JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

3D PRINTING IN TABLET DOSAGE FORM

Ms. Kalyani balnath dukare,Dr.kiran B.dhamak, Ms. Monali balasaheb shelke,

Final Year of B Pharmacy Assistant professor of pharmaceutical chemistry, Final Year of B Pharmacy
, ,

Department of Pharmacy,
PRES'S Collage of Pharmacy (For Women), Chincholi ,Nashik ,India.

Abstract:

The rise of three-dimensional (3D) printing represents an exciting advancement within the pharmaceutical sector, enabling enhanced levels of accuracy, adaptability, and customization during medication production. This innovation allows for the development of intricate medication delivery systems featuring precisely timed releases and customized dosages suited specifically to each patient's medical requirements. Following the FDA authorization of Spritam®, there is an increasing focus on utilizing additive manufacturing techniques to create personalized medications and innovative therapeutic formulations.

Using sophisticated methods like fused deposition modeling (FDM), semi-solid extrusion (SSE), stereolithography (SLA), and binder jetting, three-dimensional printers enable the creation of various tablets, encompassing immediate-, sustained-, delayed- and pulse-releasing varieties. With these technological tools, pharmacological researchers can meticulously construct molecular architectures affecting drug release speeds, absorption levels, and overall treatment effectiveness. Additionally, 3D printing facilitates quick model creation, cutting down on both timelines and expenses during pharmaceutical research without hindering personalized manufacturing for individual patients.

Nevertheless, significant hurdles remain for broad industry acceptance of this tech. Major obstacles encompass insufficient access to appropriate bio-compatible substances, absence of standardized procedures, substantial expenses for machinery, sluggish manufacturing rates, and intricate legal requirements. Furthermore, sustaining uniformity in products along with ensuring high-quality control throughout production runs is still an important issue.

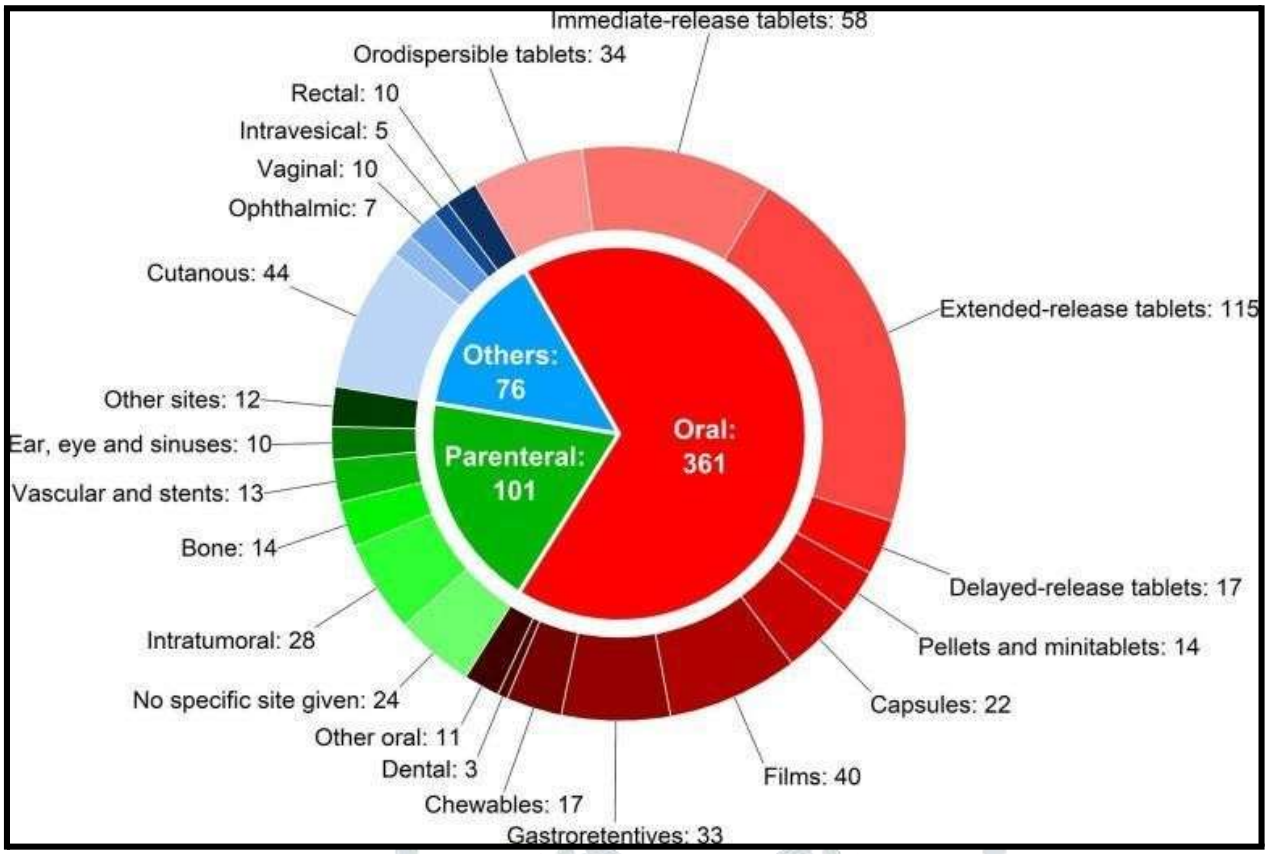
Although there are current constraints, 3D printing demonstrates considerable potential in advancing personalized healthcare strategies. As material sciences, AI, and pharmacogenomics continue to evolve, they anticipate playing an indispensable part in shaping future pharmaceutical production methods – revolutionizing how drugs are developed, manufactured, and distributed globally among patients.
Keywords: Three-dimensional (3D) printing , Drug delivery systems , Fused Deposition Modeling (FDM) , Semi-Solid Extrusion (SSE) , Personalized medicine , Controlled drug release , Pharmaceutical formulation.

Introduction

The enthusiasm for 3D printing has surged significantly within recent years. Technological advancements, often referred to as an emerging industrial shift, have begun impacting the pharmaceutical sector due to the U. S. Food & Drug Administration's endorsement of the world's first 3D-printed medication, Spritam®, introduced in 2015. Even though they achieved an important breakthrough, none of the newly developed 3D-printed medications has received regulatory clearance either from the U. S. Food & Drug Administration (FDA) or European Medicines Agency (EMA), despite ongoing efforts by firms like Triastek in testing their innovative formulations for clinical use. The ability of 3D printers to offer fine-grained manipulation of both

inner and outer structures within pharmaceutical formulations surpasses what conventional production techniques can typically accomplish efficiently. This accuracy allows for distinct shapes, predictable medication release schedules, and adaptable dosage changes while maintaining unchanged manufacturing equipment. Despite substantial advantages, present constraints like sluggish output speeds and exorbitant expenses hinder widespread industrialization efforts. Nevertheless, in cases requiring customized therapies on an individual scale, 3D printing provides both uniformity and affordability compared to traditional pharmaceutical formulation methods. As advancements in pharmacogenomics and AI-driven prescription systems increase, there's anticipated growth in the need for customized medication formulations. Organizations such as the Food and Drug Administration have been tackling these issues since before this year's report by examining it for insights into how they can address problems related to bedside manufacturing using 3D printers for healthcare equipment. Differentiating among various types of three-dimensional printing methods hinges upon their approach in depositing and fusing material layers together. As per ISO and ASTM standards, primary classifications include: The process of MEX involves forcing raw materials out via an opening in a tube-like device. Types encompass Filament Extrusion (FE), which utilizes already prepared filament materials through either hot melt extrusion or fused deposition modeling techniques commonly referred to as FDM. The Syringe Extrusion process: Utilizes pressurized or mechanically applied forces to create semisolid substances; typically necessitating subsequent drying steps for completion. The Screw Extruder (SEX) employs an auger design for shaping fine powders into desired forms. Two. In MJT technology, thin layers of melted or fluid materials like inks or electrically charged liquids are laid down atomistically through jets. Three items have been listed here. Binder jetting utilizes an adhesive substance dissolved in water to bind together individual powders into solid structures through sequential layer-by-layer deposition of material onto a moving platform. Four. Selective Laser Sintering combines powdered materials through focused light energy into solid structures. Five. Photopolymers undergo crosslinking through exposure to UV radiation in vat polymerization technology, such as those used for 3D printing techniques like SLA or DLP. Every approach boasts distinct advantages and drawbacks; thus, selecting an option hinges upon factors such as its application context, medication category, and desired administration format. Recent developments have spotlighted an innovative approach called 4D printing technology. Using this method, pharmaceuticals in tablet form may alter both appearance and performance gradually due to external factors like heat or acidity levels changing conditions around them. Choosing materials is still an important factor. Some methods utilize common medicinal ingredients as additives, whereas others necessitate unique polymers or resin materials for which thorough safet essments are required. Furthermore, it is crucial for both equipment designs and processes to adhere strictly to stringent pharmaceutical production regulations in order to guarantee product efficacy and obtain approval by authorities. Remarkably, there has been an announcement of FDA-licensed and adhering-to-GMP standards 3D printing devices designed specifically for medical application

