



جامعة الشرق الأوسط

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Amman - Jordan

**Investigating the drug release rate and
mechanical properties of tablets prepared by
3D printing assisted molding**

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for the Master's Degree in Pharmaceutical Sciences**

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دراسة معدل إطلاق الدواء والخصائص الميكانيكية للأقراص المصنعة
عبر القولية بمساعدة الطباعة ثلاثية الأبعاد

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قدّمت هذه الرسالة استكمالاً لمتطلبات الحصول على درجة الماجستير في العلوم

الصيدلانية

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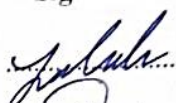

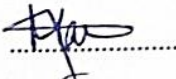
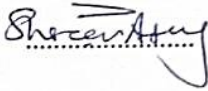
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Committee Decision


This thesis, titled "**Preparation and evaluation of rapidly disintegrating tablets made by 3D printing-assisted molding**" by Researcher Ola Hussein Alshammari, was defended and approved on 26/1/2026.

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Authorization

“I, Ola Hussein Alshammari, authorize Middle East University to provide copies of my thesis on hard copy and soft copy form, in whole or in part, to libraries, organizations, bodies, and institutions dealing with scientific research and studies upon request.

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Dedication

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List of Abbreviations

API	Active Pharmaceutical Ingredient
BJ	Binder Jetting
CAD	Computer-Aided Design
DLP	Digital Light Processing
DIW	Direct Ink Writing
DPE	Direct Powder Extrusion
FDM	Fused Deposition Modeling
FDA	Food and Drug Administration
HCl	Hydrochloric Acid
HPMC	Hydroxypropyl Methylcellulose (Hypromellose)
ICH	International Council for Harmonisation
NaCl	Sodium Chloride
PAT	Process Analytical Technology
PEG	Polyethylene Glycol
PLA	Polylactic Acid
PM	Personalised Medicine
RDTs	Rapidly Disintegrating Tablets
RPM	Revolutions Per Minute
SLA	Stereolithography
SLS	Selective Laser Sintering
SSE	Semi-Solid Extrusion
UV-Vis	Ultraviolet-Visible Spectrophotometry
w/w	Weight by Weight
3DP	Three-dimensional printing

Investigating the drug release rate and mechanical properties of tablets prepared by 3D printing assisted molding

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Abstract

Three-dimensional printing (3DP), or additive manufacturing, has emerged as a significant advancement in the production of custom pharmaceuticals, utilizing computer-aided design to create precise models. Over recent years, the application of the 3DP in the pharmaceutical sector has matured, offering substantial benefits over traditional drug preparation methods. These benefits include enhanced personalized drug production capabilities, the ability to manufacture complex drug structures, and expedited production of small drug quantities. Personalized medicine aims to tailor medical treatment to individual patients based on unique criteria. Traditional manufacturing techniques often fall short in providing the necessary diversity, which can lead to inconsistent drug formulations, including issues with tablet breakup or liquid stability. 3D printing presents a promising solution to these challenges, enabling the production of accurate and personalized drug forms. This study highlights the preparation of customized polymeric tablets using 3D printed molds.

The study focuses on evaluating a tablet preparation method utilizing 3D printed molds, specifically crafting paracetamol tablets with hydroxypropylmethylcellulose (HPMC) as the primary matrix-former. Different concentrations of polyethylene glycol 4000 (PEG) were employed as a plasticizer. The materials—HPMC, polyethylene glycol 4000 (PEG), and paracetamol—were dissolved in a 50% water-ethanol solution in various proportions and stirred at 40°C until a gel formed. This gel was then molded using 3D printed molds and dried at 50°C until completely solidified. The dried tablets were removed for further analysis, particularly focusing on dissolution studies over a six-hour period. While there was no significant difference in the dissolution rates between the two formulations tested, the 30% formulation (F3) was noted for its reliability due to consistent results, contrasting with the more variable results from the 40% formulation (F4). The calibration curve for paracetamol shows a straight line with an R^2 of 0.9994 over a concentration range of 1 to 8 mg/ml, confirming linearity as per ICH guidelines. However, formulations at 10% and 20% were not successfully created in a uniform tablet matrix. The mold for paracetamol tablets, made using 3D modeling software, consists of a cylindrical cavity, a lid, and a pressing plate, ensuring dimensional accuracy. Formulations at 30% and 40% passed friability testing with losses below 1%. In conclusion, this study confirms that 3D printed molds are a viable method for preparing customized sustained-release formulations. This innovative approach holds potential for developing a practical platform for on-demand pharmacy manufacturing, ultimately leading to safer and more precise treatment options for specific patients.

Keyword: 3D Printing (3DP), Personalized Medicine, Sustained-Release, HPMC (Hydroxypropylmethylcellulose).

دراسة معدل إطلاق الدواء والخصائص الميكانيكية للأقراص المصنعة عبر القوالب بمساعدة الطباعة

ثلاثية الأبعاد

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الملخص

تقنية الطباعة ثلاثية الأبعاد، أو ما يُعرف بتقنية التصنيع الإضافي، برزت كتطور مهم في مجال إنتاج الأدوية المخصصة، حيث تعتمد على التصميم بمساعدة الحاسوب (CAD) لإنشاء نماذج دقيقة. وخلال السنوات الأخيرة، نصح تطبيق هذه التقنية في القطاع الصيدلاني، مقدّمًا فوائد كبيرة مقارنة بطرق تحضير الأدوية التقليدية. وتشمل هذه الفوائد تعزيز القدرة على إنتاج أدوية مخصصة لكل مريض، وإمكانية تصنيع تراكيب دوائية معقدة، وتسريع إنتاج كميات صغيرة من الأدوية.

يهدف الطب الشخصي إلى تفصيل العلاج الطبي بما يتناسب مع الخصائص الفردية لكل مريض. وغالبًا ما تعجز تقنيات التصنيع التقليدية عن توفير هذا التنوع المطلوب، مما قد يؤدي إلى عدم تجانس في التركيبات الدوائية، مثل مشاكل تفكك الأقراص أو عدم استقرار المستحضرات السائلة. وهنا تبرز الطباعة ثلاثية الأبعاد كحل واعد لهذه التحديات، إذ تُمكن من إنتاج أشكال دوائية دقيقة ومخصصة. وتسلط هذه الدراسة الضوء على تحضير أقراص بوليمرية مخصصة باستخدام قوالب مطبوعة بتقنية الطباعة ثلاثية الأبعاد

تركز هذه الدراسة على تقييم طريقة تحضير الأقراص باستخدام قوالب مطبوعة ثلاثية الأبعاد، وتحديدًا تصنيع أقراص الباراسيتامول باستخدام هيدروكسي بروبيل ميثيل سليولوز كمادة أساسية لتكوين المادة الأساسية. استُخدمت تراكيز مختلفة من بولي إيثيلين جليكول 4000 كملدن. تم إذابة المواد - هيدروكسي بروبيل ميثيل سليولوزو بولي إيثيلين جليكول 4000 والباراسيتامول - في محلول من الماء والإيثانول بنسبة 50% بنسب مختلفة، مع التحريك عند درجة حرارة 40 درجة مئوية حتى تكوّن هلام. ثم تم تشكيل هذا الهلام باستخدام قوالب مطبوعة ثلاثية الأبعاد، وتجفيفه عند درجة حرارة 50 درجة مئوية حتى تصلّب تمامًا. أُخرجت الأقراص المجففة لإجراء المزيد من التحليلات، مع التركيز بشكل خاص على دراسات الذوبان على مدى ست ساعات. على الرغم من عدم وجود فرق كبير في معدلات الذوبان بين التركيبتين المختبرتين، إلا أن تركيبة 30% تميزت بموثوقيتها نظرًا لنتائجها المتسقة، على عكس النتائج الأكثر تباينًا لتركيبية 40%. يُظهر منحنى معايرة الباراسيتامول خطأ مستقيمًا بمعامل تحديد (R^2) قدره 0.9994 ضمن نطاق تركيز يتراوح بين 1 و8 مايكروغرام/مل، مما يؤكد الخطية وفقًا لإرشادات ICH. مع ذلك، لم تُصنع تركيبات بتركيز 10% و20% بنجاح في مصفوفة أقراص متجانسة. يتكون قالب أقراص الباراسيتامول، المصمم باستخدام برنامج نمذجة ثلاثية الأبعاد، من تجويف أسطواني وغطاء ولوحة ضغط، مما يضمن دقة الأبعاد. اجتازت التركيبات بتركيز 30% و40% اختبارات الهشاشة بفقد أقل من 1%.

