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Pharmaceutical 3-D Printing Technology at a Glance

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Abstract

The process of digital fabrication, commonly known as 3D printing or additive manufacturing, involves gradually adding materials to a geometric representation to make physical objects. Dr. Kodama receives the first 3D printing efforts in exchange for his creation of a quick prototyping method. He was the first to explain a layer-by-layer manufacturing process and develop the photosensitive resin that served as the prototype of SLA. 3D printing is now widely used throughout the world. 3D printing technology is progressively being applied for mass modification and manufacture of open-source designs in agricultural, healthcare, automobile, locomotive, and aviation industries. A significant amount of 3D printing technology is currently being employed in the pharmaceutical production chain to change what pharmacies do when producing particular drugs. The advantages include extremely reproducible results, a variety of pharmaceutical release patterns, and individualized pharmacological therapy. Patients may benefit from a variety of advantages provided by 3DP's customized medications. It may be better to provide a patient a printable dosage form on paper rather than one printed with powder. Used in the creation of complicated release profile formulation and customized delivery, as well as drug printing in picoliters and minimizing API side effects or adverse effects.

Keywords: *Three-dimensional printing, Solid oral dosage forms, Medical devices, Pharmaceutical development, Personalized medication, Controlled release*

1. Introduction

1.1. Three-Dimensional Printing

The purpose of 3D printing is to deliver customized and complex product in much easy way than the conventional manufacturing techniques (Perrot, 2019). Digitized production technologies are anticipated to bring striking benefits for companies and businesses, but in practice, such gains are rarely realized. Product

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Innovators are advised to be extraordinary and agile to turn to three-dimensional (3D) printing (Candi and Beltagui , 2019). 3D printing is a relatively fresh technology that was first illustrated in the early 1990s (Rengier *et al.,* 2010). Medicinal and pharmaceutical 3D printing applications are growing quickly and are expected to develop the healthcare industry (Ventola, 2014). Examples of personalized drugs, including dose, dose combination, or even actively tailored to the patient's genetics, are not yet fully understood (Kalaskar, 2017; Kamali *et al.,* 2016). 3D printing is all about digital drawing and fabrication of article layer-by-layer (Norman *et al.,* 2017). In realistic terms, this means that users can create practically anything that can be designed in a digital platform using Computer-Aided Design (CAD) software (Souto *et al.,* 2019; Izdebska and Thoma , 2016). Virtual must be created as stereo lithography (.stl) or object (.obj) files for use as templates in commercially available object printers (Panesar *et al.,* 2018). Democratization of design and production, enhanced collaboration, reduced time, customized geometrically complex objects in small quantities have helped reduce material use (Rengier *et al.,* 2010; Ursan *et al.,* 2013). The term 3D printing refers to a series of additive mechanized processes, which construct products straight from digital design by creating layers of plastics, metals or other materials (Prasad and Smyth , 2016). Due to the all-embracing research being done in this vicinity and all the investigational drug delivery systems intended and described in numerous papers over the past few years, pharmaceutical company like Aprecia® launched its first approved 3DP manufactured product (Fink, 2019). 3D printing is built-up technique in which objects fabricate by depositing material like, plastic, metal, resin, powder, liquid, etc. to construct 3D object (Ngo *et al.,* 2018). 3D printers are similar to the traditional inkjet printers though, the ending creation differs within that a 3D printed object is produced.

2. Brief History

Hull, in 1980s, was working at the Ultra Violet Products Company in California to manufacture plastic making objects from Photopolly Limers invented 3D printing(Ventola, 2014). In 1988, 1st commercial 3D printer, SLA-250, was launched. Later, Austin filed a patent designed for selective laser sintering; a process scan over a powder bed is by laser beam to produce a solid object after repetitions (Deckard, 1989). MIT Professors are accredited first for using the expression ''3D printer'' with their invention of a layering technique using standard inkjet print head to deposit ''ink'' or a binder solution into the powder bed to bind powder, again repeating this process layer-by-layer to produce the desired geometry (Sachs *et al.,* 1993). Thomas J. Bradbury and his colleagues created design of anatomically correct implants for a patient. Radiological data representing anatomical structure of anatomical body, which is to be altered, repaired or augmented and created multidimensional model, can be used (Bradbury *et al.,* 2004). David Russell *et al.* invented apparatus and method to produce 3D object (Russell *et al.,* 2007).

3. Types of 3D Printing Technologies

Over the past 20 years, wide varieties of 3D printing technologies were introduced. 3D printing is also known as the Additive Manufacturing (AM) process. Although other highly competitive processes, such as laser-based writing systems or nozzle-based deposition systems, have been extensively developed, printing-based inkjet systems is a frequently used procedure in three- dimensional method (Goole and Amighi , 2016). It can furthermore be classified in Figure 1, into 3D printing systems. 3D printing processes may also be related to (1) melt and solidify method; (2) fusing method; (3) cut and join methods. Fused deposition production method uses melting followed by liquid-based printing (Kaufui and Aldo , 2012). In stereolithographic printing, a laser is used to photo polymerize a resin. Stereo Lithography translate liquid polymers into solid layers by means of photo-curing UV blue light and used to manufacture complex nanocomposites (Melchels *et al.,* 2010; Manapat *et al.,* 2017; Gibson *et al.,* 2015). Polyjet printing is a quite novel form of rapid printing manufacture (Singh, 2011). The process was patented by Sachs *et al.* (1994) under US patent. It uses inkjet technologies to produce physical model groups (Taylor *et al.,* 2011; Cooper, 2001) Laminated Object Manufacturing is ideal for large parts production (Murr *et al.,* 2012). The layers are bound together by pressure and temperature application and by means of a thermal adhesive coating. In selective laser sintering process, the powder is sintered or fused using carbon dioxide laser beams (Kaufui and Aldo , 2012). Electron beam melting used mostly for fabricating complex polymer prototypes that have now become well established (Kaufui and Aldo,

