Recent Advances in 3D Printing Technologies for Oral Disintegrating Films: Current Status, Challenges, and Future Perspectives

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Abstract—**Oral disintegrating films (ODFs) are emerging as potential drug delivery methods based on their fast disintegration characteristics, ease of drug administration, and enhanced patient adherence particularly in the pediatric and geriatric age range. Recent breakthroughs in three-dimensional printing (3DP) processes allow creation of fine-tuned ODFs with specific geometries, controlled drug release profiles, and tailored dosing. Herein, it discusses the developments and advances in 3DP methods used for ODF fabrication, such as fused deposition modeling (FDM), semi-solid extrusion (SSE), stereolithography (SLA), inkjet printing, binder jetting, and selective laser sintering (SLS). The advantages, limitations, and pharmaceutical use of these technologies are also given a critical overview. Particular focus is given to film-forming polymers and excipients such as hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), pullulan, and related materials that have a significant influence on printability, mechanical strength, disintegration behavior, and drug release performance. The review further emphasizes important evaluation parameters like film uniformity, tensile strength, disintegration time, and dissolution performance. And, also high-priority issues of the thermal instability of the active pharmaceutical ingredients, availability of pharmaceutical-grade printable materials, scalability, and regulatory issues are reviewed. Novel paradigms, such as artificial intelligence-mediated formulation and point-of-care production, and personalized polypharmacy-based therapies, are anticipated to push the clinical utility of 3D-printed ODFs. In summary, 3DP technology provides great possibilities for patient-oriented oral film formulations and a great advancement into personalized pharmaceutical manufacturing.**

Index Terms—**3D printing; Oral disintegrating films; Semi-solid extrusion; Fused deposition modeling; Personalized medicine; Additive manufacturing**

I. INTRODUCTION

Oral disintegrating films (ODFs) are flexible polymeric dosage forms that are thin and effective in their ability to break down rapidly or dissolve in the oral cavity directly after touching with saliva, thus providing ease of drug use without the use of fluids. [1,2,7] Thanks to these benefits, these dosage forms have in recent years seen significant development in their adherence, convenience of administration, fast action, and consideration for pediatric, geriatric, and dysphagic patients.[8,9] ODFs can also be developed to serve as oral formulations for both localized action in the oral cavity and for systemic absorption via oral, buccal, sublingual routes as active pharmaceuticals. Buccal and sublingual films are favorable due to their enhancement of drug absorption in the oral mucosa with reduced hepatic first-pass metabolism and increased bioavailability.[10,11] The United States Pharmacopeia (USP) classifies oral films based on site of application and therapeutic intent.[12] These films come in a number of shapes and sizes, from strip to sheet and wafer, the thickness varies from 20 to 300 μm.[13,14] ODFs may exhibit immediate or altered drug release, according to the formulation composition and manufacturing process. ODFs compared to the conventional oral dosage forms like tablets and capsules provide certain features such as quick disintegration, better dosing efficiency, portability and better patient acceptability. [13-15] Their extensive surface area allows for rapid wetting and dissolution which leads to rapid drug release. Furthermore, ODFs

have higher flexibility and lower brittleness than orally disintegrating tablets (ODTs) for better handling and storage stability. Moreover, to use these in individualized drug-carrying systems is supported by their capability to apply the adequate dosage of individualized substances into a thin film matrix. With new pharmaceutical manufacturing technology developments and especially 3DP (3-dimensional printing), ODFs have shown enhanced potential for fabrication by the means of custom-produced patient-specific formulations with custom geometry, dose variability, and dose-controlled drug release. These advancements have established 3D-printed ODFs as promising environments for next-generation personalized medicine. [3-6]

II. IMPORTANCE OF NOVEL DRUG DELIVERY SYSTEMS

Drug delivery technologies have also greatly enhanced the therapeutic effectiveness, safety, and patient compliance of pharmaceutical formulations. Standard dosage forms usually suffer from drawbacks including poor bioavailability, variable drug release, and inadequate patient adherence, especially in pediatric and geriatric populations. These challenges have been faced with several approaches to drug delivery including PEGylation, bioadhesive systems, nanotechnology methods, microparticulate carriers, and microfabrication technologies. These technologies helped to develop personalized and targeted therapeutic systems which have enabled the emergence of new platforms like three-dimensional (3D) printed oral disintegrating films.

