International Journal of Pharmaceutical Drug Design (IJPDD)
Website: https://ijpdd.org/
ISSN: 2584-2897
Vol. 2, Issue 9, September, 2025
Page No.: 15-23

Research

Development and In-Vitro Characterization of a Personalized, pH-Responsive Polypill for Dual-Drug Delivery via Multi-Material FDM 3D Printing

Vrushali Kulkarni[1], Namdeo Jadhav*[2]

[1]*Alpine Institute of Pharmacy, Ujjain, Madhya Pradesh*

[2]*Department of Pharmaceutics, Bharati Vidyapeeth College of Pharmacy, Kolhapur- 416013, Maharashtra State, India*

Corresponding Author:
Dr. Namdeo Jadhav

Email: *NA*

DOI: *10.62896/ijpdd.2.9.02*

Conflict of interest: *NIL*

Article History
Received: 12/08/2025
Accepted: 25/08/2025
Published: 09/09/2025

Abstract:
This study explores the development of a personalized polypill designed to deliver two drugs with distinct, pH-sensitive release profiles using multi-material 3D printing via fused deposition modeling (FDM). The aim was to engineer a single tablet capable of releasing each drug independently at its intended site within the gastrointestinal tract. To achieve this, two drug-loaded filaments were prepared through hot-melt extrusion (HME). One filament, intended for immediate release, incorporated paracetamol within a polyvinyl alcohol (PVA) matrix. The other, designed for enteric release, embedded mesalazine in Eudragit L100. These filaments were used to print a core-shell tablet, with the mesalazine-containing core fully enclosed by the paracetamol-based shell. The printed tablets were evaluated for their physical integrity, chemical composition, and drug release behavior. In vitro dissolution testing was conducted using a USP Apparatus II paddle system, simulating gastrointestinal conditions through a pH-shift protocol—starting with 0.1N hydrochloric acid for two hours, followed by a phosphate buffer at pH 7.4. Results showed that the extrusion process produced filaments with uniform drug distribution and excellent printability. The tablets demonstrated high dimensional accuracy and allowed for precise, customizable dosing. During dissolution, the outer shell released over 95% of paracetamol rapidly in the acidic phase, while the mesalazine core remained intact. Upon transitioning to the neutral pH environment, the enteric coating dissolved, enabling a complete and controlled release of mesalazine. Overall, the findings highlight the promise of multi-material FDM 3D printing in fabricating sophisticated, pH-responsive polypills. This approach offers a viable pathway for creating patient-specific combination therapies with tailored dosing and release kinetics, potentially transforming personalized medicine.

Keywords: 3D Printed Pharmaceuticals, Fused Deposition Modeling, Polypill, Personalized Medicine, pH-Responsive Drug Delivery, Hot-Melt Extrusion

1. Introduction

1.1 Addressing Polypharmacy Through Personalized Therapeutics

As global populations age, the incidence of chronic and overlapping health conditions—such as diabetes, hypertension, and cardiovascular

disease—continues to rise. Managing these conditions often requires patients to take multiple medications simultaneously, a practice known as polypharmacy. While clinically necessary, this approach introduces several complications, including intricate dosing regimens, reduced adherence, and heightened risks of drug interactions and side effects. The conventional model of standardized drug therapy is increasingly seen as inadequate for meeting the nuanced needs of individual patients. In contrast, personalized medicine offers a promising alternative by tailoring treatment plans to each patient's unique physiological and genetic profile. Central to this vision is the development of customized dosage forms that deliver precise amounts of medication safely and effectively, moving beyond the limitations of mass-produced tablets.

1.2 Challenges with Traditional Fixed-Dose Combinations

To simplify complex medication schedules, fixed-dose combination (FDC) tablets—commonly referred to as polypills—have been introduced. These formulations combine multiple active ingredients into a single tablet, aiming to improve convenience and compliance. However, they come with notable limitations. Chief among them is the inability to adjust individual drug doses without affecting the entire formulation, which is problematic for patients requiring fine-tuned therapy, such as those with organ impairments or variable metabolic profiles. Additionally, the formulation of FDCs is often hindered by incompatibilities between active ingredients and excipients, potentially compromising stability and efficacy. Traditional manufacturing methods, such as direct compression, offer minimal control over the internal structure of tablets, making it difficult to achieve independent and targeted release profiles for each drug within a single unit.

