CUSTOMIZING MEDS WITH 3D PRINTING: A REVOLUTION IN PERSONALIZED DOSING BENEFIT-ORIENTED

Manea Muhdi Al Zamanan[1*], Fahad Khalid Mohammed Aldawsari[2], Nasser Saad Rashid Al Dosari[3], Abdullah Yahya Aqili[4], Shaykhah Saud Aloyayd[5], Majed Awad Maeed Alzahrani[6], Sultan Eid Eiadah Alahmadi[7], Faisal Talal Alradadi8, Khaled Saad Ali Alzhrani[9], Amer Ali Bakr Kaylani[10], Ahmed Hilal Naif Alotaibi[11], Majed Hussain Jarallah Aljarallah[12]

Abstract:
Personalized medicine seeks to revolutionize the healthcare sector by tailoring medications to individual patients, taking into account their unique physiology, drug response, and genetic makeup. The shift from conventional standardized therapy to personalized care is being propelled by several emerging technologies, with three-dimensional (3D) printing playing a significant role. 3D printing is the method of fabricating a three-dimensional object by incrementally adding material in layers, guided by digital blueprints generated by computer software. 3D printing has the ability to produce a wide variety of pharmaceutical dosage forms with varying geometries, release profiles, and combinations of medications. This technology has the potential to be used in a clinical setting for the purpose of administering drugs based on individual requirements. The study explores several 3D printing techniques and their applications in the production of pharmaceutical products for research purposes, emphasizing their strengths and weaknesses. The efficacy of tailored therapy is shown via the customization of dose, release profiles, and the combination of many drugs in a polypill. Additionally, it provides an understanding of how it accommodates various cultures. The importance of its use in a healthcare setting is also highlighted. Additionally, this breakthrough in tailored medicine has uncovered certain challenges that need resolution in order to enhance its efficacy.

Keywords: Medical devices, 3D Printing Technology, Drug delivery, Personalized dosage forms, Computer software.

[1*,2,3,4,5,6,7,8,9,10,11,12]ksa, ministry of health

***Corresponding Author:** Manea Muhdi Al Zamanan
*ksa, ministry of health

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1. Introduction

Medical treatment now uses the "one dosage that fits all" concept, giving most patients the same drugs at predictable amounts and intervals (1). The "one size fits all" concept does not apply to all treatments. When many persons get the same active ingredient at the same dosage, different reactions occur. The response may be too powerful, causing ADRs, or too weak, having no pharmacological effects. These two situations may cause patient issues. This leads to the creation of customized medicines, which tailor pharmaceuticals to patients' genetic, physiological, or pathological traits (2,3). Following the idea that "a single size does not suit all", giving the optimum medicine at the optimal dosage, for the individual's needs, at the right time. Individualized medication guarantees correct drugs.

These increase patient conformance, safety, efficacy, and cost-effectiveness (4). Three-dimensional printing, also known as additive manufacture, builds solid objects by depositing material in layers. The procedure uses CAD software to send signals to a 3D printer. The printer next converts the digital data into 2D groups, creating solid layers for item construction (4,5).

It is used in automotive, aerospace, biomedical, and pharmaceutical industries. It is utilized in fashion, accessories, building, and entertainment. Pharmaceutical companies have used this technique to make delayed-release pills, polypills, oro-dispersible films, gastrofloating pills, self-emulsifying drug delivery devices, microneedles, and transdermal patches (6). Printing advancements include inkjet, adhesive jet, fused placement, targeted laser sintering, stereolithography, and pressure-assisted microsyringe (7).

3D printing might revolutionize pharmaceutical product design, use, and manufacture. Traditional manufacturing processes, although economically feasible, may involve human work and take time for large output. Standard manufacturing methods also make it difficult to alter dose for each patient. Personalized medicine using 3D printing might change healthcare by tailoring drugs for each patient. Healthcare may be optimized with automated production (8).

The use of 3D printing for drug distribution is well documented. The quantity of papers explaining 3D printing technology, pharmaceutical applications, tailored medicine, and population-specific capabilities is limited.

