been often evoked and finally realized, thanks to the APGI.

Our contribution consisted of two presentations given by Deborah Huck, product manager for image analysis and Raman spectroscopy, and with the exceptional attendance of Paul Klippax, marketing director of the pharmaceutical sector at Malvern Panalytical, UK.

The first presentation comprised examples of the application of polymorphisms linked to dissolution speed and bioavailability and the characterization by image processing and analysis of Raman spectra. The second presentation focused more on the overall response that Malvern Panalytical can provide to the pharmaceutical industry in accordance with ICH Q6A recommendations for size, shape, and chemical and structural identification of active ingredients and excipients." Michel Terray (Marketing Manager France at Malvern Panalytical).



 **MEDELPHARM**
the tabletting instrument company







Information days

"Thanks to a long term relationship with the APGI, Malvern, the University of Clermont-Ferrand, SPS Pharma Services and the CNAM and a recent but promising collaboration with Medelpharm on Physical testing instruments, the SOTAX Sarl team had the pleasure to finally see the project of a common seminar take place the 14th of November 2019 in Paris. This event "Characterization, Compression, Dissolution" also involved interesting presentations for Skyepharma and Armor Pharma and gave to the attendees a complete overview on powder characterization. The SOTAX Sarl team hope the attendees shared the pleasure they had to participate to this event and thank again the CNAM and the APGI for their perfect organization." Michel Magnier (Product Manager Dissolution USP4) & Patrick Melot (Sales Director and Service France) from Sotax Sarl.

The APGI wishes to address special acknowledgements to the local organizing team at the CNAM.



New Technologies

Alternative excipients and ingredients for replacing titanium dioxide in film coating systems

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Titanium dioxide (TiO_2 / E171) is one of the most important additives in the food, nutraceutical and pharmaceutical industry, widely used as a whitening agent. It is the white pigment with highest refractive index and brightness and therefore, very popular for coloring solid oral dosage forms such as tablets or their film coatings.

Since few years there is a discussion in the industry about the use of TiO_2 . France had ordered a review of the substance in 2017 after a study found health effects in animals that consumed it. France's National Institute for Agricultural Research and partners in a study of oral exposure to titanium dioxide had shown that E171 crosses the intestine wall in animals to reach other parts of the body. Other studies describe a potential risk of TiO_2 nanoparticles to the human respiratory system. As a result, France wants to ban the use of the white pigment from 2020.

Parallel is a market trend for cleaner labels in nutraceutical supplements recognizable, where the consumer demands a return to real food and transparency through authenticity. Nutraceuticals should contain more natural, familiar, simple ingredients that are easy to understand, and pronounce. Beside TiO_2 also other critical excipients are no more welcome to achieve a cleaner label, such as synthetic colors, iron oxides, silicon dioxides, magnesium stearate. Last but not least, changes to regulatory requirements lead to formulation adjustments.

Under these conditions, the industry is forced to look for alternatives to replace recipes formulated with TiO_2 or other undesired ingredients. By looking at film coating users and manufacturers, they face several challenges in the development of new, TiO_2 -free, formulations:

- Alternative raw materials require a higher content in a formulation compared to TiO_2 – there are only limited possibilities due to necessary amounts of functional excipients.
- Ensuring of comparable film coating functions & film coating properties like TiO_2 containing formulations
- Decisive film coating properties for TiO_2 free film coating: brightness & opacity
- Ensuring a similar preparation & application of TiO_2 free film coatings

Possible raw materials for replacing titanium dioxide are e.g. Carbonates, Phosphates, Starch.

Evaluation of possible replacements for titanium dioxide in film coating systems for solid oral dosage forms

Material & Methods

- Investigated are 12 film coating formulations containing 5 different replacements for TiO_2 with different characteristics in a standard film-coating formulation.
- The tablet core formulation exists of different vitamins, widely used in nutritionals.
- A standardized film coating process was performed in a fully perforated drum.
- A comparison of different weight gain levels was conducted.
- All ready-to-use film coating formulas (AquaPolish®) are based on Hypromellose.

