APV FOCUS GROUP DRUG DELIVERY

COMBINING SCIENCE & TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS

INTERNATIONAL ASSOCIATION FOR PHARMACEUTICAL TECHNOLOGY

NEWSLETTER **ISSUE 2/2020 - October**

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DRUG DELIVERY EVENTS

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+ **2nd APV Interactive Workshop on ATMP: Bridging standard pharma concepts and ATMP | KN 6828**
November 19-20, 2020 | Frankfurt am Main, Germany — Details

12th World Meeting on Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology
May 11-14, 2021 | Vienna, Austria — Details

Suggest a meeting to be announced!

APV NEWS

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Provided by Univ.-Prof. Dr. Sven Stegemann

APV IS PAVING THE WAY TO MEDICINES FOR OLDER ADULTS

One of the greatest achievements of progress in the life sciences is the increase in life expectancy. However, longevity does not come without new challenges for effective patient care. For the pharmaceutical development some of the major challenges have been summarized in the "Reflection Paper on the pharmaceutical development of medicines for the use in the older population" published by the European Medicines Agency (EMA) in August 2017.

As all emerging challenges provide opportunities to develop new concepts, transdisciplinary collaboration will be essential to further support longevity and quality of life. In November 2017 APV, in collaboration with the Geriatric Medicine Society e.V., organized a first conference on "Medicines for older adults: Getting prepared for the scientific and regulatory evolution" which was held in Graz (Austria), followed by a second conference in Berlin in June 2019. The conference was also the first bringing together experts from the different scientific areas involved. Due to the encouraging discussions between the stakeholders, the experts summarized their contributions in scientific, peer reviewed publications.

The British Journal of Clinical Pharmacology has just published this series of articles in the Themed Section of the journal titled: "Medicines development to improve clinical outcomes in an increasingly older and multi-morbid patient population https://bpspubs.onlinelibrary.wiley.com/toc/13652125/current. The themed issue focuses on how each of the different disciplines and stakeholders can contribute to better medicines for older patients. The themed issue is intended to stimulate more multi- and transdisciplinary discussion and collaboration between academia, regulators, industry, pharmacists, information technology, human factor design, etc. as well as more involvement of patients in the development of pharmaceutical drug products and their prescribing.

The APV has set up the "Patient Centric Medicines Initiative (PaCeMe)" to work on practical approaches towards better medicine development for older adults in accordance with the Reflection Paper, which is expected to be finally endorsed and implemented in the coming months. To join this initiative, please contact: sven.stegemann@tugraz.at.

Despite therapies and potential vaccines for Covid 19 dominating the news for the past few months, other novel therapies were achieving regulatory approval including the two delivery-technology-enabled products discussed in this article.

MYCAPSSA® (Octreotide) Delayed-Release Capsules

On 26 June 2020 Chiasma Inc. (MA, USA) announced that the FDA had given approval for its novel oral formulation of the somatostatin analog, octreotide, based on the company's Transient Permeability Enhancer (TPE) technology, to be prescribed in the US for the long-term maintenance treatment of acromegaly patients who have responded to and tolerated treatment with octreotide or lanreotide [1, 2]. Octreotide is an octapeptide with one disulphide bridge which is included in the formulation as the acetate salt. It has been used for the treatment of acromegaly in the US since 1988 [2]. Acromegaly affects an estimated 3 to 14 individuals per 100,000, with approximately 8,000 sufferers being treated with somatostatin analog injections in the US alone. It is caused by over-secretion of growth hormone by the pituitary gland, most often due to the presence of benign pituitary adenomas. The over-secretion has profound down-stream effects as it stimulates the production of insulin-like growth factor I (IGF-I) by the liver. It is this second hormone that mediates the growth that results in the characteristic changes associated with acromegaly such as enlarged extremities and changes in blood glucose and lipid metabolism which can result in the development of type 2 diabetes, high blood pressure, and heart disease in those suffering from the condition [3, 4]. Octreotide inhibits growth hormone to a greater extent than the natural hormone inhibitor, somatostatin, resulting in a significant reduction in growth hormone and IGF-1 levels in acromegaly patients.

The peptidic nature of octreotide means it is very challenging to deliver via the oral route, and to date it has only been commercially available as a solution for injection or as a sustained release intramuscular depot. MYCAPSSA® contains 20 mg octreotide base (as the acetate salt) in a capsule coated with a methacrylate enteric coating (Acryl-EZE®) in order to minimise release and peptide exposure to stomach acid. On reaching the small intestine the capsule releases its contents and the permeation enhancer, sodium caprylate, facilitates delivery of the peptide across the intestinal wall. The duration of the increased paracellular permeability was shown in one study to occur 2 hours after MYCAPSSA® administration with levels returning to normal after 5.5 hours demonstrating that the increase in permeability is completely reversible. Other excipients in the MYCAPSSA® formulation include polyvinylpyrrolidone (PVP-12), magnesium chloride, polysorbate 80, glyceryl monocaprylate and glyceryl tricaprylate. The initial dose is 20 mg twice daily titrated based on IGF-1 levels and patient symptoms until a maximum dose of 40 mg twice daily [2].