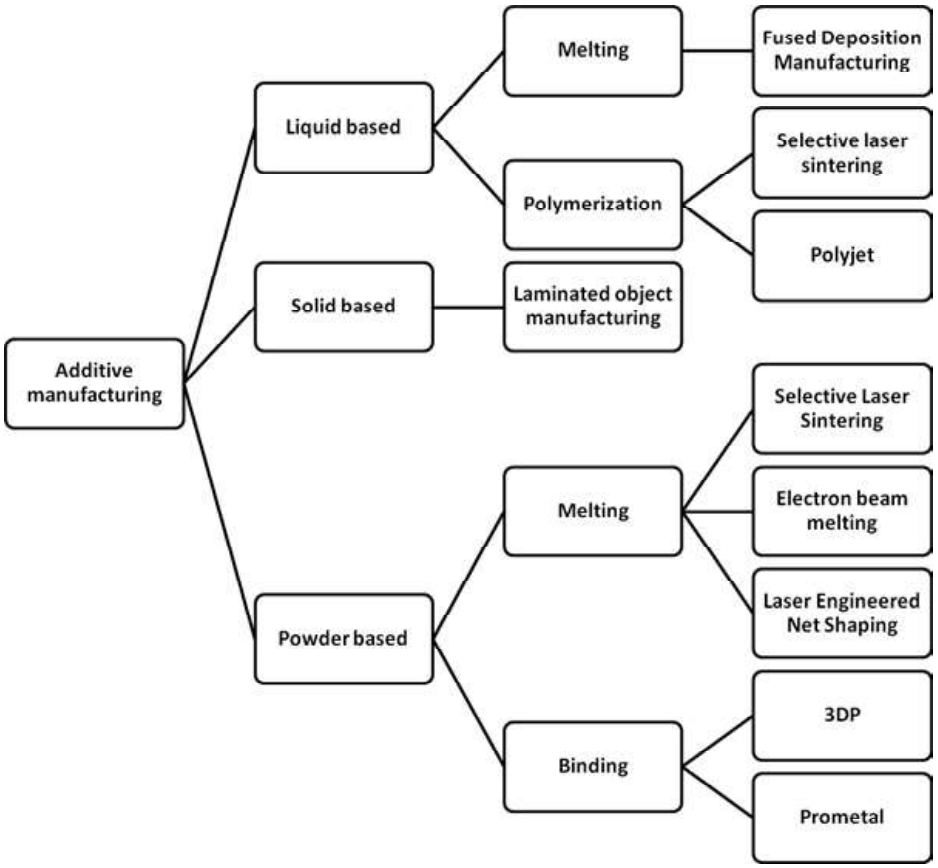

Figure 1: Categorization of 3D Printing General Additive Manufacturing Techniques Based on Type of Base

2012; Clint *et al.*, 1998). Laser Engineered Net Shaping (LENS) uses virgin metal powder as the user's choice, as processes build material (Perrot, 2019; Acosta-vélez and Wu, 2016; Hofmeister *et al.*, 1999). In MIT-licensed procedures, 3DP and prometal, a liquid binder is installed on a powder medium using inkjets for printing using Computer-Aided Design (CAD) data (Kaufui and Aldo , 2012; Murr *et al.*, 2012).

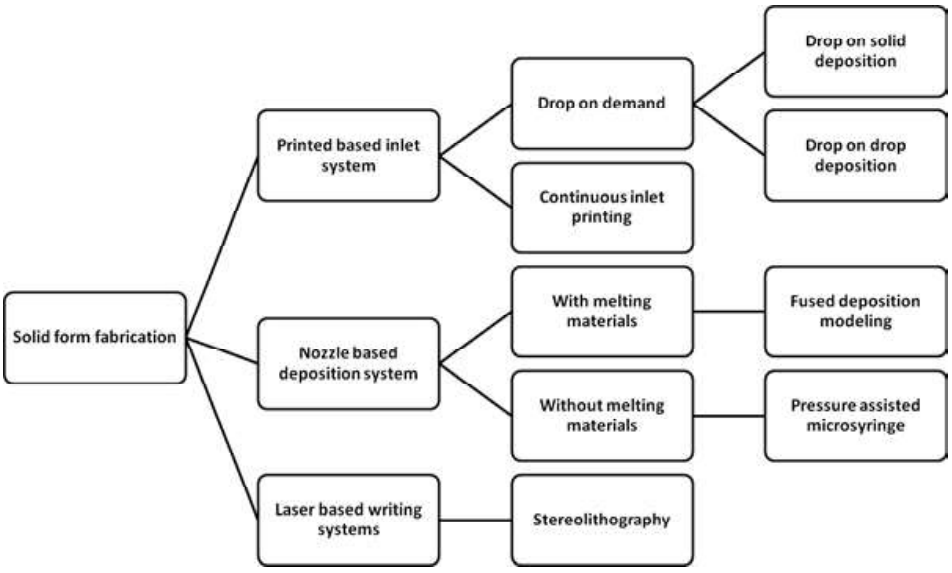

Figure 2: 3D Printing Technologies that Supports Medicine Manufactures for Solid form Fabrication

4. Techniques Widely Used by the Pharmaceutical Companies

Pharmaceutical industry uses 3D printing techniques bases on solid form fabrication that are further classified in printed based inlet system, nozzle-based deposition system and laser-based writing systems (Figure 2).

4.1. Printing-Based Inkjet Systems

Inkjet printing is the overall term for describing systems that are capable of digitally controlled configuration and residency of small liquid droplets on a substrate with a pattern-generating mechanism. There are two categories of printing-based inkjet systems: (1) Continuous Inkjet Printing (CIJ) and (2) Drop-on Demand (DoD) inkjet printing (Goole and Amighi , 2016; Yamada *et al.,* 2015). Inkjet printing is based on Lord Raley's instability theory, developed in 1878, which explains the breaking of a liquid stream or jet into droplets (Konta *et al.,* 2017; Gross *et al.,* 2014).

4.1.1. Drop-on-Demand (DoD) Inkjet Printing

DoD inkjet printers fabricate individual drops when considered necessary and are therefore more economical with ink delivery than CIJ systems (Derby, 2010). DoD classifies into two types: drop-on solid deposition and drop-on-drop deposition. The most regular types of work with DOD printing are thermal (sometimes referred to as bubbles) and piezoelectric (Goole and Amighi , 2016; Konta *et al.,* 2017). In thermal type, its heads utilize a resistor that the electrical pulses in the reservoir heat up swiftly and make a vapor bubble, these bubbles then drive the ink out of the print head; then the bubble breaks down, producing negative pressure that pulls the ink out of the reservoir to refill the chamber. In piezoelectric type, a piezoelectric component such as a crystal or ceramic is used to manufacture mechanical movement when voltage is applied. The element deformation creates a pressure signal that drains the fluid out of the nozzle breaks down, producing negative pressure that pulls the ink out of the reservoir to refill the chamber. In piezoelectric type, a piezoelectric component such as a crystal or ceramic is used to manufacture mechanical movement when voltage is applied. The element deformation creates a pressure signal that drains the fluid out of the nozzle.

4.1.2. Drop-on-Solid Deposition

Drop-on-solid deposition uses a mixture of powder-bed and binder-ink to generate a solid structure in a level-by-level way. The stability of the final product is often achieved by thermal sintering, which permits the elimination of residual volatile solvents. The binder may reason the particles of the ink to stick or the powder bed may play a role after its own solidification. These techniques are prejudiced by two powder characteristics: powder topology and the response of materials with binder.