Investigated film coating properties were: Opacity and brightness, film flexibility, strength and surface, viscosity.

Used Devices/Equipment for blending and film-coating process:

Propeller stirrer for preparing suspension

- Lab Coater Bosch Solidlab I
- Colourimeter – measuring of color intensity-opacity
- Texture Analyzer
- Viscosometer

Results and Discussion



AquaPolish® formula I



AquaPolish® formula with TiO_2

ΔE	10,13	
Opacity	-	+
Brightness	-	+
Film flexibility	+	+
Film strength	+	+
Film surface	o	+
Viscosity	475 mPa*s	513 mPa*s

Figure 1: Comparison of different film-coating formulations at **3% of weight gain** AquaPolish® formula I (formulated with one replacement). Result: bad opacity and brightness at 3% weight gain level.

New Technologies

AquaPolish® formula II

	ΔE	6,68
Opacity	o	+
Brightness	o	+
Film flexibility	+	+
Film strength	+	+
Film surface	+	+
Viscosity	466 mPa*s	513 mPa*s

AquaPolish® formula with TiO₂

	ΔE	1,2
Opacity	+	+
Brightness	o	+
Film flexibility	+	+
Film strength	+	+
Film surface	+	+
Viscosity	526 mPa*s	513 mPa*s

Figure 2: Comparison of different film-coating formulations at **3% of weight gain**

AquaPolish® formula II (formulated with one replacement). Result: bad opacity and brightness, but good film-surface at 3% weight gain level.

AquaPolish® formula III

	ΔE	3,8
Opacity	o	+
Brightness	o	+
Film flexibility	+	+
Film strength	+	+
Film surface	o	+
Viscosity	540 mPa*s	513 mPa*s

AquaPolish® formula with TiO₂

	ΔE	1,2
Opacity	+	+
Brightness	o	+
Film flexibility	+	+
Film strength	+	+
Film surface	+	+
Viscosity	526 mPa*s	513 mPa*s

Figure 3: Comparison of different film-coating formulations at **3% of weight gain**

AquaPolish® formula III (formulated with two replacements). Result: good opacity and brightness, acceptable film-surface.

Figure 4: Comparison of different film-coating formulations at **5% of weight gain**

AquaPolish® formula IV (same as formula III, with two replacements) and a weight gain level of 5%. Result: good opacity, brightness and film-surface.

Conclusion

To meet the market demand, manufacturers and users of film coating systems can reformulate existing recipes with alternative excipients to avoid the use of TiO₂. Tested replacements are suitable for nutritional and pharmaceutical industry as well. TiO₂ free film coatings can be processed and applied comparable like typical film coatings with regard to amount of weight gain, process time and product price. A comparable opacity and brightness can be achieved. Unfortunately, the tested starch, phosphate and carbonate replacements do not have the necessary characteristics to replace TiO₂ 1:1. The performed trials show that a mixture out of different replacements is recommended for combining all desired properties. By using a higher weight gain level the properties of the replacements can be increased.



New Technologies

Orodispersible film manufacturing and characterization

Authors:

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Introduction

Orodispersible films have gained popularity during the past few years and the market is growing increasingly. They are the novel approach in oral drug delivery systems. It promises patient compliance especially in case of pediatrics and geriatrics patients. They can also be used when quick action is required. They possess many advantages over conventional dosage forms and can also be used in cases of dysphagia, Parkinson's disease, mucositis, or vomiting.

They are commonly called oral thin films (OTF), oral strips, orodispersible films (ODF), fast dissolving films, buccal films...