في الختام، تؤكد هذه الدراسة أن القوالب المطبوعة ثلاثية الأبعاد تُعدّ طريقة فعّالة لإعداد تركيبات دوائية مخصصة ذات إطلاق مُستدام. ويُبشّر هذا النهج المبتكر بإمكانية تطوير منصة عملية لتصنيع الأدوية عند الطلب، مما يُؤدي في نهاية المطاف إلى خيارات علاجية أكثر أمانًا ودقة لفئات مُحددة من المرضى.

الكلمات المفاحية: الطباعة ثلاثية الأبعاد (3DP)، الطب الشخصي، الإطلاق المستدام، هيدروكسي بروبيل ميثيل سليولوز (HPMC).

Chapter One: Introduction

1.1. Personalised medicine

Individualized medicine, also known as customized or precision medicine, revolutionizes clinical care by adapting treatment to each patient's genetic, environmental, and behavioral characteristics. This strategy seeks to improve patient care by increasing the effectiveness, safety, and precision of medical therapy (Dmytro Maltsev et al.,2025) This shift is becoming increasingly important as traditional "one-size-fits-all" treatments usually neglect individual patient characteristics, resulting in poor outcomes. Individualized medicine gives a better answer to these discrepancies by striving to obtain optimal therapy by adjusting procedures to meet specific traits, thereby giving more accurate and effective care (Marques, L et al.,2024; Elemento, O et al.,2020). The core idea of personalized medicine is to use genomes, proteomics to study, discover, validate, and use biomarkers from large groups of patients with specific disease types. The goal of personalized medicine is to provide patients with accurate, individualized care while also improving illness diagnosis, treatment, and prevention.

Medical experts can gain a better understanding of how diseases evolve by studying each patient's genomes, proteomics, predicting patient reactions to medications more accurately, and developing tailored treatment strategies. Personalized therapy options can increase treatment outcomes while minimizing unwanted side effects and drug waste. As technology advances and society supports it, customized medicine is expected to broaden the scope of medical care, improve patient health, and provide more efficient medical treatment. Figure 1 illustrates the paths of personalized medicine (Junwen Su et al., 2024).

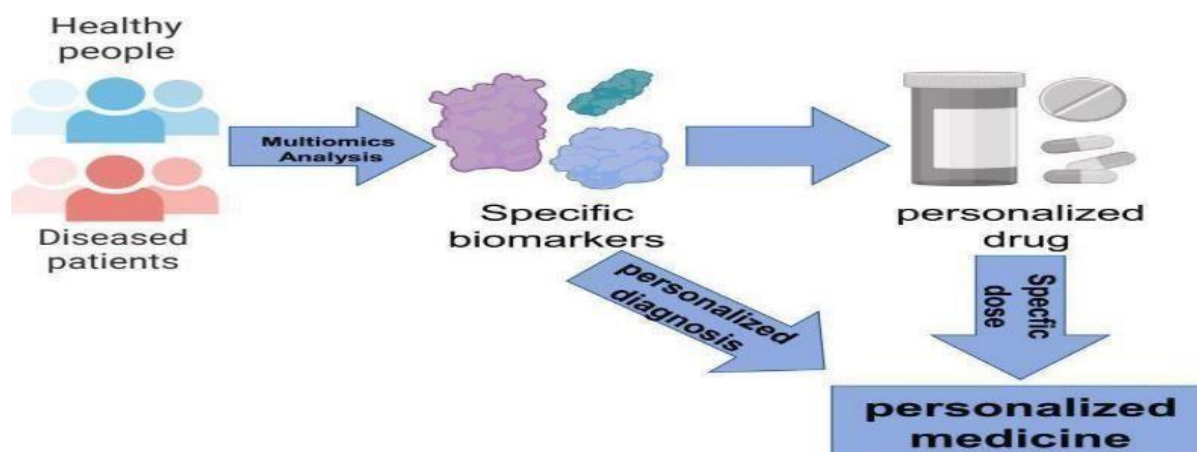


Figure 1: Paths of personalized medicine (Junwen Su et al., 2024).

The importance of personalized medicine is summed up in three points: treatment approaches, preventative strategies and monitoring and modifications (Dmytro Maltsev et al., 2025).

1.2. Pharmaceutical manufacturing of personalized medicine

Certain drugs like digoxin and phenprocoumon (long-acting anticoagulant) have a small margin between the therapeutic and toxic dose and require precise regulation during the initial phase. Clearly, appropriate drug formulation is required that can allow the selection and usage of separate drug doses to provide basic information regarding personal medicine in current practice (Standing and Tuleuet al., 2005; Kearns et al., 2003; Stegemann et al., 2010). Many drugs are designed in constant dosage suitable for most patients; however, it is not appropriate for all patients (Cohen et al., 2001). Doses may be lower or greater for some patients, and giving the same amount to everyone may have side effects. Future pharmaceutical design is aiming toward personal medicine, where the drug dosage and combination can be customized for each patient because every patient responds differently to every treatment (Alomari et al., 2015; Crommalin et al., 2016). Tablets are the most common form of medicine as they are easy to administer and cheaper (Sastry et al., 2000). However, conventional tablets are designed on a large scale and are very difficult to provide personal drug dosage. Hence, new design techniques are necessary.

1.3. Present Methods in Personalized Medicine

Liquid formulations come in many forms, such as solutions, syrups, emulsions, and suspensions. Solutions and syrups are preferred because they let to get exact doses from multi-dose containers. Droppers and spoons are the most common tools used to give doses. The main device or a separate piece can be the dose-measuring instrument. The dropper lets the patient give the right amount of medicine. But there is a chance of dose mistakes, which depends on how the device is held when it is taken.

The most often used tools at home are the etched dosing cup and a 5 mL syringe. Both dosing cups and syringes with larger capacities are suitable for measuring large volumes of medication, but syringes were more accurate than measuring cups for small volumes (Norizan et al., 2021). Graduated dosing cups will utilize a different device for dose administration other than the dose administration spoons or the oral syringes for amounts above 5ml. Hence, there will be reduced errors for multi-dose preparations. However, the devices are associated with various drawbacks, such as sticking of remaining amount in the container, particularly "sticky" liquid.

Various studies show that there is a tendency for consumers to take incorrect dose in favor of the dose measuring cups in contrast to the other devices (Griessmann et al. 2007). Even though modern instruments are prone to wrong dosing; oral syringes offer the most accurate dosage and best method.