Fig no 1from https://share.google/Ge3zCY3mPN3T6nQ4R



METHODS

The team developed methods for constructing cost frameworks specifically tailored for pharmaceutical 3-dimensional printing using stereolithography technology by initially detailing each step of this advanced additive fabrication technique's workflow. Stages were determined through previous knowledge and align with typical procedures used in pharmaceutical 3D printing technology. Subsequently, the framework underwent an intricate microeconomic cost evaluation employing M3DICORt—an advanced 3-dimensional printed corticosteroid delivery system originally created via Fused Deposition Modeling technique. A research project took place within the expansive facilities of MC, formerly known as the Erasmus Medical Centre, which is recognized for its leadership among Dutch healthcare institutions; it covers approximately 2, 654 square meters across multiple floors and accommodates over two hundred dedicated professionals. A structured methodology segmented the complete 3D printing procedure into distinct primary stages: Before printing, 2 steps were taken. Producing through printing is an activity involving text creation on paper using ink. After printing is completed. In every stage, corresponding expense classifications were consolidated into areas such as labor costs, material expenses, machinery fees, infrastructure charges, and quality control measures based on a previously utilized costing framework tailored specifically for advanced therapeutic pharmaceuticals. During Phase One - pre-processing in three-dimensional printing technology, an electronic blueprint for the tablet's shape is generated through specialized CAD programs on computers. Many of these designs can be accessed through digital downloads. Stl files undergo conversion through specific 3D printing applications for processing as readable code by machines. The program dictates precisely what actions the 3D printer should take in sequence to construct the item piece by piece. Designing plays an indispensable role here; it dictates both the tablet's structural shape and its ability to deliver drugs effectively. In this stage, the substance containing medication is manufactured alongside the printing medium used by the device. Given that these filaments aren't readily accessible on the market, manufacturers produce them internally through mixing pharmaceutical powder components and utilizing hot-melt extrusion techniques to generate an ink-like material suitable for printing applications. Stage Two - Manufacturing: In this phase, pre-prepared filaments undergo manual insertion into 3D printers, where they sequentially build up tablet components in layers until reaching the targeted formulation. In phase three - post-pressing: Following printing, tablet samples receive thorough inspection for accuracy before being sealed in their final containers. Quality control verifies that all components used in production adhere to pharmacological specifications through evaluations of factors like active ingredient concentration, consistency, durability, and physical integrity. Every product line undergoes rigorous scrutiny before being formally approved by a QP—someone well-versed in ensuring adherence to all relevant laws and regulations through their expertise in pharmaceuticals' standards of quality control.

Additional steps in post-processing involve maintaining machinery cleanliness, attaching identification tags, and preserving packaged medications for future use. Activities related to quality assurance encompass document preparation, risk evaluations, and compliance with established operational protocols, thereby guaranteeing uniformity in products. Because existing hospitals have implemented quality assurance measures in their pharmacy departments, this research focused solely on expenses related to these staff members. The system categorized expenses into two types: those that remain constant regardless of output levels (fixed) versus those whose amounts fluctuate based on production volume (variable), encompassing personnel, material procurement, machinery usage, property maintenance, quality assurance measures in each category. Fixed expenses remain constant regardless of how much is produced (for instance, machinery wearout, real estate charges). Costs fluctuate proportionally as tablet production increases; examples include material expenses and labor for technicians. A method based on cost allocation by activities determined overall production expenses. An examination was conducted through an entity's viewpoint; specifically, it focused on expenses related solely to the Erasmus MC Hospital Pharmacy. Additional expenditures like healthcare fees and operational charges were disregarded. The fixed expenses were calculated by averaging the yearly totals over the tablet production volume annually, whereas variable expenditures were assessed through an evaluation method where resource values equate to their potential alternatives' worth. The prices have been adjusted to reflect Euro values in 2022 as part of an assessment related to Dutch health care expenses. The material costs such as active substances, packaging materials, and protective gear were evaluated based on their current market rates provided by hospitals. The expenses related to equipment were considered constant and encompassed components like the three-dimensional printer, heat-melt extruder, weight-measuring device, rotor-stator blender, and labeling machine. The expense of each gadget was determined by adding up its initial value plus an allowance for wear over ten years, considering four units in total. An interest rate of two percent is paired with an annua maintenance expense of five percent. A pharmacist's team member managed manufacturing duties alongside an authorized individual who ensured product approval processes were followed. The duration of every manufacturing process was meticulously noted down by timing each operation manually with a stop watch. Estimated personnel expenses incorporated 2022-2023 university medical center wages in Netherlands, increased by 39%, including health insurance and taxes. Other tasks like maintenance and quality assurance monitoring remained constant regardless of output levels. The facility's expenses were determined by its space needs dedicated to both operational functions such as producing goods and managing offices – specifically, 26 square meters allocated for manufacturing purposes and an additional seven square meters reserved for administrative tasks. Sixty square meters is allocated for administrative areas. The annual expenses amounted to 1467 euros. The cost is 87 euros per square meter in production zones and approximately $698 in non-production spaces. The rental rate is set at 40 euros per square meter for areas not designated as production zones. Proportional adjustments were made in both space allocation for the 3D printer and staffing levels accordingly. Four percent constitutes the proportion allocated for managing all aspects of the hospital's pharmaceutical activities. For this scenario's baseline assessment, it is postulated that there would be an 0. 75 increase in productivity levels. A "keep-up-with-the-expert" approach was employed for accurately timing every stage of the procedure. Creating 250 centimeters of thread yielded enough material for 164 pills in an hour-long process. With an output speed of 120 units per hour by its 3D printer, this machine became the limiting factor for operations during peak capacity. Under normal operating conditions involving 1558 workdays each year, the plant is capable of producing approximately 186,960 units yearly. The cost of quality management software was omitted because their current infrastructure had been established. The expenses associated with quality control inspections were accounted for in both pre-validation checks of processes and routine pharmaceutical standards like consistency, disintegration rates, density measurements, brittleness assessments, contamination levels, and longevity evaluations. When QA tasks utilized common equipment or premises for either production process - whether it was filaments being manufactured into tablets through joint use of machinery or spaces allocated simultaneously by both operations - these expenses were evenly split across each activity's budget allocation.