Table 1. Advanced Drug Delivery Technologies and Their Pharmaceutical Applications

S. No.	Technology	Pharmaceutical Application
1	PEGylation	Enhances drug solubility, prolongs circulation time, and reduces immunogenicity of therapeutic agents[17]
2	Bioadhesive polymers	Improves mucosal adhesion and enhances drug permeation across biological membranes [18]
3	Chemical modification	Modifies drug molecules or conjugates to improve gastrointestinal absorption and bioavailability [18]
4	Novel transdermal systems	Utilizes techniques such as iontophoresis and ultrasound to enhance transdermal drug permeation [23]
5	Microparticulate systems	Provides controlled drug release, targeted delivery, and protection of sensitive biomolecules [21]
6	Nanotechnology-based delivery	Enhances cellular uptake, targeted delivery, and therapeutic efficacy through nanoscale carriers [19,20]
7	Microfabrication technologies	Enables precise fabrication of controlled and personalized drug delivery systems [22]

Among emerging pharmaceutical manufacturing approaches, three-dimensional printing has gained significant attention owing to its ability to fabricate personalized dosage forms with precise control over drug loading, geometry, and release characteristics.

III. 3D PRINTING TECHNOLOGY

Three-dimensional printing (3DP), also called additive manufacturing or rapid prototyping, is an advanced type of fabrication technology that creates three-dimensional structures from material deposition layer by layer based on a digital design model. Since its introduction in the late 1980s, 3DP has become widely applied in engineering, aerospace, automotive, and industrial manufacturing fields. [3,4,24] The pharmaceutical industry has focused on 3DP in recent years due to the design properties with highly configurable structures and control over the drug

formulation, dose distribution, and release characteristics. The introduction of biocompatible and computer-aided fabrication products has substantially enhanced the application for pharmaceutical applications of 3DP.[25,26] This technology was first introduced for the construction of personalized prosthetics and dental instruments, and has been increasingly utilized in designing of personalized drug delivery systems for specific individual patients, medical devices, tissue engineered scaffolds and sophisticated oral formulations. In pharmaceutical applications, for instance, 3DP permits the fabrication of dosage forms with different dimensions, drug dosage adjustment, and release profile alteration, consequently contributing to the growing demand for personalized medicine. In multiple pharmaceutical applications, 3D printing has attracted attention, especially in the context of oral disintegrating films (ODFs) fabrication, where fine deposition of drug-containing materials can be achieved while preservation of formulation flexibility and uniformity is achieved. Not only, 3DP technologies enable rapid prototyping, minimize material use and formulation optimization in drug-development processes.[27]

Fundamentals on 3D Printing in Pharmaceutics

Pharmaceutical product development utilizing 3D printing requires several key factors: digital design, formulation materials, printing parameters, and dosage form optimization. A widely applied design computer-aided CAD technique to fabricate digital models of the intended dosage form provides you with great control over dimensions, shape, geometry, and internal architecture.[28] Following that, the digital models are transformed into several printable layers of design and given the printing instructions to the components that are also machine-readable through something used by the printers in a computer-based, non-interpreting form called G-code or G-code instructions and is a language for printed form design, by slicing software. The selection of active pharmaceutical ingredients (APIs) and excipients is significantly pertinent for determining the printability, stability, mechanical strength and drug release behavior of the final preparation.[29] The physicochemical properties of APIs such as their solubility, thermal stability, and particle size have a significant influence on the printing performance and the therapeutic activities. The excipients employed in 3D printing formulations serve as printable matrices or carriers. Some of the widely used excipients are film-forming polymers, such as hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), and polylactic acid (PLA), and plasticizers, binders, and fillers that improve flexibility and structural integrity as well as enhance printability. [30] Pharmaceutical 3DP is also beneficial for the delivery of the custom dosage forms with tailored shapes, sizes, and drug dosages tailored to the patient. This increased flexibility enhances patient acceptability and enables the creation of more customized therapeutic systems, particularly for paediatric and geriatric patients.