2. The History of 3D Printing

3D printing has its roots in the late 1970s, with numerous patents filed for computer-aided additive manufacturing methods. Charles Hull, a trailblazer, developed and obtained a patent for stereolithography (SLA) in the mid-1980s, which used UV light to polymerize resins. 3D Systems, founded by Hull, commercialized SLA printers. Carl Deckard invented selected laser sintering in 1986, and Scott and Lisa Crump of Stratasys invented fused deposit modelling in 1989. Emanuel Sachs and his colleagues at MIT developed "three-dimensional printing techniques" using binding solution extruded onto a powder bed, which became the term "binder jetting" technique. Hans Langer focused on direct metal laser sintering in 1989 (10-12).

The Reproducing Rapid Prototyping (Rep Rap) project, led by Andrew Bowyer of the University of Bath, aimed to develop inexpensive, non-proprietary 3D printers. The project expanded significantly through collaborative efforts. 3D printing has been applied in various industries, including healthcare, clinical education, and pharmaceuticals. The FDA authorized Spritam (Levetiracetam), a prescribed drug for seizures, in 2015 as the first 3D-printed substance. The substance was produced via binder jet printing and has a porous structure that allows for rapid oral breakdown (13-15).

3. 3D Printing Innovations in Pharmaceutical Production

Inkjet printing refers to methods that deposit minute liquid droplets onto a substrate via design producing devices. Pharmaceuticals utilize specific drug formulations combined with the correct excipients (referred to as ink), which are applied layer by layer as tiny droplets onto an appropriate material. The two principal inkjet printing technologies are constant inkjet printing (CIJ) and droplet on delivery (DoD) (16-18). Medicinal inkjet printing is primarily used in the production of orodispersible fabric (ODF) compositions. These sheets swiftly release the drug into the mouth, where it dissolves or suspends in the saliva, eliminating the need for mastic or water intake. Thabet et al. printed enalapril maleate onto hydroxypropyl cellulose–based ODFs that were either hydrochlorothiazide-containing or drug-free using PIJ printing. By manipulating the concentrations of enalapril and hydrochlorothiazide on hydrochlorothiazide films, it was possible to produce an assortment of constant dose formulations (19,20).

In addition, mucoadhesive buccal films were created by combining TIJ with the technique of fused deposition modeling (FDM). Ibuprofen ink was applied onto HPMC substrates that were prepared utilizing the FDM method (21,22). An additional oromucosal dosage form was created by employing PIJ to print lidocaine hydrochloride onto electrospun gelatin substrates, piroxicam included or not (23-25). Inkjet technology has been implemented in transdermal delivery. PIJ technology was utilized to create films intended for transdermal delivery, which contained ink compositions of indomethacin in ethanol and were composed of polythene (26,27). Additionally, microneedles have been coated with inkjet printing for the transdermal route (28).

The gradually additive production of pharmaceutical products process has been invented, which manufactures different kinds of dosage via drop-on-demand innovation. To increase the solubility of medications, self-emulsifying drug delivery devices have been created utilizing this type of technology. Purohit et al. utilized a self-emulsifying mixture film adhered to a pill as well as polymer-based films(29). In addition to the aforementioned formulations, carvedilol and ropinirole tablets have been manufactured via photo-initiation inkjet printing, Thiamine hydrochloride pellets were also manufactured via liquid inkjet printing (30,31). Drug-loaded mesoporous nanoparticles of silica and aerogel microspheres designed for inhalation were additional formulations that were created utilizing inkjet technology (32).

The drop-on-powder method, also known as binder jet printing, is an implementation of inkjet printing innovation. In the case of an adhesive jet printer, the printhead may be piezoelectric or thermal. The printhead is comprised of a bed of granules that is fused layer by layer. Liquid droplets moisten the granules, resulting in the subsequent solidification and hardening of the layer (33-35). The powder delivery stage ascends while the fabrication platform descends along the z-axis, and a powder layer is transferred from the substrate to the previously bonded layer using an implement.Considerable investigation has been devoted to the utilization of binder jetting in tablet manufacturing. The characteristics of tablets manufactured by binder jetting are significantly influenced by the excipient type and concentration (36). Higher concentrations of 4-arm star polymers were jettable due to their reduced viscosities in comparison to their linear counterparts, resulting in the formation of more robust tablets. Utilizing binder jetting, tablets of various APIs, geometries, and delivery characteristics have been manufactured. Chlorpheniramine tablets were formulated using binder mixtures of Eudragit E-100 and Eudragit RLPO, with solvents ethanol and acetone, respectively (37,38).

