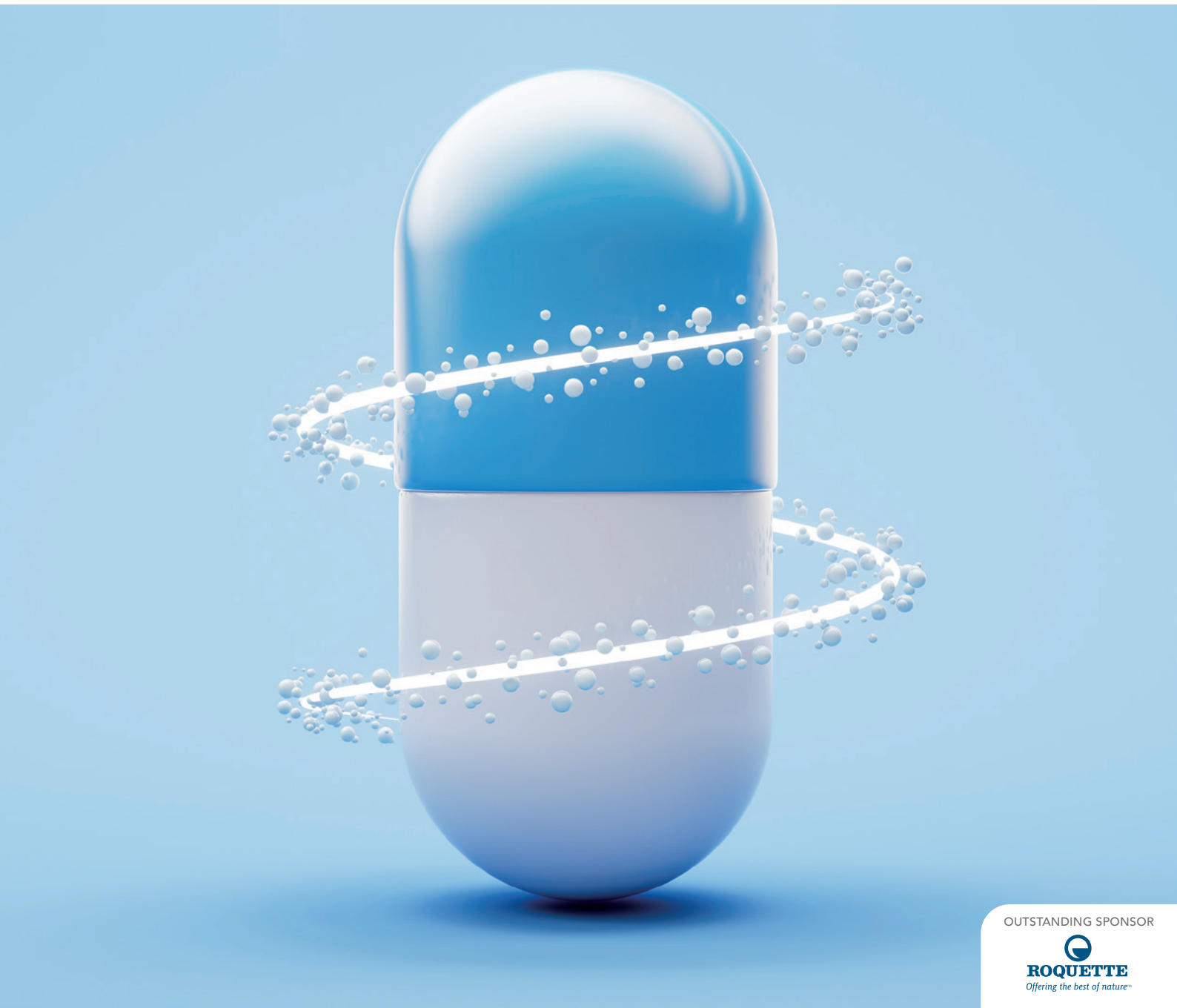
20 YEARS ON

173

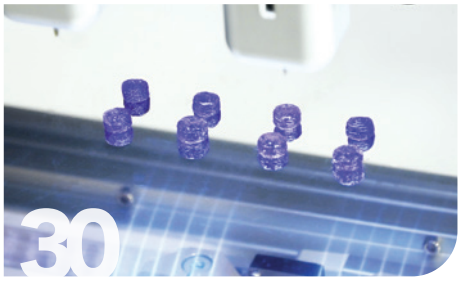
DrugDelivery

MAY 30TH 2025

ORAL DRUG DELIVERY



Contents



ORAL DRUG DELIVERY

ONdrugDelivery Issue N° 173, May 30th, 2025

This edition is one in the ONdrugDelivery series of publications. Each issue focuses on a specific topic within the field of drug delivery, and is supported by industry leaders in that field.

EDITORIAL:
James Arnold, Production Editor
james.arnold@ondrugdelivery.com
Subeditors: **Sarah Tomblin, Zoe Billyard**

CREATIVE DESIGN:
Simon Smith, Head of Creative
simon.smith@ondrugdelivery.com

SUBSCRIPTIONS:
Print + Digital subscription:
£99/year + postage.
Digital Only subscription: free.
subscriptions@ondrugdelivery.com

ADVERTISING & SPONSORSHIP:
Guy Furness, Founder and Publisher
+44 1273 47 28 28
guy.furness@ondrugdelivery.com

www.ondrugdelivery.com

ONdrugDELIVERY®

ONdrugDelivery is published by

FURNESS PUBLISHING

The Candlemakers, West Street, Lewes, East Sussex, BN7 2NZ United Kingdom

Board Directors: **Guy Furness**, **Audrey Furness**

Registered in England: Company No 8348388
ISSN 2049-145X print / ISSN 2049-1468 pdf

RECYCLED
Paper made from recycled material
FSC® C022819
www.fsc.org

WORLD LAND TRUST™
www.carbonbalancedpaper.com

GOGREEN PLUS

ONdrugDelivery Magazine is printed sustainably by Newman Thomson Ltd, West Sussex, UK, using Forest Stewardship Council® certified recycled paper, vegetable-based inks, biodegradable laminates and carbon balanced materials offset via the World Land Trust™ following ISO140001 processes. ONdrugDelivery in print is sustainably shipped to events by DHL using GoGreen Plus whereby carbon insetting of at least 30% is achieved through the use of Sustainable Aviation Fuel (SAF), a biofuel substitute for traditional jet fuel, produced from renewable sources such as vegetable oils, animal fats, waste products, and agricultural crops. The magazine is mailed to individual readers outside the UK by DHL using GoGreen, which offsets 100% of CO_2 emissions.

The toughest challenges in drug delivery.
Solved, together.

Do you believe in a world where we all have access to a healthier future? We do.

It's this belief that has inspired us to build a broad and diverse portfolio of excipient and capsule solutions, allowing our partners to move beyond the possible and deliver essential treatments to those who need them most.

From our extensive excipients range and leading formulation expertise to regulatory guidance and commercial roll-out and up-scaling assistance, you can rely on us for the tailored support that turns ambition into life-changing medications.

Get started at **roquette.com/pharma**

ROQUETTE
Offering the best of nature™

New Technology & Techniques: The Oral Drug Delivery of Tomorrow

In this issue of ONdrugDelivery, we cover the topic of oral drug delivery. Long considered a gold standard of drug delivery formats, the oral sector is currently seeing innovators looking for ways to broaden the scope of the oral route to enable formulators to deliver new medicines to more patients in a convenient and patient-centric fashion. A key facet of this innovation is in the sphere of personalised medicine and moving on from the paradigm of "one pill fits all" prescription, which is a major theme in this issue.

The issue opens with an interview with Dr Keat Theng Chow of **Roquette Health & Pharma Solutions** (Page 6), our Outstanding Sponsor, covering the twin topics of patient-centric design and regulatory compliance in the oral space. Dr Chow offers a wide-ranging overview of these subjects and how Roquette is helping pharma companies navigate the challenges presented by striking a balance between the demands of these two critical factors on drug development.

Also tackling the subject of taking a more patient-centric approach to drug development, we feature two articles on delivering personalised oral medication. First, **FABRX** (Page 22) discusses 3D printing for pharmaceutical applications, investigating how current technology can print tablets on demand as an automated alternative to conventional pharmaceutical compounding. Second, **AbbatiaLabs** and **Adare Pharma Solutions** (Page 28) introduce their novel dosing technology that enables patients to dispense variable doses of oral medication accurately at home.

PCI Pharma Services (Page 10) cover targeted protein degraders (TPDs) – a novel method for treating diseases that the pharmaceutical industry has hitherto been unable to tackle. PCI explain how the challenges presented by this new approach can be handled, and the benefits that doing so might bring to patients.

Rounding out the issue, an Expert View from **BENEO** (Page 16) shines a light on the difficulties and rewards that can come from working with plant extracts as part of pharmaceutical formulations. These ingredients can be challenging to work with but, if those challenges can be overcome, can be a valuable addition to formulators' toolkits.

James Arnold
Production Editor

2025/26 Editorial Calendar

Each issue of ONdrugDelivery focuses 100% on one specific topic *within* drug delivery.

JUN 2025 Connectivity in Drug Delivery DEADLINE PASSED	**JUL** Industrialising Drug Delivery DEADLINE PASSED	**SEP** Wearable Injectors DEADLINE: **Aug 7, 2025**
SEP/OCT **NEW ISSUE TOPIC** Dual Chamber Delivery Systems DEADLINE: **Aug 14, 2025**	**OCT** Prefilled Syringes & Injection Devices DEADLINE: **Sep 4 , 2025**	**OCT/NOV** Sustainability in Drug Delivery DEADLINE: **Sep 18, 2025**
NOV Pulmonary & Nasal Drug Delivery DEADLINE: **Oct 2, 2025**	**DEC** **NEW ISSUE TOPIC** Delivering Gene & Cell Therapeutics DEADLINE: **Nov 6, 2025**	**JAN 2026** Prefilled Syringes & Injection Devices DEADLINE: **Dec 4, 2025**
FEB Skin Drug Delivery: Dermal, Transdermal & Microneedles DEADLINE: **Jan 8, 2026**	**MAR** Ophthalmic Drug Delivery DEADLINE: **Feb 5, 2026**	**APR** Pulmonary & Nasal Drug Delivery DEADLINE: **Mar 5, 2026**
APR/MAY Sustainability in Drug Delivery DEADLINE: **Mar 19, 2026**	**MAY** Delivering Injectables: Devices & Formulations DEADLINE: **Apr 2, 2026**	**MAY/JUN** Oral Drug Delivery DEADLINE: **Apr 16, 2026**

ondrugdelivery.com/subscribe

20 YEARS ON drugDELIVERY

Interview: Patient Experience Versus Regulatory Compliance – Can Formulators Find a Middle Ground?

Dr Keat Theng Chow, Head of Applied Sciences Pharma for Greater Asia at **Roquette Health & Pharma Solutions**, outlines the essential themes on Roquette's radar regarding patient-centric drug design, upcoming regulatory changes and how drug producers can navigate both spheres to the benefit of all.

Q How would you describe the current landscape when it comes to patient-centricity? Are we still in the era of top-down drug designs, or are patient needs exerting a greater influence?

A The pharmaceutical industry is at a pivotal moment in its approach to drug design. Historically, the landscape has been dominated by a top-down methodology, where clinicians and drug developers determine what is best for patients in terms of treatment formats. This approach has contributed to significant medical advancements, but there is still opportunity for the needs and preferences of patients to be factored into the design process as early, and as regularly, as possible. The importance of this approach is underscored by the fact that approximately 50% of people do not take medications as prescribed,[1] resulting in significant consequences for both an individual's health and entire healthcare systems.[2]

Medical nonadherence is a multifaceted issue that most acutely affects people with chronic disease and older adults, though it can impact individuals of all ages and circumstances. Fortunately, the gradual shift away from the traditional one-size-fits-all approach to drug design towards one that prioritises individual patient preferences has led to the rise of improved coating and taste-masking solutions, controlled release and orally dispersible drugs, and – more recently – the incorporation of advanced technologies, such as 3D printing and artificial intelligence (AI), to support production.

Q Which specific dosage forms tend to be most popular among patients? Do these preferences differ depending on demographic factors such as age or region?

A The past decade has seen growing demand for more palatable and convenient alternatives to solid, swallowable pills, though the traditional tablet remains popular. In the pharmaceutical and nutraceutical sectors alike, chewable tablets and gummies have quickly climbed in popularity, particularly in the treatment of children, who typically find them more enjoyable and

"THE IMPORTANCE OF THIS APPROACH IS UNDERSCORED BY THE FACT THAT APPROXIMATELY 50% OF PEOPLE DO NOT TAKE MEDICATIONS AS PRESCRIBED, RESULTING IN SIGNIFICANT CONSEQUENCES FOR BOTH AN INDIVIDUAL'S HEALTH AND ENTIRE HEALTHCARE SYSTEMS."

Dr Keat Theng Chow

Head of Applied Sciences Pharma, Greater Asia

E: pharma@roquette.com

Keat Theng Chow, PhD, is the Head of the Applied Sciences Pharma team for Greater Asia at Roquette Health & Pharma Solutions' Asia Pacific Innovation Centre in Singapore. Alongside her team, Dr Chow supports the strategic management of the centre's pharma innovation portfolio and oversees its operations management. Dr Chow joined Roquette in 2017 as a Pharmaceutical Research Manager following ten years in pharmaceutical product development with Abbott, AbbVie, MSD and A*Star. She holds a BSc in Pharmacy and a PhD in Pharmaceutics from the National University of Singapore and completed a postdoctoral fellowship at The University of Texas at Austin (TX, US).

easier to swallow than standard pills. Similarly, liquids and syrups are often preferred by the parents of young children, as they offer greater flexibility in dosing and administration.

For older patients, focus has shifted to formats that address swallowing difficulties, such as orally disintegrating tablets (ODTs) and oral disintegrating films (ODFs). These dosage forms dissolve quickly in the mouth, eliminating the need for water and offering a convenient, easy-to-administer solution. Effervescent tablets and sachets are also widely used by older populations for their ease of use and, to a certain extent, separation from other drug formats that tend to trigger pill fatigue.