Table 2: Key Components Involved in Pharmaceutical 3D Printing

Component	Role in 3DP
CAD software	Digital design of dosage form
APIs	Therapeutic activity
Polymers	Film formation and printability
Plasticizers	Flexibility enhancement
Slicing software	Layer generation
G-code	Printer instructions

IV. TYPES OF 3D PRINTING TECHNOLOGIES

1. Fused Deposition Modelling (FDM):

Fused Deposition Modelling (FDM) is one of the most widely used 3D printing technologies in pharmaceutical applications because of its simplicity, affordability, and ability to produce mechanically stable dosage forms. In this technique, drug-loaded thermoplastic filaments are melted and extruded through a heated nozzle in a layer-by-layer manner based on computer-aided design (CAD) instructions to fabricate the desired structure.[24,31,32]FDM has been extensively explored for the fabrication of personalized pharmaceutical dosage forms with customized shapes, sizes, and drug release profiles. The technology enables the development of immediate- and controlled-release formulations, multilayer systems, and multi-drug dosage forms. In addition, FDM has shown potential in improving patient compliance through the production of patient-specific formulations with enhanced flexibility and dose customization. [33,35,42]

2. Semi-Solid extrusion (SSE):

Semi-solid Extrusion (SSE) is a material extrusion-based 3D printing technology widely investigated for pharmaceutical applications, particularly for oral disintegrating film (ODF) fabrication.[30,37] Unlike fused deposition modelling (FDM), SSE utilizes semisolid materials such as gels, pastes, and hydrogels, which are extruded through a nozzle in a layer-by-layer manner based on digital designs. The process operates at relatively low temperatures, making it highly suitable for thermosensitive drugs and excipients.[40]

In SSE printing, the formulation is loaded into a syringe-based system and deposited using pneumatic, mechanical, or electromagnetic extrusion mechanisms.[38,39] Among these, mechanically driven systems are commonly preferred because of their simplicity, portability, and ease of operation. SSE also supports flexible dose adjustment, multilayer fabrication, and the development of immediate- and modified-release formulations.[41]

Several studies have demonstrated the potential of SSE in producing personalized and multi-drug pharmaceutical dosage forms. Khaled et al. reported the fabrication of multi-compartment formulations with distinct release profiles and rapidly disintegrating layers using SSE technology.[42] Despite challenges such as formulation instability, viscosity-dependent printability, and limited mechanical strength, SSE remains one of the most promising approaches for developing patient-specific and heat-sensitive oral film formulations.

3. Inkjet Printing:[43-46]

Inkjet printing is a droplet-based additive manufacturing technique widely explored in pharmaceutical applications because of its high precision, accurate dose deposition, and minimal material wastage.[43–46] In this method, small droplets of drug-containing solutions or liquid binders are deposited onto substrates or powder beds according to a predefined digital pattern to form three-dimensional structures.

In powder-based inkjet printing, thin layers of powder are spread uniformly over the printing platform, followed by selective deposition of liquid binders through the printer head. This layer-by-layer process continues until the desired structure is formed, while the surrounding unbound powder acts as temporary support material during fabrication.[43]

Inkjet printing has shown significant potential in oral disintegrating film (ODF) fabrication, particularly for low-dose and personalized drug delivery systems because of its precise micro-dosing capability and uniform drug distribution.[44,45] The technique also enables rapid film formation with improved disintegration characteristics. However, limitations such as restricted formulation viscosity, nozzle clogging, and solvent-related drying issues continue to challenge large-scale application. Despite these limitations, inkjet printing remains a promising approach for the development of patient-specific oral film formulations.[46]

4. Stereo lithography:[47-50]

Stereolithography (SLA) is a light-based 3D printing technology that utilizes photopolymerization to fabricate highly precise three-dimensional structures with smooth surface morphology.[47–50] In this technique, a laser beam or light source selectively cures liquid photopolymer resin in a layer-by-layer manner based on a digital design. After each layer is solidified, the build platform moves vertically to allow the formation of subsequent layers until the final structure is completed.[47]

Because of its high spatial resolution and structural accuracy, SLA has been widely investigated for biomedical applications including microneedles, tissue engineering scaffolds, dental devices, and modified-release pharmaceutical formulations.[49,50] Compared with thermal extrusion-based techniques such as fused deposition modelling (FDM), SLA is considered more suitable for certain heat-sensitive active pharmaceutical ingredients (APIs) since it avoids exposure to elevated processing temperatures.[47]

SLA-fabricated drug delivery systems have demonstrated good structural uniformity and controlled drug release characteristics. However, the dense cross-linked architecture produced during photopolymerization may influence drug diffusion and release behavior.[48,50] Despite its advantages, the pharmaceutical application of SLA remains limited because of the restricted availability of pharmaceutically acceptable photopolymer resins, concerns regarding residual photoinitiator toxicity, and additional post-processing requirements.