Solid dosage forms consist of tablets, capsules and others; these forms represent the most used and most economical presentation of oral dosage forms. Tablets scored can be split to allow alteration of dosage for individual patients. Unscored tablets must never be split. The fundamental aim of tablet splitting should be the alteration of dosage. The other aim is to optimize costs (Quinzler et al., 2006). Tablet splitting can pose several risks due to these risks the FDA cautions patients against unsafe splitting of tablets and issued guidelines from the pharmaceutical organizations on the safe splitting of tablets (FDA, 2009). The method of tablet splitting calls for careful processing if allowed (Breitkreutz et al., 2007). Patients can benefit from tablet splitting if the dosage needs to be altered. Nonetheless, tablet splitting is neither safe nor flexible; so, designers of tablets should improve the design to allow individual patient accuracy during treatment.

Patients can use powder through measuring spoons like the metering spoon for vitamin C powder. The dosage might be difficult to ascertain if the dosage indicators on the measuring device are hard to see. This leads to inaccurate dosage (Bauriegel et al., 2007).

1.4. The Advent of 3D Printing in Personalized Medicine

Many technologies are evolving to induce this paradigm change from traditional "one size fits all" to personalized treatment, with three-dimensional (3D) printing being the most prominent example. 3D printing is the process of creating a three-dimensional item layer by layer using computer software. 3D printing can be used to create a wide range of pharmaceutical dosage forms that differ in shape, release profile, and medication combinations. Inkjet printing, binder jetting, fused filament fabrication, selective laser sintering, stereolithography, and pressure-assisted microsyringe are some of the primary 3D printing technical platforms being investigated in the pharmaceutical industry (Marcia Vaz et al., 2021).

In 2015 for instance, the FDA approved the first ever drug made with 3D printing technology; this is a drug called Spritam®, which melts instantly in one's mouth, this is FDM technology— fused deposition modeling (Goyanes et al., 2016; Melocchi et al., 2016). This technology involves melting a polymer with a heating tool and extruding it through a nozzle layer by layer for a tablet to be made; such a tablet can be modified for varying drug release by altering its dimensions, shape, internal structures, or materials. 3D printing is also being investigated for its application in personalized medications. The technique offers customized doses, forms, controlled release formulation, and small-batch production (Andreadis et al., 2022). In hospitals, personalized medications according to patients' special needs can be produced using 3D printing. In pharmacies, medications can be produced on demand. This is because, through personalization, medications will be tailored according to patients' needs, thus reducing waiting time and improving treatment (Rodriguez et al., 2025).

Pharmaceutical Applications of 3D printing method that are very crucial in the production of various drug formulations such as fast-dissolving tablets (Tranova et al.,2022), controlled release tablets (Wang et al.,2023), gastric retention tablets (Jeong et al.,2020), suppositories (Awad et al.,2023), minitablets (Krause et al.,2021), medical devices, and multiple drug formulations (Mamo et al.,2023). This, therefore, makes 3D printing very relevant in the future of pharmaceutical products.

Various 3D printing technologies that are applicable in the medical sector include fused deposition modeling (FDM), direct powder extrusion (DPE), semi-solid extrusion (SSE), selective laser sintering (SLS), binder jetting (BJ), stereolithography (SLA), digital light processing (DLP), inkjet printing, and direct ink writing (DIW) (Bernatoniene et al.,2025).

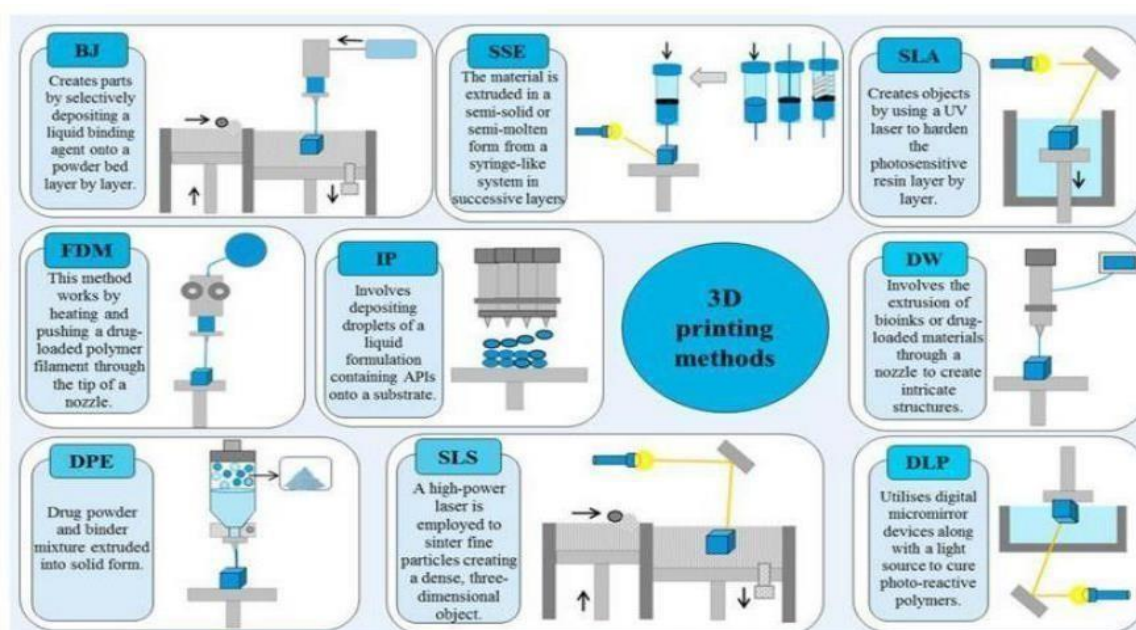


Figure 2: Overview of 3D printing methods for pharmaceuticals (Bernatoniene et al., 2025).

3D printing is highly adjustable and has the capacity to produce customized medications by altering the size, shape, or dosage of the drug content inside (Singhvi et al., 2018).

For patients who are on many drugs, it is possible to mix several drugs in one formulation to reduce errors. There are special designs or signs that would aid patients who cannot see properly. Manufacturers such as FabRx are already producing personalized drugs for children and testing them in hospitals (Goyanes et al., 2019).

3D printing technology is a revolution in healthcare, enabling the development of precision dosing and individualized medication forms like self-nano-emulsifying drug delivery systems (Bernatoniene et al., 2025).

Researchers have utilized this technology to create dosage forms with varied release profiles, enhancing the solubility and bioavailability of drugs such as dapagliflozin and glimepiride. Furthermore, this technology has been used to develop drug delivery devices like controlled-release shells, demonstrating the potential of 3D printing in personalizing medication regimens (Bernatoniene et al., 2025).

Other than the active manufacturing of tablets through 3D printing, it is also possible to integrate this technology to improve more traditional manufacturing methods. 3D printing-assisted manufacturing generally refers to the young 3D printing technology in manufacturing customized molds and dies, while additional modifications affect the design and layout of the tablet. A study by Ajamal et al. (2019) involved the use of four different 3D prints of mold designs done using computer-aided design software and 3D printing using polylactic acid (PLA). The hydroxypropyl methylcellulose (HPMC) and polyethylene glycol (PEG)-based formulation containing indomethacin as the active pharmaceutical ingredient (API) was poured into the molds. Some of them were designed with thin break lines; this was done for them to break into 2, 4, or 6 pieces once they had fully melted.

The study of Ajamal et al. demonstrated how tablets snapped because of such design, while those tablets which broke in more pieces might take less control of the drug release.

This approach can help in designing tablets with the ability to release the drug at the specified rates, thus improving personalized medicine (Ajamal et al., 2019).

This study investigates the testing of polymeric tablets prepared in 3D printed molds regarding their ability to explore using 3D printed molds in the preparation of oral solid dosage forms.

1.5. Problem Statement

There are currently few options for producing customized dosage forms for pharmaceuticals, among them 3D printing which may offer a chance to close a gap in the production of customized dosage forms, whether it is used to create tablets or molds for casting tablets. There is currently insufficient research on 3-3D printing assisted molding.