- Pre- printing
- Printing
- Post- printing

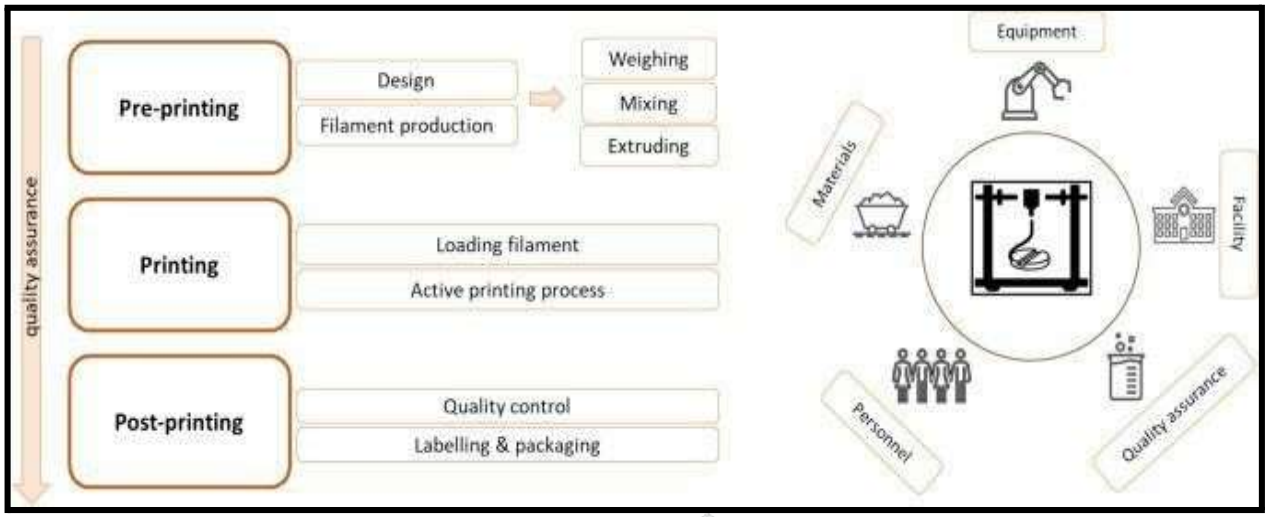


Fig no 2 from https://share.google/aVlEDGOn8qvH9O3Ys

3) Tablet types:

Types of Tablets Prepared by 3D Printing

3D printing enables the creation of a wide range of tablet types by varying their design, internal structure, and formulation. Depending on therapeutic needs, tablets can be tailored for immediate, sustained, delayed, or pulsatile drug release, as well as for combination or personalized therapy.The major categories are summarized below:

1. Immediate-Release Tablets (IR)

These tablets are designed to break apart and release their active ingredient quickly after swallowing.A well-known example is Spritam® (Levetiracetam) — the first 3D-printed tablet approved by the U.S. FDA, manufactured by Aprecia Pharmaceuticals.Using 3D printing, highly porous structures can be produced, allowing the tablet to disintegrate within seconds and deliver rapid therapeutic action.

2. Sustained-Release (SR) or Controlled-Release Tablets

In these tablets, the drug is released gradually over an extended time period.3D printing provides precise control over the tablet's matrix design, porosity, and polymer composition, which helps in achieving predictable and prolonged drug release.Materials such as hydroxypropyl cellulose and Eudragit polymers are often used for this purpose.

3. Delayed-Release or Enteric-Coated Tablets

These formulations prevent drug release in the stomach and instead release it in the intestine.
This can be achieved using pH-sensitive polymers like Eudragit L100 or S100, which dissolve only at intestinal pH.3D printing allows the creation of layered designs that effectively protect acid-labile drugs from gastric degradations.

4. Multi-Layer Tablets (Bilayer or Trilayer)

These tablets contain two or more layers, each with a distinct drug or release profile.Such designs are especially useful for combination therapy or when a staged release is required.3D printing can easily fabricate multiple layers in a single process, ensuring precise separation and control between them.

5. Pulsatile-Release Tablets

These tablets are engineered to release the drug in bursts after specific time intervals suitable for chronotherapy, where drug delivery aligns with the body's natural rhythms (e.g., for asthma or arthritis).3D printing enables the fabrication of core–shell designs that delay or trigger release after a programmed lag time.

6. Orodispersible Tablets (ODTs)

ODTs dissolve rapidly in the mouth without needing water, making them ideal for patients with swallowing difficulties.Through 3D printing, highly porous tablets can be produced that disintegrate within seconds.Binder jetting technology is commonly used to create these fast-melting dosage forms.

7. Floating or Gastroretentive Tablets

These tablets are designed to remain buoyant in the stomach for an extended period, allowing drugs with narrow absorption windows in the upper gastrointestinal tract to be more effectively absorbed.By printing hollow or low-density structures, 3D printing helps prolong gastric residence time and improve bioavailability.

8. Multiparticulate Tablets / Polypills

Multiparticulate tablets, or polypills, incorporate multiple drugs or mini-tablets into a single printed unit.This approach simplifies complex medication regimens, particularly for chronic conditions such as hypertension or diabetes, and improves patient compliance.

9. Personalized Dose Tablets

3D printing enables individualized dosing, allowing each tablet to contain a patient-specific quantity of drug.This is especially beneficial for pediatric and geriatric populations, where dose flexibility and adjustment are crucial.The design can be easily modified through digital modeling before printing.

10. Implantable or Transmucosal Tablets

Although not traditional oral tablets, 3D printing can also produce implantable or transmucosal systems that release drugs locally or over a long duration.These dosage forms are particularly useful for targeted or controlled therapy beneath the skin or via mucosal tissues

4) 3D printing technologies employed within pharmaceutical manufacturing:

The 3D Printing technology encompasses multiple distinct methods such as Binder Jetting, Fused Deposition Modeling (also known as FDM), Semi-Solid Extrusion (SSE), Selective Laser Sintering (SLS), and Stereolithography (SLA). Previously stated within the introductory section, additive manufacturing technology employs layer-by-layer deposition techniques through computer-aided design programs such as those utilized by Ngo et al. In 2018. Choosing feedstocks is contingent upon the type of 3D printer chosen; in pharmaceuticals, this process often involves using techniques such as extrusion, ink-jet printing, or binder-powder methods ailored specifically for drug formulation purposes. Furthermore, selecting the 3D printing method hinges upon considering factors such as melting points and degradability temperatures associated with the chosen APIs. Additionally, it significantly impacts the choice between different types of materials and print techniques. Different techniques differ significantly in terms of effectiveness; primarily distinguishing factors lie within how each method applies material sequentially upon its predecessor. Polymer materials exhibit distinct properties that synergize well with the sequential addition technique used in fused deposition modeling for creating three-dimensional objects. The capacity for these materials to undergo precise melting, solidification, or bonding at specified temperatures allows them to easily construct intricate and personalized pharmaceutical formulations efficiently. Moreover, polymers act efficiently as drug delivery vehicles, guaranteeing consistent distribution and regulated excretion. In 2021. Nevertheless, remember that the importance of polymers within 3D printing applications depends greatly upon their particular use case and goals. These materials are commonly used; nonetheless, based on specific projects' goals and necessary attributes, other options like ceramics, metals, or bio-based plastics might prove more suitable. Research into innovative techniques for creating drug-delivery devices using additive manufacturing frameworks can now occur due to ongoing collaboration among materials choice, dosage form creation strategies, and specific settings in 3D printing technology, maintaining its significance as a crucial area of investigation. Key features of a 3D-printed material can significantly vary based on how these settings are adjusted; changes like altering the quantity of layer prints allow precise modifications to properties including release rates, according to Samiei's research (2020). Nevertheless, it's important to remember that how the formula works significantly influences its interaction within these intertwined processes. The thorough examination of 3D printing techniques has revealed extensive applicability within pharmaceutical contexts (as detailed by Cui et al.). In 2021, researchers Kim et al. published their findings. In 2022, researchers Pitzanti et al. published their findings. In 2021, my evaluation will offer an abbreviated overview for every technological advancement discussed herein. Table 3 outlines the benefits and drawbacks associated with every widely employed 3D

printing method for creating solid oxide fuel cells.