Q Can you provide specific examples of how Roquette's offering helps pharma producers pursue more patient-centric drug design?

A Yes, certainly – APIs tend to be seen as the most important elements of pharmaceutical formulation but, when it comes to user-centric delivery, excipients are the true formulation heroes. Take chewable tablets, ODTs and ODFs as an example; the challenge at the heart of these dosage forms is the tension between long-term stability and optimal disintegration. To produce an end product capable of both, formulators need an excipient that combines excellent dispersibility with good mechanical strength, while simultaneously delivering a pleasant taste and texture. Co-processed mannitol-starches – such as our PEARLITOL® Flash solution – offer formulators excellent chemical inertness and a consistent, rapid disintegration performance, all with a pleasant flavour for maximum patient acceptance.

For manufacturers of more traditional pills, the core goals are to keep throughput speed and compression force high, and tablet sizes small to ensure maximum efficiency, quality and end-user convenience. Rapid processing rates and stronger compression forces can, however, increase the risk of capping or sticking – both of which lead to costly waste and a generally worsened patient experience.[3]

The solution for this is to select a direct-compression excipient with the optimal density and flow properties to maintain quality, even under the stress of high-pressure production. Our PEARLITOL® 200 GT mannitol was designed with these factors in mind, allowing for maximum compression force, tableting speed and API load, all without increased risk of capping or sticking. Indeed, a comparative study showed it was able to increase API load by over 100% while decreasing tablet weight by more than half.[4] This potential to create smaller, harder, more stable tablets containing higher doses of APIs means that drug manufacturers can offer patients the simplified treatment plans they need to stay on track with essential medications.

"TAKE CHEWABLE TABLETS, ODTs AND ODFs AS AN EXAMPLE; THE CHALLENGE AT THE HEART OF THESE DOSAGE FORMS IS THE TENSION BETWEEN LONG-TERM STABILITY AND OPTIMAL DISINTEGRATION."

Q Are expectations similarly in flux when it comes to regulatory standards? Are there any new developments that are having an especially significant impact on pharmaceutical producers right now?

A Yes – contrary to the perception of pharma regulations as slow moving, drug producers are often faced with near constant adaptations on a micro and macro scale. In recent months, volatile international trade regulations have hastened the introduction of measures, such as the EU's proposed Critical Medicines Act and Health Technology Assessment Regulation, both of which aim to consolidate and accelerate the production of essential drugs within the EU. Regulators are simultaneously contending with emerging challenges, including the opportunities and risks posed by AI, and long-standing risks to patient health and safety that evolve in line with ongoing research.

One such example that is still unfolding is the conversation around nitrosamine impurities. Following more than five years of recommendations from authorities on both sides of the Atlantic, in January 2025, the US FDA published new guidelines for the establishment of acceptable intake limits for N-nitrosamine drug substance-related impurities (NDSRIs). In contrast to simpler, small-molecule nitrosamines, NDSRIs present complex and unique chemical structures, which makes the establishment of accurate acceptable limits particularly challenging. Formulators have therefore been forced to apply information from structurally similar compounds or conservative defaults to establish these safe limits, but this can lead to costly or even unnecessary production changes.

The FDA's Carcinogenic Potency Categorization Approach (CPCA) proposes a new protocol that predicts the carcinogenic potency of an NDSRI by analysing its chemical makeup – whether known or merely theoretical. By combining scores awarded according to the structure of α-hydrogen atoms and the presence of activating or deactivating features, the CPCA assigns an NDSRI to a potency category, which then dictates its acceptable daily intake limit. This approach represents a notable breakthrough because it allows for a precise, risk-based assessment even in the absence of specific long-term carcinogenicity data for a particular NDSRI, making it an ideal case study for how regulatory updates don't always mean extra work for pharmaceutical brands.

Q Patient needs are central, but they are not the only stakeholders involved in drug development – do the opinions of patentors and regulators conflict with that of patients? If so, how can this be overcome?

A Though they have a final goal in common, differences in experience and aim can sometimes result in contrasting perspectives on drug development between patients, patentors and regulators. There are, however, ways to overcome

BOX 1: STUDY SPOTLIGHT – EXPLORING APPLICATIONS OF PLANT-DERIVED POLYMERS IN FUSED DEPOSITION MODELLING OF ORAL PHARMACEUTICAL TABLETS

The material requirements for the most common form of pharmaceutical 3D printing, fused deposition modelling (FDM), have, in the past, been a significant source of regulatory scepticism. In short, the process requires the use of a filament polymer with the thermophysical ability to melt, pass through an extruder, fuse with previous layers and solidify quickly.[7] Therefore, manufacturers often turn to synthetic oil-based materials, such as polyvinylpyrrolidone and polyvinyl alcohol, that, whilst effective, are not particularly popular with regulators or end users.[8]

Researchers at Roquette Health & Pharma Solutions recently set out to investigate an alternative approach to FDM production that allows for the use of widely known and trusted excipients, such as modified starches. The resultant study[8] involved the testing of two model formulations:

1. F1, which included the respiratory drug diprophylline as the API and pregelatinised hydroxypropyl pea starch as the polymer matrix excipient
2. F2, which was a combination of pregelatinised potato starch and hydroxypropyl methylcellulose (HPMC K4M) alongside a range of APIs, namely diprophylline, theophylline anhydrous, caffeine anhydrous and indomethacin.

In both formulations, sorbitol and spray-dried mannitol were included as plasticisers, while stearic acid was used as a lubricant.

The drug release kinetics of the resulting tablets (Figure 1) were evaluated in immediate and controlled release dissolution studies of 1- and 12-hour durations, some of the results of which can be seen in Figures 2 and 3. For the immediate release tests, tablets were dissolved in simulated gastric fluid (SGF) with a pH of 1.2, while the controlled-release varieties underwent a two-stage dissolution process in SGF at pH 1.2 for two hours, then in simulated intestinal fluid (SIF) at pH 6.8 for the remainder of the study.[8]

Results from the API release and later stability assessments showed that both base formulations containing hydroxypropyl starch and pregelatinised starch/HPMC (in combination with sorbitol and mannitol) were able to yield extrudable filaments with good printability, capable of achieving immediate and controlled API release for Biopharmaceutical Classification System Class 1 drugs.[6] These findings point to a more regulatory-friendly approach to 3D-printed medications, which could in turn pave the way for a more patient-focused road ahead for drug manufacturing.[8]

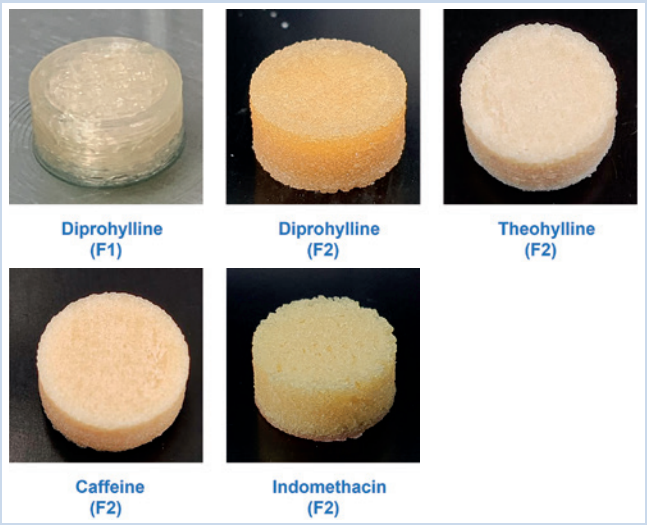


Figure 1: Photos of the tablets of F1 and F2, containing different APIs obtained by FDM.

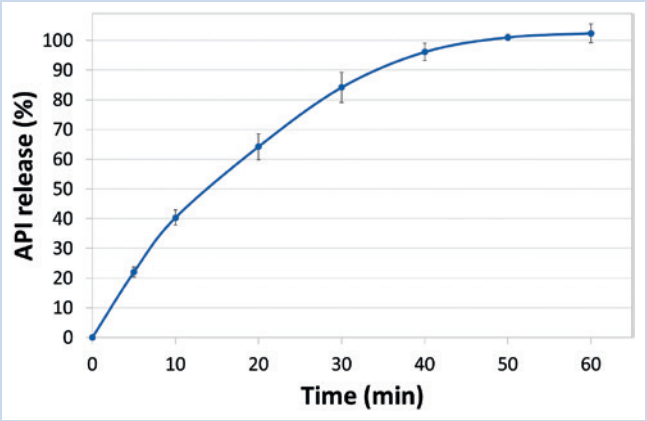


Figure 2: Dissolution profile of F1 diprophylline tablets tested using USP Apparatus 2 in SGF pH 1.2 media without enzymes. Error bars represent standard deviation (n=3).

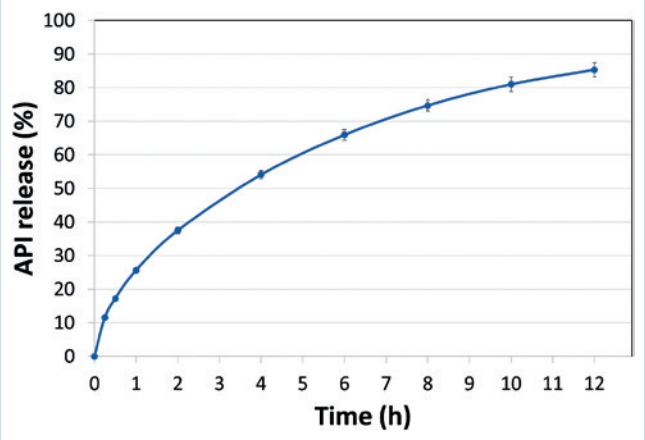


Figure 3: Dissolution profile of F2 diprophylline tablets tested using USP Apparatus 2 in SGF-SIF pH transition media without enzymes. Error bars represent standard deviation (n=3).

these differences. First, it's important to recognise the various valid considerations that are most important to each group. For patients, convenience, effectiveness and accessibility are the primary concerns, while regulators must consider safety, efficacy and quality. Patent holders' priorities, on the other hand, often centre on protecting intellectual property, securing returns on investment and navigating regulatory pathways to market.

Initiatives such as advisory boards or the inclusion of patient representatives in clinical trial design are effective methods to help bridge the gap between user expectations and other stakeholder priorities. Additionally, educational efforts at the community or frontline delivery level can help patients better understand potential regulatory constraints and the practicalities of drug product design. Through this two-way communication, all parties can align their goals and ensure that patients receive the safe, effective and accessible treatments they require.

Q How do you envision the future of patient-centric drug development? Are there any technologies or ingredients that could offer users more control or allow for closer collaboration between regulators, manufacturers and patients?

A We see the future of drug development as one where the best of advanced technologies and human ingenuity are harnessed to resolve the tension between patient experience and therapeutic efficacy. We're already witnessing the roots of this in breakthroughs, such as AI-enhanced clinical studies, wearable health-tracking technology and smart pills, all of which could transform how drugs are designed, delivered and monitored in future.

The prospect of 3D-printed drugs moving from pipedream to tangible reality is an especially exciting step in the road to a tech-enabled, patient-centric future. Offering the potential to produce personalised medicines according to need, rather than the projected return on an industrial product run, 3D printing represents a whole new model for drug manufacturing with immense potential to enhance user experience.

"AS THE FIELD OF RESEARCH CONTINUES TO MATURE AND NEW, MORE REGULATOR-FRIENDLY PROTOCOLS ARE LIKELY TO BEGIN TO EMERGE. WE THINK 3D PRINTING IS POISED TO BECOME THE NEXT LEAP FORWARD IN PATIENT-CENTRIC DRUG DELIVERY."

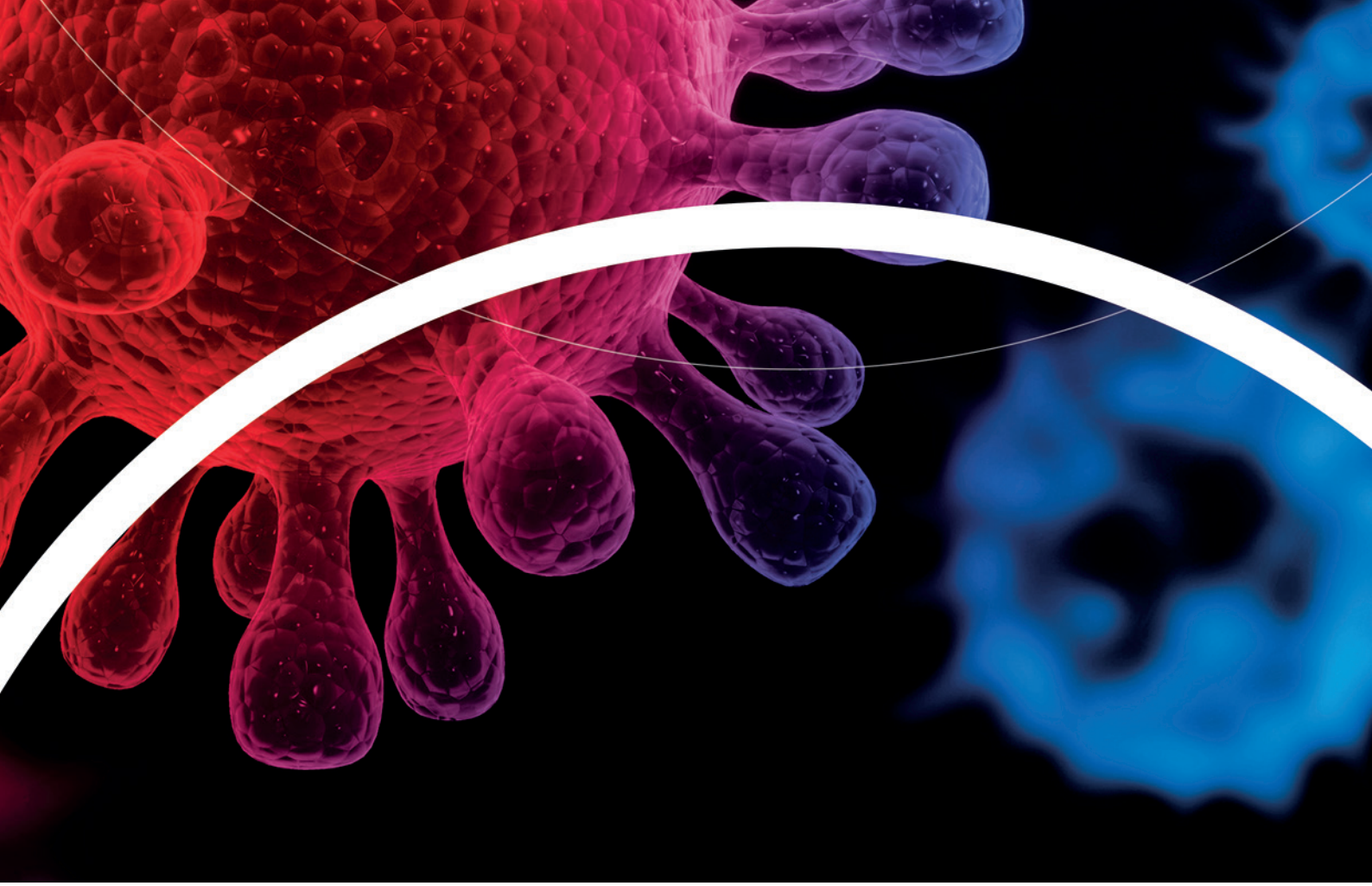
One of the main hurdles that has prevented printed medicines from entering the mainstream up until this point is regulatory reticence. In 2015, the FDA granted approval for the first 3D-printed pill, SPRITAM® (levetiracetam, Aprecia Pharmaceuticals, Mason, OH, US) but, a decade on, it remains the only drug of its kind.[5] The concerns here primarily relate to safety and consistency, with regulators questioning the fact that most 3D printing machines available to drug manufacturers were originally intended to produce plastics, rather than lifesaving pharmaceuticals.[6] However, as the field of research continues to grow, more regulator-friendly protocols are likely to begin to emerge. We think 3D printing is poised to become the next leap forward in patient-centric drug delivery (Box 1).