Approval was based on the results of a randomized, double-blind, placebo-controlled study involving 56 acromegaly patients previously stabilised on a dose of an injectable somatostatin analog. Its primary end-point was maintenance of the biochemical response (average of week 34 and 36 IGF ≤ 1.0 x Upper Limit of Normal) following a switch to either MYCAPSSA® or placebo. The results showed that 58% of the patients dosed with active met the primary end-point criteria compared with 19% on placebo. (P= 0.008). The trial also confirmed that the growth hormone response was maintained (78% of patients in the MYCAPSSA® cohort versus 30% on placebo), and that formulation was acceptable and tolerated by patients with 68% of those taking placebo reverting to their previous injectable therapy compared to 25% in the active group [4]. The main side-effects were gastrointestinal (reported in 68% of patients in the placebo-controlled trial) and were of a mild to moderate nature [2].

MYCAPSSA® launched in the US on 31 Aug 2020 [5] ahead of the Q4 anticipated schedule. The top-line results of a Phase 3 comparative trial versus injectable standard of care (octreotide and lanreotide) designed to achieve EMA approval are expected in Q4 2020 [4].

Arikayce® liposomal

At their July 2020 meeting the EMA's Committee for Medicinal Products for Human Use recommended approval of Insmed's Arikayce® liposomal (amikacin), for the treatment of non-tuberculous mycobacterial lung infections caused by Mycobacterium avium Complex (MAC) in adults with limited treatment options who do not have cystic fibrosis [6,7]. Arikayce® is a liposomal nebuliser dispersion for once daily administration containing 590 mg of the aminoglycoside antibacterial, amikacin as the sulphate salt, which acts to disrupt bacterial protein production. Incorporation of amikacin with the dipalmitoylphosphatidylcholine/cholesterol liposomes promotes its delivery to lung macrophages, while minimising the risk of systemic absorption of this antibiotic which is associated with severe side-effects such as ototoxicity and kidney damage. The dispersion is delivered once daily by means of the Lamira® Nebulizer System from PARI Pharma GmbH.

Like MYCAPSSA®, for which Chiasma received a Complete Response Letter to its original filing to the FDA in 2016 [8], this is second time lucky for the Insmed application for Arikayce® liposomal to the EMA. In 2016 the company withdrew its application for marketing authorization when it became apparent that the CHMP considered results from a Phase 2 placebo-controlled study in patients suffering from pulmonary infections caused by MAC or related bacteria provided insufficient evidence of the product's ability to clear infection permanently from sputum [9]. The approval this time around was based on

the Phase 3 randomized open-label CONVERT study which compared sputum culture conversion rates in refractory NTM lung disease patients receiving Arikayce® plus a multi-drug regimen (MDR) with MDR alone. Those who achieved conversion by Month 6 continued treatment for a further 12 months from the first month of negative sputum results. The key primary end-point with respect to the EMA application was the number of participants achieving durable culture conversion through 3 months of treatment in the Arikayce® plus MDR cohort compared to the MDR only cohort (time frame: up to Month 19) [7]. The other primary end-point was a comparison of the proportion of participants with sputum culture conversion at Month 6. This latter end-point supported the 2018 FDA approval of Arikayce® under its Limited Population Pathway for Antibacterial and Antifungal Drugs (LPAD) [10, 11]. The CHMP positive opinion, and the product's recent inclusion in international guidelines for the treatment of MAC pulmonary disease unresponsive to at least 6 months' of standard multi-drug therapy, is a boost for the estimated 1400 total refractory MAC patients in the EU and for this product whose net US sales in 2019 was $136 million [12, 13].

References and Further Information

[1] Chiasma Announces FDA Approval of MYCAPSSA® (Octreotide) Capsules, the First and Only Oral Somatostatin Analog. https://ir.chiasma.com/news-releases/news-release-details/chiasma-announces-fda-approval-mycapssar-octreotide-capsules

[2] Entry for MYCAPSSA® on Drugs@FDA https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=208232

[3] Acromegaly. The National Institute of Diabetes and Digestive and Kidney Diseases website. https://www.niddk.nih.gov/health-information/endocrine-diseases/acromegaly

[4] Presentation: Chiasma Overview September 2020 on Chiasma website. https://ir.chiasma.com/static-files/59604b38-05b1-41ce-ae04-21a2aeebe26f

[5] Chiasma Announces U.S. Commercial Launch and Availability of MYCAPSSA®, the First and Only Oral Somatostatin Analog for Patients with Acromegaly. https://www.globenewswire.com/news-release/2020/08/31/2086104/0/en/Chiasma-Announces-U-S-Commercial-Launch-and-Availability-of-MYCAPSSA-the-First-and-Only-Oral-Somatostatin-Analog-for-Patients-with-Acromegaly.html

[6] Meeting highlights from the Committee for Medicinal Products for Human Use (CHMP) 20-23 July 2020 https://www.ema.europa.eu/en/medicines/human/summaries-opinion/arikayce-liposomal