4.1. Extrusion-based printing:

The growing interest in extrusion-based 3D printing is attributed to its significant promise for use in the pharmaceutical industry. Scientists have an inclination towards this technique due to its affordability, adaptability in construction, and ease of use across various types of plastics. From among several types of extrusion methods, Fused Deposition Modeling (FDM) and Semisolid Extrusion (SSE), which have gained significant popularity in recent years, stand out as the most commonly employed approaches (Algahtani et al.). In 2018.

4.1.1. Fused deposition modelling (FDM):

Many people utilize FDM machines for their extensive use in additive manufacturing techniques; substantial efforts have been made towards refining this method through advancements and optimizations. Partly due to affordability, simplicity, and adaptability, FDM technology enjoys widespread adoption across various user groups including enthusiasts and professionals alike. In 2022. The FDM technology utilizes an extrusion-based process where melted polymers are laid down sequentially on top of each other, forming three-dimensional structures through successive layers deposited upon a base surface. In 2020. Developing drug-laden polymers containing chosen additives typically involves employing the hot melt extrusion technique. The HMEsemisolid substance is sequentially deposited in layers using the printer's tip to construct the ultimate form (Seoane-Víaño et al.). In 2021(a),. SSE differs fundamentally from conventional extrusion techniques by allowing for the creation of intricate designs under significantly reduced heat levels compared to other processes. This characteristic is highly advantageous for creating temperature-sensitive drug administration methods (Dharmawardana & Silva). In 2021. At low temperatures, SSE operates efficiently due to inherent properties of its components. Naturally occurring semi-liquid materials have significantly lower temperatures at which they melt compared to their corresponding rigid filament structures or powder forms employed by traditional FDM processes. Furthermore, SSE technologies ensure minimal heat input while achieving highly controlled temperatures, safeguarding printed materials against damage due to thermal fluctuations. More focus is now directed towards using semi-liquid preparations to develop edible tablets suitable for children's consumption, demonstrating substantial improvements in patient compliance through their palatability. In 2022. In line with this development, researchers at Tagami et al. (2021) created chewable medications targeted towards kids by integrating various components such as gelatin, HPMC, sweetened liquid, water, and lamotrigine into their formulation process. Although it has several benefits, an important disadvantage of SSE lies in its limited print quality compared to other technologies. In 2022. Frequently manufactured items tend to exhibit coarser textures, denser coatings, and simpler designs in contrast to creations achieved through more precise techniques. Despite current efforts, sustained advancements in both scientific understanding and innovation continue to enhance SSE's accuracy, indicating potential breakthroughs in overcoming existing constraints within the foreseeable timeframe (Funk et al.). In 2022.

4.1.3. Direct powder extrusion (DPE):

The direct powder extrusion method is categorized within the broader family of extrusion techniques. In place of using a thread-like substance, DPE utilizes an extruder mechanism through which powders or granules derived from HME technology flow out as it passes over the printhead component within the 3D printing device. In 2019. DPE offers an advantageous feature by avoiding common limitations in loading drugs encountered during traditional HME and FDM procedures. Through initiating an evenly dispersed drug-polymers mixture at its outset, DPE ensures uniform medication dispersion throughout the system. The mixture undergoes continuous extrusion to ensure uniform medication levels during production. The DPE enables meticulous management of settings, guaranteeing reliable administration methods suitable for diverse applications. Moreover, this approach reduces drug clustering and guarantees even distribution of medications. Consequently, this approach could streamline the production method into an efficient two-step procedure at reduced expense. In 2021. Another advantage of using DPE involves its ability to use small quantities of medication and additives while being highly effective in developing formulations specifically designed for early-stage scientific studies. In 2021B. Recent applications of DPE in pharmaceutics pertain less than those utilizing FDM and SSE methods; thus, additional investigation remains necessary (Lafeber et al.). In 2022.

5) Various techniques used in 3D printing:

Whether employing any form of 3D printing method, the general procedure typically consists of these core phases: Next, an electronic blueprint for the intended item is generated using softwarools. The document subsequently undergoes conversion into a stereolithography format (. A STL file specifies an object's geometric shape. Conclusively, thusly. The STL file undergoes conversion into machine-dependent instructions (.). The g-code instructs the printer on how to create the ultimate three-dimensional object [(8], Figure 1].

Techniques involving 3D printing may be classified according to various criteria such as the method used for adding layers together, the kind of material employed during fabrication, how layers interact within each other, or characteristics related to printer components like print heads. According to Figure 2, various techniques tend to be categorized based on the type of primary components employed. Amongst several methods utilized, stereo lithography (SLA), selective laser sintering (SLS), binder jetting, and fused deposition modelling (FDM) stand out as being extensively employed within the pharmaceutical industry for creating drug formulations [10].

The stereolithography process employs resin materials that harden sequentially through exposure to intense UV light emitted by an illuminating device. Using this technique yields meticulously crafted items boasting fine surfaces; it's commonly applied in fabricating prosthetics or detailed medical replicas based on individual scan data.

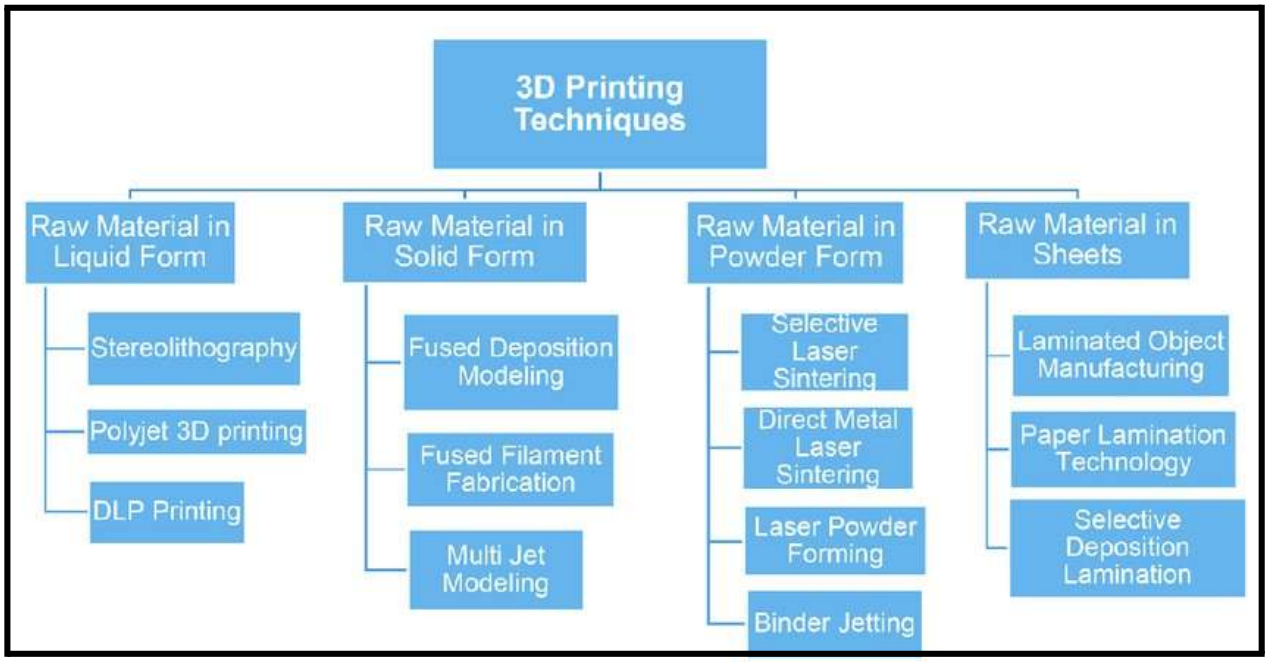
In contrast, Selective Laser Sintering utilizes powders as its raw material component. An intense light pulse precisely heats up and welds together individual granules into coherent three-dimensional structures. Various uses of SLS technology have included creating synthetic tissues.