Q Do you have any final thoughts on the intersection between patient experience and regulatory compliance?

A Whether drug manufacturer, safety inspector, patient advocate or excipients expert, the end goal is the same – better health and wellbeing for all. Ultimately, collaboration and empathy are the keys to achieving this aim, though advancing technology also has a significant role to play. These are the simple facts I see carrying the industry towards a future where regulation and user experience are two halves of the same whole.

REFERENCES

1. *Brown MT, Bussel JK, "Medication adherence: WHO cares?". Mayo Clin Proc, 2011, Vol 86(4), pp 304–314.*
2. *"€125 billion lost each year across Europe due to non-adherence to medication". International Longevity Centre UK, Apr 2022.*
3. *"Preventing Capping and other Tablet Defects". Company Web Page, Natoli, accessed May 2025.*
4. *Lefèvre P et al, "Optimizing API Load and Minimizing Tablet Weight Leveraging an Innovative DC Mannitol". Presentation, 14th PBP World Meeting, Mar 2024, Vienna (Austria).*
5. *Sultana N et al, "3D Printing in pharmaceutical manufacturing: Current status and future prospects". Mater Today Commun, 2024, Vol 38, art 107987.*
6. *Milliken RL et al, "Application of 3D printing in early phase development of pharmaceutical solid dosage forms". Int J Pharm, 2024, vol 653, art 123902.*
7. *H Peng et al, "3D printing processes in precise drug delivery for personalized medicine". Biofabrication, 2024, Vol 16(3), art 032001.*
8. *Chow KT et al, "Exploring Applications of Plant-Derived Polymers in Fused Deposition Modeling of Oral Pharmaceutical Tablets". Presentation, AAPS 2023 PharmSci360, Oct 2023, Orlando (FL, US).*



TPDs: DEVELOPING THE NEXT GENERATION OF ORAL THERAPEUTICS

Dr Anshul Gupte of **PCI Pharma Services**

looks at how targeted protein degraders are redefining the landscape of drug delivery, creating new strategies for previously untreatable diseases. The article goes on to consider the scientific, manufacturing and regulatory challenges ahead, while considering the role specialised CDMOs can play in overcoming these obstacles.

Targeted protein degraders (TPDs) are transforming the landscape of modern drug discovery and development, introducing a groundbreaking method for tackling diseases that have previously been deemed untreatable. In contrast to traditional small-molecule inhibitors that only block protein function, TPDs harness the body's natural degradation systems to eliminate harmful proteins altogether.

This pioneering approach paves the way for novel therapies in oncology, neurodegenerative diseases and immune-related conditions. Reflecting this potential, investment in TPDs has surged – venture funding soared from US$33 million (£25 million) in 2017 to $707 million in 2022, an increase of more than 2,000%.[1] The global TPD market, valued at roughly $544 million in 2024, is projected to expand at a compound annual growth rate of 20.8% between 2025 and 2030.[2] However, despite their vast potential, TPDs still face major obstacles, including formulation complexity, limited bioavailability and challenges in scaling up manufacturing.

ENGINEERING PRECISION

The scientific foundation of TPDs lies in their unique ability to selectively and irreversibly eliminate specific proteins by exploiting the body's ubiquitin-proteasome system. Unlike traditional therapies – such as tyrosine kinase inhibitors, which focus on blocking protein function and often provide only temporary suppression

– TPDs offer a more permanent solution by binding to the target protein and guiding it towards degradation. This results in a more sustained therapeutic effect and helps to overcome the issue of drug resistance. TPDs are especially valuable in situations where conventional small-molecule inhibitors fail to achieve adequate specificity or efficacy.

In oncology, TPDs are showing strong therapeutic potential, with active investigations underway for their use in treating lung cancer, breast cancer, multiple myeloma and lymphoma. Their applications are not limited to cancer; research is expanding into neurodegenerative disorders such as Parkinson's disease, where protein misfolding and aggregation are central to the progression of the disease. TPDs also hold significant promise for immunological conditions, offering a novel way to selectively target and eliminate proteins that drive chronic inflammation and immune system dysregulation. With thousands of proteins performing diverse roles in the human body, the scope of TPDs is vast, making them one of the most compelling emerging areas in modern drug development.

Leading TPD strategies currently under exploration include proteolysis-targeting chimeras (PROTACs) and molecular glues, both of which have already progressed to clinical trials. PROTACs are bifunctional molecules that simultaneously bind to the target protein and an E3 ubiquitin ligase, initiating the degradation cascade. In contrast, molecular glues facilitate the degradation process by strengthening the interaction between a target protein and a ubiquitin ligase, subtly recruiting the body's degradation machinery with greater efficiency. As both technologies continue to evolve, they are expected to fundamentally reshape the future of therapeutic intervention.

DEVELOPMENT CHALLENGES WITH TPDs

The therapeutic promise of TPDs is substantial, however, their development presents a series of complex challenges. Unlike conventional small-molecule drugs, which generally align with well-characterised pharmacokinetic and pharmacodynamic behaviours, TPDs often possess atypical properties that complicate formulation and delivery.

A key hurdle in formulation arises from the structural complexity of TPDs. Their relatively high molecular weights, along with the inclusion of multiple functional groups required for effective target binding and E3 ligase recruitment, frequently result in poor solubility and limited membrane permeability. These physicochemical characteristics can significantly impair oral bioavailability, prompting the need for advanced formulation techniques to enhance absorption. Among the two main classes of TPDs, molecular glues – being smaller and structurally simpler – have demonstrated better potential for oral delivery, whereas PROTACs typically require additional solubility-enhancement strategies.

Figure 1: Interior of a high-potent isolator.

"THE THERAPEUTIC PROMISE OF TPDs IS SUBSTANTIAL, YET THEIR DEVELOPMENT PRESENTS A SERIES OF COMPLEX CHALLENGES."

To address these solubility limitations, researchers are investigating a variety of formulation methods, including hot-melt extrusion, spray drying, nano-milling and lipid-based delivery systems. Each approach offers specific advantages depending on the unique attributes of the compound. For instance, spray drying and hot-melt extrusion can increase the bioavailability of poorly soluble drugs by generating amorphous solid dispersions. On the other hand, nano-milling enhances dissolution by reducing particle size, while lipid-based formulations exploit the body's endogenous lipid absorption pathways to facilitate drug uptake.

Further complicating development is the fact that many TPDs do not conform to Lipinski's Rule of Five, a widely accepted guideline for predicting the oral bioavailability of small-molecule drugs. TPDs often exhibit characteristics such as elevated molecular weight, limited permeability and high numbers of hydrogen bond donors and acceptors. These deviations necessitate comprehensive solubility screening and early-stage optimisation to ensure alignment between the formulation strategy and the intended route of administration. Moreover, excipients play a pivotal role in stabilising the final dosage form and ensuring content uniformity, particularly important for TPDs, which often require low drug loads due to their high potency (Figure 1).

PHASE-APPROPRIATE DEVELOPMENT

When working with complex modalities such as TPDs, pharmaceutical development must be approached as a continuous, adaptive process rather than a fixed set of activities. A scientifically rigorous, strategically flexible and operationally collaborative framework is essential for guiding molecules from discovery to commercial readiness.

Scientifically, the foundation lies in quality by design. This approach begins with a clear understanding of the desired product attributes, including quality, safety and efficacy, defined by the target product profile (TPP). However, the TPP is not static – it starts broad during early development and becomes more refined as the programme progresses, ultimately aligning with regulatory expectations and real-world patient needs.

Strategically, a phase-appropriate plan is vital. Each phase should build intelligently upon the last, with clear inputs, outputs and technical goals tailored to where the product is in its lifecycle. In early-phase development, speed is paramount. Simple formulations, such as a neat API in a capsule, can provide sufficient stability for first-in-human studies. As the product advances, more robust and scalable formulations are introduced to meet the demands of later-stage trials and commercial production.

Operationally, communication and collaboration are key. Development cannot occur in silos; alignment across drug substance; chemistry, manufacturing and controls (CMC); and clinical teams is critical. CDMOs must be able to interpret the sponsor's vision and translate it into viable, scalable and patient-friendly formulations without locking themselves into inflexible paths. This requires not only scientific expertise but also a willingness to adapt based on new data or shifting priorities.

PCI applies this philosophy through a stage-gated pharmaceutical development process that mirrors the clinical lifecycle, spanning from formulation and analytical development, through toxicology batches to Phase I/II/III studies. As development progresses, the focus shifts from flexibility to robustness, with increasing attention to identifying and controlling critical material, quality and process parameters. These elements inform the control strategies and specifications that underpin a successful product.

Figure 2: PCI's analytical development laboratory.

Given the concurrent scale-up of drug substance and drug product, close co-ordination is especially important. Understanding how an API's characteristics, such as morphology or impurity profile, might evolve during scale-up is essential to avoid formulation issues downstream. In the context of targeted therapies such as TPDs, where precision is paramount, the margin for error is razor-thin. A phase-appropriate, science-led development strategy is not just ideal – it is imperative.

MANUFACTURING AND STABILITY

Manufacturing TPDs demands a highly sophisticated approach that accounts for their potency, scalability and stability. Due to their precise mechanism of action, TPDs are frequently highly potent compounds, necessitating rigorous containment protocols to ensure safety during production. As a result, manufacturing environments must be equipped with high-containment capabilities – something not all facilities possess. This limitation makes strategic partnerships with CDMOs a critical component of TPD development and scale-up.

Containment is only part of the equation; the structural complexity that grants TPDs their therapeutic precision can also render them more vulnerable to chemical or physical degradation under various conditions. As these compounds move from laboratory to large-scale production, ensuring their stability becomes a significant focus. Maintaining formulation integrity throughout scale-up and commercial manufacturing requires the judicious selection of excipients, optimised processing techniques and advanced analytical tools for continuous monitoring (Figure 2). Robust in-process controls are essential not only for maintaining batch-to-batch consistency but also for ensuring that the final drug product meets all regulatory and quality requirements.

THE ROLE OF A CDMO

As drug development becomes increasingly complex, biotech and pharmaceutical companies are increasingly turning to CDMOs to navigate the unique challenges of TPDs. A strong CDMO partner provides essential support across the development lifecycle, offering deep expertise in the handling of highly potent compounds, advanced formulation technologies and contained manufacturing. A CDMO's infrastructure can be critical for supporting the seamless transition of TPDs from preclinical stages through to commercial scale supply.

A particularly crucial area of support lies in analytical development. The characterisation of TPDs requires a suite of highly specialised techniques, including surface plasmon resonance, mass spectrometry, fluorescence polarisation, X-ray crystallography and bio-nuclear magnetic resonance spectroscopy. These advanced methods are indispensable for assessing key attributes, such as protein-binding efficiency, degradation kinetics and molecular stability. Given the complexity of these analytical tools and the expertise required to operate them effectively, many pharmaceutical companies partner with CDMOs to gain access to the necessary infrastructure and know-how.

In addition to its strengths in manufacturing and analytical services, PCI Pharma Services has more than 35 years of experience in the development of highly potent drug products. The company has also formed strategic partnerships to further expand its capabilities in solubility enhancement and particle engineering, two areas that are particularly relevant to the development of TPDs. Through cutting-edge techniques, such as hot-melt extrusion, amorphous solid dispersion formation and nano-milling, PCI's partner network helps to optimise bioavailability and ensure consistent product performance, enabling the successful development of TPD candidates that might otherwise be limited by poor solubility or inconsistent pharmacokinetics.

TPDs: LOOKING AHEAD

The field of TPD research is advancing at a remarkable pace, fuelled by ongoing innovation in medicinal chemistry, structural biology and computational modelling. Over the next five to ten years, the pipeline of new TPD candidates is expected to grow substantially, with a strong focus on enhancing oral bioavailability and expanding the spectrum of druggable proteins. Continued progress in the discovery and refinement of E3 ligase ligands will further improve the specificity and efficiency of TPD design, enabling more precise and effective therapeutic outcomes.