[7] Insmed Receives Positive CHMP Opinion for ARIKAYCE Liposomal 590 mg Nebuliser Dispersion for the Treatment of NTM Lung Infections Caused by MAC in Non-CF Patients with Limited Treatment Options. https://investor.insmed.com/2020-07-24-Insmed-Receives-Positive-CHMP-Opinion-for-ARIKAYCE-Liposomal-590-mg-Nebuliser-Dispersion-for-the-Treatment-of-NTM-Lung-Infections-Caused-by-MAC-in-Non-CF-Patients-with-Limited-Treatment-Options

[8] Chiasma Provides Update Regarding FDA's Complete Response Letter for Mycapssa™ New Drug Application. https://www.globenewswire.com/news-release/2016/04/18/829612/0/en/Chiasma-Provides-Update-Regarding-FDA-s-Complete-Response-Letter-for-Mycapssa-New-Drug-Application.html

[9] Arikayce: Withdrawal of the marketing authorisation application. https://www.ema.europa.eu/en/medicines/human/withdrawn-applications/arikayce

[10] Daley et al. Treatment of Nontuberculous Mycobacterial Pulmonary Disease: An Official ATS/ERS/ESCMID/IDSA Clinical Practice Guideline: Executive Summary. *Clinical Infectious Diseases*, Volume 71, Issue 4, 15 August 2020, Pages e1–e36.

[11] Entry for Arikayce® on Drugs@FDA https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/207356s004lbl.pdf

[12] Rosenmayr-Templeton, L. Drug Delivery Products, APV Drug Delivery Focus Group Newsletter 3rd Edition 2018.

[13] Investor Presentation on Insemed Inc. website https://investor.insmed.com/events

NANOMERICS LTD. (London, United Kingdom)

Nanomerics Ltd is a speciality pharmaceutical company based in London, UK. Nanomerics was spun out of University College London, a top 20 global university, and was founded to commercialise the Molecular Envelope Technology (MET) developed in the UK academic sector. Nanomerics' MET enables the transport of drugs across key biological epithelial barriers and this allows Nanomerics to create uniquely differentiated products, underpinned by high quality science.

Fact sheet:

Founded:	2010
Location:	London, United Kingdom
Ownership:	Private
Employees:	Undisclosed
Key technology:	Molecular Envelope Technology (MET) Nanomerics' MET involves the self-assembly of specifically engineered polymers that wrap around and incorporate hydrophobic drugs and peptides creating a protective molecular envelope. MET enables the delivery of hydrophobic and amphiphilic drugs across biological barriers, increasing bioavailability over 5-fold and specifically targeting therapeutics to the brain or to ocular tissues. Nanomerics' MET also significantly increases drug bioavailability via the oral route.
Products:	• NES100 – a nano-enabled pain therapeutic out-licensed to and being developed by Virpax Pharmaceuticals. • I33 – a nano-enabled eye drop formulation out-licensed to and being developed by Iacta Pharmaceuticals.
Development status:	IND enabling
Partnerships:	Multiple Global Partnerships around the world, e.g. Iacta Pharmaceuticals and Virpax Pharmaceuticals
Website:	http://www.nanomerics.com
Contact:	Professor Ijeoma F. Uchegbu Chief Scientific Officer Nanomerics Ltd. New Bridge Street House 30-34 New Bridge Street London EC4V 6BJ United Kingdom Tel: +44 (0)2033972183 ijeoma.f.uchegbu@nanomerics.com

NEXT GENERATION ZYDIS® TECHNOLOGIES

By Niamh Barrat, Leon Grother, Susan Banbury, Desmond Wong
Catalent Pharma Solutions, Frankland Road, Blagrove, Swindon, SN5 8RU, UK

Catalent's Zydis® technology was initially developed in 1986, and it was first applied to a commercial program in 1993. The technology is used to create a unique orally disintegrating tablet (ODT) that dissolves, typically, in less than 3 seconds to aid swallowing without the requirement for water. Zydis technology has been shown to be an excellent technology to improve compliance (e.g., pediatrics, geriatrics, psychiatrics and for animal health applications). This delivery system can potentially be beneficial in obtaining pre-gastric absorption of appropriate drug candidates, by bypassing first-pass metabolism. The portfolio of Zydis technologies has grown over the past 30+ years, to extend the range to Zydis® Bio, Zydis® Nano and Zydis Ultra® (to be discussed further in this article).

What is Zydis?

Zydis technology is applied to make a solid dosage form, where the drug is dissolved or dispersed in an aqueous polymer matrix. Additional structure formers and other excipients, such as flavors, sweeteners, pH modifiers etc., are added to the mix as required. The resulting mix is then dosed directly into preformed blister pockets as a liquid, frozen, freeze-dried and finally sealed, as shown in Figure 1.