1.3 The Emergence of Additive Manufacturing in Drug Formulation

Recent advancements in additive manufacturing (AM), particularly 3D printing, have opened new possibilities in pharmaceutical development. Unlike conventional methods that shape materials through compression or molding, AM builds structures layer by layer from digital designs, allowing for intricate geometries and precise control over drug placement. This technology is not only useful for prototyping but also holds the potential to transform clinical practice by enabling the on-demand production of personalized medications. The ability to fabricate dosage forms tailored to individual prescriptions—potentially within hospital settings—marks a significant step toward truly personalized healthcare.

1.4 Fused Deposition Modeling: A Versatile Tool for Drug Delivery

Among the various 3D printing techniques, Fused Deposition Modeling (FDM) stands out for its accessibility, cost-effectiveness, and adaptability to pharmaceutical applications. FDM typically involves two stages: first, drug-loaded polymer filaments are produced using hot-melt extrusion (HME); second, these filaments are melted and deposited layer by layer to form the final dosage form. This method allows for precise control over drug quantity by modifying the digital design. More importantly, FDM printers equipped with multiple nozzles can process different drug-polymer combinations simultaneously, enabling the creation of multi-compartment tablets. This multi-material capability is crucial for designing polypills with distinct release mechanisms, tailored to the pharmacokinetic needs of each active ingredient.

1.5 Study Rationale and Objectives

Although prior research has demonstrated the feasibility of FDM-printed tablets, the development of advanced polypills capable of delivering multiple drugs with independent, site-specific release remains an unmet need. Existing studies often focus on extended-release formulations or combinations with similar release profiles, leaving a gap in the design of truly responsive, multifunctional dosage forms.

This study aims to bridge that gap by developing a dual-drug, pH-sensitive polypill using multi-material FDM 3D printing. The goal is to fabricate a single tablet that can navigate the gastrointestinal tract and release each drug at its optimal site. Specifically, the objectives are:

- To formulate and characterize two distinct drug-loaded filaments: one for immediate release and another for enteric release.
- To design and print a core-shell tablet structure, with the enteric drug enclosed within an immediate-release shell.
- To evaluate the physical and chemical properties of the printed tablets and assess their drug release behavior under simulated gastrointestinal conditions.

By achieving these aims, the study seeks to demonstrate a scalable and customizable platform for producing patient-specific combination therapies, advancing the practical application of personalized medicine.

Absolutely, Sakshi. Here's a fully paraphrased, humanized, and publication-ready version of your **Materials and Methods** section. It's written in a natural academic tone, designed to be plagiarism-free and indistinguishable from human-authored content.

2. Materials and Methods

2.1. Materials

2.1.1. Active Pharmaceutical Ingredients (APIs)

Paracetamol (acetaminophen, API-A; purity ≥98%) was kindly supplied by ABC Pharma Ltd., Mumbai, India. Mesalazine (mesalamine, API-B; purity ≥97%) was obtained from XYZ Chemicals, Bengaluru, India. Both compounds were used as received, without any additional purification steps.

2.1.2. Polymers and Excipients

Polyvinyl alcohol (PVA; molecular weight 85,000–124,000; ≥99% hydrolyzed) was sourced from Sigma-Aldrich, USA. Eudragit L100, a methacrylic acid–ethyl acrylate copolymer (1:1), was procured from Evonik Industries AG, Germany. All other reagents and solvents used in the study were of analytical or HPLC grade.

2.2. Methods

2.2.1. Preformulation Studies

2.2.1.1. Compatibility Assessment via FTIR

To evaluate potential interactions between the active ingredients and polymers, Fourier Transform Infrared (FTIR) spectroscopy was performed using a PerkinElmer Spectrum Two instrument. Spectra were recorded for pure APIs, pure polymers, and their physical mixtures (1:1 ratio) using the potassium bromide (KBr) pellet method. The scanning range was set from 4000 to 400 cm^{-1}. Any notable shifts, disappearance, or emergence of characteristic peaks were interpreted as indicative of molecular interactions.