4.1.1.1. Drop-on-Drop Deposition

The drop-on-drop deposition is a direct-writing inkjet printing method capable of creating microscopic drug formulations with diverse geometries and comparatively high drug loadings. Multi-droplets allow the creation of overlapping, high-resolution three-dimensional compositions. Piezoelectric print heads are frequently used because they do not restrict the selection of solvent. The droplets produced are characterized by the volume of some pico liters, which corresponds to the normal range of 18-50 μm. The major negative aspect of the process is that the three-dimensional structures are very fragile and irregular, deficient hardness, unconvinced resolution finish, and low drug loadings. The unbound powder serves as a supporting material during the process and is removed after the forgery (Goole and Amighi , 2016; Konta *et al.,* 2017; Gross *et al.,* 2014).

4.1.3. Continuous Inkjet Printing (CIJ)

CIJ printing uses a pressure stream to generate a continuous flow of drops. The droplets are taken after exiting the nozzle and are directed to the substrate or the waste again by electrostatic plates (Derby, 2010; Cooley *et al.,* 2002).

4.2. Nozzle-Based Deposition Systems

Technologies are ever evolving and new technologies are continuously developed to overcome limitations of previous ones (Khatri *et al.,* 2018). The nozzle-based deposition method consists of a combination of drugs

and polymers and other solid materials prior to 3D printing. Nozzle-based deposition systems permit direct writing, which is based on computer-controlled production methods thatink through the nozzle to create a 3D pattern layer-bilayer with controlled structure and architecture. Such systems can be divided into processes based on content melting and non-melting processes. There are two types of printing, depending on the kind of material use: fused deposition modeling, which uses dissolved components, and pressure-assisted micro syringes, which do not use dissolved materials.

4.2.1. Fused Deposition Modeling

In Fused deposition modeling process, the copy or part is usually produced by extruding slim 200-400 µm threads of polymer-based matter that alleviate immediately to structure a solid layer (Kaufui and Aldo, 2012). Process has limitation of various shapes that can be fabricated. Yet, using a detachable holdup structure, any form can be constructed. These thin supports are added without human intervention to the model throughout processing and can be broken down during the finishing procedure.

4.2.2. Pressure-Assisted Micro Syringes (PAM)

This technique uses a syringe extruder for oily and semi-liquid material deposition according to the geometry design. Viscosity, apparent elastic limit and viscoelasticity, are the root parameters that establish the fertility of this technology. It has the potential to work continuously with an oven and at room temperature. Solvents used can be sometimes toxic to health and may cause stability problem in certain APIs. Tissue printing substitutes or soft tissue scaffolds, as well as multifaceted medicine delivery systems are its key applications (Goole and Amighi , 2016; Konta *et al.*, 2017).

4.2.3. Stereo Lithography

In stereolithographic printing, a laser is used to photo polymerize a resin. Stereo Lithography converts liquid polymer resins and composites into solid layers using photo-curing UV blue light (Bradbury *et al.*, 2004). This technology produces high-quality components for biomedical applications or gears with integrated moving components and complex nanocomposites.

5. Biological Applications/Medical Application for 3D Printing

Additive manufacturing was used to design and manufacture lightweight machines for various purposes like parts of rocket, plane, formula one car (Bletzinger and Ramm, 2001; Milewski, 2017). In the early 2000s, the expertise was first used to create dental implants and custom prosthetics (Ventola, 2014; Konta *et al.*, 2017). After that, medical applications of 3D printing have advanced extensively. Recently published reviews tell the use of 3D printing intended for skeleton, ears, exoskeleton, windpipes, stem cells, jawbones, spectacles, vascular network, cell culture, blood vessels, organs and tissues, novel dosage forms, and drug delivery devices (Schubert *et al.*, 2014). Additive manufacturing have been extensively used as a tool for bioengineered tissue, varying in composition from bone and tooth to vascular and organ scaffolding. However, in some cases the required scaffolds area is so large that autogenous tissue sampling is not possible for the patient (Gross *et al.*, 2014). 3D printing has become an attractive booth for the development of biological material that is reproducible. Table 1 shows the various biological applications of 3D printing.

6. Pharmaceutical Applications

6.1. Commercially Existing 3D Printed Drugs

The FDA granted approval to the antiepileptic API, the first 3D printed drug-containing levetiracetam, Spritam® (Aprecia Pharmaceuticals, East Windsor, NJ, USA). Pharmacological effectiveness was found to be analogous conventional tablets, but porous and soluble matrix composition led to improved dissolution (Gross *et al.*, 2014). Also used for tablets with immediate-release, monolithic sustained-release, pulsatile drug release, biphasic release, fast-disintegrating, enteric release, and zero-order release, or odispersible films, Floating Drug Delivery System (FDDS), multi-active solid dosage forms, and nano capsule formulation (Khatri *et al.*, 2018).

Table 1: Biological Applications of 3D Printing	
Tissue Engineering	The current treatment for organ failure is largely based on organ transplantation of live or else deceased donors. On the other hand, present is a stretched scarcity of human organs obtainable for transplantation (Cui *et al.*, 2012). Researchers are working on methods to grow complete human organs, which can be used, for selection purposes at some stage in drug discovery (Ventola, 2014; and Acosta-vélez and Wu, 2016). 3D bioprinting have been doing well in produce knee meniscus, heart valves, artificial ears as well as the manufacture of custom-made barrier absorbable trachea, which has already been implanted in neonates with tracheobronchomalacia (Konta *et al.*, 2017; and Ji and Guvendiren, 2017).
Customized Implants and Prostheses	Planting and prosthesis can be made in almost any conceivable geometry by translating X-ray, MRI or CT scan digital.stl 3D print documents. 3D printing is productively used in the health care, both standard and complex, used for surgical implant and prostheses, sometimes within 24 hours (Ventola, 2014). Used for fabricating dental, spinal, and hip implants.
Surgical Anatomical Models	3D Printed neuro anatomical providing can be especially helpful for neurosurgeons by introducing some of the most complex structures in the human body. A real model, modeling the relationship between lesions with regular brain structure, can help determine the safest surgical corridors and may be useful for rehearsing challenging cases for neurosurgeons. Multipart spinal deformity can be better studied using the 3D model. Models for colonoscopy and liver transplant studies have been designed in USA and Japan, respectively. Polypeptide chain models with secondary folds structures were designed by inclusion of bond rotating barriers.
Aesthetic Surgery	In the future, using a three-dimensional printed model will be able to print personalized breast implants to suit any patient's anatomy and personal needs. Not only the shape but also the implant's design can be adjusted, giving the breast a more natural appearance and a natural experience.
Hand Surgery	Recently, customized three-dimensionally printed prostheses have emerged, and various commercial companies offer personalized three-dimensionally printed finger, hand, and arm prosthetics. It is now doable to order a 3D printed finger or arm prosthetic for only $20 to $50. Print biomimetic prosthetics combined with diverse neurons layers may probably make prosthetic limbs a entirely functional piece of the body.
Treatment of Burn Wounds	Researchers at the Wake Forrest Institute of Regenerative Medicine used this method to bioprint amniotic fluid-derived stem cells and skin cells directly onto wounds and burn defects. The escalating speed and resolution of three-dimensional bioprinters, this approach may develop into viable for the in vivo regeneration of tissues straight away after injury or during surgery.