1.6. Aims and Objectives

The objectives of this study are:

1. Preparation of the tablet molds using Fused Deposition Modeling (FDM) 3D printing.
2. Preparation of the tablets' blend using hydroxypropyl methyl cellulose (HPMC) as the API carrying polymer with PEG as plasticizer. The design involves different ratios of polymer to optimize the tablets' characteristics.
3. Molding of the tablets in the prepared molds made by the 3D printing technique.
4. Evaluation of the result tablets in terms of drug assay, friability, hardness, and drug release.

Chapter Two: Literature Review

Hamburg & Collins et al., 2010 and Schork, 2015 showed that personalised medicine (PM) enables “the right treatment for the right person at the right time” as patients are treated for their biological, genetic, or demographic characteristics. PM clinical trials need precise research methods for correct targeting of study volunteers and appropriate medications. A review of existing research design efforts for this research area forms a basis for better suggestions for personalized medicine clinical research.

Chung, 2017; Mascaux, 2017 and Bonsignore, 2017 found that the concept of personalized medicine impacts all domains of respiratory medicine, such as asthma, chronic obstructive pulmonary disease, bronchiectasis, pulmonary cancer, interstitial lung disease, pulmonary vascular disease, pulmonary sleep disorders, and pulmonary rehabilitation. These applications are all based on humanomics methods and biological systems related to the disease being assessed. When combined, these studies show how much personalized medicine can improve respiratory healthcare.

Meisel, 2016 and Middleton, 2018 explained that personalized medicine is gradually being incorporated with traditional clinical medicine, especially in cancer care. Patients and the public's acceptance and involvement are essential to their success. Evidence has indicated that patients have a better understanding and acceptance of personalized medicine compared to the general population although misperceptions surrounding genetic testing were prevalent.

Personalised medicine (PM), Ashley, 2016 and Jameson & Longo et al., 2015 showed that arose from recognition of differences existing at a molecular, physiological, environmental, and behavioral level among individuals, which needed designed interventions. Breakthroughs in genome sequencing, proteomics, imaging, and digital biomedical technology have been characterised by a great degree of variability among individuals.

Despite some success, problems exist regarding accessibility. Although PM has potential in improving health outcomes, there is potential related to high costs and unclear cost-effectiveness associated with personalized medicine.

Isaacs, 2016 showed that in Rheumatoid Arthritis; Biological drugs with the aim of various molecular pathways have shown equal efficacy in patients. Present biomarkers have limited predictive capability beyond clinical disease activity, suggesting that innovative research design needs to be pursued to discover novel biomarkers to distinguish personal treatment approaches.

Phillips, 2014 found that there remains significant uncertainty about how to assess the value of personalised medicine because of the different methods of economic evaluation. The establishment of guidelines is important to improve the quality of the economic evaluation of personalised medicine.

Nicholson, 2012 and Everett, 2015 showed that Pharmacometabolomics is the integration of the result of drugs on metabolism and combines the concepts of pharmacoproteomics and pharmacogenomics.

Pavan, 2023 found that 3D printing enables quick design, bioprinting, and manufacture in comparison to traditional techniques. Layer-by-layer deposition of a predetermined, flexible polymer in a range of geometries, thicknesses, release profiles, and configurable designs is used to build compositions for pharmaceutical producers. The foundations of 3D printing are examined in this examination before moving on to techniques and tactics. The justification for customized medications is the main focus. Applications for 3D printing integrated customized delivery and devices include medical implants, multidrug composition, dose customisation, modified release systems, and customization for certain demographics.

Dolores, 2023 showed that 3D printing technology makes it possible to customize medications to meet the needs of individual patients. Although there are a number of 3D printing methods, nozzle-based extrusion, laser writing systems, and powder binder jetting are used to print the majority of dosage forms and medical devices. Solid, semi-solid, and locally administered or implanted medications are among the many applications of 3D printing that have been shown to be in development.

To enhance patient compliance, facilitate deglutition, customize the release profile, or create new medications for which no dosage form is currently available, 3D-printed solid dosage forms enable the mixing of one or more drugs within a single solid dosage form. Cardiovascular applications, medical prosthesis, and joint replacement treatments have been the primary uses for sustained-release 3D-printed implants, stents, and medical devices. Medicated contact lenses, microneedles, and wound dressings are examples of locally applied medications that have also been produced by 3D printing. Choosing the best 3D printing method for each application and the kind of pharmaceutical ink that should be created with the necessary physicochemical and biological performance are difficult tasks. When biopharmaceuticals and nanotechnology-based medications are combined with 3D printing, or "nanoprinting," printed tailored nanomedicines become one of the most revolutionary ideas for the years to come.

Kalyani,2023 found that 3D printing makes it possible to fabricate biological structures, medical devices, and implants with high precision, improving treatment accuracy and lowering clinical risks. The technology also aids in the creation of customized drug delivery plans meant to maximize therapeutic effectiveness. Even with these encouraging developments, issues with material biocompatibility, legal frameworks, and economic viability continue to be major obstacles to broad adoption. To overcome these obstacles, the review emphasizes the need for interdisciplinary cooperation between researchers, medical professionals, industry stakeholders, and regulatory bodies. According to the study's findings, 3D printing has the potential to significantly improve healthcare outcomes and personalized treatment plans, making it a game-changing tool in contemporary biomedical practice.

Lorca,2023 explained that three-dimensional (3D) printing has demonstrated substantial potential in healthcare by enabling customized drug delivery systems, patient-specific implants, prosthetics, and biofabricated tissues, leading to improved patient outcomes. The integration of nanotechnology has further enhanced drug delivery accuracy and material biocompatibility.

Additionally, 3D printing supports cost-effectiveness and sustainability through efficient material utilization and recycling. By facilitating personalized medical solutions across diverse applications, including implants, radiation shielding, and drug delivery, 3D printing promotes a patient-centered healthcare model. However, challenges related to material biocompatibility, standardization, and ethical considerations must be addressed to ensure its responsible and widespread implementation.

Alomari, 2015 and Norman, 2017 showed that three-dimensional printing is one of the most prominent driving forces in transitioning from traditional “one-size-fits-all” therapy towards personalised medicine. It allows for the constricting of tailored dosage forms of medications with individually selected doses, shapes, release kinetics, and combinations. Different 3D printing methods are being explored for their applicability in pharmacy. However, certain constraints need to be overcome for it to become applicable on a clinical scale.

Trenfield, 2018 and Awad, 2019 found that the results of improvements in pharmacokinetic and pharmacogenomics areas also strengthened the need for personalized medicine. Three-dimensional printing is an attractive technology for manufacturing because it has the capacity for the safe, flexible, and inexpensive preparation of customized dosage forms. This technology has the "personalised medicines" that are accessible down to the pharmacy level. Though there are some disadvantages to modern methods of manufacturing, which must be overcome to achieve success, coupled with Biopharmaceutics in 3D printing has immense future scope in PM.

Ventola, 2014 and Li, 2020 explained that three-dimensional printing has numerous revolutionary applications in personalized healthcare, such as customized drug delivery systems, improved implants, prosthetics, and bio fabrication. The combination with nanotechnology enables improved specificity, biocompatibility, and efficacy for drug delivery. The technology enables patient-centric healthcare in addition to promoting cost-effectiveness and sustainability. Nevertheless, its constraints in regard to material biocompatibility, standardization, and ethics should be managed for proper adoption.