Nevertheless, SLA continues to be a promising technology for the development of highly precise and complex drug delivery systems.

5. Binder Jetting:[51,52]

Binder jetting is a powder-based additive manufacturing technique in which a liquid binding agent is selectively deposited onto layers of powder particles to produce three-dimensional structures.[51,52] During the printing process, thin layers of powder are spread over the build platform, followed by controlled deposition of the binder solution through a print head to selectively join particles in predefined regions. The process is repeated layer by layer until the desired structure is formed, after which the unbound powder is removed.[51]

Binder jetting has gained interest in pharmaceutical applications because of its rapid fabrication process, formulation flexibility, and ability to produce highly porous dosage forms with enhanced disintegration characteristics.[52] The technology also allows precise control over geometry and drug loading, making it suitable for personalized drug delivery systems.

However, its application in oral disintegrating film (ODF) fabrication remains limited compared with other 3D printing technologies. Challenges such as poor mechanical strength, powder flow variability, and post-processing requirements may affect formulation stability and product handling. Despite these limitations, binder jetting continues to be explored as a promising approach for developing rapidly disintegrating and personalized pharmaceutical dosage forms.

6. Selective Laser Sintering (SLS):[53-55]

Selective Laser Sintering (SLS) is a powder-based additive manufacturing technique that uses laser energy to selectively fuse powder particles in a layer-by-layer manner to form three-dimensional structures.[53–55] During the printing process, thin layers of powder are spread across the build platform, and a laser beam selectively sinters specific regions according to a predefined digital design. This process is repeated sequentially until the final structure is completed.[53]

SLS has gained considerable attention in pharmaceutical applications because it enables solvent-free fabrication, precise control of dosage form geometry, and the development of porous structures that can influence drug release and disintegration properties.[54,55] The technology also supports the production of personalized dosage forms with adjustable size, internal architecture, and drug loading.

In oral drug delivery, SLS has been investigated for the fabrication of rapidly disintegrating and modified-release formulations with improved mechanical stability and minimal post-processing requirements.[54] However, the high temperatures generated during laser sintering may result in degradation of thermosensitive active pharmaceutical ingredients (APIs) and excipients.[55] In addition, challenges related to powder flow properties, thermal stress, and limited availability of pharmaceutical-grade printable materials continue to restrict broader pharmaceutical application. Nevertheless, SLS remains a promising technology for the development of complex and personalized drug delivery systems.

Table 3. Comparison of Major 3D Printing Technologies Used in Oral Disintegrating Film Fabrication

S. No.	Technology	Principle	Materials Used	Advantages	Limitations	Applications in ODFs	Temperature Requirement
1	Fused Deposition Modelling (FDM)	Layer-by-layer extrusion of drug-loaded thermoplastic filaments under elevated temperature	Thermoplastic polymers (PLA, PVA, HPMC), plasticizers	Cost-effective, reproducible, good mechanical strength, controlled drug release	High processing temperature may degrade thermosensitive drugs	Fast-dissolving films, controlled-release formulations, personalized dosage forms	High