6.2. Personalized Topical Treatment Device

Nose-shaped masks for acne treatment filled with salicylic acid have been developed efficiently. Here, facial scan of patient was exported to the program, after which the section was selected. The most promising technique was for mask manufacturing, allowing high drug loading for the significant conductivity of salicylic acid during 3D printing (Konta *et al.*, 2017).

6.3. 3D Printing of Transdermal Delivery Systems

To avoid first-pass metabolism and/or pH mediated degeneration or ease of administration for patients with chronic illnesses such as diabetes, transdermal delivery systems may be beneficial. Layer-by-layer 3D printing technology can with no trouble used for the foundation of multifaceted transdermal patches of films. 3D technology offers the unique advantage of printing drug-filled micro needles for transdermal delivery. Microneedles are usually less than 500 μm in height and are meant to penetrate the stratum corneum (10-15 μm) to deliver active agents (Prasad and Smyth, 2016). SL was used to produce microneedles of biodegradable polymer (methyl vinyl ether-alt-maleic anhydride). To coat a quantum dotted needle as a model active agent inkjet printing can be used.

Table 2: Studies of 3D Printing for Use in Drug Formulation Development

The 3D Technique (Equipment)	API and/or Dosage form	Application/Remark	Reference
Selective laser sintering and fused deposition modeling or UV curing of resin as in stereolithography	Captopril, Nifedipine Glipizide	3D extrusion-based printing was used as a drug product technology. It was used to produce a multi-active tablet with well-defined and separate controlled release profile, for three different drugs.	Khaled *et al.* (2015)
FDM (fused deposition *Modeling)	Metronidazole	Printed 3D printed tablet, which has a hole of 2.0 mm, air volume of 132 mm3, is released zero-order drug. In this research, indicate That has promised in the development of the existing 3D printing tablet housing platform Floating drug delivery systems.	Huanbutta and Sangnim (2019)
The desktop extrusion-based 3D printer (Fab@Home)	Guaifenesin	This research was a noteworthy step towards the revelation and validation of easy, low-cost 3D printing for the adapted manufacture of medicines, with the impending possibility to play a decisive role in future developments, both in personalized care and treatment.	Khaled *et al.* (2014)
RegenHU 3D printer (3D based extrusion)	Ramipril, pravastatin sodium, Atenolol, aspirin, and hydrochlorothiazide	Demonstrate 5 drugs in one tablet (polypill) in one tablet, immediate and sustained release, shun incompatibility of drug, no detection of interaction.	Khaled *et al.* (2015)
Fused deposition Modeling (FDM) 3D printing and Hot Melt Extrusion (HME)	Theophylline	FDM-based 3D printing proved compatible with the drug load filament produced by HME.	Pietrzak *et al.* (2015)
3DP	Chlorpheniramine maleate, Diclofenac sodium	3DP technology different release mechanism (erosion, diffusion), Pulsatory devices fabrication one pulse generate in stomach and second pulse generate in the intestine. 3DP techniques used for fabricating pulsatile release fabrication.	Rowe *et al.* (2000)
Thermal Ink-Jet (TIJ) Printing	Salbutamol Sulphate	Salbutamol Sulphate used as a model drug and treatment of Asthma in pediatric patient. TIJ printing makes it possible to personalized dose as per patient age, body surface area and sex.	Buanz *et al.* (2011)
Inkjet printing	Riboflavin sodium phosphate, propranolol hydrochloride	Inkjet-printed solid dose forms showed excellent content Consistency for both APIs. Also used for water-insoluble and oxygen labile drug and increase the stability of the drug.	Genina *et al.* (2012)
FDM 3DP	Paracetamol	Five diverse shaped tablets were printed - pyramid, cube, sphere, cylinder, and torus. Here, it was concluded that drug release was dependant on surface are to volume ratio rather than simply on surface area and there comes the role of geometric shape.	Goyanes *et al.* (2015)

Table 2 (Cont.)

Inkjet printing	Rifampicin	Antibiotic and calcium eluting micropatterns were revealed as fresh means of prevention. Microfluidic motile cultures were used. Rifampicin absolutely kills the ability of the micropattern to have as an effective means of preventing biofilm colony. *S. Epidermidis* composition is an effective means of preventing biofilm colony development.	Gu *et al.* (2012)
Inkjet printing	Levofloxacin(LVFX)	A 3D printing process that yields a dual-model profile i.e., pulsatile and sustains release from an implant was developed.	Huang *et al.* (2007)
Hot-melt 3D inkjet printing	Fenofibrate	Higher spatial resolution is achieved by the formulation testifies to and benefits from very small volumes of ink (picoliters). Accurate dose is be very desirable when managing Chronic illnesses like hypertension and anti-depression for maximum therapeutic reasons.	Kyobula *et al.* (2017)
Piezoelectric inkjet printing	Paclitaxel (PTX)	PTX loaded PLGA microparticles with different geometries display different drugs release rate mainly due to different surface areas to volume ratio. The release rate was a downward rate categorized as honeycomb > grid, ring > circle.	Lee *et al.* (2012)
Extrusion printing	dexamethasone-21-phosphate disodium salt (Dex21P)	The printed 3-dimensional compositions are represented by the spatial distribution of the drug. Two types of drug encapsulation designs (rolled and sealed as well as layer-by-layer) were successfully fabricated using printing technology.	Rattanakit *et al.* (2012)
ZMorph® 3D printer(co-extrusion based 3Dprinting)	Aripiprazole	The underlying principle of this research was to estimate the value of dual co-extrusion fluid-loaded soluble free filament and insoluble drug-free with 3D printed tablet with aripiprazole (ARP) assigned to BCS class II. The synchronized co-extrusion of drug-free filament was chosen because feedstock material demonstrates a promising approach to be a viable preparation method for prints with modified release.	Jamróz *et al.* (2018)
Fused Deposition Modeling (a.k.a. FDM-3D printing)	Metformin and glimepiride	Formulated bilayer tablet dosage form encloses two anti-diabetic drugs having di erent daily dosage regimens. It is desirable to include added more than one API into the formulation, as it increase patient fulfillment and reduce the cost of treatment, especially when different doses of API are tailored to the explicit requirements of each patient, provided by printing.	Gioumouxouzis *et al.* (2018)

Table 2 (Cont.)