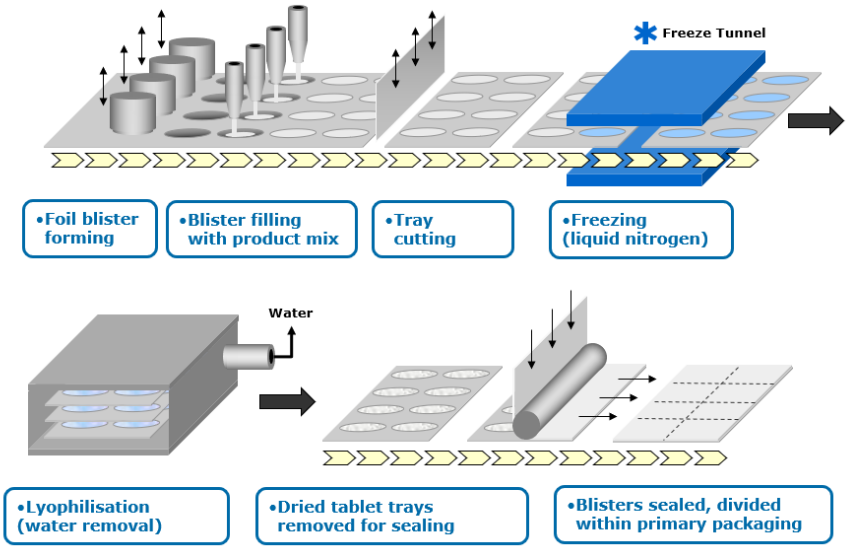

Figure 1: The Zydis® ODT Process

Once frozen, a polymer crystal structure matrix is obtained which, upon removal of water (freeze-drying), creates channels/pores in the unit dose, that on dose administration effectively act as a sponge absorbing saliva in the mouth and dispersing rapidly. Figure 2 shows schematically the freeze drying of a Zydis unit.

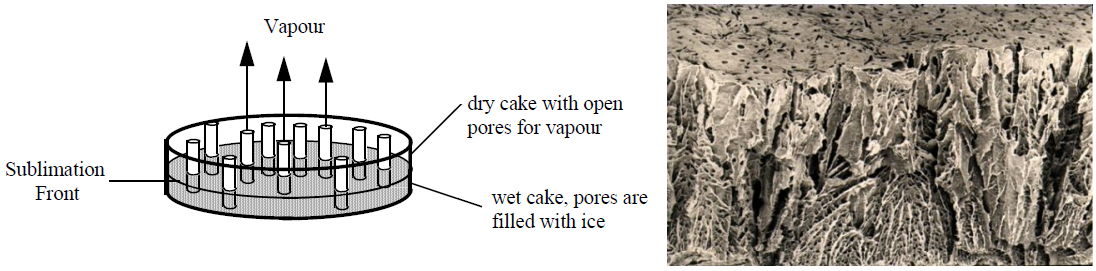

Figure 2: Freeze Drying Diagram and SEM image of a cross-section of a Zydis® unit dose

Next Generation Zydis Technology - Sequential Dosing

The multi-phasic Zydis ODT is produced through a manufacturing process that layers two or more homogenous formulations sequentially into the blister pocket under different conditions, prior to freeze-drying. This multi-phasic form of the Zydis ODT addresses issues of incompatible Active Pharmaceutical Ingredients (APIs)/excipients or temperature sensitive API. The application could also be extended to create a buffer layer to modify the oral pH to aid API uptake without affecting the drug stability in the finished product.

An exemplary biphasic product is made using the following process. Two mixes are prepared with different physical properties, such as density and gelling characteristics. The first layer of the matrix former mix is dosed into the blister pocket followed by the second layer of the matrix former mix. The blisters are then frozen and freeze-dried as per conventional Zydis ODT. Figure 3 shows a photograph of a sequentially-dosed unit. A blue dye was used to determine that the layers did not mix.

Figure 3: Sequentially-dosed Zydis® orally disintegrating tablet

Next Generation Zydis Nano

Zydis Nano technology has extended the effectiveness of the Zydis ODT, by using API nanoparticulates. The benefit of using nanoparticulates is in the increased surface-to-mass ratio that improves the dissolution rate of the API, which in turn can lead to an increase in in vivo bioavailability for API that suffer dissolution rate limited absorption. Due to improved bioavailability, reduction of dose/dosing frequency is possible and thereby potentially reducing toxicity while maintaining therapeutic effect. Nanoparticulates are however prone to agglomeration, and this can negatively influence the rate of dissolution and hence the bioavailability for the drug. The physical stability of the nanoparticulates in the Zydis dosage form is maintained by the matrix components of the formulation to prevent agglomeration. This, in combination with the rapid dispersion in the finished dosage form, has resulted in enhanced bioavailability and rapid dispersion compared to the micronized API typically used (Zydis "As is"); refer to Figure 4 for data for fenofibrate (48 mg dose strength).