The first time fast dissolving drug delivery systems have been developed was in the late 70's as an alternative to conventional dosage forms. These systems consist of solid dosage forms that disintegrate and dissolve quickly in the oral cavity without the need of water. Fast dissolving drug delivery systems include orally disintegrating tablets (ODT) and (OTF). The Centre for Drug Evaluation and Research (CDER) defines ODT as, "a solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue". The food and drug administration (FDA) defines OTF as, "a thin, flexible, non-friable polymeric film strip containing one or more dispersed active pharmaceutical ingredients (API) which is intended to be placed on the tongue for rapid disintegration or dissolution in the saliva prior to swallowing for delivery into the gastrointestinal tract". The first approved prescription OTF was Zuplenz (Ondansetron hydrochloride) which was approved in 2010. The second approved one was Suboxone (Buprenorphine and Naloxone). Statistics have shown that four out of five patients prefer orally disintegrating dosage forms over conventional solid oral dosage forms [1].

Usually, fast dissolving oral films are ultra-thin film (50-150µm), which dissolves within a minute in the oral cavity after being in contact with the saliva, resulting in quick absorption and instant bioavailability of the drugs [2].

Advantages of ODF

An ODF dissolves more rapidly than other conventional dosage forms. They are less friable and easy to carry dosage form compared to commercialized orally fast disintegrating tablets, which need special packing. They are easy to administrate and no water is required which has led to better satisfactoriness amongst the dysphasic patients. Besides, the dosage form can be consumed at any place and any time as per convenience of the patient.

ODF have the ability to provide similar advantages to liquid medication in the form of solid preparation. They give accurate dosing as compared to liquids and provide good chemical stability.

ODF can be developed within 12-16 months, thus provides improved product development life-cycle time.

ODF are easy to swallow and don't present a risk of choking. As a matter of fact, patients suffering from dysphagia, repeated emesis, hypertension, heart attack, asthma, motion sickness, paralysis and mental disorders prefer this dosage form [1-3].

Disadvantages of ODF

ODF has some disadvantages but, their major limitations are the absence of specifications in the pharmacopeia and a limited drug load capability.

Commonly films are hygroscopic thus, special precaution should be taken during manufacturing and packaging.

Dose uniformity is difficult to maintain in ODF and combining more than one drug concomitantly is very challenging [1, 2].

Formulation and composition of ODF

Formulation includes consideration regarding; API - excipient compatibility, mechanical properties, taste masking, fast disintegration, physical appearance, mouth feel. ODF are generally with an area of 5-20 cm². APIs can be incorporated up to 50 mg [4]. From the regulatory point of view, all the excipients used should be generally regarded as safe (GRAS) listed and should be used as per Inactive Ingredients Limit (IIG limit) [1]. Various components of fast dissolving oral thin films are shown in (Table 1).

Table 1: ODF composition

Components	% w/w
API	0-50
Film forming agents	30-70
Plasticizers	5-20
Emulsifiers	0-25
Stabilizing agents	4-25
Disintegrants	1-5
Surfactants	0-5
Salivary stimulating agents	1-5
Sweeteners	3-6
Taste maskers	0-2
Coloring agents	Up to 1
Flavoring agents	Up to 10

New Technologies

1. Active pharmaceutical ingredient

Several class of active pharmaceutical ingredient (API) can be formulated as mouth dissolving films. The ideal characteristics of API to be incorporated into a fast dissolving film are: efficient at low dose, good palatability, small molecular weight, good solubility and stability in saliva. Insoluble API can be also incorporated and dispersed uniformly into ODF but, the API granulometry must be taken into account so particle size does not exceed the thickness of the final film.

2. Film forming agents

Water soluble polymers are commonly used in ODF in order to achieve rapid disintegration. The chosen polymer for ODF formulation must exhibit good properties such as good wettability, good mouth feel, optimum peel and tensile strength, non-toxic and non-irritant.

A variety of soluble polymer are available for ODF preparation. Natural polymers such as starch, pectin, gelatin, pullulan, sodium alginate...

Semi synthetic polymers like cellulose derivates; hydroxypropyl cellulose (HPC), hydroxylpropylmethyl cellulose (HPMC), Hydroxyethyl cellulose (HEC)...

Synthetic polymers such as polyvinyl alcohol (PVA), polyvinyl pyrrolidone (PVP), polyethylene oxide (PEO), methacrylate copolymers...