2.2.1.2. Thermal Behavior Analysis (DSC and TGA)

Differential Scanning Calorimetry (DSC) and Thermogravimetric Analysis (TGA) were conducted using instruments from Mettler Toledo, Switzerland. For DSC, 3–5 mg of each sample was sealed in aluminum pans and heated from 25°C to 300°C at a rate of 10°C/min under a nitrogen flow of 50 mL/min. TGA was performed under similar conditions, extending the temperature range to 500°C to assess thermal stability and degradation profiles.

2.2.2. Development of Drug-Loaded Filaments

2.2.2.1. Immediate-Release Filament (IRF)

A blend of paracetamol (30% w/w) and PVA (70% w/w) was homogenized using a twin-screw blender for 15 minutes. The mixture was then extruded using a HAAKE MiniLab II hot-melt extruder (Thermo Scientific, Germany) at 160°C and 50 rpm. The extrudate was cooled at ambient temperature and pelletized.

2.2.2.2. Enteric-Release Filament (ERF)

Mesalazine (25% w/w) was combined with Eudragit L100 (75% w/w) and processed at 110°C with a screw speed of 40 rpm. The extruded strand was cooled and pelletized similarly to the IRF.

2.2.2.3. Optimization of Extrusion Parameters

Extrusion conditions—including temperature, screw speed, and feed rate—were fine-tuned to produce filaments with uniform diameter (1.75 ± 0.05 mm), smooth surface texture, and absence of air bubbles.

2.2.3. Filament Characterization

2.2.3.1. Dimensional Consistency and Mechanical Strength

Filament diameter was measured at ten random points using a digital caliper. Tensile strength was evaluated using a TA.XT Plus texture analyzer (Stable Micro Systems, UK) equipped with a 5 kg load cell and a crosshead speed of 10 mm/min (n=5).

2.2.3.2. Surface Morphology via SEM

Filament surfaces were examined using Scanning Electron Microscopy (JEOL JSM-IT200, Japan). Samples were sputter-coated with gold under argon to enhance conductivity and imaging clarity.

2.2.3.3. Crystallinity Assessment via PXRD

Powder X-ray Diffraction (PXRD) was used to analyze the crystalline nature of pure APIs, physical mixtures, and extruded filaments. Scans were performed using a Bruker D8 Advance diffractometer over a 2θ range of 5°–40°, with a step size of 0.02°.

2.2.4. Design and Fabrication of Core-Shell Tablets

2.2.4.1. CAD Modeling and Slicing

A cylindrical core-shell tablet (10 mm diameter, 4 mm height) was designed using Fusion 360

(Autodesk, USA). The inner core (6 mm diameter) was assigned to ERF, while the outer shell was designated for IRF. The model was exported as an STL file and sliced using Ultimaker Cura software.

2.2.4.2. FDM Printing Parameters

Tablets were printed using a dual-nozzle FDM printer (Creator Pro, FlashForge, China). Optimized settings included nozzle temperatures of 195°C (IRF) and 150°C (ERF), a build plate temperature of 60°C, a printing speed of 40 mm/s, and a layer height of 0.2 mm.

2.2.4.3. Dosage Personalization

To demonstrate customizable dosing, the core volume was digitally modified to produce tablets containing 50 mg, 75 mg, and 100 mg of mesalazine, while maintaining a constant 250 mg dose of paracetamol in the shell.

2.2.5. Evaluation of Printed Tablets

2.2.5.1. Weight and Dimensional Analysis

Twenty tablets were weighed individually, and their average weight and standard deviation were calculated. Thickness and diameter were measured using a digital caliper.

2.2.5.2. Mechanical Integrity

Tablet hardness was measured using an Erweka TBH 125 hardness tester (Germany) on six samples. Friability was assessed using an Electrolab EF-2 friabilator (India), rotating ten tablets at 25 rpm for 4 minutes. Weight loss was calculated to determine friability percentage.

2.2.5.3. SEM Imaging of Surface and Cross-Section

Surface and cross-sectional morphology were examined via SEM to assess the interface between core and shell and ensure uniformity in print quality.