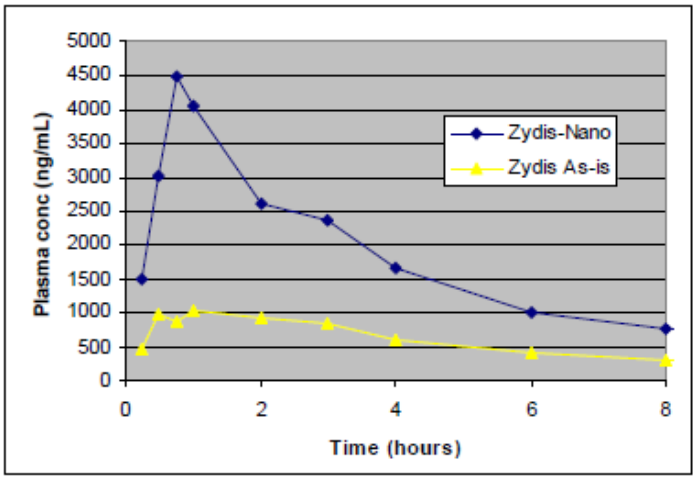

Figure 4: Zydis® Nano ODT (Fenofibrate)

Next-Generation Zydis Bio

Delivery of large molecules, peptides and protein drugs via the oral route has seen considerable interest and market growth in recent years. The Zydis format has proved beneficial in achieving oral dose delivery by offering: low temperature processing conditions (dosing an aqueous mix at sub ambient temperature); formulation flexibility (e.g. pH for optimum stability); good content uniformity, even at low dose strengths (e.g., 50 µg – API dispersed in a solution or suspension); containment of potent API in a liquid mix; solid dosage form with protective pack to prevent moisture stability issues; and the potential for sublingual/buccal absorption.

The pre-gastric delivery of biomolecules offers a significant benefit as it avoids first-pass metabolism and the biomolecule is protected from the harsh environment of the gastrointestinal tract. For example, the pH of saliva in the mouth ranges from pH 5.5 to 7.2, which is more favorable in aiding stability compared to the acidic environment of the stomach. The oral cavity also has a good blood supply with the thickness of the sublingual epithelium varying between 100-200 µm and buccal epithelium thickness of 500-800 µm, increasing the potential for uptake of biomolecules (e.g., calcitonin study using Zydis technology, refer to Figure 5).

Zydis technology was used successfully in the development of ALK's Grazax®. Previous therapies for grass pollen allergy (hay fever) involved injection-based therapy, often requiring monthly subcutaneous injections at a clinic for severe cases, plus monitoring of the patient for adverse effects. Zydis Grazax contains an extract of grass pollen allergen (Timothy grass), which stimulates the body to produce antibodies against grass pollen. This immunotherapy can be administered daily at home as a sublingual Zydis ODT.

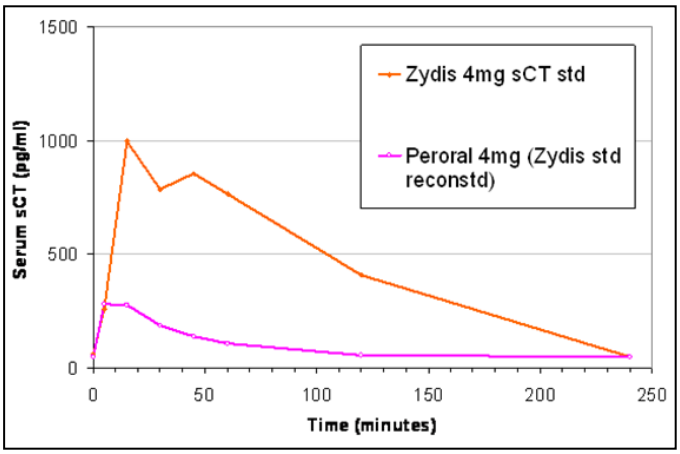

Figure 5: Zydis calcitonin sublingual versus peroral administration

Applications for the Zydis Bio technology do not stop here – another area of interest is for the oral delivery of vaccines. Zydis Bio ODT vaccines may have advantages compared to traditional vaccines such as improved stability with increased robustness to transit and climate conditions that may reduce reliance on cold chain storage. Currently, there are several studies underway to assess Zydis technology to deliver vaccine delivery systems.

Next-Generation Zydis Ultra® Technology

Zydis Ultra Coating Technology is the next generation of ODT. The technology was voted the winner of the 2018 Medicine Maker Innovation Award for ground-breaking innovation.

A limitation of traditional Zydis ODT was drug loading (insoluble API ~ 200 mg and soluble API ~60 mg). The Zydis Ultra platform offers increased drug loading in addition to taste masking by the incorporation of coated API in the ODT format, with drug loading > 200 mg and the potential for functional coating for controlled/sustained release application with great taste masking capabilities. To create the enhanced capabilities of Zydis Ultra technology, the API is first coated with coating materials using a resonance acoustic mixing (RAM) process involving low frequency, high intensity acoustic pressure waves.