Binder jetting is commonly known as drop-on-demand inkjet printing or simple three-dimensional printing; it constructs objects through layer-by-layer deposition of liquid binding agents on top of a powdered base material until they fuse into solid form [9,10]. The technique is part of an inkjet-printing system that also includes continuous inkjet technology. Its application has yielded successful results in creating both implantable devices and solid pharmaceutical formulations, notably exemplified by Spritam® - the world's first FDA-licensed three-dimensional printed pill.

Currently, Fused Deposition Modeling stands as the leading choice for 3D printing technology. This material employs thermoplastics as its building blocks; these plastics melt within an oven-like chamber before being pushed out through tiny holes, creating successive layers of plastic sheeting. Upon being placed on a cold base, the substance hardens into its complete shape. An alternative method called semi-solid extrusion (SSE) utilizes gelatinous substances instead of traditional plastics when creating prints using an inkjet-style nozzle device [10]. In recent times, these extrusion techniques have extensively been employed for creating various types of gels like hydrogels as well as coatings on pills along with numerous other applications within the realm of pharmaceutics [11].

In summary, through Figures 1-2, it is evident how various additive manufacturing techniques, whether preliminary research tools or commercial applications, significantly alter the approach for creating pharmaceutical formulations and production processes.

Fig no 3 from: https://share.google/PD2uOstHxj0DwPdLV .
3D printing techniques categorisatio



6) Working:
Involving multiple layers sequentially, this technology constructs customized medication forms utilizing pharmaceutical additives. The process starts by creating an electronic blueprint through specialized CAD tools. Another way this design could be created is through using a 3D scanner to capture an actual item in three-dimensional space, allowing for the creation of a virtual copy on computer software.

- Step involved in 3D printing 1.Design:

To begin, use computer-aided design (CAD) tools to produce an exact digital replica of what you want, enabling it to appear as if physically presentable in space through 3D visualization techniques.
2. Converting the design to a machine-readable format:
After being created, the 3D model transforms into an STL file type which specifies the exterior shape of the item and allows for its interpretation by the printer.
3. Raw material preparation:
Materials chosen for use undergo processing until they achieve appropriate shapes like powders, threads, or adhesive liquids so they can be used in print-making techniques effectively.
4. Inking: During ink application, pre-mixed substances are sequentially laid down on substrates using machinery, ultimately culminating in the creation of entire items. Five. The process includes removing excess material followed by treatments such as drying, sintering, or finishing touches for achieving optimal characteristics and aesthetics of the end result after printing.

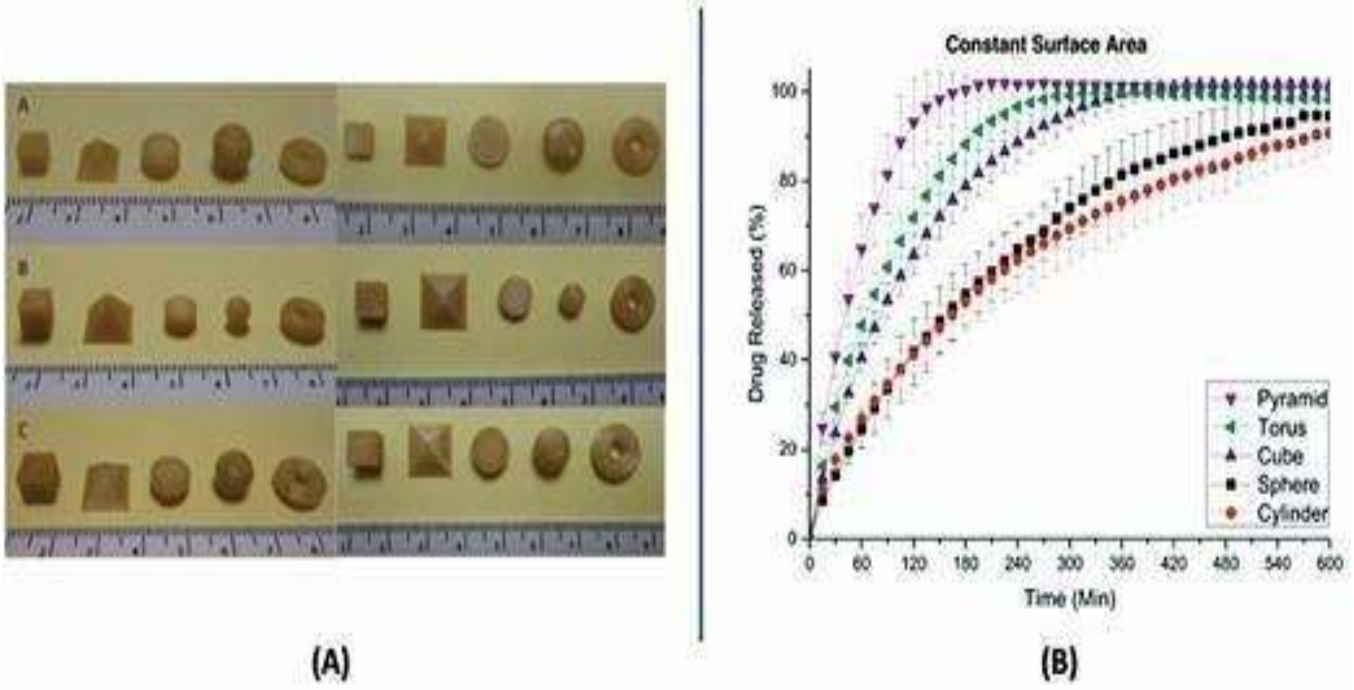
7) Tablet:

2. Certainly. Here's an alternative version of your input: Incorporating digital technology in printing has its roots as far back as 1996; at this time, scientists utilized small-scale printers alongside materials such as poly(lactic acid) and polyethylene oxide, often mixed with pigments for clarity during testing phases. A groundbreaking research project showcased how three imensional printing technology enabled scientists to create intricate drug delivery mechanisms through modifications of tablets' inner composition and production techniques. During the initial phase of utilizing 3D printing technology in drug manufacturing processes, it commonly employed droplets as components to create medication doses. In place of traditional polymer-based adhesives like those found in Eudragit®, alternative binding agents including mannitol were utilized instead. The studies demonstrated efficacy in utilizing erosion and diffusion techniques for controlled drug delivery