3. Plasticizers

Plasticizers are very important excipients in ODF formulation. They improve mechanical properties and flexibility they also reduce film fragility and improve the processability.

The commonly used plasticizers are glycerol and polyethylene glycols. However, other plasticizers can be used like; sorbitol, monoacetin, triacetin, propylene glycol, corn syrup etc [5, 6].

Plasticizers interact with the film-forming polymers by lowering their glass transition temperature and thereby improving plasticity and elasticity of the resulting films. Plasticizers may affect solubility of the API and drug absorption. High concentrations of plasticizers may cause an impaired moisture resistance, resulting in stability problems or tacky films [7].

4. Superdisintegrants

Disintegration has a significant emphasis on the bioavailability of the drug. The mechanisms of action of disintegrants are swelling or chemical reaction or enzymatic action [8].

Superdisintegrants, such as sodium starch glycolate, crospovidone, croscarmellose, provide quick disintegration as a result of combined effect of both swelling and water absorption, when they are added in the formulation. Superdisintegrants absorb water and swell which promotes the dispersibility of the system, thereby enhancing disintegration and dissolution [1].

Marketed ODF and future potential

The market for fast-disintegrating dosage forms including ODF, fast-disintegrating tablets and lyophilisates is growing fast. Between 2003 and 2007, more than 50 different ODF brands were launched in the US and Canada; a further increase is assumed. For companies, the ODF technology is suitable for life cycle management and extending patent protection of branded API [7]. Several companies including AdhexPharma offer platform technologies and development of ODF ready for licensing. ODF may not be the solution for all problems, because drug load is limited. Nevertheless, they will compete with orodispersible tablets, immediate-release dosage forms and oral lyophilisates in future.

Further potential API include loperamide, fentanyl, triptans or sildenafil. However, future decisions of the authorities on equivalence of ODF and orally disintegrating tablets as well as other dosage forms will influence the market [7]. Below, some examples of commercialized ODF are given in table 2.

Table 2: Examples of commercialized ODF

Brand name	Distributor	API
Zuplenz™	Stratava pharmaceuticals	Ondansetron
Suboxone® sublingual film	Indivior	Buprenorphine+ naloxone
Gas-X® thin strips	Novartis Consumer Health	Simethicone
Listerine® pocket paks	Pfizer	Peppermint
Chloraseptic® sore throat relief strips	Prestige Brands	Benzocaine
Novanuit®	Sanofi	Melatonin
Sudafed® PE quick dissolve strips	McNeil-PPC	Phenylephedrine HCl
Klonopin® Wafers	Roche Laboratories	Clonazepam

Different techniques for manufacturing ODF

There are various manufacturing process that can be used for ODF preparation. The most used in the pharmaceutical industry are the solvent casting and hot melt extrusion processes. The different manufacturing processes are described below.

1. Solvent casting

Solvent casting is the most used and widespread technology as the manufacturing process is accessible, easy to implement and cost-effective. Most commonly used solvents are water or ethanol. Film forming water-soluble polymers are dissolved or dispersed in the solvent. The API and other excipient are added to the mixture and stirred until total homogenization. The mixing process could introduce air bubbles into the mixture therefore, de-aeration is performed afterwards to remove this bubbles.

New Technologies

Rheological properties, drying temperature, API solubility and compatibility should be taken into account since they affect the stability of the system.

Casting is performed by spreading out of the mix on a continuous roll of release media like plastic or paper. Wet film thickness is given by a gap between the release media and the coating blade (figure 1). After casting on the relevant substrate, the product is dried by passing through an oven or a similar system in order to evaporate the solvent. This process leads to a dry polymeric film loaded with the drug substance.

Dried films are cut and stored under roll forms known as 'rollstock' before the converting step. However, it is highly recommended to cut the product directly after the casting step to avoid stability issues.