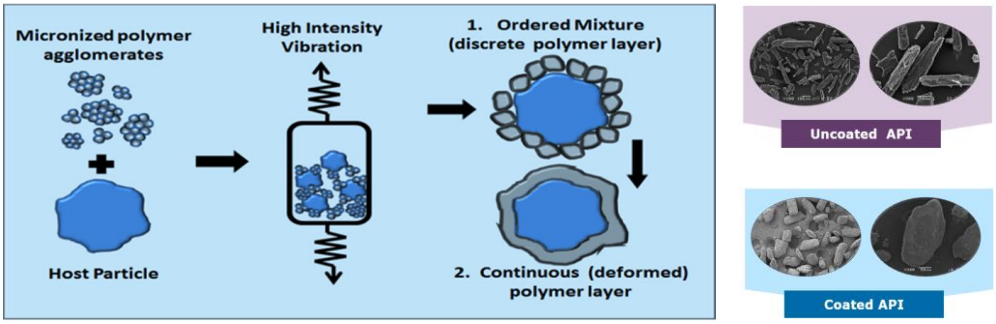

Figure 6: Zydis® Ultra API Coating Process and SEM Images

The coating process is dry (no solvent), uses no impellers for mixing and has the potential for higher potency than other coating processes (e.g. 70% - 80% w/w). This coated API is then combined with the wet phase (matrix system) just prior to dosing and is subsequently processed into blister packs as per conventional Zydis ODT (frozen and freeze-dried), as shown in Figure 7.

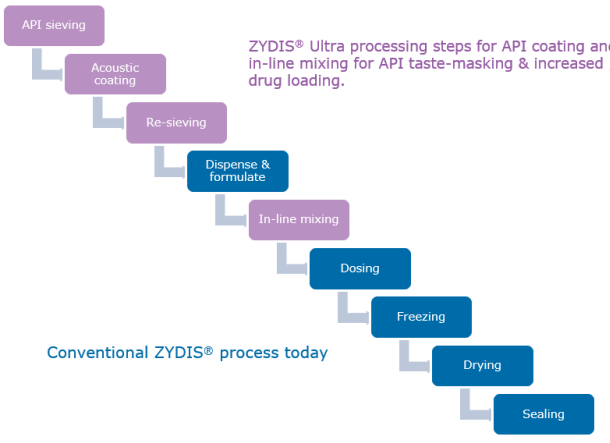

Figure 7: Zydis Ultra Manufacturing Process

In summary, the Zydis technology has been shown to be a versatile delivery system. Initially it is a very specific system which brought the benefits of orally disintegrating tablets, and the potential for pre-gastric absorption, for the administration of many drug products. The technology has now progressed to offer solutions in areas where Zydis would not have previously been considered. These solutions; whether sequential dosed Zydis where incompatible components can be separated to maintain stability, Zydis Bio incorporating peptide/protein molecules or vaccines with the benefit of low temperature process conditions and potential for reduced cold storage requirements for the finished product, Zydis Nano delivering stable API nanoparticles without the risk of agglomeration, or Zydis Ultra addressing the limitation of conventional Zydis drug loading with the added potential of taste masking. The question now remains, where will Zydis take us to next?

References

[1] Seager, H. "Drug Delivery Products and the Zydis® Fast-Dissolving Dosage Form", J. Pharm. Pharmacol., 50 (1998) 375-382.

[2] "Zydis® Fast-Dissolve" oral presentation, Rosie McLaughlin, University of Dusseldorf, 18th July 2013.

[3] "Oral Dispersion Tableting Technology" oral presentation, Leon Grother, Robert Gordon University, 4th March 2016.

[4] "A sequential dosing approach for the Zydis® freeze-dried orally disintegrating tablet" poster presentation, Niamh Barrat, Leon Grother, Lisa Garrett, Rosie McLaughlin, Pharmaceutics, Biopharmaceutics and Pharmaceutical Technology (PBP) Conference, Glasgow, 2016.

[5] "Use of Cyclodextrins for taste masking Cetirizine HCl 10mg formulated in the Zydis® dosage form" poster presentation, L. Grother, K. Hau, P. Axe, D. Wong, AAPS 2012.

[6] Grazax® is a registered trademark of ALK-Abelló Ltd.

DRUG DELIVERY PEOPLE

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Provided by Dr. Lea Ann Dailey

For this issue of the Newsletter, **Pieter R. Cullis, Ph.D.** FRSC, FNAI (USA) is our featured Drug Delivery Scientist. Dr. Cullis gained both his BSc and PhD in Physics from the University of British Columbia, Canada, before expanding his research interests into the biological sciences by completing postdoctoral fellowships in biochemistry departments at the University of Oxford, UK, and Utrecht University. He is currently Scientific Director & CEO, of the NanoMedicines Innovation Network, Canada's National Centre of Excellence in nanomedicines and also Director, of the NanoMedicines Research Group and Professor, Department of Biochemistry and Molecular Biology, University of British Columbia.

Dr. Cullis and co-workers have been responsible for fundamental advances in the design and development of nanomedicines employing lipid nanoparticle (LNP) technology for cancer therapies and gene therapies. This work has contributed to four drugs that have been approved by regulatory agencies in the U.S., Europe and Canada. Three of these (ABELCET, Myocet and Marqibo) are LNP systems that contain small molecule drugs and are used to treat cancer and its complications. The fourth (Onpattro) is an LNP formulation of short interfering RNA (siRNA) and was approved by the FDA and EMA in 2018 to treat the hereditary condition transthyretin-induced amyloidosis (hATTR). Onpattro employs an LNP delivery system devised by Dr. Cullis and colleagues and is the first RNAi drug to receive regulatory approval. Similar technologies can be used to enable other gene therapies employing mRNA and gene editing constructs.