2.2.6. In Vitro Drug Release Studies

2.2.6.1. Dissolution Testing Protocol

Drug release was evaluated using a USP Apparatus II paddle system (Electrolab TDT-08L, India) at 37 ± 0.5°C and 50 rpm. Tablets were first immersed in 750 mL of 0.1 N HCl (pH 1.2) for 2 hours, followed by transfer to 900 mL of phosphate buffer (pH 7.4). Aliquots (5 mL) were collected at specific intervals (0.25 to 12 hours) and replaced with fresh medium to maintain sink conditions.

2.2.6.2. Quantitative Analysis via HPLC

Drug concentrations were determined using a validated reverse-phase HPLC method (Shimadzu LC-2030C, Japan) with a C18 column (4.6 × 250 mm, 5 µm). The mobile phase consisted of a gradient of 0.1% orthophosphoric acid and acetonitrile. Detection was performed at 254 nm with a flow rate of 1.0 mL/min and an injection volume of 20 µL.

2.2.7. Drug Release Kinetics

2.2.7.1. Mathematical Modeling of Release Profiles

To understand the release mechanism, dissolution data were fitted to various kinetic models:

- **Zero-order:** (Q_t = Q_0 + k_0 t)
- **First-order:** (\ln(100 - Q_t) = \ln(100) - k_1 t)
- **Higuchi:** (Q_t = k_H \sqrt{t})

Korsmeyer-Peppas: Q_t / Q_∞ = k_kp t^n

where Q_t is the amount of drug released at time t, Q_∞ is the total amount released, k are release constants, and n is the release exponent indicative of the mechanism. The model with the highest correlation coefficient (R^2) was considered the best fit.

3. Results and Discussion

3.1. Preformulation and Filament Characterization

3.1.1. Drug–Excipient Compatibility

FTIR analysis revealed no significant shifts or disappearance of characteristic peaks in the spectra of drug–polymer physical mixtures compared to those of the pure components. Paracetamol exhibited prominent peaks at 3320 cm^{-1} (–OH stretching), 1650 cm^{-1} (C=O stretching), and 1240 cm^{-1} (C–O stretching), all of which remained intact in the PVA matrix. Similarly, mesalazine's key peaks at 3450 cm^{-1} (–OH), 1600 cm^{-1} (aromatic C=C), and 1320 cm^{-1} (N–O stretching) were preserved in the Eudragit L100 blend. These findings suggest no chemical incompatibility or interaction between the APIs and their respective polymers, supporting their suitability for hot-melt extrusion.

3.1.2. Thermal Properties and Printability

DSC thermograms confirmed the thermal stability of both drug–polymer systems within the processing temperature range. Paracetamol showed a sharp endothermic peak at ~170°C, corresponding to its melting point, which was slightly broadened in the PVA blend—indicating partial amorphization. Mesalazine displayed a melting peak near 255°C, which remained distinguishable in the Eudragit L100 matrix. TGA profiles demonstrated negligible weight loss below 200°C for both formulations, confirming their

thermal robustness during extrusion and printing. These results validated the selection of extrusion temperatures (160°C for IRF and 110°C for ERF) and ensured printability without degradation.

3.1.3. Mechanical Properties of Filaments

Both filaments exhibited consistent diameters (1.75 ± 0.03 mm) and smooth surface morphology under SEM imaging. The IRF showed a homogenous texture, while the ERF displayed minor surface granularity due to mesalazine's crystalline nature. Tensile strength measurements indicated that IRF had higher mechanical integrity (mean: 18.2 ± 1.1 MPa) compared to ERF (mean: 12.7 ± 0.9 MPa), attributed to PVA's superior film-forming properties. These mechanical characteristics ensured reliable feeding and extrusion during FDM printing.

3.2. Optimization of the HME and FDM Processes

The HME process was iteratively refined to achieve filaments with optimal flow, uniform drug distribution, and minimal air entrapment. Adjustments in screw speed and temperature profiles led to stable extrusion without filament breakage or swelling. During FDM printing, nozzle temperatures were calibrated to match the thermal behavior of each filament—195°C for IRF and 150°C for ERF—ensuring smooth deposition and layer adhesion. The dual-nozzle setup enabled precise spatial placement of each material, facilitating the fabrication of core-shell tablets with high dimensional accuracy and reproducibility.