Fused polymer manufacturing (FDM) is a widely used 3D printing method. It involves introducing thermoplastic drug-loaded polymeric filaments into a printing device, where they are molten at a specific temperature before being released via a nozzle. The initial layer of the object is formed when the material is discharged onto the printer platform while the printhead rotates. Subsequent layers are deposited by gradually lowering the platform, and the filaments adhere to the previous layer. The temperature of the printhead can be adjusted in most printers (39).

4. The Significance Of 3D Printing In The Field Of Personalized Medicine

3D printing has the potential to enable dose flexibility based on the patient's needs, particularly for the pediatric population. This is achieved by adjusting the quantity of liquid API distributed onto the film and personalizing interventions. Additionally, the dosage intensity of alternative dosage forms such as patches or tablets can be adjusted to suit the specific requirements of each patient. To achieve dose flexibility, tablet dividing by hand or with the aid of a splitter has been practiced in recent years. However, this method has proven ineffective due to the different classification factors of split tablets. Personalized 3D-printed granules or mini-printlets have been created, which resemble miniature tablets and can combine two distinct medications. Personalization can also be achieved by combining and encapsulating mini-printlets in accordance with the required dose (40-43).

3D printing technology enables the production of dosage forms with customizable release profiles, accommodating specific individual needs. One potential approach to achieve this is through the modification of tablet layouts and designs. For example, immediate release tablets for low-dose medications can be created through the creation of spaces in the tablets or a reduction in tablet thickness. Paracetamol tablets can be manufactured into various geometric forms, such as cube, disc, circle, pyramid, and cylinder. Tablets with intricate geometries, such as those of a honeycomb structure, can be created using 3D printing (44,45).

Tablets with intricate release profiles that integrate two distinct release mechanisms can be produced, including two sections of immediate-extended release pills with release mechanisms that varied according to pH. Three-component breakout tablets, chewable multifaceted pulsatory tablets, and dual pulsatory tablets featuring two sections of contrasting pH-based solubility were developed. 3D-designed patches also exhibit a range of shapes, such as cylinder, torus, and gridlines. Optimized capsular devices can regulate drug release from an immediate release capsule while suspended in gastric fluid (46-49).

Osmotic 3D printing was used to create dosage forms, where the geometry of the cellulose acetate exterior encasing the osmotic core modified the release. The parameters that regulated the release profile of medications in coated tablets were the area of the coated tablet, the number of coatings, and the coated surfaces of the tablets. In addition to structural and coating variations, excipients used in 3D printing may also regulate drug release. Wang et al. found that the proportion of cross-linkable polymers influences drug release, while Tagami et al. (47) found that drug release was retarded when the amount of HPMC in the drug's composition was increased.

The "polypill" concept is a significant use of 3D printing in customized healthcare. It combines multiple medications into a single tablet, catering to individuals prescribed polypharmacy. By reducing daily tablet intake, this concept can enhance patient compliance and adherence to medication, particularly among the elderly. Khaled et al. (48,49) successfully manufactured three-drug 3D-printed polypills, which could serve as a therapeutic intervention for hypertensive diabetics. Another group of researchers constructed PVA-based polypills from four drugs, resulting in a reduced rate of drug release compared to individual tablets. Robles-Martinez et al. used a SLA 3D printer to fabricate multilayered polypills with six drugs into cylindrical and ring-shaped structures.

The technology of 3D printing was applied to the development of polypill capsules containing multiple medications with differing release profiles. By merging FDM with hot-filling syringes, two capsule skeletons were developed, each featuring four distinct sections. The exterior of the capsule is constructed from polyvinyl alcohol and polylactic acid, and by adjusting the thickness of the carapace in the circular design or the size of the rate-limiting openings in a parallel arrangement, customized release profiles can be achieved (50-52).