According to Goyanes, 2016 and Scoutaris et al.,2018 explained that three-dimensional printing is currently revolutionizing the pharmaceutical industry as it is now capable of producing customized medications based on the characteristics of patients, such as age, weight, co- morbidities, and pharmacogenetics. There are three methods currently used: inkjet printing, nozzle-based deposition, and laser-based writing. However, some of the disadvantages include the limited availability of appropriate polymers and the need for compatibility of drug properties with printing needs. It is very crucial to understand the approaches and the corresponding materials to achieve success in the production of customized medication. With regards to the application of 3D printing within personalized medicine, according to Prasad & Smyth in 2016, the process is still slow. This is due to the difficulties related to cost and privacy concerns. There is a need to come together to achieve success within the three parties: researchers, practitioners, and regulators. The FDA has been promoting the coming together of stakeholders to resolve these difficulties. 3D printing is a technology that cannot replace traditional treatments on its own but will serve as supplementation within personalized medicine.

However, according to Chen, 2022 and Zhang, 2021 studies conducted on 3D printing in customised medicines have shown increased momentum in terms of number and scope between 2012 and 2022. The United States and United Kingdom have emerged as pioneering nations in 3D printing studies. Some key contributors to such studies include University College London and the International Journal of Pharmaceutics. Some of the latest trends in 3D printing studies include release and formulation studies and thus its unparalleled utility for developing personalised medicines.

Jamróz, 2018 and Seoane-Viaño, 2020 showed that three-dimensional printing facilitates customized dosing of medications for the purpose of addressing individual patient requirements through methods such as extrusion-based printing, laser writing, and powder binder jetting. It also facilitates the preparation of solid, semi-solid, locally administered, and implantable formulation of medications in customized combinations with controlled release of the medications to ensure patient compliance. Its application includes sustained release of implants, medical devices, as well as locally administered products such as microneedles, contact lenses, and topical dressings for wounds. Despite many difficulties in deciding on printing techniques and formulation combinations, nanotechnology.

Murphy and Atala, 2014 and Vijaya Venkataraman, 2018 showed that the use of 3D bioprinting is revolutionizing personalized medicine with innovative approaches for personalizing transplant practices, tissue reconstruction, medication discovery, surgical simulations, and educational modeling for healthcare professionals. The current study has shown the benefits of various bioprinting techniques while accepting current impediments that should be conquered for their use in practical healthcare practices. The use of 3D bioprinting has vast potential for establishing a base for future personalized healthcare practices.

Norman, 2017 and Alhnan, 2016 found that three-dimensional printing is altering the way medications are distributed because it is possible to have customized dosages, complex mixtures of drugs, and formulations manufactured based on demand. In this regard, unlike previous approaches, 3DP could provide personalized medications based on an individual's requirements, which may serve as a supplement or replacement for existing medications. The differences in 3DP techniques provide varying benefits as well as disadvantages. These differences may be noted in the formulation, release, and control of drugs. In short, 3DP carries immense challenges and opportunities and bright prospects in the field of personalized medicines.

Konta, 2017 and Lamichhane, 2019 explained that additive manufacturing (3D printing) is also revolutionizing the pharmaceutical sector as it allows to produce customized medications on- demand via FDM, SSE, SLA, SLS, inkjet, and binder jetting. However, there are still limitations related to the materials, scalability, reproducibility, and adaptability to regulation that still require further investigation. With the adaptability challenges and incorporation with AI, there is great potential for 3D printing to allow hospitals and medical clinics to manufacture their own tailor-made medications on demand as it can distribute the drug manufacturing sector.

Young & Lovell, 2011 and Mark, 2007 showed that the development of polymer materials has significantly transformed engineering by replacing traditional materials and enabling novel applications that expand human capabilities. Over the past century and a half, plastics have emerged as the most dominant class of polymers, followed by fibers and elastomers.

Gauthier, 2004 and Nicolas, 2013 found that recent advances in polymer bioconjugation, which involves the covalent attachment of synthetic polymers to biological objects such as proteins, nucleic acids, enzymes, carbohydrates, viruses, or cells, have been achieved. Initially driven by the biological interest community in the biomedical applications community, the polymer bioconjugate has currently flourished in the materials science community.

The most recent methodologies, such as clicking reactions, ring opening metathesis polymerization, and controlled radical polymerization, have enabled the preparation of highly customized polymer bioconjugates, echoing the most important progress in polymer science.

Description, Rubinstein & Colby et al., 2003 found that polymers are described as large molecules with covalently bonded units in long chains, and their unique properties arise from their structure. This key text relies on modern polymer physics theory. The text discusses scaling theory, concentration fluctuations, gels, reptation, and statistical aspects of chain formation. The text is a crucial resource for advanced undergraduate and graduate-level students who study polymer physics.

The 2019 polymers developed by Zhang find specific applications in laser ablation because the material has the capability to be melted and vaporized at high temperatures. Various polymer substrates have been considered for laser ablation technology, thus enabling the creation of multiple micro- and nanostructures. The present study focuses on the mechanism of laser ablation, the types of lasers, the factors at which the results depend, the choice of material, and the applications.

Makadia & Siegel, 2011 and Woodruff & Hutmacher et al., 2010; this study also points to the similarities and differences that exist in the degradation process for polymeric coatings and bulk polymers. It discusses biodegradable polymers that are widely used in drug delivery systems. A literature survey has been conducted in this study to evaluate biodegradable polymer degradation by mass loss measurement, surface analysis, and chemical analysis. Current research is needed for a better understanding of dynamic degradation in biodegradable polymeric coatings.

Laurichesse & Avérous et al., 2014 and Thakur, 2014 found that the use of lignin in thermoplastic polymers is viewed as a viable method of converting lignin to high-quality lignin. It is necessary to highlight the use of lignin in structural and functional forms of thermoplastic polymers, in which modifications are required. Methods of copolymerization of lignin, as well as the utilization of lignin in thermoplastics, will be noted.

The applications of sequence-defined polymers have received widespread attention in the fields of material science, chemistry, and biological sciences. The knowledge of the microscopic details of sequences, configurations, self-assembling properties, as well as phase separation phenomena in sequences is paramount for the application of the inverse design of sequences. The recent achievement in the application of machine learning algorithms in the simulation of molecular dynamics in sequences has allowed for the efficient exploration of the relationship between sequences and properties.

Chapter Three: Materials and Methods

3.1. Chemicals and Equipment

All chemicals and reagents used in this research were of analytical grade and were used as received without further purification. Sodium chloride (NaCl) was obtained from Loba Chemie® (India). Hydroxypropyl methylcellulose (HPMC) was supplied by Global Tech®. Polyethylene glycol 1500 (PEG 1500) was purchased from Hayat® (Jordan). Hydrochloric acid (HCl) was obtained from Merck® (Germany), while paracetamol was supplied by BBC Biochemical® (United States).

The equipment utilized in this thesis included a friability tester (Model CS-2) supplied by Tianjin City Optical® (China), a tablet hardness tester (Model THT-1) from Biobase® (China), and a UV–Visible spectrophotometer supplied by BEL Photonics® (Italy). An INCU-SHAKER 10LR incubator from Benchmark Scientific® (USA) was used during dissolution and mixing procedures, and voltage stability was ensured using an SVC-1500VA voltage stabilizer supplied by Taileoik® (China). All instruments were operated according to the manufacturers' instructions.

3.2. Calibration Curve of Paracetamol

The calibration curve of the paracetamol was done using a wavelength of 242 nm. The calibration curve was created by reading the UV-Vis absorbance levels of the paracetamol samples with concentrations of 1, 2, 2.5, 5, 6, 8 mcg/ml. Each concentration was analyzed in triplicate, and the absorbance values were taken three times, then calculated average and standard deviation. The software used in the analysis was Microsoft Excel 2016. The output produced in the excel software included the linear equation and R^2 value.