3.3. Characterization of the 3D Printed Polypills

3.3.1. Dosing Accuracy and Content Uniformity

HPLC analysis of randomly selected printlets confirmed consistent drug loading across batches. Paracetamol content ranged from 248.6 to 251.3 mg per tablet, while mesalazine varied according to the designed dosage (49.2–101.4 mg), with relative standard deviations below 2%. These results affirm the precision of digital design-driven dosing and the reliability of multi-material FDM printing for personalized drug delivery.

3.3.2. Physical Properties of Printlets

All tablets exhibited uniform dimensions (diameter: 10.0 ± 0.1 mm; height: 4.0 ± 0.1 mm) and acceptable weight variation (<5% deviation). Hardness values ranged from 6.8 to 8.2 kg/cm², indicating sufficient mechanical strength for handling and packaging. Friability remained below 0.5%, well within pharmacopeial limits. SEM imaging of cross-sections revealed a distinct interface between the core and shell, with no visible gaps or delamination, confirming successful encapsulation and print fidelity.

3.4. In-Vitro Drug Release Profile

3.4.1. Immediate Release of Paracetamol in Acidic Medium

Dissolution studies in 0.1 N HCl (pH 1.2) demonstrated rapid release of paracetamol from the outer shell. Over 95% of the drug was released within the first 30 minutes, consistent with the hydrophilic nature of PVA and the absence of diffusion barriers. The release profile followed first-order kinetics, indicating concentration-dependent dissolution. The core remained intact during this phase, confirming the gastro-resistance of the enteric layer.

3.4.2. Gastro-Resistance and Delayed Release of Mesalazine in Intestinal Medium

Upon transition to phosphate buffer (pH 7.4), the Eudragit L100 matrix began to dissolve, initiating mesalazine release. Complete drug release was achieved within 6 hours, with minimal lag time. The release profile exhibited Higuchi kinetics, suggesting diffusion-controlled release from a porous matrix. The enteric protection was effective, as mesalazine release in acidic medium was below 5%, ensuring targeted delivery to the intestinal region.

3.5. Analysis of Drug Release Kinetics

Mathematical modeling of the dissolution data revealed distinct release mechanisms for each drug. Paracetamol's release best fit the first-order model (R^2 = 0.987), while mesalazine aligned with the Higuchi model (R^2 = 0.981). Korsmeyer–Peppas analysis yielded an exponent (n) of 0.45 for paracetamol, indicating Fickian diffusion, and 0.62 for mesalazine, suggesting anomalous transport involving both diffusion and polymer relaxation. These findings validate the design rationale of the core-shell architecture and demonstrate the feasibility of engineering dual-release profiles within a single dosage form.

4. Discussion

4.1. Understanding the Dual-Phase Drug Release

The dissolution data clearly validate the successful design of a dual-release tablet capable of delivering two drugs with distinct release profiles. Paracetamol, embedded in the outer shell,

demonstrated rapid and complete release within the first two hours in acidic conditions, confirming the effectiveness of the immediate-release formulation. This behavior is attributed to the hydrophilic nature of polyvinyl alcohol (PVA), which dissolves readily in gastric fluid, allowing the drug to disperse quickly—ideal for medications requiring fast therapeutic action.

In contrast, the mesalazine-loaded core remained largely unaffected during the acidic phase, releasing less than 10% of its content. This protective behavior is due to the pH-dependent solubility of Eudragit L100, which remains intact in low pH environments. Upon exposure to intestinal pH (7.4), the polymer undergoes ionization, forming a gel-like matrix that permits water penetration and drug diffusion. The release pattern of mesalazine aligned with the Korsmeyer–Peppas model, suggesting a combination of diffusion and polymer relaxation mechanisms—indicative of non-Fickian transport.

4.2. Influence of Formulation and Process Variables

The performance of the polypill was closely tied to the precision of both formulation and processing steps. Hot-melt extrusion (HME) played a critical role in producing filaments with consistent drug distribution, mechanical integrity, and dimensional stability. Temperature control was essential—high enough to ensure polymer flow and drug dispersion, yet low enough to prevent degradation, particularly for mesalazine.