Dr. Cullis has co-founded ten biotechnology companies that now employ over 300 people, published over 350 scientific articles that have received over 50,000 citations and is an inventor on over 60 patents. He also co-founded the Centre for Drug Research and Development (CDRD, a National Centre of Excellence) in 2004, the Personalized Medicine Initiative (PMI) in 2012 and the NanoMedicines Innovation Network in 2019. Dr. Cullis was elected a Fellow of the Royal Society of Canada in 2004 and was also awarded the Prix Galien, Canada's premier prize for achievements in pharmaceutical R&D, in 2011.

RECENTLY PUBLISHED LITERATURE REVIEWS IN THE FIELD OF DRUG DELIVERY

Peptide, Protein-based Drug Delivery

Overcoming negatively charged tissue barriers: Drug delivery using cationic peptides and proteins
Vedadghavami A, Zhang C, Bajpayee AG. Nano Today. 2020 Oct;34:100898
Advances using examples of negatively charged tissues (cartilage, meniscus, tendons and ligaments, nucleus pulposus, vitreous of eye, mucin, skin) are discussed and how each of their structures, tissue matrix compositions and high negative fixed charge densities creates barriers to drug entry. The review explores how charge interactions are being used to overcome these barriers. Work on tissue targeting cationic peptide and protein-based drug delivery is reviewed, compared and drug delivery designs contrasted. Examples of technologies that are entering clinical trials are presented.

Dermal and Transdermal Drug Delivery

Lipid vesicles: A versatile drug delivery platform for dermal and transdermal applications
Chacko IA, Ghate VM, Dsouza L, Lewis SA. Colloids Surf B Biointerfaces. 2020 Jul 17;195:111262
This review article describes the various vesicular systems reported for skin delivery of actives with relevant case studies.

Intrathecal/Intracranial delivery

Targeted Drug Delivery (Intrathecal and Intracranial) for Treatment of Facial Pain
Dupoiron D. Prog Neurol Surg. 2020 Aug 19;35:1-13
The review discusses targeted drug delivery of pain medication for the treatment of refractory head and face pain which is a relatively recent, little-used, and rather poorly defined technique, despite its proven efficacy. The introduction of a new generation of catheters connected to implantable pumps, enable established techniques to become simpler to implement, and these techniques are expected to grow in popularity over the next few years because of their reversibility and efficacy in fighting refractory head and face pain.

Nanosystem-based Drug Delivery

Nanomedicine and Chemotherapeutics Drug Delivery: Challenges and Opportunities
Nezhadi S, Handali S, Dorkoosh F. J Drug Target. 2020 Aug 8:1-39
In this review, TME (tumor microenvironment) features, current drug delivery approaches, challenges, and promising strategies toward cancer treatment are discussed.

Nanomedicine and drug delivery systems in cancer and regenerative medicine
Garbayo E, Pascual-Gil S, Rodríguez-Nogales C, Saludas L, Estella-Hermoso de Mendoza A, Blanco-Prieto MJ. Wiley Interdiscip Rev Nanomed Nanobiotechnol. 2020 Sep;12(5):e1637
The present review summarizes the most important steps carried-out by the group of Prof Blanco-Prieto in nanomedicine and drug delivery technologies. The latest research by this group has shown that drug delivery systems combined with cell therapy can achieve a more complete and potent regenerative response. Cutting-edge areas such as noninvasive intravenous delivery of cardioprotective nanomedicines or extracellular vesicle-based therapies are also being explored.

Carbon nanostructures: The drug and the delivery system for brain disorders
Henna TK, Raphey VR, Sankar R, Ameena Shirin VK, Gangadharappa HV, Pramod K. Int J Pharm. 2020 Jul 28;587:119701
This review focuses on different carbon nanostructures for brain-targeted drug delivery and their CNS activities. As a carrier and CNS therapeutic agent, carbon nanostructures can revolutionize the treatment of brain disorders.

Ocular Drug Delivery

Evaluation of commercial soft contact lenses for ocular drug delivery: a review
Fan X, Torres-Luna C, Azadi M, Domszy R, Hu N, Yang A, David AE. Acta Biomater. 2020 Aug 24:S1742-7061(20)30485-2
The review critically appraises the rationale for using commercially available soft contact lenses for ocular drug delivery; summarizes the evolution of materials used in lens fabrication; and explores various methods used to improve the drug release characteristics and its tissue uptake.

Pulmonary Drug Delivery

Scope and limitations on aerosol drug delivery for the treatment of infectious respiratory diseases
Douafer H, Andrieu V, Brunel JM. J Control Release. 2020 Sep 10;325:276-292
The review article has been written with the objective to compile information about various existing modern technologies developed to provide greater patient compliance and reduce the undesirable side effect of the drugs. In conclusion, aerosol antibiotic delivery appears as one of the best technologies for the treatment of pulmonary infectious diseases and has the ability to limit the systemic adverse effects related to the high drug dose and to make life easier for patients.