Artificial intelligence (AI) and machine learning are also set to play transformative roles in TPD discovery. By streamlining compound identification and optimising lead selection, AI-driven high-throughput screening is poised to reduce development timelines and increase the likelihood of clinical success. These technologies will enable researchers to prioritise the most promising molecules for synthesis and biological evaluation, accelerating the journey from concept to candidate.

As regulatory pathways for TPDs continue to evolve, early engagement with regulatory agencies will be essential for ensuring alignment and avoiding delays. Proactive dialogue can help to clarify requirements and facilitate smoother approvals. Throughout this process, CDMOs will remain invaluable partners – bringing deep regulatory experience, advanced formulation capabilities and scalable manufacturing infrastructure to support the development of stable, high-quality TPD-based therapies.

SUMMARY

TPDs are ushering in a new era of drug development, offering a fundamentally different approach through the selective and irreversible elimination of disease-causing proteins. Although their development is accompanied by a distinct set of scientific and logistical challenges, specialised CDMOs are playing a pivotal role in overcoming these obstacles – supporting everything from advanced formulation to high-containment manufacturing and regulatory navigation. With continued progress in medicinal chemistry, bioengineering and computational tools, the momentum behind TPDs is only expected to grow. This promising modality stands poised to deliver transformative therapies across a broad range of diseases, potentially reshaping the future of modern medicine.

REFERENCES

1. *"Venture financing for targeted protein degraders soared in 2022". Pharmaceutical Technology, Oct 27, 2023.*
2. *"Targeted Protein Degradation Market Trends". Grand View Research, 2024.*

Dr Anshul Gupte

Anshul Gupte, PhD, RAC-Drugs, joined PCI in March 2024 as Vice-President, Pharmaceutical Development. Dr Gupte has over 16 years of experience in concept, pharmaceutical development and commercialisation of drug products. He has experience in working on broad range of dosage forms, including solid orals, liquids, sterile and topicals, and has contributed to several branded and generic regulatory submissions for the US and worldwide markets. Dr Gupte previously served as Senior Director Pharmaceutical Development and Scientific Affairs at Catalent and Senior Director, Scientific and Technical Affairs at Catalent Pharma from 2022 to 2024. Dr Gupte previously held several positions at Metrics Contract Services including Senior Director, Scientific and Technical Affairs, Senior Director, Drug Product Development, Director and Associate Director of Pharmaceutical Development. Additionally, Dr Gupte was based in Australia for four years and served as Head of Formulation at Mayne Pharma and led development activities for complex generics.

E: anshul.gupte@pci.com

PCI Pharma Services

3001 Red Lion Road, Philadelphia, PA 19114, United States

www.pci.com

15th Annual

PODD® PARTNERSHIP OPPORTUNITIES IN DRUG DELIVERY

October 27-28, 2025 · Westin Copley Place, Boston, MA

Covering Cutting-Edge Scientific and Business Trends

Program Features

- 1000+ Attendees from Pharma, Biotech, Drug Delivery, Academia, Investors and More
- 10 Tracks Covering a Wide Range of Drug Delivery Technologies
- Partnering Opportunities including One-on-One Scheduled Meetings
- Keynotes
- Plenary Sessions
- Cutting-Edge Panels
- Pharma Company Spotlights
- Key Trends
- Case Studies
- PODD Soapbox

And Much More!

COMING SOON

2025 Agenda Coming Soon

Celebrating 15 Years!

PODDConference.com

20% Off with Code ONDD20 for the ONdrugDelivery Community


pci
PHARMA SERVICES
pci.com
Your world leading CDMO.
High Potent Manufacturing.
talkfuture@pci.com
Building capacity today, based on demand predictions of the future.
Significant investment at our world-class high potent facilities doubles manufacturing and packaging capacity, addressing the growing need for expert integrated oncology outsourcing solutions.
High potent solutions include:
· High potent pharmaceutical development, clinical trial and commercial manufacture
· Containment down to an OEL of 0.01µg/m³
· Xcelodose® microdosing technology and roller compaction
· Tablets, capsules, powders, liquids, suspensions, semi-solids and drug-in-capsule/vial
· Analytical laboratory and QP services
· Clinical and commercial packaging
Together, delivering life changing therapies | Let's talk future™

Expert View

A STICKY ISSUE: TRANSFORMING OILY PLANT EXTRACTS INTO SOLID ORAL DOSAGE FORMS

Dr Maj-Britt Cepok of BENEO discusses the increasing prevalence of plant extracts in the oral solid dosage market, considering how the common physical properties of these ingredients can both provide benefits and pose a challenge to formulators looking to capitalise on this rapidly growing market segment.

"THE PRINCIPAL DRIVERS FOR THIS GROWTH INCLUDE THE INCREASING HEALTH-CONSCIOUS CONSUMER BASE AND THE RISE OF CLEAN-LABEL TRENDS IN THE PHARMACEUTICAL, FOOD AND BEVERAGE INDUSTRIES."

In numerous pharmaceutical and nutraceutical dosage forms, plant extracts have gained significance as key ingredients. However, they can have sticky or oily characteristics that make them challenging to incorporate into solid formats, such as tablets and capsules. When it comes to oral solid dosage (OSD) forms containing phytopharmaceuticals, production hurdles such as compressibility must be overcome. As such, the creation of specific excipients, such as an agglomerated isomalt that acts as a filler-binder, has become a necessity.

MARKET DYNAMICS

Herbal extracts are concentrated forms of plant materials that contain beneficial compounds, such as phytochemicals, flavonoids, alkaloids and essential oils. According to Precedence Research, the global herbal extract market size is predicted to increase from US$48.9 billion (£37 billion) in 2025 to approximately $103.6 billion by 2034, expanding at a compound annual growth rate of 8.69% from 2025 to 2034.[1] The principal drivers for this growth include the increasing health-conscious consumer base and the rise of clean-label trends in the pharmaceutical, food and beverage industries.

By region, Asia-Pacific generated more than 53% of the revenue share in 2024 and is expected to sustain this position during the 2025–2034 forecast period. Countries such as China, India, Japan and South Korea have a long history of traditional medicine practices that utilise herbal extracts. These geographies boast a wealth of knowledge and expertise when it comes to identifying, cultivating and processing medicinal plants.

North America is another fast-growing region in the herbal extract market; it is actively involved in research and innovation related to botanical extracts. Academic institutions, research organisations and companies in this area are conducting studies on their medicinal properties, efficacy and safety. Globally, in terms of the use of herbal extracts in different types of products, the pharmaceutical and dietary supplement industries accounted for the biggest market share (37%) in 2024, compared with 34% in foods and 19% in cosmetics, respectively.[1]

Michael Black, Head of Sales, Pharma, at BENEO, comments: "The rising application of herbal extracts is being driven by consumer demand for natural and functional ingredients, the growth of nutraceuticals and functional foods, scientific research supporting health claims and the trend toward customisation and personalisation. Furthermore, herbal extracts derived from plant sources are seen to be natural ingredients that align with ongoing clean-label trends."

FORMULATION CONSIDERATIONS

"When incorporating plant extracts, there are generally two main hurdles — of a technical and sensorial nature — to overcome. From a technical perspective, plant extracts are often difficult to compress and sensitive to moisture. Another prevalent issue is achieving the desired dose in an acceptable tablet size," observes Michael Black. Working with hygroscopic materials can create challenges with storage and stability. The inclusion of a low-hygroscopic excipient with a suitably high dissolution rate could eliminate the need for super-disintegrants, which are also hygroscopic.

Figure 1: From a technical perspective, plant extracts are often difficult to compress and sensitive to moisture.

Similarly, temperature and humidity are critical parameters when working with herbal extracts. Under suboptimal conditions, they can become sticky, which is a technical disadvantage, and subsequently degrade (Figure 1).

Further work by Carpanzano *et al* has also identified hurdles that must be overcome when processing oily or greasy substances into tablets or capsules.[2] Notable obstacles include adhesion to processing equipment, oil migration or leaching during storage or compression and incompatibility with conventional excipients. Among other criteria, the material to be compressed must be free-flowing and, most importantly, must possess sufficient cohesiveness to ensure that the OSD form remains intact after compression. In addition, material flowability and lubricity are crucial for uniform die filling and easy ejection of the compressed material from punch faces. Numerous solutions — and their limitations — have been attempted and recorded, such as using porous carriers or simply forming an admixture with powders.[2] However, the ensuing outcomes most often resulted in suboptimal dosage form, stability or uniformity.

Tablet formulation methods are used to impart desirable characteristics to materials being compressed into solid dosage forms. Typically, the material to be compressed comprises one or more excipients; as such, lubricants, diluents, binders and disintegrants are commonly added to improve flow, bulk, cohesion and disintegration rates. Oily drugs, or those that dissolve in oil, are usually made into softgel capsules. Although many commonly used excipients can absorb oils or oily drugs, they can only absorb a limited amount when the goal is to manufacture tablets. Many of these excipients don't retain the oil sufficiently to prevent partial loss during the compression process (Figure 2).[2]

"Many plant extracts have a bitter or unpleasant aftertaste and mouthfeel. Although the complete mechanism of action is not fully understood, an agglomerated isomalt can reduce these characteristics in both solid and liquid forms compared to other sugars and sugar alcohols," says Michael Black. Whereas the most common application for isomalt is the production of compressed tablets, agglomerate grades can also be used in powder mixtures to make sachets, stickpacks and as a fill for hard gelatine capsules. Owing to the surface characteristics of the agglomerates, high levels of homogenous component mixing within a powder preparation can be obtained. This enhances content uniformity and, subsequently, facilitates accurate dosing within each finished format.

Compared with other excipients, agglomerated isomalt is unaffected by electrostatic charging during transport and movement in stainless steel processing equipment. As such, it does not stick to the sides of the machinery, thereby ensuring high content uniformity and accurate dosing in the finished form.

Beretta *et al* noted that tribo-charging is often a root cause of mass flow deviations and powder adhesion during continuous feeding that may impact product quality.[3] They characterised the volumetric (split- and pre-blend) feeding behaviour and process-induced charge of two direct compression grades of polyols under different processing conditions.

Figure 2: The development of oral solid dosage forms with plant extracts requires a high level of technological and formulation expertise.

"PARTICULARLY WHEN USING OILY PLANT EXTRACTS, A WATER-SOLUBLE FILLER-BINDER ENABLES MANUFACTURERS TO OVERCOME COMMON FORMULATION ISSUES."

Feeding mass flow range and variability, hopper end-fill level and powder adhesion were all profiled and, whereas both isomalt and mannitol showed comparable feeding performances, the authors recorded a lower tribo-charging propensity and less tendency to adhere to the screw outlet for isomalt. The results suggested that, when fed as a single excipient, isomalt performed better in continuous feeding operations. Both aspects were deemed to be relevant for formulation and process development.

SOLID DOSAGE EXAMPLES: TABLETING HERBAL EXTRACTS

Particularly when using oily plant extracts, a water-soluble filler-binder enables manufacturers to overcome common formulation issues. Offering a high oil-binding capacity, agglomerate stability and flowability, it acts like a sponge by absorbing the oily plant extracts and then remaining as a dry flowable powder (Figure 3). The excipient's morphology helps to retain the homogeneity of the mixture and makes the production of robust tablets with a high content uniformity much easier. Plus, being water-soluble, plant extract tablets often disintegrate rapidly without the use of a super-disintegrant. In addition, isomalt reduces the unpleasant taste of oily plant extracts, thus enhancing the palatability of the tablet and promoting patient compliance.

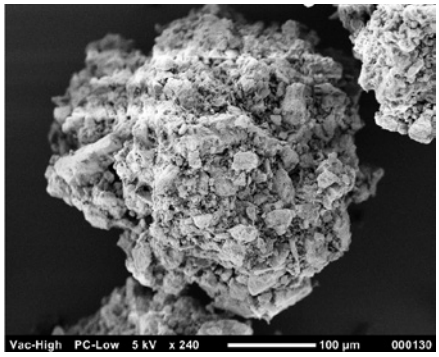


Figure 3: Offering a high oil-binding capacity and flowability, agglomerated isomalt acts like a sponge by absorbing the oily extracts and remaining a dry flowable powder.

To explore the versatility of agglomerated isomalt, a simple direct compression formulation with *echinacea purpurea* was developed. Echinacea, obtained from Bionorica (Neumarkt, Germany), is a dry-pressed juice that tends to stick together and/or leaves residues on tablet punches. This recipe (Table 1) only comprised the extract, a filler-binder (isomalt with a solubility of 42 g/100 g at 20 °C and a bulk density of 0.40 g/cm³) and magnesium stearate as a lubricant.

When a uniform blend of the extract and the isomalt had been obtained by mixing, the lubricant was added. The combined powders were then compressed into round, 250 mg convex tablets using a 9 mm punch. Suitable tablet hardness was achieved (78 N), the tablet disintegrated in a good time (293 s) and the abrasion was very low (0.07%). The API content was 80 mg, approximately one-third of the tablet's entire weight.

Similarly, the formulators were able to incorporate 200 mg of salicis extract, again obtained from Bionorica, into a formulation comprising just three ingredients (Table 2). This time, the salicis cortex extract comprised two-thirds of the entire tablet weight and was blended with isomalt and magnesium stearate. The same production process was used and the blend was compressed into round, 204 mg convex tablets using a 9 mm punch. Very good results in terms of the tablet's hardness, disintegration and abrasion parameters were obtained.

Owing to the higher concentration of the extract, however, it was necessary to include a precompression step (in the rotary tablet press) before the main compression. This was necessary to prevent capping. A common problem with this type of OSD form is that the extracts are elastic, meaning that the tablets can cap or tear apart horizontally when the post-compression tension decreases.

"In both examples," notes Michael Black, "the use of an agglomerated isomalt meant that relatively simple formulations

Item	Component	Description	[w/w, %]	Mass per Tablet [mg]	Batch Mass [g]
1	*Echinacea purpurea* extract	Herbal extract	32.0	80.0	480
2	Isomalt (galenIQ™ 721)	Filler/Binder	67.0	167.5	1005
3	Magnesium stearate	Lubricant	1.0	2.5	15

Table 1: Recipe of Echinacea tablet (80 mg) herbal extract.