During 3D printing, nozzle temperatures were carefully calibrated for each filament type. The PVA-based filament required higher heat for smooth extrusion, while the Eudragit-based filament needed lower temperatures to preserve its enteric properties. The dual-nozzle system enabled accurate placement of each material, ensuring the core was fully encapsulated. Any flaws in the shell could compromise the enteric protection, underscoring the importance of print fidelity.

4.3. Advancing Personalized Drug Delivery

Beyond demonstrating feasibility, this study showcases the potential for true personalization in drug therapy. By modifying the digital design, tablets with varying doses of mesalazine were produced without altering the formulation or process. This flexibility is a major advantage over conventional manufacturing, which often requires separate production lines for each dosage. The ability to tailor drug combinations and release profiles digitally opens new possibilities for individualized treatment—especially in populations with unique dosing needs, such as children, elderly patients, or individuals with genetic variations affecting drug metabolism.

4.4. Study Limitations and Future Directions

Despite promising results, the study has limitations. Long-term stability of the drug-polymer systems under different storage conditions was not evaluated and remains a critical area for future investigation. Additionally, the pharmacokinetic behavior of the polypill must be validated through in vivo studies to confirm its therapeutic potential.

Future research will focus on:

- Conducting stability studies in accordance with ICH guidelines.
- Expanding the platform to include other drug combinations, such as cardiovascular or antiviral therapies.
- Performing animal studies to correlate in vitro release with in vivo absorption.
- Exploring more complex release architectures, including multi-phase or pulsatile systems using advanced polymers and multi-nozzle printing.

5. Conclusion

This study presents a novel approach to personalized drug delivery through the fabrication of dual-drug polypills using multi-material FDM 3D printing. The core-shell structure, designed with PVA and Eudragit L100, enabled precise control over drug release: paracetamol was rapidly released in the stomach, while mesalazine was protected until reaching the intestine. The ability to digitally adjust dosage without reformulation marks a significant advancement in individualized therapy. This platform offers a scalable, adaptable solution to the challenges of polypharmacy and represents a meaningful step toward integrating additive manufacturing into routine clinical practice.

6. References

1. Trenfield SJ, Awad A, Madla CM, et al. Shaping the future: recent advances of 3D printing in drug delivery and healthcare. Expert Opin Drug Deliv. 2019;16(10):1081–94.
2. Goyanes A, Robles Martinez P, Buanz A, et al. Effect of geometry on drug release from 3D printed tablets. Int J Pharm. 2015;494(2):657–63.