During the converting step, the film is cut into the required shape and size related to the desired dosage and packed. Final packaging generally consists in an individual package sealed in atmospherically resistant pouch that provide a moisture barrier as films properties are very sensitive to humidity [8, 9].

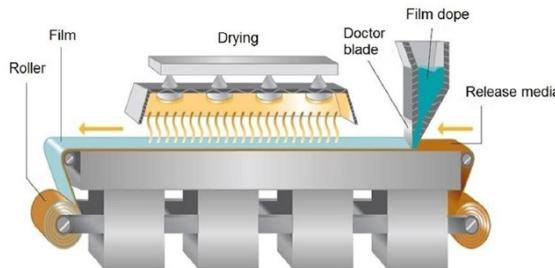


Figure 1: Equipment for solvent-casting manufacturing

2. Hot melt extrusion

In this method, polymers with low molecular weight and low viscosity are preferred, a combination of different polymer grades can also be used. This technology is coming from plastic, rubber and food industry then, it has been adopted for thin films. It represents an alternative to solvent casting when no organic solvent is required in the product.

Hot melt extrusion equipment consists in; one hopper connected with an extruder. The extruder is moving inside a barrel equipped with heaters and manufactured in different sections to shorten material residence time and avoid material degradation. A die gives the final shape of the product (figure 2).

During the manufacturing process, drug is first mixed with carrier in solid form. Film components are introduced in the extruder via the hopper and are mixed and melt thanks to the shearing forces generated by the extruder rotation. The melt mix is flowing through the die to obtain the final shape. Processing temperatures within the extruder should be between 65°C and 115°C depending on the extruder area and profile, with a screw speed around 15 rpm.

Thanks to this process, solubility and bioavailability of

poor soluble components can be improved.

Hot melt extrusion allows also to have good dispersion uniformity due to intense mixing and agitation. Besides stability is enhanced for a wide pH and moisture levels. This process can be considered as environmental friendly as no organic solvent or water are required. It also permit to reduce production time and operations.

The major drawback of the hot melt process is the restriction to non-thermo-labile API and sensitive polymers [12].

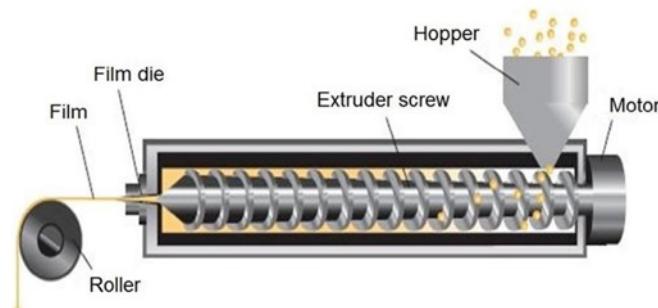


Figure 2: Equipment for hot-melt extrusion

3. Semi-solid casting

In this method, first a solution of water-soluble film forming polymer is prepared. Then to the resulting solution is added a solution of acid insoluble polymer (e.g. cellulose acetate phthalate) which was prepared by ammonium or sodium hydroxide. The ratio of the acid insoluble polymer to film forming polymer should be (1:4). A gel mass is obtained as a suitable amount of plasticizer is added to the mixture. Finally the gel mass is casted into ribbons or film using heat controlled drums [10, 11].

4. Rolling method

In rolling method, both the drug solution and film forming polymer solution are mixed thoroughly and the resultant solution or suspension is subjected to the roller. The solution or suspension should have specific rheological consideration. The film is dried on rollers and cut into desired shapes and sizes [13].

5. Solid dispersion extrusion

This method is a mixt of previous technology where API is mixed with suitable solvent and the solution is added in melted polymer along with immiscible components then the mixture is extruded which gives formulation in the form of solid dispersion. Finally, the dispersion is shaped into film [14].

6. Printing technologies

Printing technologies in ODF is the latest technique in which drug is printed on the surface of the polymer.

New Technologies

This technique exhibits many advantages, these include flexibility, cost effectiveness, possibility of customized medicines, preventing counterfeit, identification and labelling of the dosage form, homogeneous distribution and accurate dosage of API. However, it is useful only for high potent drugs.