Item	Component	Description	[w/w, %]	Mass per Tablet [mg]	Batch Mass [g]
1	*Salicis cortex* extract	Herbal extract	66.7	202.8	1000.5
2	Isomalt (galenIQ™ 721)	Filler/Binder	32.3	98.2	484.5
3	Magnesium stearate	Lubricant	1.0	3.0	15.0

Table 2: Recipe of salicis tablet (202.8 mg) herbal extract.

could be created and no disintegrating agents were necessary. Both the echinacea and salicis tablets exhibited good compressibility and, because the isomalt protected the moisture-sensitive extracts from water absorption, there was no sticking of the extracts to the punches."

NEW MARKET OPPORTUNITIES: COMPRESSED CBD LOZENGES

While regulations vary and some regions remain cautious, cannabidiol (CBD) is increasingly recognised worldwide for its medicinal potential, particularly in North America and most European countries. CBD is increasingly being incorporated into nutraceuticals for its potential therapeutic benefits, including alleviating anxiety, reducing inflammation and improving sleep quality (Figure 4).

According to Grand View Research, the global CBD nutraceuticals market was valued at approximately $8.99 billion in 2024 and is projected to grow at a compound annual growth rate of 12.6% from 2025 to 2030.[4] This expansion is being driven by a rising consumer awareness of CBD's health advantages, a preference for plant-based supplements, the ongoing legalisation of cannabis in various countries and increased research into its medical applications. The market's development is further supported by the launch of new products and the broadening of geographical reach by innovator companies in the pharmaceutical and greater life sciences ecosystem.

As such, formulations containing this versatile ingredient present a wide range of market opportunities. One example is a compressed lozenge-type tablet containing 10 mg of CBD. To create the dosage form, a liquid self-microemulsifying drug delivery system (SMEDDS) preparation was made using the cannabidiol distillate (Table 3), which was mixed with a silica carrier to produce a free-flowing powder and then tumble-blended with the remaining ingredients. The uniform mixture was then compressed into 200 mg flat-face, bevel-edged "tablets" using an 8 mm punch. The result was a lozenge with a sweet taste, a pleasant mouthfeel and an instant and long-lasting peppermint flavour.

Figure 4: CBD is increasingly being incorporated into nutraceuticals for its potential therapeutic benefits, including alleviating anxiety, reducing inflammation and improving sleep quality.

Item	Component	Description	[w/w, %]	Mass per Tablet [mg]	Batch Mass [g]
1	Cannabidiol distillate 80% purity – thick viscous oil ranging from 30,000–50,000 cps	Active ingredient	5.85	10.00	60.00
2	Proprietary* SMEDDS technology	Cannabinoid delivery system	4.88	10.00	50.00
3	Silicon dioxide	Adsorbent/ Oil carrier	9.76	20.00	100.00
4	Isomalt (galenIQ™ 721)	Filler/Binder	48.78	100.00	500.00
5	Sorbitol (DC grade)	Filler/Binder	9.76	20.00	100.00
6	Xylitol (DC grade)	Filler/Binder	9.76	20.00	100.00
7	Stevia powder (milled grade)	Sweetener	4.88	10.00	50.00
8	Partially pregelatinised maize starch	Filler	2.44	05.00	25.00
9	Peppermint flavour	Flavouring agent	2.44	05.00	25.00
10	Magnesium stearate	Lubricant	1.46	03.00	15.00

** by Genova Biosciences (Toronto, Canada)*

Table 3: Recipe of CBD (10 mg) compressed lozenge tablets.

CONCLUSION

The use of an agglomerated (spherical) isomalt with defined hygroscopicity, solubility and bulk density properties could be used to optimise the formulation of a wide range of nutraceutical and pharmaceutical OSD forms, particularly if it delivers a natural taste profile, contributes to enhanced overall palatability and has a plant-based origin. Real-world examples have noted that, depending on the application, only very low compression forces are required during tableting (for both low- and high-dose formulations) and additional binders are generally not required (filler-binder functionality). Furthermore, when in use, high agglomerate stability and excellent flow have been demonstrated, with final forms showing good mix homogeneity and a high level of content uniformity.

ABOUT THE COMPANY

BENEO is part of the Südzucker Group (Germany) and a member of the International Pharmaceutical Excipients Council (IPEC). The company produces galenIQ™ (Isomalt), a multifunctional range of water-soluble filler-binders, according to cGMP conditions for pharmaceutical excipients that is available in a wide variety of median particle sizes, morphologies and solubilities, and is therefore readily used in solid and liquid dosage forms such as tablets, sachets, effervescents, lozenges and syrups. It is physically and chemically stable, has low hygroscopicity and enhances the palatability of the final dosage form.

"THE USE OF AN AGGLOMERATED (SPHERICAL) ISOMALT WITH DEFINED HYGROSCOPICITY, SOLUBILITY AND BULK DENSITY PROPERTIES COULD BE USED TO OPTIMISE THE FORMULATION OF A WIDE RANGE OF NUTRACEUTICAL AND PHARMACEUTICAL OSD FORMS."

Dr Maj-Britt Cepok

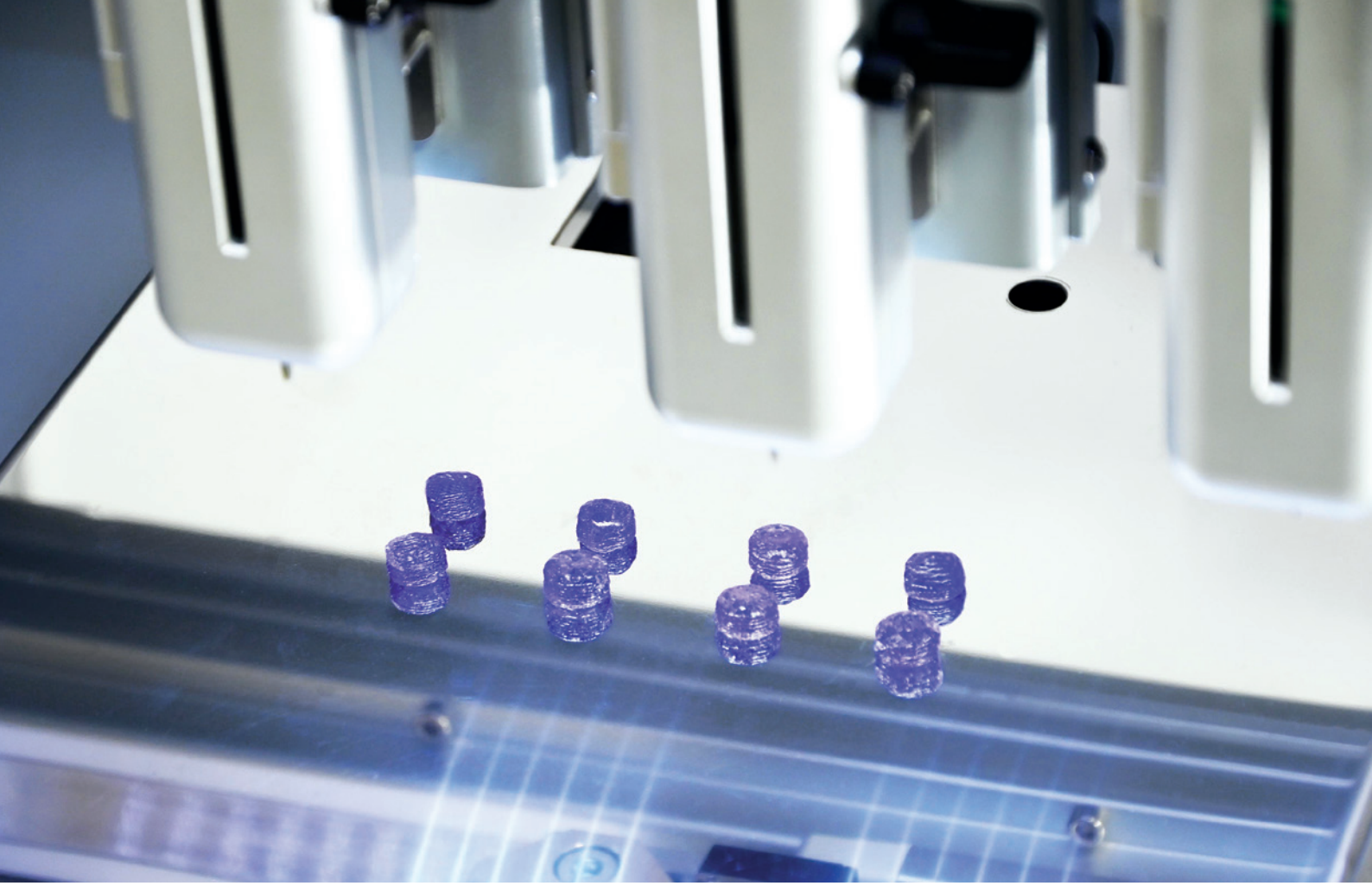
Maj-Britt Cepok, PhD, Head of Business Development, Pharma, at BENEO, is a Food Chemistry graduate and holds a PhD in Analytical Chemistry. She has experience in both the food and pharmaceutical industries, with particular specialties in pharmaceutical development of solid dosage forms and taste profiling. Dr Maj-Britt Cepok joined BENEO in 2005 and has held a variety of roles in global sales, technical services, product management and business development for the Pharma business unit of the company, currently leading the Pharma department.

T: +49 621 421 170
E: maj-britt.cepok@beneo.com

BENEO GmbH
Maximilianstrasse 10, 68165 Mannheim, Germany
www.beneo.com

REFERENCES

1. *"Herbal Extract Market Size, Share, and Trends 2025 to 2034". Market Report, Precedence Research, 2025.*
2. *Carpanzano A, Nagel M, "Excipient and oral solid dosage forms for oily drugs". Patent WO2016201119A1, 2016.*
3. *Beretta M et al, "Assessment of Tribo-charging and Continuous Feeding Performance of Direct Compression Grades of Isomalt and Mannitol Powders". AAPS PharmSciTech, 2023, Vol 24(4), art 91.*
4. *"CBD Nutraceuticals Market Size & Trends". Market Report, Grand View Research, 2024.*



3D PRINTING: THE FUTURE OF PERSONALISED MEDICINES

Anna Kirstine Jørgensen and **Dr Abdul Basit** both at **UCL School of Pharmacy**, along with **Dr Alvaro Goyanes** at **FABRX**, discuss the role of 3D printing in shaping the future of personalised medication, and explain how FABRX's two pharmaceutical 3D printers can help unlock its potential – extending even beyond Earth.

The "standard medicine for standard patient" paradigm is well-known to be unsuitable, risking the safety of certain patients and patient groups, as well as being a factor for reduced efficacy and treatment adherence.[1] Although conventional and large-scale manufacturing processes offer significant cost and production efficiencies, they remain highly inflexible in terms of varying dosage and product characteristics according to patient needs.

Three-dimensional (3D) printing is capable of accurately and effectively producing small batches of pharmaceuticals with tailored characteristics (such as dose differentiation, taste masking and release profiles). This technology is no longer just a crazy vision but is now actively being used to treat patients who are not benefitting from the one-size-fits-all approach.[2,3]

3D printing is a process whereby a 3D object is designed through computer-aided design software for subsequent printing in a layer-by-layer manner. While upscaling of binder jetting (a specific 3D printing technology) manufacturing processes has resulted in the successful commercialisation of Aprecia Pharmaceuticals' (Mason, OH, US) SPRITAM® (levetiracetam) to treat epileptic seizures, it remains the only mass-manufactured 3D-printed medication available off-the-shelf to date, nearly a decade after receiving market authorisation.[4]

Since then, it has become increasingly evident that the small-scale and flexible nature of 3D printing might actually be its major selling point and the key to achieving personalised oral medicines through the so-called "virtuous cycle" (Figure 1).

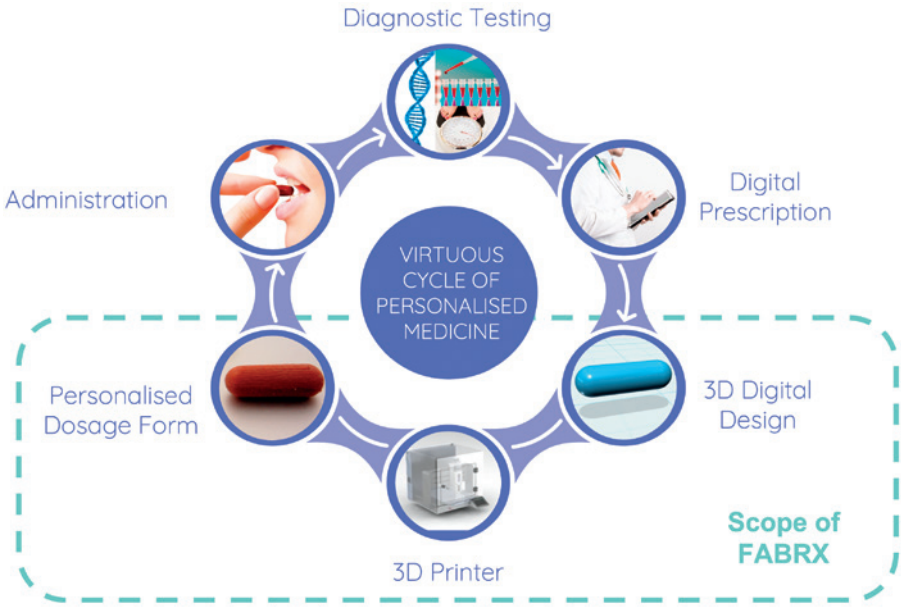


Figure 1: The virtuous cycle of personalised medicines and how FABRX's 3D printing technologies help realise this.

FABRX has been a driving force in advancing 3D printing of personalised drug products from novel research and translating it into real-world clinical impact.