2	Semi-Solid Extrusion (SSE)	Extrusion of semisolid formulations through pneumatic or mechanical pressure	Hydrogels, pastes, semisolid polymers, bio-inks	Low-temperature processing, suitable for heat-sensitive drugs, easy dose customization	Limited mechanical strength, formulation instability, phase separation	Pediatric formulations, chewable films, multi-drug ODFs	Low
3	Inkjet Printing	Controlled deposition of drug-containing droplets onto substrates or powder layers	Drug solutions, binders, polymer dispersions	High precision, accurate micro-dosing, minimal material wastage	Nozzle clogging, limited viscosity range, solvent-related challenges	Rapidly disintegrating thin films, low-dose personalized formulations	Low
4	Stereolithography (SLA)	Photopolymerization of liquid resin using laser or light irradiation	Photopolymers, photoinitiators	High resolution, smooth surface finish, precise geometry	Limited availability of biocompatible resins, post-processing requirements	Modified-release films, highly precise oral formulations	Moderate
5	Binder Jetting	Selective deposition of liquid binders onto powder layers	Powder blends, binding agents	Rapid fabrication, porous structure formation, cost-effective processing	Fragile structures, post-processing requirements	Porous ODFs with rapid drug release characteristics	Moderate
6	Selective Laser Sintering (SLS)	Laser-induced sintering of powder particles to form solid structures	Polymer powders, drug-loaded blends	Solvent-free process, high precision, improved mechanical strength	Thermal degradation risk, high energy requirement	Controlled-release systems, complex drug delivery formulations	High

V. MATERIALS AND EXCIPIENTS FOR ODF's:[56 – 62]

The selection of suitable polymers and excipients plays a crucial role in the development of 3D-printed oral disintegrating films (ODFs), as they significantly influence printability, mechanical strength, flexibility, disintegration, drug release, and patient acceptability.[56–62] Both natural and synthetic polymers have been widely investigated because of their film-forming ability, biocompatibility, and compatibility with various 3D printing technologies.

Commonly used film-forming polymers include hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), pullulan, and polyvinyl alcohol (PVA), which provide good mechanical properties and rapid disintegration characteristics.[56–58] Polymer blends such as pullulan–HPMC and HPC–HPMC have also been explored to improve film flexibility, uniformity, and dissolution behavior.

Natural biopolymers including sodium alginate, chitosan, gelatin, starch, and carrageenan have attracted considerable interest because of their biodegradability, mucoadhesive properties, and ability to enhance drug release and absorption.[59] These materials are particularly suitable for semi-solid extrusion (SSE)-based printing systems that process hydrogel and paste-like formulations under relatively mild conditions. The printability of such formulations largely depends on rheological properties, viscosity, crosslinking behavior, and temperature sensitivity during the printing process.[62]

In addition to polymers, functional excipients are incorporated to improve film performance and patient compliance. Plasticizers such as polyethylene glycol (PEG) and glycerol are commonly used to enhance flexibility and reduce film brittleness.[60] Disintegrants facilitate rapid saliva uptake and faster film disintegration, while sweeteners and flavoring agents improve palatability, especially for pediatric and geriatric patients.[15,60] Recent taste-masking strategies, including pH-sensitive polymers and nanoparticle-based encapsulation systems, have also shown promise in improving patient acceptability and therapeutic compliance.[61]

Overall, careful selection and optimization of polymers and excipients are essential for achieving desirable printability, mechanical integrity, rapid disintegration, and controlled drug release in 3D-printed ODF formulations.

Table 4. Common Materials and Excipients Used in 3D-Printed Oral Disintegrating Films

Category	Materials	Examples	Functions in ODFs
Primary film-forming polymers	Natural and synthetic polymers	HPMC, Pullulan, HPC, PVA	Form film matrix, improve mechanical strength, and facilitate rapid disintegration
Single polymer systems	Hydrogel-forming polymers	HPMC	Excellent film-forming ability and rapid dissolution characteristics
Polymer blends	Combination polymer systems	Pullulan + HPMC; HPC + HPMC	Improve flexibility, elasticity, film uniformity, and dissolution performance
Natural biopolymers	Biodegradable polymers	Sodium alginate, chitosan, gelatin, starch, carrageenan	Enhance biodegradability, mucoadhesion, and drug release
Synthetic polymers	Water-soluble synthetic polymers	PVA, PVP, PEGDA	Improve structural integrity, solubility, and printability
Plasticizers	Flexibility-enhancing agents	PEG 300, glycerol	Improve flexibility and reduce brittleness
Disintegrants	Rapid disintegration agents	Sodium starch glycolate, crospovidone	Promote rapid saliva uptake and film disintegration
Taste-masking agents	Sweeteners and flavor modifiers	Aspartame, sucralose, flavoring agents	Improve palatability and patient compliance