3.3. Preparation of tablets

Table 1: Detailed quantitative composition of HPMC-based paracetamol tablet formulations prepared at different polymer concentrations (10–40% w/w), specifying the amounts of polymer (HPMC), active pharmaceutical ingredient (paracetamol), plasticizer (PEG), solvent composition (water–ethanol), and final preparation volume.

Sample (%W/W)	HPMC (%w/w)	Paracetamol (mg)	PEG (%w/w)	Solvent composition	Total volume (mL)
F1 10% W/W	87.80	125	9.76	25 mL water+25 mL ethanol	50
F2 20% W/W	88.89	125	9.88	25 mL water +25 mL ethanol	50
F3 30% W/W	89.26	125	9.92	25 mL water+25 mL ethanol	50
F4 40% W/W	89.44	125	9.94	25 mL water+25 mL ethanol	50

Tablets were prepared using different polymer concentrations of HPMC at 10, 20, 30, and 40% w/w. For each formulation, a fixed amount of paracetamol (0.125 g) was used, while the amount of HPMC was increased proportionally from 4.5 g to 18.0 g, polyethylene glycol (PEG) was incorporated as a plasticizer in amounts ranging from 0.5 g to 2.0 g. The solvent system consisted of a hydroalcoholic mixture of distilled water and ethanol in a 1:1 ratio (25 mL water and 25 mL ethanol), giving a total volume of 50 mL for all formulations. This approach allowed the evaluation of the effect of varying HPMC concentrations on tablet preparation while maintaining constant drug content and solvent volume. After pouring these mixtures into 3D printing molds, the prepared mixtures were left to dry under suitable conditions. Embossing features were incorporated in the mold to ensure proper formation of the tablets.

3.4. Mold printing

The tablets were printed using a FDM 3D printer. Nozzle temperature: 200 °C, build plate temperature: 55 °C, layer height: 0.2 mm, printing speed: 60 mm/s.



Figure 3: Creality Ender-3 (FDM 3D Printer)

3.5. Friability of tablets

Friability test were carried out using the pharmacopoeial method. The tablets for each formulation were accurately weighed and rotated using a friability apparatus for 3 tablets for 4 minutes at a speed of 25 RPM. The tablets were then removed, dedusted, and reweighed for calculation of friability as equation demonstrated below:

$$friability = \frac{Initial\ weight - final\ weight}{Initial\ weight} \times 100$$

[equation 1]

3.6. Hardness of tablets

Hardness test were carried out using the pharmacopoeial method. Tablet hardness was evaluated on 3 tablets using a standard hardness testing method. The prepared tablets were individually placed in a manual hardness tester, where a gradually applied compressive force was exerted by a slowly compression plate. The force at which each tablet slipped one was accurately recorded as the tablet hardness.

3.7. Dissolution method

The dissolution test was conducted in accordance with the United States Pharmacopeia.

Apparatus and Conditions:

- Apparatus: USP Dissolution Apparatus II (Paddle)
- Dissolution Medium: 900 mL of phosphate buffer pH 6.8 and PH 1.2
- Temperature: 37 ± 0.5 °C
- Paddle Speed: 100 rpm
- Sampling Times: every 10 minutes
- Sample Volume: Defined volumes withdrawn at each time point
- Analysis: UV-visible spectrophotometry at the appropriate λ_{\max} for paracetamol
- Replacement: After each withdrawal, an equal volume of fresh medium at 37 °C was returned to the vessel to maintain constant volume.

Chapter Four: Results

4.1. Calibration Curve

The calibration curve presents straight-line graph between paracetamol concentration and absorbance.

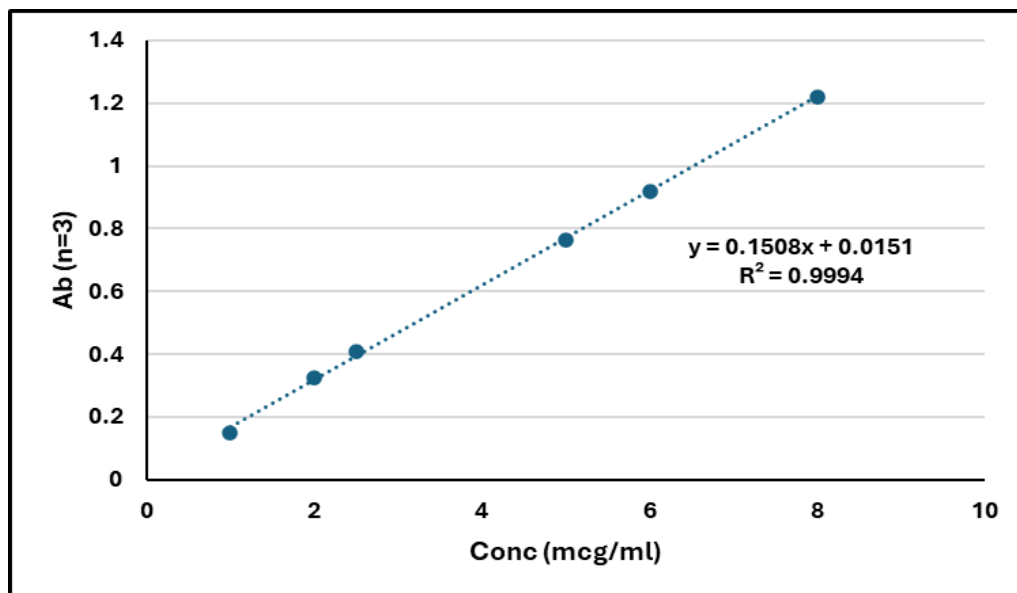


Figure 4: Calibration curve of paracetamol (n=3, 0.631 ± 0.0135)

Table 2: Analytical calibration data for paracetamol, showing replicate absorbance measurements (a1–a3), mean absorbance (AV), standard deviation (SD), and relative standard deviation (RSD) at different concentrations.

Concentration (mcg/ml)	a1	a2	a3	AV	SD	RSD
1	0.15	0.153	0.149	0.151	0.002	0.014
2	0.32	0.33	0.32	0.323	0.006	0.018
2.5	0.4	0.41	0.41	0.407	0.006	0.014
5	0.76	0.756	0.78	0.765	0.013	0.016
6	0.91	0.92	0.93	0.92	0.01	0.011
8	1.22	1.23	1.21	1.22	0.01	0.008

Our calibration curve is a straight line with an R^2 of 0.9994. The range was a straight line, and it ranges from 1 to 8 mg/ml.

The analytical method for determination of paracetamol was validated in accordance with ICH guidelines, focusing on linearity. Linearity was assessed by analyzing standard solutions at six concentration levels ranging from 1 to 8mg/ml.

The calibration curve demonstrated a direct and proportional relationship between concentration and absorbance over the studied range, confirming the linear behavior of the method.

Precision was evaluated through repeatability by analyzing each concentration in triplicate. The low standard deviation and relative standard deviation (RSD) values obtained at all concentration levels indicate good repeatability and acceptable precision of the method. The consistently low RSD values, all within acceptable limits, confirm that the method produces reliable and reproducible results. Overall, the validation results demonstrate that the proposed analytical method is precise, linear, and suitable for the quantitative analysis of paracetamol.

4.2. Tablet formation

A uniform tablet matrix could not be obtained in the 10% and 20% formulations. As shown in Figures 6, 7,8 & 9.