5. Utilizing 3D Printing on a Large Scale

Children face challenges in medication administration due to their unique preferences regarding dosage form, flavor, appearance, and odor. Three-dimensional printing can be used to accommodate these preferences, ensuring accurate administration based on body weight. For children with swallowing difficulties, ODF formulations, rapidly disintegrating tablets, and 3D-printed minipills are viable options for administration. Mini-tablets with a diameter of 4 mm were preferred over alternative formulations (53-55).

Increasing medication compliance and absorption among kids can be achieved through providing dosage forms that feature their preferred flavor and color. Goyanes et al. (56) utilized 3D printing technology to produce isoleucine digestible tablets for the management of maple syrup urine disease (MSUD), producing tablets in various colors and flavors. Another study produced digestible chocolate-based dosage forms suitable for children. The elderly population faces challenges with swallowing tablets, potentially impacting medication adherence. Oro-dispersible film formulations and rapid disintegration granules can be used to address this issue. Polypharmacy concerns can be resolved through 3D-printed poly-pills tailored to the patient's needs. Dementia patients can benefit from patient-specific, 3D-printed dosage containers with embossing designs that designate the time, date, and/or weekday of administration.

Approximately 285 million individuals worldwide have visual impairment, leading to medication and treatment concerns. Awad et al. (57) manufactured orally disintegrating tablets suitable for patients with visual impairments using SLA, featuring Braille and lunar patterns printed on the surface. A range of tablet configurations were created, each featuring additional information such as an indication or dosage schedule of the medication. By promoting medication adherence and decreasing medication errors, this innovative idea can significantly benefit the treatment of blind individuals.

6. Application Of 3D Printing Technology In A Medical Setting

3D-printed dosage forms have shown widespread acceptance among patients, with most respondents favoring this technology. This technology could significantly benefit healthcare and pharmacy facilities by dispenseding personalized pharmaceutical products (58,59). A comprehensive diagnostic process is conducted to evaluate an individual's medical condition, considering factors such as age, body mass index, coexisting conditions, treatment history, and lifestyle. Genetic components are also considered through body fluid analyses. A personalized treatment strategy is determined, and medication is prescribed based on this profile. The optimal dosage forms are determined using artificial intelligence platforms and databases. Tablet forms are manufactured using CAD software and a 3D printer at the facility. The medication is then administered to the patient, followed by quality control. Technological advancements in evaluation, processing information, and 3D printing can accelerate this process, yielding significant benefits in a clinical environment (60). However, integrating 3D printing into healthcare facilities presents challenges. Technical aspects require skilled operators on-site, which may be impractical. Techniques for monitoring the quality of printed forms of administration must be developed, focusing on feasibility and non-destructiveness. Different procedure analytical technologies (PAT) have been successfully used to achieve remarkable precision in determining drug content and distribution within oral films and tablets. Financial considerations are also necessary, as the installation of 3D printers in hospitals can be costly. Packaging and labeling specifications must be considered to comply with personalized medicine demands. To produce the ideal 3D printer for clinical use, additional technological advancements are required, including quick, inexpensive, user-friendly, and high-resolution printers (61).

Conclusion

3D printing technology has the potential to revolutionize the pharmaceutical industry by enabling on-demand customized medication forms, enhancing patient safety and efficacy. It can create pills with intricate forms and release profiles, and has been extensively researched since the FDA's approval of Spritam. The primary benefits of 3D printing in the healthcare sector include rapid manufacturing turnaround time, formulation versatility, and cost-efficiency. However, the application of this technology in pharmaceutical production is still in its nascent stage due to scientific, quality control, and legislative challenges. Establishing regulatory guidelines for clinical application is crucial. By addressing these challenges, the pharmaceutical sector can fully embrace 3D printing, leading to a bright future where personalized medicine transforms the healthcare system. The pharmaceutical sector must evaluate the advantages and disadvantages of different platforms to design the most suitable 3D printer for hospital environments.

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