The versatility of 3D printing in terms of creating unique oral solid dosage forms for a range of different diseases and populations has been demonstrated through several publications. In addition, through partnerships with high-profile institutions, FABRX is now proving how its 3D printing systems can help patients achieve better therapy than currently available options. Even NASA wants to 3D print medications in space to provide better therapy during long-haul missions while greatly reducing occupied space aboard its spacecraft.[5,6]

"FABRX HAS BEEN A DRIVING FORCE IN ADVANCING 3D PRINTING OF PERSONALISED DRUG PRODUCTS FROM NOVEL RESEARCH AND TRANSLATING IT INTO REAL-WORLD CLINICAL IMPACT."

As a result of tireless discussions and engagement with regulatory agencies, backed by scientific evidence and case studies, a new paradigm for personalised and on-demand medicines manufacture is now set to commence through new legislative framework.

FABRX'S STATE-OF-THE-ART PHARMACEUTICAL 3D PRINTING SYSTEMS AND SERVICES

Two 3D Printing Setups for Enhanced Flexibility

FABRX has successfully commercialised two pharmaceutical 3D printers (Figure 2), varying in their levels of printing complexities to offer flexibility for the users' needs. Back in 2020, FABRX launched the world's first pharmaceutical-grade 3D printer, the M3DIMAKER1, capable of printing with fused-deposition modelling (FDM), semisolid extrusion (SSE) and direct powder extrusion (DPE) technologies through interchangeable printheads. The printer is GMP-certified and comes with inbuilt quality control add-ons, such as an integrated analytical balance for monitoring of mass deposit and a near-infrared spectrometer accessory for API quantification for each individual dosage unit.[7,8]

The more advanced M3DIMAKER2 was launched in 2023 to enable even more process and product versatility through simultaneous operation of three separate printheads using the same technologies as the M3DIMAKER1, namely FDM, DPE and SSE. The quality control features (analytical balance and near-infrared spectrometer) are also available for this printing system, along with a high-efficiency particulate-arresting filter unit to ensure safe working with hazardous APIs and particle-free printing environments.[9]

Advanced Software with Easy-To-Use Interface

To help clients and clinicians benefit from all the versatile functions of the printing systems, the M3DIMAKER Studio™ software accompanies the printers. The software allows users to easily select printing models (i.e. size and shape), printing parameters and control the printer. Generating pharma-ink (drug-loaded formulation for 3D printing) profiles accelerates printing of previously developed pharma-inks. The software may be used in R&D mode, where all specifications and parameters are changeable according to the client's workflow. It can also be operated

Figure 2: FABRX's two pharmaceutical 3D printers, M3DIMAKER1 (left) and M3DIMAKER2 (right).

"FABRX OFFERS VERSATILE CONSULTATION SERVICES FOR ITS CLIENTS TO HELP THEM ACHIEVE THEIR GOALS, RANGING FROM BRIEF CONSULTATIONS TO FULL FORMULATION DEVELOPMENT AND ANALYSIS PACKAGES."

(A) (B)

Figure 3: A) Chewable, combination printlets produced in a hospital tested for efficacy and acceptability among children with rare metabolic disorders. Six different colour and flavour combinations were assessed. B) Part of the evaluation process recorded on an app developed by FABRX AI. Figures reprinted from Rodríguez-Pombo L *et al.* (2024).[11]

in "clinical" mode, in which developed and stored protocols can be locked and employed for printing according to the saved protocols.

Pharma-Ink Development

Developing the right pharma-ink is important to achieve dosage units with the desired properties and requires general knowledge about formulation and the specific API(s) to be printed. FABRX offers versatile consultation services for its clients to help them achieve their goals, ranging from brief consultations to full formulation development and analysis packages.

CLINICAL TRIALS DEMONSTRATE EFFICACY AND ACCEPTABILITY OF PERSONALISED 3D-PRINTED MEDICINES

FABRX has been involved in two published clinical trials to date, where the efficacy and acceptability of chewable medications tailored to children have been demonstrated. The world's first clinical study evaluating the efficacy and patient acceptability of 3D-printed personalised medicines was conducted in 2018.[10] Children affected by maple syrup urine disease were treated with chewable isoleucine printlets (3D-printed tablets) produced by SSE 3D printing in six different colour and flavour combinations and compared with isoleucine medicines compounded via traditional methods.

Following three months of treatment with each medication type, it was clear that the 3D-printed, chewable dosage units achieved narrower isoleucine plasma levels closer to the target level, and that the 3D-printed pharmaceuticals were well-accepted among the patients. A second clinical study investigated the efficacy and acceptability of treating children affected by rare metabolic disorders with chewable printlets containing more than one active and of different taste and colour profiles (Figure 3).[11] The printlets, containing personalised levels of amino acids, were produced in a hospital through the M3DIMAKER1, and good control of plasma levels was achieved for all printlets. The printlets were also well-accepted, and participants indicated that future therapy with these colour- and taste-masked medicines could improve adherence and quality of life.

Additional clinical trials assessing the efficacies and acceptability of 3D-printed medicines are already underway. A clinical trial to treat children suffering from adrenal insufficiency with hydrocortisone medicines printed with the M3DIMAKER1 in a hospital is being conducted,[12] along with a clinical trial in 200 breast cancer patients treated with multi-active dosage units produced by the M3DIMAKER2 in Europe's leading cancer research hospital.[13]

DM OF PERSONALISED MEDICINES IN THE UK

New Legislation Supporting Small-Batch Pharmaceuticals Production

Multiple conversations between developers of 3D-printed personalised medicines and the UK MHRA have now led to new legislation empowering the implementation of decentralised 3D printing manufacturing facilities to produce more bespoke therapies for patients. In the "Statutory Instruments: The Human Medicines (Amendment) (Modular Manufacture and Point of Care) Regulations 2025" legislation signed into law on January 23, 2025, decentralised medicines manufacture may take place through a so-called "modular manufacture" strategy, where multiple decentralised manufacturing (DM) sites will be connected to a licensed centralised control site, responsible for overseeing and ensuring the medicine's product quality. Parallels can be drawn to "hub-and-spoke" model frameworks, where multiple spokes are connected to a single, centralised hub, which, in the case of modular manufacture, would be represented by modular manufacturing sites connected to a single control site. DM facilities could result in

"THE MODULAR MANUFACTURE FRAMEWORK WOULD ENABLE PRESCRIPTIONS, IN ANONYMISED FORM, TO BE MANUFACTURED AT A DECENTRALISED, MODULAR SITE VIA PHARMACEUTICAL 3D PRINTING."

multiple benefits, such as less-sensitive supply chains and the adoption of smaller-scale technologies for more flexible drug production processes.

The control site is an integral part of the new modular manufacture framework. The MHRA manufacturing licence is given to a control site, which then authorises, on-boards, supervises, oversees, validates, audits and decommissions its modular manufacturing units through a so-called Master File.[14] The control site and Master File will be subject to regular inspections by the MHRA, whereas the modular units will undergo occasional inspections to certify appropriate oversight from the control site. Decentralised, or modular, sites manufacturing medications via 3D printing could include licensed pharmacies, both community and hospital, as well as facilities focusing solely on medicines production. With the new legislation coming into effect on July 23, 2025, it is a substantial milestone in moving towards personalised medicines to enhance therapeutic outcomes for patients. While the UK is a first-mover for implementing decentralised manufacture by legislation, other regulatory territories are already in the process of effectuating equivalent frameworks, marking a global shift in the medicines manufacture paradigm.[15–17]

Envisaged Workflow for 3D Printing Personalised Medicines as Modular Manufacture

The DM sites may produce medicines via GMP-certified 3D printers; hence production of personalised drug products may be attained on much smaller scales than currently possible. In essence, the modular manufacture framework would enable prescriptions, in anonymised form, to be manufactured at a decentralised, modular site via pharmaceutical 3D printing. Product and process data would be obtained through in-line sensors and measures and would be digitally transferred, potentially in real-time, between the modular manufacturing site and the centralised control site, for recording of quality data and quality assurance. Once approved, dispensing of the medicines to the patient may happen either via their point-of-care location (i.e. community pharmacy or hospital) or potentially through delivery directly to their home (Figure 4). Pharma-inks could either be produced directly at the DM sites as part of the modular manufacturing process or in large batches by another site (i.e. a pharmaceutical company) for distribution to the modular sites, as described by a recent case study.[8]

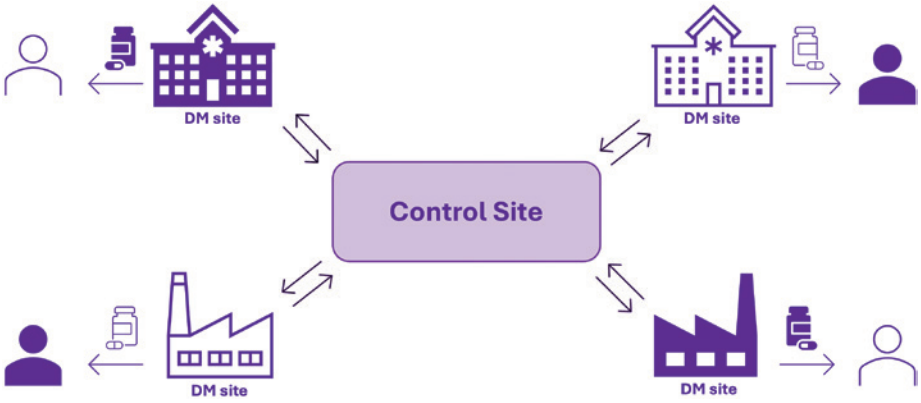


Figure 4: Schematic representation of the new MHRA modular manufacture framework, where multiple DM units are connected to a single control site with two-way communication and data transfer for overall aim of delivering better medicines to patients.

STREAMLINING PHARMACEUTICAL COMPOUNDING – FROM PROCESS TO PRODUCT

Pharmaceutical Compounding – The Original Personalised Medicines

Pharmaceutical compounding is a century-old process where a specific medicine is prescribed for a patient and then prepared by a pharmacist, usually according to specific monographs in national formularies and/or prescriber instructions. The process of pharmaceutical compounding is highly manual, often involving the crushing of commercially available tablets for filling of capsules. Evidently, the process is prone to human-induced errors, which can jeopardise the quality of the final product and thereby patient safety and therapeutic effect. Moreover, compounding requires vast pharmacist resources and is associated with higher costs than off-the-shelf pharmaceuticals. Unsurprisingly, in many countries, pharmaceutical compounding has been heavily reduced even though the practice itself is of great importance for healthcare systems.[18] Hence, automating compounding processes, ensuring medications of reproducible qualities, can help to bring much-needed personalised medicines to patients.

"PHARMACEUTICAL 3D PRINTING OF MEDICINES IS ALREADY BEING USED TO TREAT PATIENTS WHERE COMMERCIALLY AVAILABLE PRODUCTS DO NOT MEET THE REQUIREMENTS OF THE SPECIFIC PATIENT OR PATIENT GROUP."

3D Printing Automates Pharmaceutical Compounding

Pharmaceutical 3D printing of medicines is already being used to treat patients where commercially available products do not meet the requirements of the specific patient or patient group, such as through two M3DIMAKER2 printers in the Clinical Pharmacy department of Gustave Roussy Cancer Campus – a leading cancer research hospital in Paris, France.[19] Although 3D printing is considered an "advanced manufacturing technology", the use of pharmaceutical-grade 3D printers as a means to automate compounding processes is already possible under many existing compounding guidelines. Pharmacists in another European hospital have also been reported to be in favour of automating compounding with 3D printing.[20]

(A) (B)

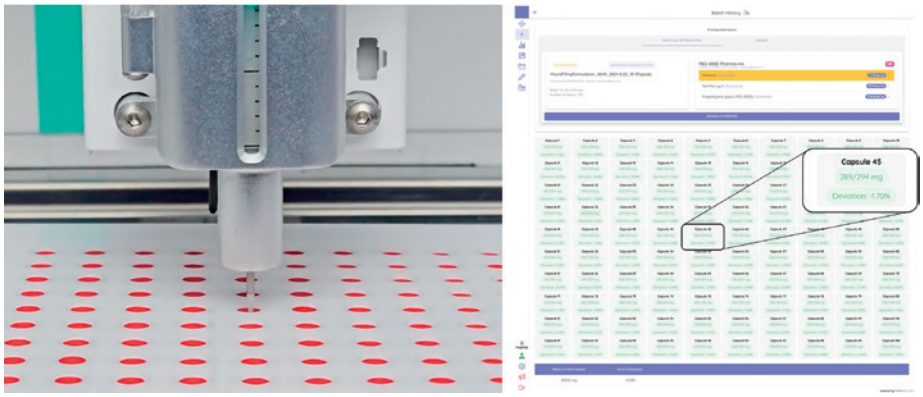


Figure 5: A) Capsule filling via the M3DIMAKER1 printer in a community pharmacy as an automated compounding process resulting in 55% less manual labour. B) M3DIMAKER Studio software interface upon recording of each individual capsule fill weight with indication of mass variation according to target fill weight for individual units and the entire batch. Figures reprinted from Rodríguez-Maciñeiras X *et al.* (2025).[21]

What pharmaceutical 3D printing offers compared with conventional compounding procedures is greater process control through an automated system, thereby resulting in medicines of greater quality and less room for manual errors. A recent publication has highlighted the benefits of installing a M3DIMAKER2 in a community pharmacy to automate the production and dispensing of oral minoxidil medications directly to patients.[21] Correct masses of the medicines were ensured through the integrated analytical balance and an uninterrupted printing process was monitored by the SSE printhead pressure sensor in real-time, all connected to the M3DIMAKER Studio™ software (Figure 5). Overall, the 3D-printed medicines were produced with a 55% reduction in required pharmacist working time compared with conventionally compounded dosage units, thereby providing not only enhanced process and product control but also the potential for resource relocations to bring compounded medicines to a larger array of patients.

CONCLUSION

3D printing of personalised medicines has multiple implications, extending even beyond Earth. Providing more efficient medical therapy during long-duration space missions and space tourism is also on the cards for 3D printing of medicines. Hospital pharmacies are already 3D printing medicines for patients where commercially available products do not meet the patient needs and to conduct clinical trials among these patient groups. Successful implementation of a pharmaceutical 3D printer in a community pharmacy has also highlighted its potential impact for the public by making pharmaceutical compounding more effortless for pharmacists and potentially more accessible overall. Large pharmaceutical companies are currently interested in 3D printing technologies to accelerate prototyping and produce dosage units for first-in-human studies. The future of personalised medicines is being printed – already!