Respiratory Tract: Structure and Attractions for Drug Delivery Using Dry Powder Inhalers
ElKasabgy NA, Adel IM, Elmeligy MF. AAPS PharmSciTech. 2020 Aug 21;21(7):238
In this review, different types of inhaler devices are illustrated like metered dose inhalers (MDIs), dry powder inhalers (DPIs), nebulizers, and the new soft mist inhalers (SMIs).

Intranasal Drug Delivery

Intranasal Antiviral Drug Delivery and Coronavirus Disease 2019 (COVID-19): A State of the Art Review
Higgins TS, Wu AW, Illing EA, Sokoloski KJ, Weaver BA, Anthony BP, Hughes N, Ting JY. Otolaryngol Head Neck Surg. 2020 Jul 14:194599820933170. doi: 10.1177/0194599820933170
A state-of-the-art review of intranasal antiviral drug delivery which discusses current applications, adverse reactions, and future considerations in the management of coronavirus disease 2019 (COVID-19).

New Opportunity to Formulate Intranasal Vaccines and Drug Delivery Systems Based on Chitosan
Popescu R, Ghica MV, Dinu-Pîrvu CE, Anuța V, Lupuliasa D, Popa L. Int J Mol Sci. 2020 Jul 16;21(14):5016
The aim of this review is to present the influence of the properties of chitosan and its derivatives (mucoadhesion, permeability enhancement, surface tension, and zeta potential) on the development of suitable nasal drug delivery systems and on the nasal bioavailability of various active pharmaceutical ingredients

Oral Drug Delivery

Challenges in oral drug delivery and applications of lipid nanoparticles as potent oral drug carriers for managing cardiovascular risk factors
Okur NÜ, Siafaka PI, Gökçe EH. Curr Pharm Biotechnol. 2020 Aug 4
In this review, the most current and promising studies involving Solid Lipid Nanoparticles and Nanostructured Lipid Carriers as oral drug carriers are reported with the aim to assist researchers who focus their research on lipid-based nanoparticles.

Micro and nanoscale technologies in oral drug delivery
Ahadian S, Finbloom JA, Mofidfar M, Diltemiz SE, Nasrollahi F, Davoodi E, Hosseini V, Mylonaki I, Sangabathuni S, Montazerian H, Fetah K, Nasiri R, Dokmeci MR, Stevens MM, Desai TA, Khademhosseini A. Adv Drug Deliv Rev. 2020 Jul 22:S0169-409X(20)30096-X
The review briefly describes biological barriers to oral drug delivery and micro and nanoscale fabrication technologies.

Self-emulsifying Drug Delivery System Improve Oral Bioavailability: Role of Excipients and Physico-chemical Characterization
Zhang Q, Zhu Y, Ye J. Pharm Nanotechnol. 2020 Aug 10
This review explores the role of ingredients (drugs, oils, surfactant and cosurfactant) of self-emulsifying drug delivery systems (SEDDS) in increasing oral drug bioavailability and discusses the influence of the physicochemical properties (particle size and zeta potential) of SEDDS on the oral drug bioavailability enhancement. This review would provide an approach to develop a rational SEDDS for improving oral drug bioavailability.

The APV Drug Delivery Focus Group (APV DD) is a section of the APV (Arbeitsgemeinschaft für Pharmazeutische Verfahrenstechnik e.V. / International Association for Pharmaceutical Technology), a major European society for those sharing a professional interest in pharmaceutical sciences. The Focus Group was established in 2003 in response to the increasing importance of drug delivery within modern pharmaceutics.

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COMBINING SCIENCE AND TECHNOLOGY TO CREATE ADVANCED DRUG DELIVERY SYSTEMS

OUR MISSION STATEMENT:

Modern drug delivery research and development is a truly multidisciplinary approach and must combine all relevant scientific, technical, medical and regulatory aspects required for the design, preparation, testing, manufacturing and registration of drug delivery systems and their components. It is the mission of the APV Drug Delivery Working Group to foster and promote all aspects of research and development required to transform drug molecules into safe, applicable and acceptable drug delivery systems, which provide therapeutic benefit, convenience to the patient and improve patient compliance.

Our mission includes in particular the following tasks:

- Thoroughly understanding the physical-chemical and biopharmaceutical properties of the drug substance to be delivered and the components of the drug delivery system
- Understanding the biological barriers and the interactions of the drug molecule and its delivery system with the biological environment and the biological target including PK/PD and PK/safety relationships
- Research on excipients, materials and technologies required for the design, preparation and manufacturing of drug delivery systems for a selected route of administration
- Development and understanding of methods for in vitro and in vivo evaluation of drug delivery systems and their components
- Knowledge of regulatory requirements for clinical testing, manufacturing and registration of drug delivery systems

All disciplines relevant to the above-mentioned areas of drug delivery R&D are invited to contribute to the APV Drug Delivery Group:

Pharmaceutics, Biopharmaceutics, Analytics, Biology, Physical Chemistry, Biochemistry, Physics, Engineering Sciences, Nano Technology, Material Sciences, Polymer Science, Toxicology, Drug Safety, Clinical Research, Drug Regulatory Affairs, etc.

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