Here below, some printing technologies that have been used for preparation of ODF.

7. Inkjet printing

Inkjet technology is versatile, accurate, repeatable and inexpensive method, it's usually divided into two types: Continuous inkjet printing is based on liquid ejection through a nozzle leading to a drop stream generated thanks to surface tension force. Continuous stream production can be obtained by driving the drops to a particular targeted site. Deviation of the stream can be obtained thanks to electrical charge application that will remove some of the drops from their main axis. Drop on demand (DoD) is following the same principle except that ejection of the drop is occurring only when the drop is necessary. Production of individual drop happens after response to a trigger signal. DoD is composed of multiple nozzles with a number varying between 100 to 1000. Printability characteristics may be impacted by density and viscosity of the ink, which can therefore cause variation of the uniformity and dosage accuracy of the drug substance [2].

The major drawback of Inkjet technology is a low throughput, thus these technologies may not be relevant for high throughput industrial productions where flexography is more suitable.

Flexographic Printing Technology

Flexography principal is to transfer the API to the film by contact printing. The ink is loaded with the drug substance leading to a solution which is transferred to a printing cylinder. Mix should have specific rheological properties. In most cases, water or mix of water and alcohol is used as solvent.

This process has many advantages, it is useful for heat of sensitive products like proteins and peptides, high production efficiency can be reached and it is transferable to large scale. Besides, after printing API, no effect on film's mechanical properties has been noticed [2].

Patented technologies for manufacturing ODF

BioProgress has developed a platform technologies like as XGEL™, Soluleaves™, WaferTab™, Foamburst™, for formulating fast dissolving ODF [5, 13, 15, 16, 17].

XGel: Alternative to the gelatin capsules, XGel™ was the world first non-animal- based soft capsule system using a formulation of PVA film. Different film formulations and thickness are available and make possible to design the dissolution time in the mouth or in other site of the body by tailoring the film formulation. XGel™ film is genetically modified organism (GMO) free and continuous production processing provides an economic and competitive manufacturing platform. XGel™ film can be taste masked,

colored, layered, and capable of being enteric properties whilst also having the ability to incorporate active pharmaceutical ingredients. The XGel™ film systems can be made to encapsulate any oral dosage form and can be soluble in either cold or hot water. XGel™ film is comprised of a range of different water soluble polymers, specifically optimized for the intended use.

Soluteaves: Technology allowing incorporation of active ingredients, colors and flavors into a non-genetically modified, non-animal derived film which is dissolving in the mouth on contact with saliva. Soluteaves products can also be tailored to adhere to mucous membranes and deliver the active ingredient on a slower time scale over 15 minutes.

Wafertab: Process to prepare drug loaded thin films. Drug delivery system incorporating API into edible film-strip with rapid dissolution and active ingredient release. Many possibilities of innovative products with different shapes and sizes.

Foamburst: It is a special variant of the Soluteaves™ technology where an inert gas is sent into the film during production. This results in a film with a honeycombed structure, which dissolves rapidly giving a novel mouth sensation.

Micap: Micap plc signed an option agreement in 2004 to combine its expertise in microencapsulation technology with the Bio Progress water soluble films. It was initially developed for smoking cessation products incorporated in water soluble films. This rapid film with disintegration occurring in 20s potentially induces a faster release of nicotine than previous methods.

ODF characterization

ODF are not listed in the pharmacopoeias yet. Despite that characterization method are conducted in order to ensure safe product, robust manufacturing process and patient compliance.

Besides typical parameters such as content uniformity, impurity profile, disintegration, dissolution and mechanical properties are investigated.

Below we described some evaluation method.

1.Content Uniformity

This is determined by any standard assay method described for the particular API in any of the standard pharmacopoeia. The content uniformity is determined using 10 films and estimating the API content in individual film.