REFERENCES

1. *"Personalised prescribing: Using pharmacogenomics to improve patient outcomes". Royal College of Physicians and British Pharmacological Society, 2022.*
2. *Seoane-Viaño I et al, "Translating 3D printed pharmaceuticals: From hype to real-world clinical applications". Adv Drug Deliv Rev, 2021, Vol 174, pp 553–575.*
3. *Krueger L et al, "Clinical translation of 3D printed pharmaceuticals". Nat Rev Bioeng, 2024, Vol 2 (10).*
4. *"FDA approves the first 3D printed drug product." Press release, Aprecia Pharmaceuticals, Aug 3, 2015.*
5. *"3D Printing at University College of London (UCL) School of Pharmacy". NASA, www.nasa.gov/ochmo-3d-printing-at-ucls-school-of-pharmacy/.*
6. *Seoane-Viaño I et al, "To infinity and beyond: Strategies for fabricating medicines in outer space". Int J Pharm X, 2022, Vol 4, art 100121.*
7. *Bendicho-Lavilla C et al. "Ensuring the quality of 3D printed medicines: Integrating a balance into*

a pharmaceutical printer for in-line uniformity of mass testing". J Drug Deliv Sci Technol, 2024, Vol 92, art 105337.

8. *Seoane-Viaño et al. "A case study on decentralized manufacturing of 3D printed medicines". Int J Pharm X, 2023, Vol 5, art 100184.*
9. *Mora-Castaño G et al, "Optimising 3D printed medications for rare diseases: In-line mass uniformity testing in direct powder extrusion 3D printing!. Int J Pharm, 2025, Vol 668, art 124964.*
10. *Goyanes A et al, "Automated therapy preparation of isoleucine formulations using 3D printing for the treatment of MSUD: First single-centre, prospective, crossover study in patients". Int J Pharm, 2019, Vol 567, art 118497.*
11. *Rodríguez-Pombo L, de Castro-López MJ, et al. Paediatric clinical study of 3D printed personalised medicines for rare metabolic disorders. Int J Pharm, 2024, Vol 657, art 124140.*
12. *Rodríguez-Pombo L et al, "3D printed personalized therapies for pediatric patients affected by adrenal insufficiency". Expert Opin Drug Deliv, 2024, Vol 21(11), pp 1665–1681.*
13. *Denis L et al, "Developing an innovative 3D printing platform for production of personalised medicines in a hospital for the OPERA clinical trial". Int J Pharm, 2024, Vol 661, art 124306.*
14. *"Collection: Decentralised manufacture hub". Medicines and Healthcare Products Regulatory Agency, Mar 2025.*
15. *"Distributed Manufacturing of Drugs: Stakeholder Feedback and Action Plan". US FDA, Nov 2023.*
16. *"Draft Guidance for Industry: Considerations for Complying With 21 CFR 211.110". US FDA, Jan 2025.*
17. *"Fourth listen-and-learn focus group meeting of the Quality Innovation Group". European Medicines Agency, Nov 2024.*
18. *Carvalho M, Almeida IF, "The Role of Pharmaceutical Compounding in Promoting Medication Adherence". Pharmaceuticals (Basel), 2022, Vol 15(9), art 1091.*
19. *"Améliorer les traitements pédiatriques grâce à l'impression 3D." ("Improving pediatric treatments with 3D printing".) Press Release, Gustave Roussy, Feb 11, 2025.*
20. *Levine VR et al, "Off-the-shelf medication transformed: Custom-dosed metoprolol tartrate tablets via semisolid extrusion additive manufacturing and the perception of this technique in a hospital context". Int J Pharm X, 2024, Vol 8, art 100277.*
21. *Rodríguez-Maciñeiras X et al, "Advancing medication compounding: Use of a pharmaceutical 3D printer to auto-fill minoxidil capsules for dispensing to patients in a community pharmacy". Int J Pharm, 2025, Vol 671, art 125251.*

Anna Kirstine Jørgensen

Anna Kirstine Jørgensen is a final-year PhD student at the UCL School of Pharmacy (London, UK), conducting research on 3D-printed personalised medicines as part of the Basit Research Group and is funded by the EPSRC. She has published multiple high-impact papers on pharmaceutical drug printing. Ms Jørgensen holds an MSc in Pharmaceutics from UCL and a BSc in Pharmacy from University of Copenhagen, Denmark, during which spent half an academic year on exchange at ETH Zurich (Switzerland). Prior to starting her doctoral degree, she spent one year working for Evotec and Intract Pharma.

E: anna.jorgensen.19@ucl.ac.uk

Dr Abdul Basit

Abdul Basit, PhD, is a Professor of Pharmaceutics at the UCL School of Pharmacy. He has also founded multiple biotech companies and is internationally recognised for his research. Over a million patients benefit annually from treatments developed in his group. Dr Basit has published more than 300 peer-reviewed publications, and his group's research interests are on additive manufacturing of personalised medicines, sex differences in pharmaceutical research, microbiome interaction with drugs and colonic drug delivery.

E: a.basit@ucl.ac.uk

Dr Alvaro Goyanes

Alvaro Goyanes, PhD, is the CEO and co-founder of FABRX and FABRX AI, and is a professor of Pharmacy and Pharmaceutical Technology at the University of Santiago de Compostela, Spain. He joined the Basit Research Group as a postdoctoral researcher in 2013, during which he co-founded FABRX as a spin-out. Dr Goyanes holds PhD and BPharm degrees from the University of Santiago de Compostela, and has published more than 100 peer-reviewed publications and book chapters. He is ranked among the world's most highly influential researchers.

E: a.goyanes@fabrx.co.uk

FABRX Ltd

UCL School of Pharmacy, 29-39 Brunswick Square, London, WC1N 1AX, United Kingdom

www.fabrx.co.uk/home

ENHANCING PERSONALISED MEDICINE: POWDOSE AND DIFFUCAPS FOR PRECISE ORAL SOLID DOSING

Thierry Jomini, **Stéphane Baronnet** and **Dr John van den Anker**, all of **AbbatiaLabs**, along with **Giuseppe De Franza** of **Adare Pharma Solutions**, evaluate the performance of the POWDOSE® system in delivering precise and repeatable doses of different formulations of Diffucaps®. The authors analyse the functionalities of combining Diffucaps with POWDOSE and highlighting its potential for improving personalised dosing regimens.

Accurate dosing of oral solid forms is increasingly recognised as crucial for achieving optimal therapeutic outcomes while minimising adverse effects.[1] Indeed, the era of the "one-tablet-fits-all" is in the past. Patients now seek personalised treatments for their individual needs. Tailoring drug doses will facilitate precise titration (e.g. in neurological diseases, ADHD[2] and cardiovascular diseases[3]), help mitigate the development of antibiotic resistance[4] and enable weight-based dosing, particularly in paediatric populations.[5] Such individualised approaches are therefore critical for enhancing the safety, efficacy and overall effectiveness of treatment regimens.

Figure 1: POWDOSE device.

AbbatiaLabs has developed a novel dosing technology that enables precise dose titration for oral solid medications by the end user. The POWDOSE device, a two-step mechanism, allows users to first preset the desired dose using a ring and then accurately dispense the medication by turning a knob. This user-centric design is optimised for ease of use and aims to minimise the risk of dosing errors, enhancing the reliability and safety of self-administered treatments (Figure 1).

Adare Pharma Solutions' Diffucaps technology is a multiparticulate system that uses polymer membranes to create multilayered beads, allowing precise drug release and enhanced solubility in targeted gastrointestinal regions. Diffucaps can minimise side effects, such as gastric irritation, and reduce the impact of food on absorption.

This article evaluates and assesses the performance of the POWDOSE system in delivering precise and repeatable doses of different formulations of Diffucaps, demonstrating the system's capacity to achieve consistent and reproducible dosing.

TEST MATERIAL

The POWDOSE device can deliver incremental doses constituting a fraction of the maximum deliverable amount. The technology is fully customisable, allowing adjustment of both the number of increments and the maximum dose to suit the specific requirements of the administered medication. In this study, four (1–4) POWDOSE devices were manufactured and tested. Each device was evaluated for its ability to deliver four distinct dose sizes, corresponding to 25%, 50%, 75% and 100% of the maximum deliverable dose. The reservoir was customised to accommodate up to 30 full-dose deliveries (Table 1).

Dose Percentage (max)	Doses
25%	120
50%	90
75%	60
100%	30

Table 1: Percentage of max delivered dose for this device configuration with the corresponding number of doses delivered.

"THE POWDOSE DEVICE, A TWO-STEP MECHANISM, ALLOWS USERS TO FIRST PRESET THE DESIRED DOSE USING A RING AND THEN ACCURATELY DISPENSE THE MEDICATION BY TURNING A KNOB."

With the flexibility needed to meet diverse patient requirements, Adare's Diffucaps can be used in multiple dosage forms, including capsules, orally disintegrating tablets, rapidly disintegrating tablets and sprinkle formulations. When combined with other Adare technologies, Diffucaps can enhance solubility, broadening its applicability across various drug compounds and therapeutic areas.

For the purpose of this study, Diffucaps sugar sphere core granules were used for testing. These granules did not contain any API, meaning that no specific therapeutic dose was targeted or considered during the testing. As a result, the mean delivered dose for each dosing series was not compared with a predefined or target delivered dose. Instead, the study focused on evaluating the device's ability to consistently deliver precise and reproducible increments of the granules across the specified dose fractions. This approach allowed for a comprehensive assessment of the device's performance in terms of dose precision, independent of any therapeutic dose considerations:

- Devices #1, #2 and #3 were tested with Diffucaps sugar spheres size 30 LOT: 2310458 (sphere diameter between 500 and 700 µm).
- Device #4 was tested with Diffucaps sugar spheres size 18/20 LOT: 2410135 (sphere diameter between 800 and 1,000 µm).

TEST SETUP

The devices were fully loaded with the sugar spheres for the test. Each device was mounted on a laboratory stand positioned above a calibrated KERN F1 balance (capacity 240 g, precision 0.001 g). The test engineer operated the device per the test protocol, delivering the doses into a receptacle placed on the balance, which was used to measure the amount of material dispensed by the device during each test iteration.

The testing sequence for each device was as follows:

1. 30 deliveries at the maximum dose
2. 60 doses at 75% of the maximum dose
3. 90 doses at 50% of the maximum dose
4. 120 doses at 25% of the maximum dose.

Each delivery was logged in a test sheet.

METHODOLOGY

The objective of this study was to evaluate dose delivery variability by a device during its development, rather than to establish a quality control release testing protocol. A straightforward approach was employed, focusing on the total variability of the assay and the variability observed at different dosing stages (beginning, middle and end of the dosing process). As already described, placebo Diffucaps granules were used to assess the variability in the mass of doses dispensed by the device. Statistically, the relative standard deviation (RSD) is considered a practical acceptance criterion.

While the European Pharmacopoeia 2.9.40 on Uniformity of Dosage Units was referenced, the T value was not applied due to the absence of API in the granule batch tested. Instead, the limit of ±25% of the mean value was considered the critical parameter. Therefore, for the test to be considered successful, dose could not deviate by more than ±25% from the mean value.

The test was passed if the RSD was <7%, or if all doses were within ±25% of the mean for each device.

% of Maximum Dose	Type of Diffucaps Granules	Devices Tested	All Values Are Within ± 25%	RSD	Target Value	Min and Max Values
25	Sugar spheres 500–700 µm	#1, #2, #3	Yes	< 1.5%	142 mg	133 mg < x < 154 mg
50	Sugar spheres 500–700 µm	#1, #2, #3	Yes	< 1.4%	285 mg	255 mg < x < 297
75	Sugar spheres 500–700 µm	#1, #2, #3	Yes	< 1.2%	428 mg	413 mg < x < 461 mg
100	Sugar spheres 500–700 µm	#1, #2, #3	Yes	#1 < 0.75% #2 6.7% #3 < 0.75%	570 mg	558 mg < x < 585 mg #2 2 doses at 412 mg & 428 mg

Table 2: Results for X% of the maximum delivered dose with devices #1, #2 and #3.

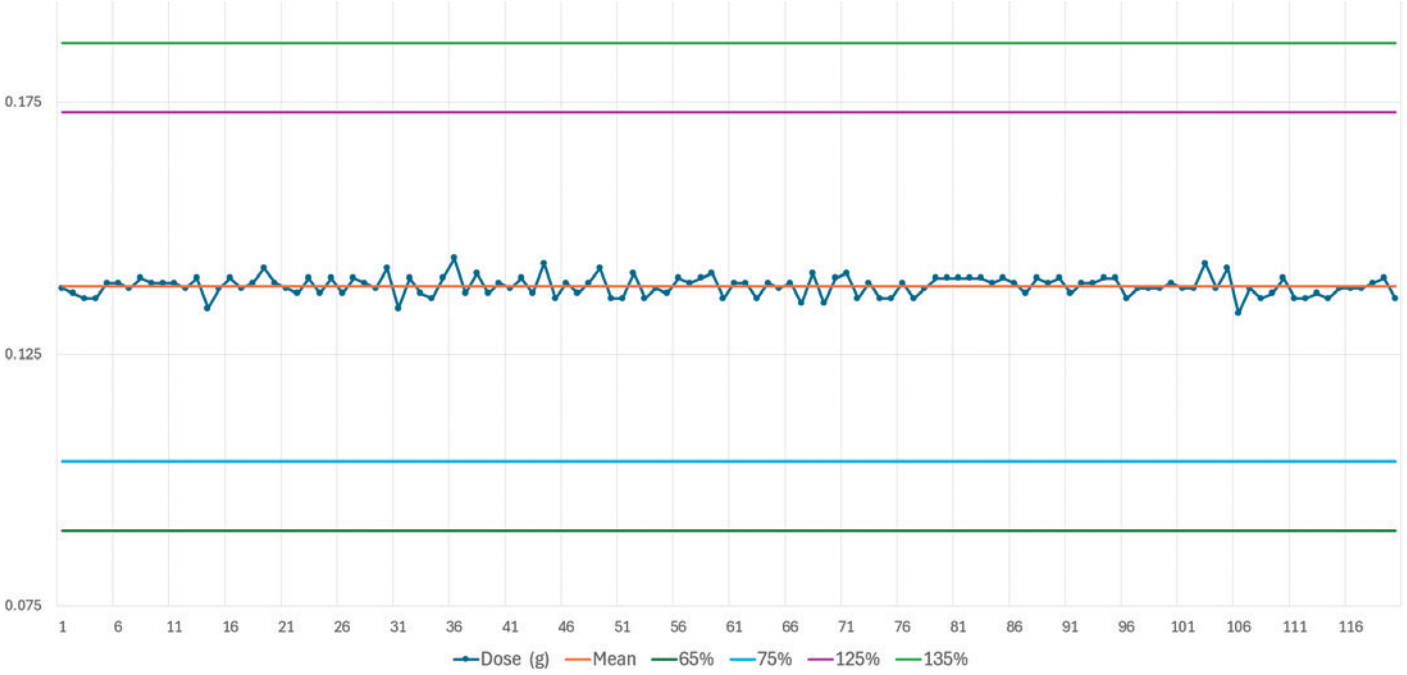


Figure 2: Delivered doses for targeted 25% of max dose with sugar spheres between 500 and 700 µm.