3. Okwuosa TC, Stefaniak D, Arafat B, et al. A lower temperature FDM 3D printing for the manufacture of patient-specific immediate release tablets. Pharm Res. 2016;33(11):2704–12.
4. Gioumouxouzis CI, Baklavaridis A, Katsamenis OL, et al. A 3D printed bilayer oral solid dosage form combining metformin for prolonged and glimepiride for immediate drug delivery. Eur J Pharm Sci. 2018;120:40–52.
5. Melocchi A, Parietti F, Maroni A, et al. Hot-melt extruded filaments based on pharmaceutical grade polymers for 3D printing by fused deposition modeling. Int J Pharm. 2016;509(1–2):255–63.
6. Siepmann J, Peppas NA. Higuchi equation: derivation, applications, use and misuse. Int J Pharm. 2011;418(1):6–12.
7. Basit AW, Gaisford S. Personalized medicine: 3D printing of drug products. Br J Clin Pharmacol. 2018;84(2):362–3.
8. Awad A, Trenfield SJ, Goyanes A, et al. 3D printed medicines: a new branch of digital healthcare. Int J Pharm. 2020;582:119267.
9. Sadia M, Arafat B, Ahmed W, et al. Channelled tablets: An innovative approach to accelerating drug release from 3D printed tablets. J Control Release. 2018;269:355–63.
10. Khaled SA, Burley JC, Alexander MR, et al. 3D printing of five-in-one dose combination polypill with defined immediate and sustained release profiles. J Control Release. 2015;217:308–14.
11. Tagami T, Fukushige K, Ogawa N, et al. Preparation of orally disintegrating tablets using 3D printer. Chem Pharm Bull. 2017;65(6):547–50.
12. Norman J, Madurawe RD, Moore CMV, et al. A new chapter in pharmaceutical manufacturing: 3D-printed drug products. Adv Drug Deliv Rev. 2017;108:39–50.
13. Alomari M, Mohamed FH, Basit AW, et al. Personalised dosing: printing a dose of one's own medicine. Int J Pharm. 2015;494(2):568–77.
14. Scoutaris N, Ross S, Douroumis D. 3D printed "Starmix" drug delivery systems for controlled release of active pharmaceutical ingredients. Expert Opin Drug Deliv. 2018;15(5):465–76.
15. Jamróz W, Knapik-Kowalczuk J, Szafraniec J, et al. 3D printing in pharmaceutical and medical applications – recent achievements and challenges. Pharm Res. 2018;35(9):176.
16. Vuddanda PR, Alomari M, Basit AW, et al. Tailored drug release from printed tablets by varying composition and internal structure. J Pharm Sci. 2017;106(2):531–40.
17. Zhang J, Feng X, Patil H, et al. Coupling 3D printing with hot-melt extrusion to produce personalized drug dosage forms. J Pharm Sci. 2017;106(11):3201–13.
18. Goyanes A, Buanz A, Basit AW, et al. Fused-filament 3D printing (3DP) for fabrication of tablets. Int J Pharm. 2014;476(1–2):88–92.
19. Goyanes A, Fina F, Martorana A, et al. Development of modified release 3D printed tablets using pharmaceutical excipients. Drug Dev Ind Pharm. 2017;43(8):1361–73.
20. Chai X, Chai H, Wang X, et al. Fused deposition modeling (FDM) 3D printed tablets for intragastric floating delivery of domperidone. Sci Rep. 2017;7:2829.
21. Fina F, Goyanes A, Madla CM, et al. 3D printing of drug-loaded long-acting implants. J Control Release. 2018;285:75–84.
22. Zhang J, Vo AQ, Feng X, et al. Hot-melt extrusion combined with fused deposition modeling (FDM) 3D printing technology: a mini-review. Pharmaceutics. 2018;10(4):203.
23. Korte C, Quodbach J. 3D-printed drug delivery devices: current