systems, thereby validating the applicability of employing such methods to develop appropriate oral pharmaceutical preparations. In those initial trials, investigators concentrated mainly on choosing suitable 3D-printing methods, fine-tuning print settings, investigating different types of tablets for quick vs. slow release, and studying how drugs behave under various conditions such as absorption rates in the body. Gubereck et al. A novel approach was introduced through initial fabrication of bioceramic tablets via powder extrusion, subsequently coated with antibiotics during an antibiotic retention phase lasting for seven days, ultimately resulting in functional drug-containing pills. Yuan et al. Later, they created acetaminophen-containing tablet matrices through an inkjet printing process on flat surfaces, where the medication is deposited into thin film coatings mixed with modifiers for controlled release properties. A year after their initial modification, which involved changing the tablet's inner-layer alignment so it printed upright rather than horizontal for altering how drugs dissolve, they subsequently employed an extruded three-dimensional printing technique to create gaiter-structured controlled-release bi-laminar pills. New pharmaceuticals showed they could mimic released versions found in current market products, validating 3D printing's accuracy for intricate systems; this was marked by an important milestone in 2015: The US Food & Drug Administration granted approval to Spritam® -the world's first printed medication intended for treating seizures- through innovative 3D technology. Produced through ZipDose® innovation, this is currently the sole 3D-printed medicinal item granted official approval in its entirety for use as of that specific time period by researchers Goyanes et al. Several groundbreaking research papers showcased how flexible FDM 3D printers can work effectively with PVA filament materials. Scientists added substances like 5-amino salicylic acid and 4-amino salicylic acid onto threads and created pills with various fill-in designs and thicknesses, demonstrating how those factors impact when medicines come out of their capsules. Next, they started looking at ways to combine multiple medications through 3-D printing techniques. Another notable advancement involved "a polypill," manufactured through an extrusion process utilizing the RegenHU technology, featuring distinct sections for storing medications like nifedipine, captopril, and glipizide separately. In each section of the formulation, unique extraction methods were employed—diffusion for releasing substances through molecular movement and osmosis via solvent-driven absorption—to create an integrated drug delivery system capable of delivering various treatments simultaneously. Following this breakthrough technology, researchers subsequently created a pill comprising six medications: mesalamine, thiazides, beta-blockers like propranolol, angiotensin-converting enzyme inhibitors such as enalapril, and statins including simvastatin. A precise design ensured certain medications were administered rapidly upon administration, whereas other substances were gradually released via cellulose acetate films over an extended period. Additional research focused on examining the physical characteristics such as mechanics and flow behavior in drug-containing threads. To illustrate, researchers combined nitrofurantoin with cellulose-based polymers during extrusion experiments aimed at understanding how particle non-dissolution and polymer concentrations affected drug release speeds in solution. [38]. Moreover, Okwuosa et al. Utilized thermally stable additives like kaolin for enabling FDM 3D printing below ~110°C while preserving API integrity throughout manufacturing processes. An innovative approach suggested by Sadia et al. Integrated a thermally stable additive called TCP within fibers, enhancing uniformity in material properties for easier creation of customized release-rate pills. Despite consistent stability in many drug formulations throughout production processes, captopril exhibited slight thermal decomposition between 1996 and 2016. These improvements laid the groundwork for advancing tablet-based three-dimensional printing technologies, progressing from experimental prototypes towards practical applications by mid-century. Subsequent innovations incorporated novel materials alongside innovative methodologies. Acosta-Vélez developed an injectable photopolymer suitable for inkjet-based three-dimensional printing, facilitating swift manufacturing of tablets containing water-soluble medications like roperidone hydrochloride. Integrating nanotechnology into 3D-printed constructs through encapsulation of nanoparticles inside them improves pharmaceutical release management. -Chai et al.

Created an inflatable Domperodine pill made of Hydroxypropyl Cellulose; its unique shape contributed to floatability and prolonged stomach dwell time. Additionally, research by Genina et al. demonstrated similar properties in their study. Developed a multi-chamber pill for segregating unmixable tuberculosis medications like rifampicin and isoniazid in a single capsule, ensuring distinct dissolution rates; additional innovations encompassing DualCapsules, latticed cubes, and pierced lozenges tailored towards precise drug delivery mechanisms and individualized treatment requirements. To illustrate, for instance, Scoutari et al. Researchers utilized 3D printing technology to manufacture chewable pediatric tablets resembling various animal shapes in an effort to enhance children's medication adherence by ensuring sustained-release properties over twenty-four hours through innovative drug-loading techniques as early as 2017-2018. Showed how they developed tasty, user-friendly printed materials specifically designed for hard-to-treat conditions like maple syrup urine

disorder, proving that 3D technology can create customized medication formats suited to individual needs. Fig no from https://doi.org/10.1093/jpp/rgab136



Challenging and Regulatory Consideration:

Despite promising advancements in 3D printing technology for medicine applications, numerous hurdles hinder its broad implementation across industries. A significant obstacle involves insufficiently developed printing standards alongside scarce access to eco-friendly biomedical components. Moreover, effective testing techniques lacking in reliability impede advancements, alongside the lack of established oversight rules. Given how significantly different multiple 3D printing methods operate based on distinct underlying theories, pinpointing precisely what needs adjustment is crucial for creating formulations that remain durable, secure, and efficacious. A disadvantage includes instances where certain printing techniques utilize UV lights or intense energies, potentially leading to drug deterioration. To illustrate, Fused Deposition Modeling utilizes elevated temperatures; thus, this technique is appropriate exclusively for stable drug substances and additives. Additionally, limited availability of suitable components poses an obstacle due to requirements for compatibility in living tissues, ease of decomposition without producing harmful substances upon use. Some 3D printing techniques necessitate additional processing stages for enhancing the physical attributes of their resultant pharmaceutical formulations. A prevalent task in after-printing procedures involves eliminating auxiliary elements employed for maintaining an object's form. Carefully dismantle these components free of any harm to the finished item. For different technologies like SLA/DLP printing requires post-processing steps including washes and cures; while inkjets need drying after printing, and powder-based processes necessitate heat treatment afterwards. Nevertheless, including those additional procedures extends overall manufacturing duration. A secondary issue pertains to the visual appeal of the manufactured medication dispersions. Methods using three-dimensional printing often result in textured or bumpy exteriors because they frequently incorporate substantial amounts of extraneous plastic fragments or flaws after finishing steps. Unappealing features might decrease patients' adherence to treatment regimens. Easing batch-to-batch consistency often proves challenging due to difficulties in ensuring homogeneous materials and avoiding phase segregation, both of which contribute significantly to stable outcomes. Over 100 medical products made through additive manufacturing techniques were produced recently; however, their application as drug formulations remains at an embryonic stage. In 2017, the United States Food and Drug Administration approved regulations concerning 3D-printed medical equipment; however, comparable remain absent in relation to pharmaceutical drug formulations. Despite various current methods for additive manufacturing, there is currently no single standard approach available globally. In general, substances employed in creating orally administered pharmaceuticals through 3D printing should meet the GRAS criteria set forth by the Food and Drug Administration. Essential GMP standards ought likewise to be adhered to; only safe chemicals without toxins

and suitable heating conditions need apply for avoiding medication deterioration. To achieve efficient production through custom fabrication, stringent need establishment for maintaining item precision and worker competency. Firms preparing for implementation of 3D printing technology at pharmacies and medical facilities must allocate specific areas free from contaminants and secure supplies of various dosage levels of "ink" materials. The stipulations hinder pharmaceutical firms' transition towards individualized healthcare through additive manufacturing techniques like stereolithography. Despite its potential for producing personalized medication in response to unique patients' requirements, additive manufacturing technology is still not widely adopted as an industrial process. Primarily attributed to technological constraints, insufficiently formulated prints, and inadequate quality assurance measures, integrating 3D printing technology into healthcare settings faces several hurdles as well. Proficient experts are required for printer operation and upkeep, alongside innovative methods of ensuring high-quality checks without causing damage. Furthermore, hospital setups often involve significant expenses due to necessitating specific packaging and labelling for individualized medications. An uncontaminated setting is crucial for preventing spoilage; thus, computational analysis tools like CAD should be employed to create medications with consistent medication dispersion rates. Nowadays, due to numerous types of 3D printing techniques being accessible, choosing an optimal method for medical applications continues to pose considerable difficulty.

Advantages and disadvantage:Advantages:

Integrating 3D printing tech enhances therapy applications significantly, potentially revolutionizing contemporary medicine. Benefits encompass customization of therapies, creation of complex patterns, precise dosage delivery management, and quickening product development cycles. Despite obstacles like insufficient raw materials, technical limitations, capacity problems, and legal barriers, achieving maximum benefit from using 3D printers for medical purposes remains an ongoing challenge.

I) Personalization :

The ability to create 3D-printed personalized medicine solutions enables precise customization in both drug administration methods and healthcare equipment designed specifically for unique patients' requirements. Implementing this tailored method improves accuracy in care delivery, boosts efficacy of treatments, and maximizes positive health results for patients.