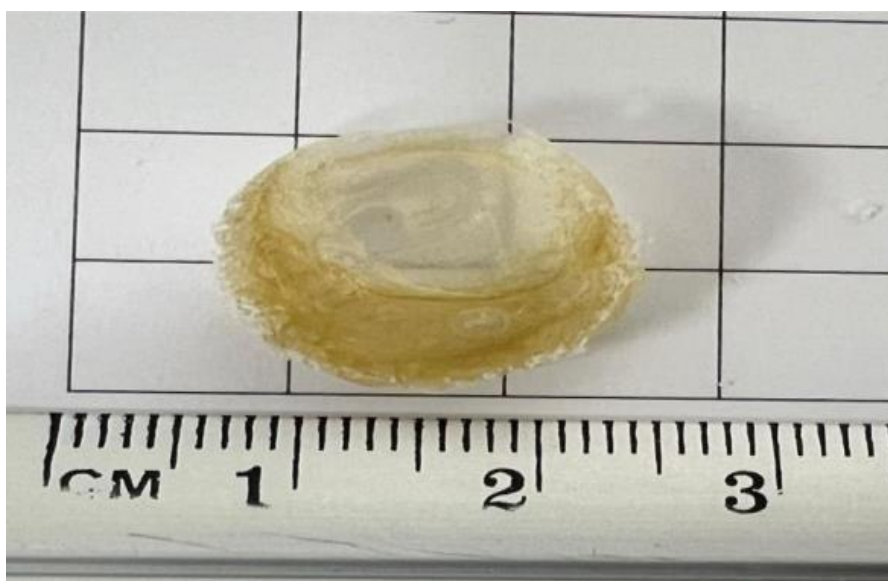


Figure 5: (F1) 10%w/w formulation

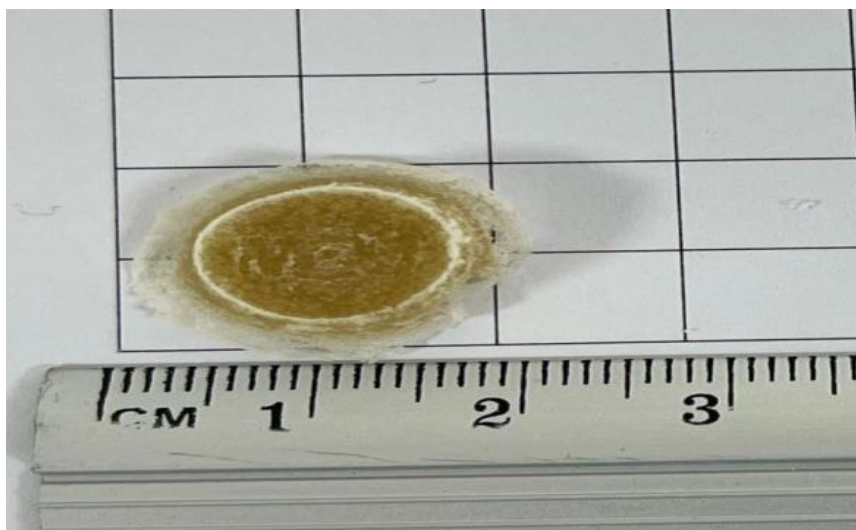


Figure 6: (F2) 20%w/w formulation

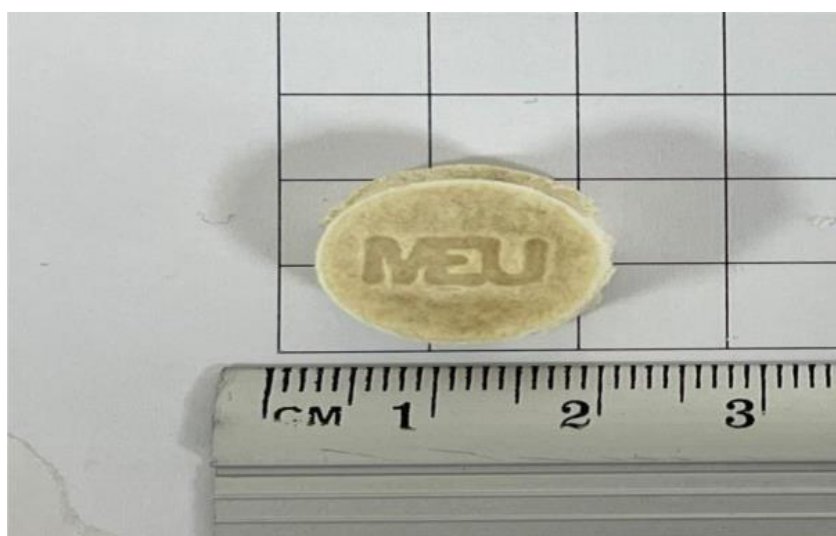


Figure 7: (F3) 30%w/w formulation



Figure 8: 40%w/w formulation

Formulation 10%, 20% were not successfully form in uniform tablet matrix

4.3. Mold printing

The mold's computer-aided design (CAD), which is utilized in the production of paracetamol tablets. To guarantee exact dimensional control and dosage form reproducibility, 3D modeling software was used to design the mold. A cylindrical base cavity and a matching lid/pressing plate engraved with the desired tablet imprint make up the design's three parts : body,lid and bottom. The top and bottom components share the same circular geometry to ensure proper alignment and uniform tablet formation.

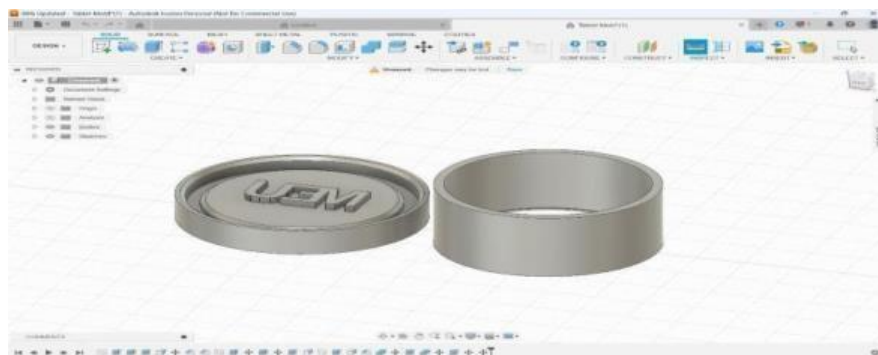


Figure 9: Design of mold of paracetamol

4.4. Friability test

In both the 30% and 40% formulation, the loss on friability testing was less than 1%. As can be seen in Table (3)

Table 3: Friability test results

30%		40%	
Weight before	Weight after	Weight before	Weight after
0.703	0.643	0.784	0.790
0.649	0.659	0.802	0.859
0.619	0.699	0.829	0.780
0.647	0.645	0.864	0.818
0.660	0.618	0.794	0.799
0.638	0.636	0.823	0.800
Average Loss 0.34% STD=0.0280		Average Loss 0.83% STD=0.0285	

4.5. Hardness test

Table 4: Hardness test results

30%w/w	40%w/w
6.790	5.741
6.470	8.840
3.290	2.520
Average=5.517 STD=1.935	Average=5.700 STD=3.161

The hardness test results for the formulated tablets are summarized in Table 4.

For the tablets containing 30% w/w polymer, hardness values of 6.790 g, 6.470 g, and 3.290 g were recorded. In comparison, tablets formulated with 40% w/w polymer exhibited hardness values of 5.741 g, 8.840 g, and 2.520 g. These results demonstrate variability in tablet hardness within each formulation, reflecting differences in mechanical resistance among individual tablets.

During the hardness test, the tablets did not exhibit complete fracture; however, the maximum hardness value was not recorded because the tablets slipped from the tester before full breakage occurred. Consequently, the hardness values reported in the table represent the final recorded readings obtained immediately prior to tablet displacement.

4.6. Dissolution test

Table 5: Dissolution data of paracetamol tablets, showing absorbance values recorded at predetermined time intervals for three independent samples (Tablet 1 – Tablet 3) during the in vitro dissolution study.