Dual extrusion fused deposition modeling	Pantoprazole sodium	The model drug used different printing plans for tablets with the acid- and thermo-labile drug pantoprazole sodium were evaluated for various characteristics. The acetate phthalate bottom and the almost insoluble polycaprolactone at the top are printed only at 58 °C. Coated tablets with a thermo-labile API were successfully implemented showing no visible signs of thermal degradation.	Kempin *et al.* (2018)
Hot melt ram extruder 3D printers	Paracetamol	Paracetamol used as the model drug in Orodispersible film (ODF). This work describes a novel approach to print ODF intended for adapted therapy. This should be the uniformity of the drug amount per unit of medicinal products Goals for the benefit of patients can be certain.	Musazzi *et al.* (2018)
3DP	Paracetamol	3DP technology development of new oral fast-disintegrating dosage form devices. The porosity of the pellets is inversely related to the compressive pressure. However, high compression pressure is needed to ensure sufficient strength of the tablet. 3DP has some advantages over traditional compression techniques for the manufacture of solid dosage forms and can grant inventive strategies for the design, development, production, and commercialization of many types of solid dosage forms.	Yu *et al.* (2009)
3DP	Acetaminophen	Desired drug release in conventional manufacture techniques requires multistep process different materials used in the different processes and unfriendly effect on accuracy repeatability. Desired release profile tablet formulated in single easy step. Also powerful way to compete with controlled-release tablets formulating.	Yu *et al.* (2009)
3-DP™ Technology	Pseudoephedrine hydrochloride (PEH)	Primary difficulties in maintaining a constant release rate include initial dose explosion, loss of driving force to maintain target release rate over the desired period, and premature changes in its properties due to the length of the drug release path. Prepare the near zero-order release of water-soluble drug by this technology. These techniques produce products insensitive to both changes in pH and hydrodynamic stress of the dissolution medium.	Wang *et al.* (2006)

Table 2 (Cont.)

Inkjet printing	Felodipine	Felodipine is poorly water-soluble anti-hypertensive drug and bioavailability and dissolution is poor, inkjet printing able to produce droplet size in picoliters so adverse/side effect is reduced. This technology used to prepare the solid dispersion to boost the dissolution profile.	Scoutaris *et al.* (2011)
3DP technology	Fenofibrate (FEN) and Cinnarizine (CINN)	Fenofibrate (FEN) and cinnarizine (CINN) are used as the model drug for the preparation of solid self-micro emulsifying drug delivery systems (SSMEDDS) with defined surface area to volume (SA/V) ratios. Drugs selection was based on their poor water solubility and their broad use as lipophilic compounds in a variety of studies with lipid-based drug formulations. These formulations controlled three-dimensional geometry without a solid-phase carrier. The dispersal kinetics of the drug-filled SSMEDDS formulation showed a clear dependence on the SA/V ratio values, showing the effect of geometric shaping on the dispersion time.	Vithani *et al.* (2019)
HME FDM	Haloperidol	In 3D printed tablet drug in amorphous state and drug, release is faster and immediate. Potential delivery of medicine avoidance of side effects by personalized delivery, 3D printed tablets prepared by fused deposition modeling with the aim of would afford comparatively rapid drug release.	Solanki *et al.* (2018)

7. Summary of Research Carried Out Using 3D Printing for Dosage Form Development

Variety of research has been carried out on dosage form development ranging from controlled release profile of drug to immediate release solid dispersions. Table 2 summarizes various research reported and their outcome to guide further course of research in future.

8. Future Trends

3D printing is anticipated to execute a significant role in the attitude towards individual medicine, the use of customize dietary foodstuffs, drugs and organs. Pharmaceutical API/dosage forms could be made-up on demand. Drug manufacturing and distribution will be more cost effective. 3D printing in fabricating the complex organ and prosthetics for the individual patient will surely help healthcare system. Pharmaceutical industry, like aerospace, could use the complex designed equipment for manufacturing processes. The advances in the programmed bioprinters and robot-assisted surgical treatment may also be fundamental in the direction of the development of this technology. There are challenges but a promising progress is continuing.

9. Conclusion

Our well-thought-out review summarizes the accessible literature on current techniques designed for pharmaceutical manufacturing and dosage form development. Useful individual/personalized drug delivery for the narrow therapeutic window drug in 3D printing technology printing in the picoliters and reduce the adverse effect or side effect of the API for pediatrics and geriatrics. 3D printed fabrication of the products with complex release profile and personalized delivery. Effect of formulation geometry on release rate was

studied which gives a way and idea to study other factors using printing technology produced dosage forms.

References

Acosta-vélez, G.F. and Wu, B.M. (2016). 3D Pharming: Direct Printing of Personalized Pharmaceutical Tablets. *Polymer Sciences,* 2(1), 1-10. https://doi.org/10.4172/2471-9935.100011

Bletzinger, K.U. and Ramm, E. (2001). Structural Optimization and Form Finding of Light Weight Structures. *Comput Struct*., 79(22-25), 2053-2062. https://doi.org/10.1016/S0045-7949(01)00052-9

Bradbury, T.J., Gaylo, C.M., Fairweather, J.A., Chesmel, K.D., Materna, P.A. and Youssef, A. (2004). System and Method for Rapidly Customizing Design, Manufacturing and/or Selection of Biomedical Devices. US6772026B2.

Buanz, A.B.M., Saunders, M.H., Basit, A.W., Gaisford, S. (2011). Preparation of Personalized-dose Salbutamol Sulphate Oral Films with Thermal Ink-jet Printing. *Pharm Res*, 28(10), 2386-2392. https://doi.org/10.1007/s11095-011-0450-5

Candi, M. and Beltagui, A. (2019). Effective use of 3D Printing in the Innovation Process. *Technovation*, 80-81: 63-73. https://doi.org/10.1016/j.technovation.2018.05.002

Clint, A., Grifûth, M., Harwell, L., Schlienger, E., Mark, E., John, S., Tony, R., Don, G. and Daryl, R. (1998). Laser Engineered Net Shaping (LENS®): A Tool for Direct Fabrication of Metal Parts, in: Proceedings of ICALEO '98, 85, Orlando, FL, USA, p E-1.

Cooley, P., Wallace, D. and Antohe, B. (2002). Applications of Ink-Jet Printing Technology to BioMEMS and Microfluidic Systems. *JALA*., 7(5), 33-39. doi:10.1016/S1535-5535(04)00214-X

Cooper, K.G. (2001). *Rapid Prototyping Technology: Selection and Application*. 1st ed. Marcel Dekker, Inc., New York.