II) complex geometry:

Using 3D printers allows for creating detailed objects that would be challenging to produce using traditional manufacturing techniques. This feature enables the development of targeted medication delivery mechanisms tailored for precise locations in the body, enhancing the effectiveness of treatment administration.

III) control drug released:

Integrating medicinal substances within fabricated structures through 3D printing allows for precise management of delivery schedules. This kind of management facilitates continuous medication release in response to external factors like stimulation, enhancing treatment efficacy while maintaining patient security.

IV) Rapid Prototyping and Manufacturing:

The use of 3D printing dramatically reduces both the duration required for designing products, conducting tests, and manufacturing them. The swift progression enables quicker transition of concepts into practical applications—in critical situations where immediate healthcare interventi

Disadvantage:

The duration of making something and its expenses often result in lengthy processes and potentially wasteful expenditures when dealing with significant quantities.

Resource constraints:

Certain methods of three-dimensional printing necessitate elevated heat levels, potentially compromising thermostable medications. Compatibility between materials and various medications remains an obstacle.

Inadequate uniformity in regulatory and evaluation procedures hampers the broad adoption of 3D-printed medications on the market.

Ensuring high-quality standards is crucial but maintaining consistent product batches across different production runs remains an ongoing challenge in quality management.

Meeting demands for vast numbers requires overcoming substantial scalability hurdles.

Challenges arise in achieving both high image quality and flexibility due to present technological constraints.

9) future in pharmacy:

Numerous studies have shown how three-dimensional printers can be utilized effectively in various

applications.
medicines manufacture and patient care. Figure 2 illustrates an overview of advancements in three-dimensional printing within the pharmaceutical industry, emphasizing key milestones.
The significant achievements within this technological domain have been highlighted.
Significant progress has been achieved in addressing those obstacles. Today, 3D printing is utilized in numerous applications.
clinical application in research institute. Previously, commercial-grade three-dimensional printers lacked uniformity and compatibility.
For the production of pharmaceuticals without validation against Good Manufacturing Practice standards. Currently, there is an event taking place today.
A diverse array of three-dimensional-printed items finds application within biotechnological fields—from miniature growth enclosures to microlithographic systems.
Miniaturized diagnostic tools on chips have been implemented globally within laboratories.
[52] Among the various 3D
Technological advancements in printing methods, particularly fusing filament through extrusion technology (Fused Deposition Modeling), have garnered attention due to their potential use in drug development.
As an exceptionally strong contender in producing medical treatments for children.
[53] Pharmaceutical industries continue
Creating more effective formulations for quick-dissolving tablets through binder jetting technology is being explored.

10) conclusion:

Integrating 3D printing in medicine now allows for innovative changes in how drugs are made and administered. This groundbreaking method facilitates tailored healthcare by offering controlled dosing precision and intricate medication delivery schedules. Even though obstacles like resource constraints, legal barriers, and production difficulties hinder progress, ongoing improvements indicate an optimistic outlook for 3D-printed medicines. As more studies are conducted and improvements made, it's anticipated that 3D printing will play an increasingly significant role within contemporary medicine, fundamentally altering how drugs are developed and manufactured.

Referance:

1. Siamidi A, Tsintavi E, Rekkas DM, Vlachou M. 3D-printed modified-release tablets: a review of the recent advances. Pharmaceutics. 2023;15(3):xxx–xxx https://www.researchgate.net/publication/338668625_3D-Printed_Modified-Release_Tablets_A_Review_of_the_Recent_Advances
2 .Mulay AA, More SD, Mhetre RL. A review on 3D printing technologies in pharmaceutical science.https://share.google/r3jwYffJYclJEbkYZ .
3. Bácskay I, Ujhelyi Z, Fehér P, Arany P. The evolution of the 3D-printed drug delivery systems: A review. [Journal Name]. [Year];Volume:[Page numbershttps://pmc.ncbi.nlm.nih .gov/article s/PMC9318419 /.
4. Pitzanti G, Mathew E, Andrews GP, Jones DS, Lamprou DA. 3D printing: an appealing technology for the manufacturing of solid oral dosage forms. Open Accesshttps: //share.google/ Jmb6EzUXSxowvhgK2.
5. Chate AL, Devkate AB. 3D Printing in Pharmaceutical Industry: A Review. Review Article. Review Article Topic 3D Printing In Pharmaceutical Industry.pdf https://share.google/zWK2OSpHh5jnxeEsw
6. Siamidi A, Tsintavi E, Rekkas DM, Vlachou M. 3D-printed modified-release tablets: a review of recent advances. Pharmaceutics. 2023;15(3):567. Available from: https://doi.org/10.3390/pharmaceutics15030567
7. Algahtani MS, Ahmad MZ, Ahmad J. 3D printing of pharmaceuticals: an overview of the technology and its applications. Drug Discov Today. 2018;23(5):1023–1030. Available from: https://doi.org/10.1016/j.drudis.2018.01.023
8. Pitzanti G, Mathew E, Andrews GP, Jones DS, Lamprou DA. 3D printing: an appealing technology for the manufacturing of solid oral dosage forms. Open Access J Pharm Res. 2022;8(4):25–40. Available from: https://doi.org/10.3390/pharmaceutics14040810
9. Goyanes A, Wang J, Buanz ABM, Martinez-Pacheco R, Telford R, Gaisford S, Basit AW. 3D printing of medicines: engineering novel oral devices with unique design and drug release characteristics. Mol Pharm. 2015;12(11):4077–4084. Available from: https://doi.org/10.1021/acs.molpharmaceut.5b00510
10. Scoutari E, Scoutaris N, Gaisford S, Basit AW. Towards printed paediatric medicines: a novel chewable dosage form. Int J Pharm. 2017;518(1–2):86–92. Available from: https://doi.org/10.1016/j.ijpharm.2016.12.014
11. Seoane-Viaño I, Trenfield SJ, Awad A, Goyanes A, Basit AW. 3D printed pharmaceutical drug delivery: opportunities and challenges. Adv Drug Deliv Rev. 2021;173:497–520. Available from: https://doi.org/10.1016/j.addr.2021.03.012
12. Krueger L, Brambilla M, Goyanes A. Fused deposition modelling in pharmaceutics. Int J Pharm. 2022;611:121303. Available from: https://doi.org/10.1016/j.ijpharm.2021.121303

13. Tagami T, Fukushige K, Ogawa E, Hayashi N. Fabrication of 3D-printed chewable medicines for children. J Pharm Sci. 2021;110(1):150–158. Available from: https://doi.org/10.1016/j.xphs.2020.10.038