Time (Minute)	Tablet 1	Tablet 2	Tablet 3
0	0.044±0.019	0.009±0.019	0.041±0.019
10	0.020±0.089	0.100±0.089	0.199±0.089
10	0.133±0.023	0.106±0.023	0.151±0.023
15	0.157±0.054	0.110±0.054	0.050±0.054
10	0.060±0.038	0.005±0.038	0.079±0.038
15	0.072±0.036	0.014±0.036	0.081±0.036
30	0.091±0.044	0.030±0.044	0.116±0.044
30	0.092±0.043	0.045±0.043	0.130±0.043
60	0.129±0.048	0.055±0.048	0.146±0.048
60	0.209±0.077	0.068±0.077	0.083±0.077
60	0.187±0.065	0.076±0.065	0.191±0.065
60	0.249±0.081	0.092±0.081	0.205±0.081

The dissolution test was done for the two concentrations: 40% and 30%, for 6 hours. The drug release of the 40% formulation was 6.22%, while that of the 30% was 5.59%, though in slow sustained release, with less than 3% for the six hours for both percentages. No difference was detected in drug release for the 30% and 40% preparations. The 40% formulation had greater variability between replicates, with higher standard deviations of 1.58% than standard deviations of 0.48% for the 30% formulation.

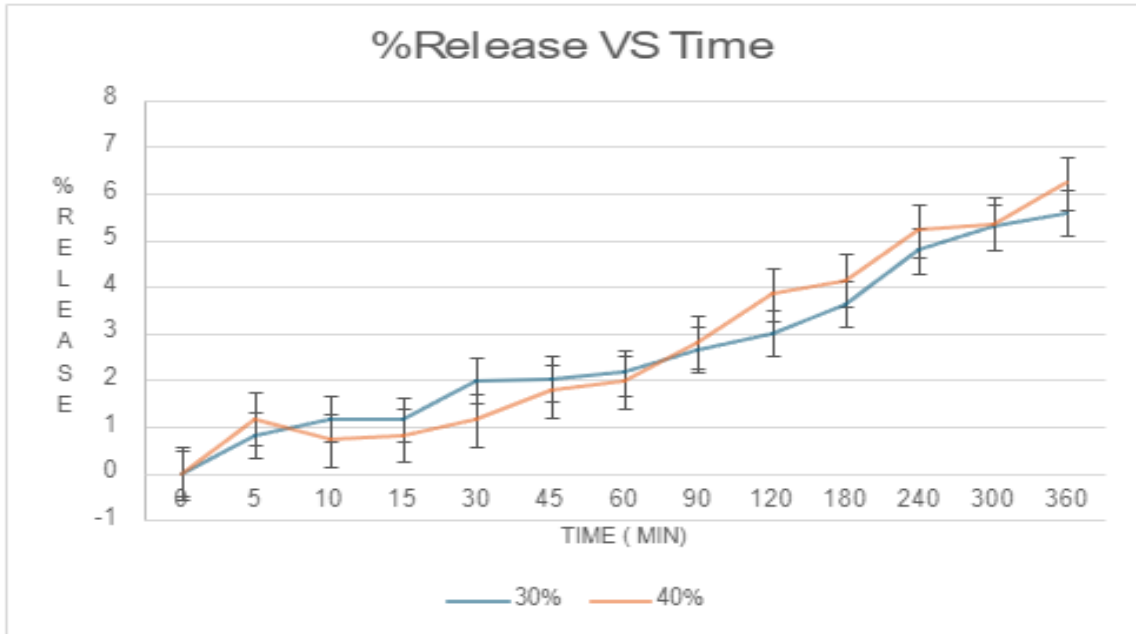


Figure 10: Percentage release over time for two different concentrations (30% and 40%) HPMC in dissolution apparatus at PH=6.8, rpm=100, temperature=37±0.5°C

Chapter five: Discussion

5.1. Tablet printing

Formulations with a 10% and 20% polymer failed to prepare tablets successfully; this shows there was not a sufficient binding capacity in these concentrations. This shows there was a lack of particle cohesion in 10% and 20% polymer concentrations; this aligns with findings suggested in previous studies for (Aulton and Taylor et al., 2018; Lachman et al., 1986) to provide a sufficient binder concentration for tablets to be successfully prepared. The 30% and 40% polymer concentrations perfectly prepared tablets and thus were chosen to proceed with the experimental study.

From the results obtained, the conclusion can be drawn that choosing an optimal concentration of the polymer and adequate plasticizer concentration is equally important in overcoming the challenges of formulation. The results obtained are in correlation with previous studies and support the fact that both 30% and 40% formulations work.

5.2. Friability and Hardness tests

Friability tests revealed a weight loss of less than 1% in both formulations, satisfying the limits set by the pharmacopeial standards, and it can be concluded that both tablets possessed good resistance and hardness.

These results have also been supported by other studies in the literature, where an improvement in tablet hardness and reduction in friability were observed with an increased concentration of polymers (Rowe et al., 2009). In addition to this, a greater concentration of polymers also led to a better difference between the two formulations, especially in relation to their integrity, mechanical properties, and overall performance.

From the hardness test result, the mechanical strength of all the tablets was revealed to withstand the applied mechanical pressure without any cracking or breakage. The results obtained are within the acceptable range depicted in literature studies of conventional compressed tablets.

For the pharmacopeial requirements to be met, compressed tablets are expected to exhibit hardness values typically between 4 and 10kgf (United States Pharmacopeia). Hence, the mechanical strength result has proved the tablets to exhibit sufficient hardness and mechanical strength (Aulton et al., 2015).

5.3. Calibration curve

It depicts a straight-line graph between concentration and absorbance. The graph passes through the origin and has an R^2 value of 0.9994, indicating the data has very high precision over the concentration range from 1mcg/ml to 8 mcg/ml. The graph is useful in determining the concentration of an unknown solution since changes in concentration result in remarkable changes in the absorbance.

5.4. Dissolution test

There was no significant difference observed regarding the dissolution rate of 30% vs. 40% formulation over a period of 6 hours. This is because both formulas show dissolution releases in the first 45 minutes, possibly because of surface dissolution, and thereafter, there is controlled dissolution, possibly because of diffusion, and there is high reproducibility in the 30% groups, showing less standard deviation, whereas high standard deviation is shown by the 40% groups, especially, possibly because of degradation or agglutination at higher concentrations. The sustained release formula is because there is no porosity present in the cast tablet formulation.

Chapter six: Conclusion

This study effectively illustrated a novel strategy for pharmaceutical preparation that combines conventional tablet formulation with contemporary FDM-based 3D printing technology. The successful design, formulation, and evaluation of HPMC-based paracetamol tablets demonstrated that polymer concentration plays a crucial role in regulating the dosage forms' physical properties and drug-release behavior. To ensure constant tablet geometry and bridge the gap between digital design and physical pharmaceutical compounding, a Creality Ender-3 printer was utilized to produce highly reproducible and economical molds.

To ensure accurate drug content and dissolution measurement, a robust UV–Vis spectrophotometric technique at 242 nm with outstanding linearity ($R^2 = 0.9994$) supported the analytical evaluation. After being plasticized with PEG 1500, the produced formulations (10–40% w/v HPMC) exhibited regulated drug-release behavior in phosphate buffer media (pH 1.2 and 6.8) and satisfied USP physical quality standards. The release mechanism was predominantly controlled by HPMC swelling and diffusion, hence validating the function of hydrophilic polymer matrices in regulating the release of paracetamol.

The study's overall findings position 3D-printed molding systems as a useful and expandable instrument for pharmaceutical research, providing a platform that may be tailored for future uses in customized medicine and controlled drug delivery.

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