Cui, X., Boland, T., D'Lima, D. and Lotz, M. (2012). Thermal Inkjet Printing in Tissue Engineering and Regenerative Medicine. *Recent Pat Drug Deliv Formul*., 6(2), 149-155. https://doi.org/10.2174/187221112800672949

Deckard, C.R. (1989). Method and Apparatus for Producing Parts by Selective Sintering. US4863538.

Derby, B. (2010). Inkjet Printing of Functional and Structural Materials: Fluid Property Requirements, Feature Stability, and Resolution. *Annu Rev Mater Res*., 40(1), 395-414. https://doi.org/10.1146/annurev-matsci-070909-104502

Fink, J.K. (2019). *3D Industrial Printing with Polymers,* 1st ed.: John Wiley & Sons Inc. https://doi.org/10.1002/9781119555308.ch6

Genina, N., Fors, D., Vakili, H., Ihalainen, P., Pohjala L., Ehlers, H., Kassamakov, I., Haeggström, E., Vuorela, P., Peltonen, J., Sandler, N. (2012). Tailoring Controlled-release Oral Dosage Forms by Combining Inkjet and Flexographic Printing Techniques. *Eur J Pharm Sci*; 47(3), 615-623. https://doi.org/10.1016/j.ejps.2012.07.020

Gibson, I., Rosen, D. and Stucker, B. (2015). *Additive Manufacturing Technologies: 3D Printing, Rapid Prototyping, and Direct Digital Manufacturing*, 2nd ed. Springer New York, London. Heidelberg Dordrecht; https://doi.org/10.1007/978-1-4939-2113-3

Gibson, I., Rosen, D. and Stucker, B. (2015). *Additive Manufacturing Technologies: 3D Printing, Rapid Prototyping, and Direct Digital Manufacturing*, 2nd ed. Springer New York, London. Heidelberg Dordrecht; https://doi.org/10.1007/978-1-4939-2113-3

Genina, N., Fors, D., Vakili, H., Ihalainen, P., Pohjala L., Ehlers, H., Kassamakov, I., Haeggström, E., Vuorela, P., Peltonen, J., Sandler, N. (2012). Tailoring Controlled-release Oral Dosage Forms by Combining Inkjet and Flexographic Printing Techniques. *Eur J Pharm Sci*; 47(3), 615-623. https://doi.org/10.1016/j.ejps.2012.07.020

Gioumouxouzis, C.I., Baklavaridis, A., Katsamenis, O.L., Markopoulou, C.K., Bouropoulos, N., Tzetzis, D. and Fatouros, D.G. (2018). A 3D Printed Bilayer Oral Solid Dosage Form Combining Metformin for Prolonged and Glimepiride for Immediate Drug Delivery. *Eur J Pharm Sci*, 120, 40-52. https://doi.org/10.1016/j.ejps.2018.04.020

Goole, J. and Amighi, K. (2016). 3D Printing in Pharmaceutics: A New Tool for Designing Customized Drug Delivery Systems. *Int J Pharm.*, 499(1-2), 376-394. https://doi.org/10.1016/j.ijpharm.2015.12.071.

Goyanes, A., Robles Martinez, P., Buanz, A., Basit, A.W, Gaisford S. (2015). Effect of Geometry on Drug Release from 3D Printed Tablets. *Int J Pharm*; 494(2), 657-663. https://doi.org/10.1016/j.ijpharm.2015.04.069

Goyanes, A., Robles Martinez, P., Buanz, A., Basit, A.W, Gaisford S. (2015). Effect of Geometry on Drug Release from 3D Printed Tablets. *Int J Pharm*; 494(2), 657-663. https://doi.org/10.1016/j.ijpharm.2015.04.069

Gross, B.C., Erkal, J.L., Lockwood, S.Y., Che, C. and Spence, D.M. (2014). Evaluation of 3D Printing and its Potential Impact on Biotechnology and the Chemical Sciences. *Anal Chem.,* 86(7), 3240-3253. https://doi.org/10.1021/ac403397r

Gu, Y., Chen, X., Lee, J.H., Monteiro, D.A., Wang, H., Lee, W.Y. (2012). Inkjet Printed Antibiotic- and Calcium-eluting Bioresorbable Nanocomposite Micropatterns for Orthopedic Implants. *Acta Biomater,* 8(1), 424-431. https://doi.org/10.1016/j.actbio.2011.08.006

Gu, Y., Chen, X., Lee, J.H., Monteiro, D.A., Wang, H., Lee, W.Y. (2012). Inkjet Printed Antibiotic- and Calcium-eluting Bioresorbable Nanocomposite Micropatterns for Orthopedic Implants. *Acta Biomater,* 8(1), 424-431. https://doi.org/10.1016/j.actbio.2011.08.006

Hofmeister, W., Wert, M., Smugeresky, J., Philliber, J.A., Griffith, M. and Ensz, M. (1999). Investigating Solidification with the Laser-engineered Net Shaping (LENSTM) Process. *JOM*, 51(7), 1-6.

Huanbutta, K. and Sangnim, T. (2019). Design and Development of Zero-order Drug Release Gastroretentive Floating Tablets Fabricated by 3D Printing Technology. *J Drug Deliv Sci Technol*., 52, 831-7. https://doi.org/10.1016/j.jddst.2019.06.004

Huang, W., Zheng, Q, Sun, W., Xu, H., Yang, X. (2007). Levofloxacin Implants with Predefined Microstructure Fabricated by Three-dimensional Printing Technique. *Int J Pharm,* 339(1-2), 33-38. https://doi.org/10.1016/j.ijpharm.2007.02.021

Izdebska, J. and Thoma, S. (2016). 3-D Printing. In: Thomas, D.J. and Claypole, T.C. (Eds.), *Printing on Polymers: Fundamentals and Applications,* 293-306,William Andrew, Oxford. https://doi.org/10.1016/B978-0-323-37468-2.00018-X

Jamróz, W., Kurek, M., Czech, A., Szafraniec, J., Gawlak, K., Jachowicz, R. (2018). 3D Printing of Tablets Containing Amorphous Aripiprazole by Filaments Co-extrusion. *Eur J Pharm Biopharm,* 131, 44-47. https://doi.org/10.1016/j.ejpb.2018.07.017

Ji, S. and Guvendiren, M. (2017). Recent Advances in Bioink Design for 3d Bioprinting of Tissues and Organs. *Front Bioeng Biotechnol*., 23(5), 1-8. https://doi.org/10.3389/fbioe.2017.00023

Kalaskar, D.M. (2017). 3D Printed Pharmaceutical Products. In: Gaisford, S. (Ed.). *3D Printing in Medicine.* 155-166, Woodhead publishing, Duxford. https://doi.org/10.1016/B978-0- 08-100717-4.00007-7

Kamali, P., Dean, D., Skoracki, R., Koolen, P.G.L., Paul, M.A., Ibrahim, A.M.S. and Lin, S.J. (2016). The Current Role of Three-Dimensional Printing in Plastic Surgery. *Plast Reconstr Surg,* 137(3), 1045-1055. https://doi.org/10.1097/01.prs.0000479977.37428.8e

Katstra, W.E., Palazzolo, R.D., Rowe, C.W., Giritlioglu, B., Teung, P. and Cima, M.J. (2000). Oral Dosage forms Fabricated by Three Dimensional PrintingTM. *J Controlled Release*., 66(1), 1-9. https://doi.org/10.1016/S0168-3659(99)00225-4

Kaufui, V.W. and Aldo, H. (2012). A Review of Additive Manufacturing. *Int Sch Res Notices,* 1-10. doi:10.5402/2012/208760.