2. Disintegration

Disintegration time is the time when an oral film starts breaking when brought in contact with water or saliva. For a fast dissolving film, disintegration time should be in range of 5-30 s. United State Pharmacopoeia (USP) disintegration apparatus can be used to study disintegration time.

New Technologies

In another method, the disintegration time can be visually determined by dipping the film in 25 mL water in a beaker. The beaker should be shaken gently and the time was noted when the film starts to breaks or disintegrates [13].

3.Dissolution

Dissolution is defined as the amount of drug substance that goes into the solution per unit time under standardized conditions of liquid/solid interface, temperature, and solvent concentration.

Dissolution test is performed with USP dissolution test apparatus (paddle method, apparatus 2). The USP dissolution apparatus is thermostated at the temperature of 37 ±0.5°C and stirred at rate of 50 revolutions per minute. Each film is placed in a sinker. Then the sinker is immersed in the vessel containing 500 mL of phosphate buffer pH 6.8. The aliquots of one ml are withdrawn at the time interval of 2, 4, 6, 8, 10 minutes and replaced with equal volume of dissolution medium. The sink conditions are maintained throughout the study. The absorbance is checked by selected analytical method [1, 13].

4.Stability study

Stability study should be carried out according to the International Conference on Harmonization (ICH) guidelines. The storage conditions at which formulations are kept should be:

Long term: 25°C/60% RH

Intermediate: 30°C/65% RH

Accelerated: 40°C/75% RH.

After 3 months, the films are evaluated for drug content, disintegration time, and appearance.

5.Surface pH

The surface pH of the oral dissolving film is measured in order to investigate the risk of any side effects *in vivo*. Since acidic or alkaline pH may cause irritation to the oral mucosa, it is determined to maintain the surface pH as close to neutral as possible. A combined pH electrode is used for this purpose. Films are left to swell for 2 hours on the surface of an agar plate. The pH is measured by bringing the electrode in contact with the surface of the swollen film. This study is performed in six films of each formulation and mean±S.D is calculated [1, 3].

6. Moisture loss

Percent moisture loss is a parameter that determines the hygroscopicity of a film. Usually, this parameter is determined by first finding the initial weight of the film, afterward, putting this film in a dessicator.

Percentage moisture loss = {(initial weight - final weight / initial weight) x 100} [18].

7. Tensile strength

It is calculated by using a small oral film fixed to assembly. The weight required to break the film is noted and simultaneously film elongation is measured with the help of pointer mounted on the assembly. Where W, T and L are width, thickness, and length of the strip, and ΔL is the

elongation at break.

$$\text{Tensile strength} = \{\text{Break force} / \text{WT} (1 + \Delta L/L)\} [18].$$

8. Percentage elongation

It was calculated by the distance travelled by pointer before the break of the film on the graph paper.

$$\% \text{ Elongation} = \{(\text{increase in length}/\text{original length}) \times 100\} [18].$$

Conclusion

ODF are new emerging novel drug delivery system of great importance, they offer many advantages over conventional oral dosage such as rapid onset of action, ease of administration, good bioavailability which draw the attention of many pharmaceutical companies. An ODF should have good mechanical properties, fast disintegration and good dissolution profile.

The application of ODF now extends beyond traditional immediate release oral dosage forms. Development of topical films, probiotic strips, and controlled-release ODF products are new forms made possible through this delivery format's flexibility, proven robustness and stability.

Future applications include incorporation of incompatible APIs in a single formulation using multilayer films laminated together. An inactive film layer separating the incompatible APIs can be introduced in between.

So far, the major drawback of ODF is that only high potent API can be used but, research is still going on. The future potential for these products is promising because of the availability of new technologies combined with strong market acceptance and patient demand.

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FURTHER INFORMATION

For further information regarding this vacancy, please contact Professor Stefaan De Smedt (Stefaan.desmedt@Ugent.be, <https://www.ugent.be/fwl/pharmaceutics/biochemphypfarm/en>) at the faculty pharmaceutical sciences, Department of Pharmaceutics).

Agenda



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