RESULTS

The results are summarised in Table 2. Figure 2 shows the delivered doses (g) targeted for 25% of the maximum dose with sugar spheres between 500 and 700 µm. Following the test with the sugar spheres 500 < x < 700 µm, another lot of Diffucaps sugar spheres was tested with a higher particle size: Diffucaps sugar spheres 800 < x < 1,000 µm. The results are shown in Table 3. Figure 3 shows the delivered doses targeted for 25% of the maximum dose with sugar spheres between 800 and 1,000 µm.

DISCUSSION

With 1,200 doses administered, the POWDOSE device demonstrated high precision and repeatability in delivering doses of Diffucaps sugar spheres. It is important to note that the devices used in this study were pre-production prototypes that have not yet undergone full industrialisation. As a result, the inner surfaces of the devices have not been optimised to minimise friction between the granules and the device walls. This optimisation will be addressed during the development and industrialisation process, which will occur prior to the product's commercial release.

In typical usage, the POWDOSE device will be manipulated by the user between dose deliveries. This handling introduces slight shaking, which helps to prevent issues such as granule bridging, clogging, or sticking – phenomena that likely contributed to the two low doses observed in the fixed-device test setup.

The results also indicated that the doses remain consistent throughout the entire usage period of the device: 30–120 doses. No variation in dose delivery was observed, regardless of whether the

% of Maximum Dose	Type of Diffucaps Granules	Devices Tested	All Values Are Within ± 25%	RSD	Target Value	Min and Max Values
25	Sugar spheres 800–1,000 µm	#4	Yes	< 1.9%	130 mg	118 mg < x < 133 mg
50	Sugar spheres 800–1,000 µm	#4	Yes	< 1.5%	261 mg	248 mg < x < 270
75	Sugar spheres 800–1,000 µm	#4	Yes	< 3.0%	394 mg	347 mg < x < 443 mg
100	Sugar spheres 800–1,000 µm	#4	Yes	< 3.1%	525 mg	480 mg < x < 574 mg

Table 3: Results for X% of the maximum delivered dose with device #4.

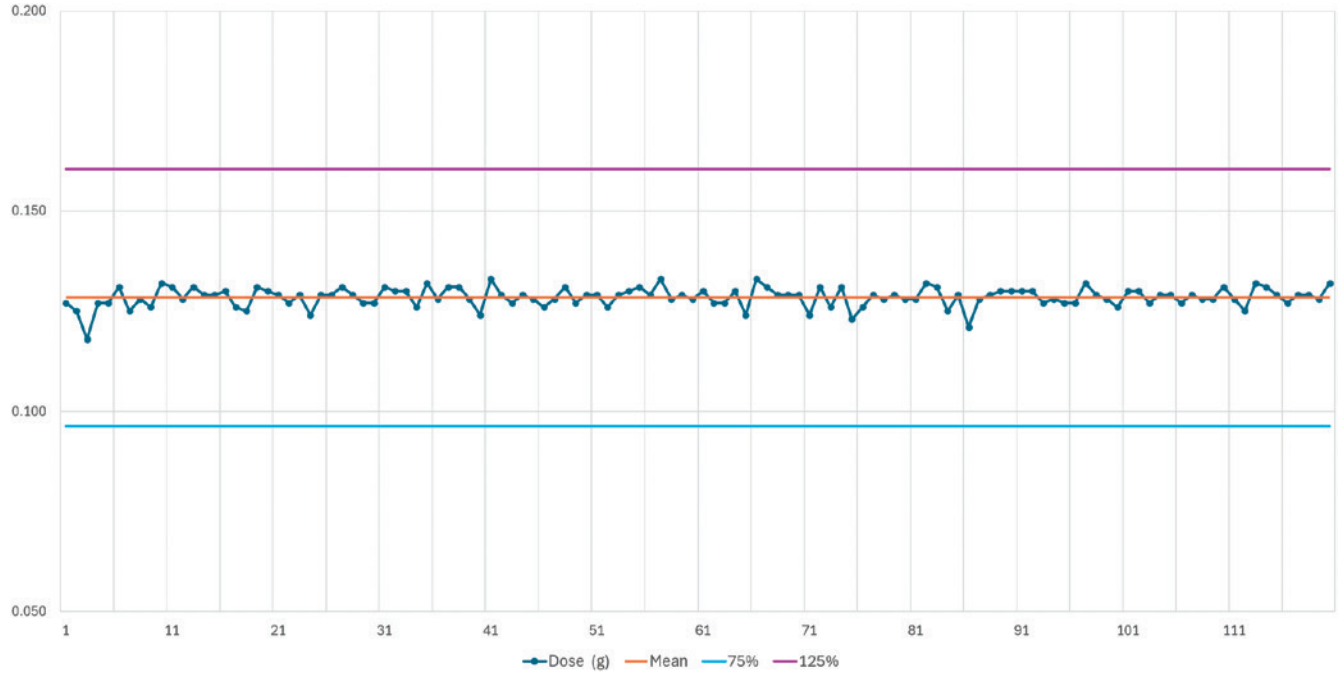


Figure 3: Delivered doses for targeted 25% of max dose with sugar spheres between 800 and 1,000 µm.

dose was administered at the start of the device's use (with a full reservoir) or at the end of its lifetime (when the reservoir was nearly empty).

Overall, the results indicate that Diffucaps granules in combination with the POWDOSE device provide a reliable and adequate solution for delivering customised doses of oral solid dosage forms. It provides a valuable tool for drug, chemistry, manufacturing and controls formulation teams, offering a means for patients to self-administer personalised doses of solid drugs with high accuracy and ease.

REFERENCES

1. *Singh BS, "The Impact of Pharmacogenomics in Personalized Medicine. Advances in Biochemical Engineering/biotechnology". Adv Biochem Eng Biotechnol, 2020, Vol 171, pp 369–394.*
2. *Farhat LC et al, "The effects of stimulant dose and dosing strategy on treatment outcomes in attention-deficit/hyperactivity disorder in children and adolescents: a meta-analysis". Mol Psychiatry, 2022, Vol 27, pp 1562–1572.*
3. *Mauriello A et al, "Pharmacogenomics of Cardiovascular Drugs for Atherothrombotic, Thromboembolic and Atherosclerotic Risk". Genes, 2023, Vol 14, p 2057.*
4. *Mouton JW et al, "The role of pharmacokinetics/pharmacodynamics in setting clinical MIC breakpoints: the EUCAST approach". Clin Microbiol Infect, 2012, Vol 18(3), pp E37–E45.*
5. *Bartelink IH et al, "Guidelines on paediatric dosing on the basis of developmental physiology and pharmacokinetic considerations". Clin Pharmacokinet, 2006, Vol 45(11), pp 1077–1097.*

Thierry Jomini

Thierry Jomini, CEO of AbbatiaLabs, is a mechanical engineer with more than 15 years of experience with the development of drug delivery devices and combination products, primarily focusing on sterile products for subcutaneous administration in areas such as diabetes, Parkinson's disease and hormone therapies. In 2019, he co-founded Anteris Helvetia, a consulting firm that supports pharma and biotech companies in bringing their drug delivery devices to market, where he served as General Manager. In 2023, Anteris Helvetia was acquired by Kymanox, a US-based company.

T: +41 79 703 3180
E: info@abbatialabs.com

Stéphane Baronnet

Stéphane Baronnet, Chief Technical Officer of AbbatiaLabs, is an expert in development of medical devices, including those containing and dosing drug products. His knowledge encompasses mechanics, injection moulding, biocompatibility, formulation, project management and quality standards. Holding key management roles in the pharmaceutical industry, Mr Baronnet led the device engineering team at AstraZeneca's Swedish site until 2018 and contributed to a successful start-up as Chief Technical Officer between 2018 and 2022, leading the development of a connected oral solid dosing dispensing device. Since joining AbbatiaLabs in 2024, Mr Baronnet has led the development of the device with a team of experts in device development.

T: +46 76 636 36 00
E: s.baronnet@abbatialabs.com

Dr John van den Anker

John van den Anker, PhD, MD, Chief Scientific Officer of AbbatiaLabs, is a Professor of Pediatrics, Pharmacology, Physiology, Genomics and Precision Medicine at the George Washington University School of Medicine and Health Sciences (Washington, DC, US). He has been the President of the American College of Clinical Pharmacology (2016–2018) and the European Society of Developmental, Perinatal and Paediatric Pharmacology (2006–2008 and 2017–2019). His research has focused on developmental, neonatal and paediatric pharmacology. He has authored over 600 peer-reviewed publications and has received NIH funding, as well as funding from the EU, to support his research and the development of training programmes in paediatric clinical pharmacology.

E: jvandena@childrensnational.org

AbbatiaLabs
Chemin de Pramey 18, 1530 Payerne, Switzerland
www.abbatialabs.com

Giuseppe De Franza

Giuseppe De Franza is Director of Pharmaceutical Development at Adare Pharma Solutions. He leads all formulation activities within the Italian pharmaceutical development team. With nearly 30 years of experience in the pharmaceutical industry, Mr De Franza has held a range of roles at Adare with increasing responsibility across manufacturing, technology transfer, industrialisation and continuous improvement. A certified Lean Six Sigma Black Belt, Mr De Franza brings over a decade of hands-on experience in applying Lean methodologies to drive process optimisation, enhance productivity and improve quality. His work is underpinned by deep expertise in pharmaceutical technologies and industrial processes. He holds a bachelor's degree in biology from the University of Milan, Italy.

E: giuseppe.defranza@adareps.com

Adare Pharma Solutions
Via Martin Luther King, 13, 20042 Pessano con Bornago (MI), Italy
www.adarepharmasolutions.com

ROQUETTE

Offering the best of nature™

OUTSTANDING SPONSOR

Roquette Health & Pharma Solutions is a family-owned provider of plant-based ingredients and pharmaceutical excipient and capsule solutions, using raw materials of natural origin. Founded in 1933, the company currently operates in more than 100 countries, through more than 30 manufacturing sites and employs almost 10,000 people worldwide. The company offers innovative ingredients for the food, nutrition and healthcare markets.

Keat Theng Chow
pharma@roquette.com
www.roquette.com/pharma

To learn more, see **Page 06**

ABBATIALABS

Thierry Jomini
info@abbatialabs.com
www.abbatialabs.com

AbbatiaLabs is a Swiss-based company specialising in the development of innovative drug delivery devices for oral solid medications. Its solutions are designed to support patients with complex or variable dosing schedules during treatment. AbbatiaLabs is dedicated to enhancing the patient experience by providing new and improved solutions.

To learn more, see **Page 28**

ADARE® PHARMA SOLUTIONS

Giuseppe De Franza
giuseppe.defranza@adareps.com
www.adarepharmasolutions.com

Adare Pharma Solutions is a global technology-driven CDMO providing end-to-end integrated services, with small molecule expertise focusing on oral dosage forms, including taste-masking, customised release, solubility enhancement and patient-centric dosing solutions. With a proven history in drug delivery, Adare's seven facilities in the US and Europe have developed and manufactured more than 65 products sold by customers worldwide.

To learn more, see **Page 28**

FABRX pharmaceutical 3D printing

Dr Abdul Basit
a.basit@ucl.ac.uk
www.fabrx.co.uk/home

FABRX is a pioneering company for 3D printing of personalised medicine founded as a spin-out from the UCL School of Pharmacy (London, UK) in 2014. Now partnering with world-renown institutions and companies, FABRX is determined to bring better therapies to patients, one layer at a time.

To learn more, see **Page 22**

pci PHARMA SERVICES

talkfuture@pci.com
www.pci.com

PCI Pharma Services is a global contract development and manufacturing organisation that provides integrated end-to-end drug development, manufacturing and packaging solutions to increase product speed to market and opportunities for commercial success. PCI's experience includes more than 90 successful product launches each year and over five decades in the delivery of supply chain healthcare services.

To learn more, see **Page 10**

WANT TO APPEAR IN A FUTURE ISSUE?

SCAN THE QR CODE TO FIND OUT MORE

www.ondrugdelivery.com/participate

ONdrugDELIVERY

The toughest challenges in drug delivery, solved through transformative innovation.

You never stop searching for new ways to improve patients' lives – so neither do we.

It's our mission to support the development of the most innovative drug delivery systems and get them to the people who need them most.

With a legacy of pioneering innovations, global network of specialized research centers and a program of continuous innovation, we harness our expertise and extensive portfolio of industry-leading excipient solutions to help you bring groundbreaking treatments to market faster, changing and saving lives for good.

Discover more at **roquette.com/pharma**

ROQUETTE

Offering the best of nature™