Kempin, W., Domsta, V., Brecht, I., Semmling, B., Tillmann, S., Weitschies, W. and Seidlitz, A. (2018). Development of a Dual Extrusion Printing Technique for an Acid- and Thermo-labile Drug. *Eur J Pharm Sci,* 123, 191-198. https://doi.org/10.1016/j.ejps.2018.07.041

Khaled, S.A., Burley, J.C., Alexander, M.R., Yang, J. and Roberts, C.J. (2015). 3D Printing of Tablets Containing Multiple Drugs with Defined Release Profiles. *Int J Pharm*., 494(2), 643-650. https://doi.org/10.1016/j.ijpharm.2015.07.067

Khaled, S.A., Burley, J.C., Alexander, M.R. and Roberts, C.J. (2014). Desktop 3D Printing of Controlled Release Pharmaceutical Bilayer Tablets. *Int J Pharm*, 461(1-2), 105-11. https://doi.org/10.1016/j.ijpharm.2013.11.021

Khaled, S.A., Burley, J.C., Alexander, M.R., Yang, J, Roberts, C.J. (2015). 3D Printing of Five-in-one Dose Combination Polypill with Defined Immediate and Sustained Release Profiles. *J Controlled Release*, 217: 308-314. https://doi.org/10.1016/j.jconrel.2015.09.028

Khatri, P., Shah, M.K. and Vora, N. (2018). Formulation Strategies for Solid Oral Dosage form Using 3D Printing Technology: A Mini-Review. *J Drug Deliv Sci Technol.,* 46, 148-155. https://doi.org/10.1016/j.jddst.2018.05.009

Konta, A.A., Garc, M. and Serrano, D.R. (2017). Personalised 3D Printed Medicines : Which Techniques and Polymers Are More Successful?. *Bioeng*, 4(79), 1-16. https://doi.org/10.3390/bioengineering4040079

Kyobula, M., Adedeji, A., Alexander, M.R., Saleh, E., Wildman, R., Ashcrof,t I., Gellert, P.R., Roberts, C.J. (2017). 3D Inkjet Printing of Tablets Exploiting Bespoke Complex Geometries for Controlled and Tuneable Drug Release. *J. Control. Release,* 261, 207-215. https://doi.org/10.1016/j.jconrel.2017.06.025

Lee, B.K., Yun, Y.H., Choi, J.S., Choi, Y.C., Kim, J.D., Cho, Y.W. (2012). Fabrication of Drug-loaded Polymer Microparticles with Arbitrary Geometries using a Piezoelectric Inkjet Printing System. *Int J Pharm,* 427, 305-310. https://doi.org/10.1016/j.ijpharm.2012.02.011

Manapat, J.Z., Chen, Q., Ye, P. and Advincula, R.C. (2017). 3D Printing of Polymer Nanocomposites via Stereolithography. *Macromol Mater Eng*., 302(9), 1600553. https://doi.org/10.1002/mame.201600553

Melchels, F.P.W., Feijen, J. and Grijpma, D.W. (2010). A Review on Stereolithography and its Applications in Biomedical Engineering. *Biomater.,* 31(24), 6121-6130. https://doi.org/10.1016/j.biomaterials.2010.04.050

Milewski, J.O. (2017). Additive Manufacturing of Metals. *From Fundamental Technology to Rocket Nozzles, Medical Implants, and Custom Jewelry,* 134-57. https://doi.org/10.1007/978-3- 319-58205-4

Murr, L.E., Gaytan, S.M., Ramirez, D.A., Martinez, E., Hernandez, J., Amato, K.N., Shindo, P.W., Medina, F.R. and Wicker, R.B. (2012). Invited Review Metal Fabrication by Additive Manufacturing using Laser and Electron Beam Melting Technologies. *J Mater Sci Technol.,* 28(1), 1–14. https://doi.org/10.1016/S1005-0302(12)60016-4

Murr, L.E., Gaytan, S.M., Ceylan, A., Martinez, E. andMartinez, J,L. (2010). Characterization of Titanium Aluminide Alloy Components Fabricated by Additive Manufacturing using Electron Beam Melting. *Acta Mater.,* 58, 1887-1894. https://doi.org/10.1016/j.actamat.2009.11.032

Musazzi, U.M., Selmin, F., Ortenzi, M.A., Mohammed, G.K., Franzé, S., Minghetti, P. and Cilurzo, F. (2018). Personalized orodispersible films by hot melt ram extrusion 3D printing. I*nt J Pharm,*; 551(1-2), 52-59. https://doi.org/10.1016/j.ijpharm.2018.09.013

Ngo, T.D., Kashani, A., Imbalzano, G., Nguyen, K.T.Q. and Hui, D. (2018). *Additive Manufacturing (3D printing): A Review of Materials, Methods, Applications and Challenges.* Compos Part B-Eng; 143, 172-196. https://doi.org/10.1016/j.compositesb.2018.02.012

Norman, J., Madurawe, R.D., Moore, C.M.V., Khan, M.A. and Khairuzzaman, A. (2017). A New Chapter in Pharmaceutical Manufacturing: 3D-printed Drug Products. *Adv Drug Deliv Rev,* 108, 39-50. https://doi.org/10.1016/j.addr.2016.03.001

Panesar, S.S., Belo, J.T.A. and D'Souza, R.N. (2018). Feasibility of Clinician-Facilitated Three-Dimensional Printing of Synthetic Cranioplasty Flaps. *World Neurosurg,* 113, e628-e637. https://doi.org/10.1016/j.wneu.2018.02.111

Perrot, A. (2019). 3D Printing in Concrete: General Considerations and Technologies. In: Perrot ,A. and Amziane, S. (Eds.). *3D Printing in Concrete,* 1-40, London and New Jersey: ISTE Ltd and John Wiley & Sons, Inc. https://doi.org/10.1002/9781119610755.ch1