14. Genina N, Holländer J, Jukarainen H, Mäkilä E, Salonen J, Sandler N. Ethylene vinyl acetate (EVA) as a new drug carrier for 3D printed medical devices. Eur J Pharm Sci. 2016;90:53–63. Available from: https://doi.org/10.1016/j.ejps.2015.11.008
15. Sadia M, Sośnicka A, Arafat B, Isreb A, Ahmed W, Kelarakis A, Alhnan MA. Adaptation of pharmaceutical excipients to FDM 3D printing for the fabrication of patient-tailored immediate release tablets. Int J Pharm. 2016;513(1–2):659–668. Available from: https://doi.org/10.1016/j.ijpharm.2016.09.050
16. Goyanes A, Buanz AB, Basit AW, Gaisford S. Fused-filament 3D printing of drugs. Int J Pharm. 2014;476(1–2):88–92. Available from: https://doi.org/10.1016/j.ijpharm.2014.09.044
17. Khaled SA, Burley JC, Alexander MR, Roberts CJ. Desktop 3D printing of controlled release pharmaceutical bilayer tablets. Int J Pharm. 2014;461(1–2):105–111. Available from: https://doi.org/10.1016/j.ijpharm.2013.11.021
18. Awad A, Fina F, Goyanes A, Gaisford S, Basit AW. 3D printing: principles and pharmaceutical applications. Pharmacol Res. 2020;165:105409. Available from: https://doi.org/10.1016/j.phrs.2021.105409
19. Pereira BC, Isreb A, Forbes RT, Douroumis D. 3D printed oral films for personalized drug delivery. Int J Pharm. 2020;589:119798. Available from: https://doi.org/10.1016/j.ijpharm.2020.119798
20. Scoutari E, Gaisford S, Basit AW. 3D printed polypills: individualized therapy for polypharmacy patients. Pharmaceutics. 2018;10(4):204. Available from: https://doi.org/10.3390/pharmaceutics10040204
21. Lafeber T, Prinsen R, van Riet-Nales DA, et al. Direct powder extrusion 3D printing of medicines. Eur J Pharm Biopharm. 2022;173:90–99. Available from: https://doi.org/10.1016/j.ejpb.2021.12.009
22. Vithani K, Goyanes A, Jannin V, Basit AW, Gaisford S, Boyd BJ. An overview of 3D printing technologies for pharmaceutical applications. J Control Release. 2021;339:283–300. Available from: https://doi.org/10.1016/j.jconrel.2021.09.004
23. Rahman Z, Barakh Ali SF, Ozkan T, Kuttolamadom MA, Akhtar S, Siddiqui A, Khan MA. Additive manufacturing with 3D printing: progress from bench to bedside. AAPS J. 2018;20(6):101. Available from: https://doi.org/10.1208/s12248-018-0248-4
24. Chai XY, Zhang H, Zhang X, Sun Y, Dai X, Chen W, Liu J, Zhong G. Development of a floating 3D printed tablet for gastroretentive drug delivery. Int J Pharm. 2017;530(1–2):282–290. Available from: https://doi.org/10.1016/j.ijpharm.2017.07.021
25. Khaled SA, Burley JC, Alexander MR, Roberts CJ. 3D printing in pharmaceutics: promises and challenges. Pharmacol Ther. 2015;147:43–52. Available from: https://doi.org/10.1016/j.pharmthera.2014.10.007
26. Norman J, Madurawe RD, Moore CMV, Khan MA, Khairuzzaman A. A new chapter in pharmaceutical manufacturing: 3D printing. J Pharm Sci. 2017;106(4):415–424. Available from: https://doi.org/10.1016/j.xphs.2016.10.002
27. Long J, Gholizadeh H, Lu J, Bunt C, Seyfoddin A. 3D printing of mini-tablets for pediatric drug delivery: formulation optimization. Eur J Pharm Biopharm. 2021;162:139–148. Available from: https://doi.org/10.1016/j.ejpb.2021.02.004
28. Ibrahim M, Goyanes A, Basit AW, Edirisinghe M. Selective laser sintering in drug delivery and manufacturing. Int J Pharm. 2019;558:328–342. Available from: https://doi.org/10.1016/j.ijpharm.2018.12.035

9. Skowyra J, Pietrzak K, Alhnan MA. Fabrication of extended-release patient-tailored prednisolone tablets via fused deposition modelling. Eur J Pharm Sci. 2015;68:11–17. Available from: https://doi.org/10.1016/j.ejps.2014.11.009
30. Daly R, Harrington TS, Martin GD, Hutchings IM. Inkjet printing for pharmaceutical applications. Mater Today. 2015;18(1):43–49. Available from: https://doi.org/10.1016/j.mattod.2014.07.002
31. Wang J, Goyanes A, Gaisford S, Basit AW. Stereolithographic (SLA) 3D printing of oral modified-release dosage forms. Int J Pharm. 2016;503(1–2):207–212. Available from: https://doi.org/10.1016/j.ijpharm.2016.02.020
32. Ching S, Gupta M, Li J. Review of 3D printing for drug delivery applications. Int J Pharm. 2021;599:120443. Available from: https://doi.org/10.1016/j.ijpharm.2021.120443
33. Norman J, Madurawe RD. 3D printing in personalized medicine. Drug Dev Ind Pharm. 2020;46(8):1325–1331. Available from: https://doi.org/10.1080/03639045.2020.1770897Katstra WE, Palazzolo RD, Rowe CW. Oral dosage forms fabricated by 3D printing. J Control Release. 2000;66(1):1–9. Available from: https://doi.org/10.1016/S0168-3659(99)00225-4
34. Khaled SA, Burley JC, Alexander MR, Roberts CJ. 3D printing in pharmaceutics: challenges and prospects. Pharmacol Ther. 2015;147:43–52. Available from: https://doi.org/10.1016/j.pharmthera.2014.10.007
35. Daly R, Harrington TS, Martin GD. 3D printing in healthcare: future perspectives. Adv Drug Deliv Rev. 2020;157:1–5. Available from: https://doi.org/10.1016/j.addr.2020.06.013
36. Kimura SI, Terashima T, Irie S. Recent advances in additive manufacturing of pharmaceutical dosage forms. J Pharm Sci. 2022;111(5):1225–1238. Available from: https://doi.org/10.1016/j.xphs.2022.01.023
37. Kjar A, Huang Y. 3D printing of micro- and nanoscale drug delivery systems. Bio-Design Manuf. 2019;2(2):93–113. Available from: https://doi.org/10.1007/s42242-019-00044-8
38. Cui M, Pan H, Fang D. 3D printing of oral tablets for personalized drug delivery. Drug Discov Today. 2021;26(1):172–180. Available from: https://doi.org/10.1016/j.drudis.2020.09.003
39. Goyanes A, Fina F, Martorana A. Printing of personalized medicines: a new paradigm. Pharmaceutics. 2020;12(12):1216. Available from: https://doi.org/10.3390/pharmaceutics12121216
40. Scoutari E, Scoutaris N, Basit AW. 3D printed drug-loaded chewable tablets for pediatrics. Pharmaceutics. 2018;10(3):176. Available from: https://doi.org/10.3390/pharmaceutics10030176
41. Pardeike J, Strohmeier DM, Schröder B. 3D printing of solid lipid tablets. Eur J Pharm Sci. 2019;139:105065. Available from: https://doi.org/10.1016/j.ejps.2019.105065
42. Okwuosa TC, Pereira BC, Arafat B. Fabrication of drug-loaded filaments for 3D printing. Int J Pharm. 2017;533(2):285–292. Available from: https://doi.org/10.1016/j.ijpharm.2017.09.003
43. Chai XY, Zhang X, Liu J. 3D printing of floating gastroretentive tablets. Int J Pharm. 2017;530(1–2):282–290. Available from: https://doi.org/10.1016/j.ijpharm.2017.07.021
44. Ibrahim M, Edirisinghe M, Goyanes A. Selective laser sintering for pharmaceutical manufacturing. Addit Manuf. 2019;27:534–544. Available from: https://doi.org/10.1016/j.addma.2019.03.005
45. Rahman Z, Khan MA. Applications of 3D printing in drug delivery. AAPS J. 2018;20(6):101. Available from: https://doi.org/10.1208/s12248-018-0248-4

46. Scoutari E, Basit AW, Gaisford S. Personalized chewable pediatric dosage forms using 3D printing. Eur J Pharm Sci. 2021;156:105584. Available from: https://doi.org/10.1016/j.ejps.2020.105584
47. Daly R, Martin GD. Additive manufacturing in pharmaceutical sciences. Adv Drug Deliv Rev. 2020;170:19–41. Available from: https://doi.org/10.1016/j.addr.2020.06.013
48. Kim H, Park J. Emerging trends of 3D printed drug delivery systems. Pharmaceutics. 2021;13(2):187. Available from: https://doi.org/10.3390/pharmaceutics13020187
49. Bácskay I, Ujhelyi Z, Fehér P, Arany P. The evolution of 3D-printed drug delivery systems: a review. Pharmaceutics. 2022;14(3):612. Available from: https://doi.org/10.3390/pharmaceutics14030612