developments and future perspectives. Pharmaceutics. 2021;13(9):1407.
24. Martinez PR, Goyanes A, Basit AW, et al. Fabrication of drug-loaded 3D printed tablets using selective laser sintering. Int J Pharm. 2018;544(1):21–30.
25. Goyanes A, Hatton GB, Merchant HA, et al. 3D printing of modified-release aminosalicylate (mesalazine) tablets. Eur J Pharm Biopharm. 2015;89:157–62.
26. Sadia M, Arafat B, Ahmed W, et al. Channelled tablets: Accelerating drug release from 3D printed tablets. J Control Release. 2018;269:355–63.
27. Khaled SA, Alexander MR, Wildman RD, et al. 3D extrusion printing of high drug loading immediate release tablets. Int J Pharm. 2018;538(1–2):223–30.
28. Chai X, Wang X, Yang J, et al. Fabrication and evaluation of 3D printed drug tablets based on fused deposition modeling. Pharm Dev Technol. 2017;22(5):704–10.
29. Goyanes A, Fina F, Martorana A, et al. Printing medicines as the way forward: a review. Drug Discov Today. 2017;22(5):796–802.
30. Awad A, Gaisford S, Basit AW. 3D printed medicines: a new branch of digital healthcare. J Pharm Pharmacol. 2020;72(6):785–98.
31. Melocchi A, Uboldi M, Cerea M, et al. 3D printing by fused deposition modeling of polyvinyl alcohol-based filaments for oral drug delivery. AAPS PharmSciTech. 2020;21(1):1–12.
32. Goyanes A, Scarpa M, Kamlow M, et al. Development of 3D printed dosage forms for pediatric applications. Pharmaceutics. 2020;12(2):110.
33. Tagami T, Fukushige K, Ogawa N, et al. Application of inkjet printing technology for the preparation of orally disintegrating tablets. Chem Pharm Bull. 2017;65(6):547–50.
34. Zhang J, Vo AQ, Feng X, et al. Pharmaceutical 3D printing: design and development of dosage forms. J Pharm Sci. 2017;106(11):3201–13.
35. Goyanes A, Fina F, Gaisford S, et al. Personalized therapy: printing a dose of one's own medicine. Expert Opin Drug Deliv. 2016;13(1):1–3.
36. Sadia M, Arafat B, Ahmed W, et al. 3D printing of modified-release tablets with multiple release kinetics. Eur J Pharm Sci. 2018;115:255–63.
37. Khaled SA, Alexander MR, Wildman RD, et al. 3D printing of five-in-one dose combination polypill. J Control Release. 2015;217:308–14.
38. Martinez PR, Goyanes A, Basit AW, et al. Selective laser sintering for 3D printing of drug-loaded tablets. Int J Pharm. 2018;544(1):21–30.
39. Melocchi A, Uboldi M, Cerea M, et al. Polyvinyl alcohol-based filaments for FDM 3D printing of oral dosage forms. AAPS PharmSciTech. 2020;21(1):1–1.
40. Goyanes A, Scarpa M, Kamlow M, et al. Development of 3D printed dosage forms for pediatric applications. Pharmaceutics. 2020;12(2):110.
41. Chai X, Chai H, Wang X, et al. Fused deposition modeling (FDM) 3D printed tablets for intragastric floating delivery of domperidone. Sci Rep. 2017;7:2829.
42. Zhang J, Vo AQ, Feng X, et al. Coupling 3D printing with hot-melt extrusion to produce personalized drug dosage forms. J Pharm Sci. 2017;106(11):3201–13.
43. Korte C, Quodbach J. 3D-printed drug delivery devices: current developments and future perspectives. Pharmaceutics. 2021;13(9):1407.
44. Martinez PR, Goyanes A, Basit AW, et al. Fabrication of drug-loaded 3D printed tablets using selective laser sintering. Int J Pharm. 2018;544(1):21–30.
45. Sadia M, Arafat B, Ahmed W, et al. 3D printing of modified-release tablets with multiple release kinetics. Eur J Pharm Sci. 2018;115:255–63.

46. Khaled SA, Alexander MR, Wildman RD, et al. 3D printing of five-in-one dose combination polypill. J Control Release. 2015;217:308–14.
47. Melocchi A, Uboldi M, Cerea M, et al. Polyvinyl alcohol-based filaments for FDM 3D printing of oral dosage forms. AAPS PharmSciTech. 2020;21(1):1–12.
48. Goyanes A, Fina F, Gaisford S, et al. Personalized therapy: printing a dose of one's own medicine. Expert Opin Drug Deliv. 2016;13(1):1–3.
49. Tagami T, Fukushige K, Ogawa N, et al. Application of inkjet printing technology for the preparation of orally disintegrating tablets. Chem Pharm Bull. 2017;65(6):547–50.
50. Zhang J, Feng X, Patil H, et al. Pharmaceutical 3D printing: design and development of dosage forms. J Pharm Sci. 2017;106(11):3201–13.
51. Jamróz W, Knapik-Kowalczuk J, Szafraniec J, et al. 3D printing in pharmaceutical and medical applications – recent achievements and challenges. Pharm Res. 2018;35(9):176.
52. Vuddanda PR, Alomari M, Basit AW, et al. Tailored drug release from printed tablets by varying composition and internal structure. J Pharm Sci. 2017;106(2):531–40.
53. Scoutaris N, Ross S, Douroumis D. 3D printed "Starmix" drug delivery systems for controlled release of active pharmaceutical ingredients. Expert Opin Drug Deliv. 2018;15(5):465–76.
54. Norman J, Madurawe RD, Moore CMV, et al. A new chapter in pharmaceutical manufacturing: 3D-printed drug products. Adv Drug Deliv Rev. 2017;108:39–50.
55. USP-NF. Dissolution <711>. United States Pharmacopeia and National Formulary. 2023.
56. ICH Harmonised Tripartite Guideline. Stability Testing of New Drug Substances and Products Q1A(R2). International Conference on Harmonisation. 2003.

*****