Perrot, A. (2019). 3D Printing in Concrete: General Considerations and Technologies. In: Perrot, A. and Amziane, S. (Eds.). *3D Printing in Concrete,* 1-40, ISTE Ltd and John Wiley & Sons, Inc, London and New Jersey. https://doi.org/10.1002/9781119610755.ch1

Pietrzak, K., Isreb, A., Alhnan, M.A. (2015). A Flexible-dose Dispenser for Immediate and Extended Release 3D Printed Tablets. *Eur J Pharm Biopharm,* 96, 380-387. https://doi.org/10.1016/j.ejpb.2015.07.027

Prasad, L.K. and Smyth, H. (2016). 3D Printing Technologies for Drug Delivery: A Review. *Drug Dev Ind Pharm,* 42(7), 1019-1031. https://doi.org/10.3109/03639045.2015.1120743

Rattanakit, P., Moulton, S.E., Santiago, K.S., Liawruangrath, S., Wallace, G.G. (2012). Extrusion Printed Polymer Structures: A Facile and Versatile Approach to Tailored Drug Delivery Platforms. *Int J Pharm,* 422, 254-263. https://doi.org/10.1016/j.ijpharm.2011.11.007

Rengier, F., Mehndiratta, A., Tengg-Kobligk, H., Zechmann, C.M., Unterhinninghofen, R., Kauczor, H.U. and Giesel, F.L. (2010). 3D Printing Based on Imaging Data: Review of Medical Applications. *Int J CARS*; 5, 335-341. https://doi.org/10.1007/s11548-010-0476-x

Rowe, C.W., Katstra, W.E., Palazzolo, R.D., Giritlioglu, B., Teung, P., Cima, M.J. (2000). Multimechanism Oral Dosage Forms Fabricated by Three Dimensional Printing™. *J Controlled Release,* 66(1), 11-17.

Russell, I.D., Hernandez, A., Kinslfy, J. and Berlin, A. (2007). Apparatus and Methods for 3D Printing, US7291002B2.

Sachs, E.M., Haggerty, J.S., Cima, M.J. and Williams, P.A. (1993). Three-dimensional Printing Techniques. US5204055.

Sachs, E.M., Haggerty, J.S., Cima, M.J. and Williams, P.A. (1994). Three-Dimensional Printing Techniques. US5340656, Massachusetts Institute of Technology.

Schubert, C., Van Langeveld, M.C. and Donoso, .LA. (2014). Innovations in 3D Printing: A 3D Overview from Optics to Organs. *Br J Ophthalmol*, 98(2), 159-161. https://doi.org/10.1136/bjophthalmol- 2013-304446

Scoutaris, N., Alexander, M.R., Gellert, P.R. and Roberts, C.J. (2011). Inkjet Printing as a Novel Medicine Formulationtechnique. *J Controlled Release,* 156(2), 179-185. https://doi.org/10.1016/j.jconrel.2011.07.033

Singh, R. (2011). Process Capability Study of Polyjet Printing for Plastic Components. *J Mech Sci Technol*., 25(4), 1011-1015. https://doi.org/10.1007/s12206-011-0203-8

Solanki, N.G., Tahsin, M., Shah, A.V. and Serajuddin, A.T.M. (2018). Formulation of 3D Printed Tablet for Rapid Drug Release by Fused Deposition Modeling: Screening Polymers for Drug Release, Drug- Polymer Miscibility and Printability. *J. Pharm. Sci.,* 107(1), 390-401. https://doi.org/10.1016/j.xphs.2017.10.021

Souto, E.B., Campos, J.C., Filho, S.C., Teixeira, M.C., Martins-Gomes, C., Zielinska, A., Carbone, C. and Silva, A.M. (2019). 3D Printing in the Design of Pharmaceutical Dosage Forms. *Pharm Dev Technol*., 24(8), 1044-1053. https://doi.org/10.1080/10837450.2019.1630426

Taylor, P., Petrovic, V., Vicente, J., Gonzalez, H., Jordá, O., Gordillo, J.D., Blasco, J.R. and Griñan, LP. (2011). Additive Layered Manufacturing: Sectors of Industrial Application Shown Through Case Studies. *Int J Prod Res;* 49(4), 1061-1079. https://doi.org/10.1080/00207540903479786

Ursan, I., Chiu, L. and Pierce, A. (2013). Three-dimensional Drug Printing: A Structured Review. *JAPhA;* 53(2), 136-144. https://doi.org/10.1331/JAPhA.2013.12217

Vehse, M., Petersen, S., Sternberg, K., Schmitz, K. and Seitz, H. (2014). Drug Delivery from Poly (Ethylene Glycol) Diacrylate Scaffolds Produced by DLC Based Micro-Stereolithography. *Macromol Symp*, 346(1), 43-47. https://doi.org/10.1002/ masy.201400060

Ventola, C.L. (2014). Medical Applications for 3D Printing: Current and Projected Uses. *Pharmacy and Therapeutics*, 39(10), 704.

Vithani, K., Goyanes, A., Jannin, V., Basit, A.W., Gaisford, S. and Boyd, B.J. (2019). A Proof of Concept for 3D Printing of Solid Lipid-based Formulations of Poorly Water-soluble Drugs to Control Formulation Dispersion Kinetics. *Pharm Res*, 36(7), 102. https://doi.org/10.1007/s11095-019-2639-y

Wang, C.C., Tejwani, M.R., Roach, W.J., Kay, J.L., Yoo, J., Surprenant, H.L., Monkhouse, D.C. and Pryor, T.J. (2006). Development of Near Zero-order Release Dosage Forms Using Three-dimensional Printing (3-DPTM) Technology. *Drug Dev Ind Pharm*, 32(3), 367-376. https://doi.org/10.1080/03639040500519300

Yamada, K., Henares, T.G., Suzuki, K. and Citterio, D. (2015). Paper Based Inkjet Printed Microfluidic Analytical Devices. *Angew Chem Int Ed.*, 54(18), 5294-310. https://doi.org/10.1002/anie.201411508

Yu, D.G., Shen, X.X., Branford-White, C., Zhu, L.M., White, K. and Yang, X.L. (2009). Novel Oral Fast-Disintegrating DrugDelivery Devices with Predefined Inner Structure Fabricated by Three-Dimensional Printing. *J Pharm Pharmacol*, 61(3), 323-329.https://doi.org/10.1211/jpp/61.03.0006

Yu, D.G., Branford-White, C., Yang, Y.C., Zhu, L.M., Welbeck, E.W. and Yang, X.L. (2009). A Novel Fast DisintegratingTablet Fabricated by Three-dimensional Printing. *Drug Dev Ind Pharm.*, 35(12), 1530-1536. https://doi.org/10.3109/03639040903059359

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