VI. COMPOSITION OF ORAL DISINTEGRATING FILMS (ODFS)

Oral disintegrating films (ODFs) comprise a number of important constituents and together ensure quick disintegration efficiency, pleasant taste, mechanical longevity, and successful drug delivery. The basic components are presented as follows:

1. Film-Forming Polymers: [14,56,58]

The film-forming polymer forms the base of ODFs and gives structural support to the film. They should also be non-toxic, biocompatible, and able to form a thin film that is flexible. Polymers often include hydroxypropyl methylcellulose (HPMC), polyvinyl alcohol (PVA), pullulan, and sodium alginate. The

polymer choice makes a huge difference in the disintegration time and drug release profile.

2. Plasticizers: [59,60]
Plasticizers are used to make films more flexible and less brittle. Their strength of joints increases and the possibility of cracking during handling and storage decreases. Plasticizers include glycerol, polyethylene glycol (PEG), and propylene glycol. The plasticizer volume is important in determining the film's elasticity as well as tensile strength.

3. Sweeteners: [15,60]
Sweeteners are introduced to counteract the bitter taste and improve patient comfort rates, especially among the pediatric and geriatric populations. Both natural and artificial sweeteners, such as sucrose, mannitol, aspartame, and saccharin, are widely used.

4. Flavoring Agents: [15,61]
Flavoring agents are included to adjust ODFs for palatability. They help to mask the taste of unpleasant drug agents, and when taken, make them taste pleasant. Common flavors include mint, orange, strawberry, and lemon. The choice of taste profile depends on the demographic and the specific properties of the drug.

5. Saliva-Stimulating Agents: [14]
Saliva-stimulating agents facilitate the rapid disintegration of the film by increasing saliva production in the oral cavity. Organic acids such as citric acid, malic acid, and tartaric acid are often used for that.

6. Active Pharmaceutical Ingredient (API): [14,58]
The active pharmaceutical ingredient is used as the medicinal agent part of ODF. It needs to be conducive for mixing with other excipients to perform its action well and it should be as soluble as appropriate for quick action. API has typically low dosage for ODFs because of the constraints of film dimensions and thickness.

VII. DESIGN AND FABRICATION OF 3D PRINTING ODF's:

The design and fabrication of 3D-printed oral disintegrating films (ODFs) mainly rely on computer-aided design (CAD) software and additive manufacturing techniques to develop personalized dosage forms with optimized geometry, uniform drug distribution, and rapid disintegration properties.[63,64] CAD models are converted into printable layers through slicing software, allowing optimization of parameters such as film thickness, infill density, layer orientation, and polymer composition to achieve desired mechanical and drug release characteristics.
Technologies including fused deposition modelling (FDM), semi-solid extrusion (SSE), and inkjet printing have been widely explored for fabricating multilayer and patient-specific ODFs.[65] Customized geometries and porous structures can further influence disintegration behaviour and drug release profiles.[66] In addition, 3D printing supports flexible dose adjustment and personalized therapy, particularly for paediatric and geriatric patients.
Despite these advantages, challenges related to formulation stability, printing reproducibility, and mechanical integrity continue to limit large-scale pharmaceutical applications.[67] Nevertheless, advances in digital design tools and printable materials are expected to further expand the role of 3D-printed ODFs in personalized drug delivery.

VIII. CHARACTERIZATION AND EVALUATION

Demographic analysis and characterization of 3D-printed oral disintegrating films (ODFs) is needed to evaluate mechanical integrity, uniformity, rapid disintegration, and drug delivery activity. For evaluation of formulation quality and pharmacopeial compliant standards numerous physicochemical, mechanical and performance-based parameters are established.
Physical Characterization. [68]
The physical characterization of ODFs ranges from surface morphology, thickness uniformity, porosity, transparency, structural integrity. In the current research, the thickness of films is generally recorded in different places under digital Micrometer or coating thickness gauge for homogeneity of appearance and the consistency of dose. Microscopic techniques are used for the characterization of the surface morphology and porosity, which also serve to evaluate layer deposition, structural homogeneity and internal architecture of the printed films. Porosity plays a

major part in determining the tendency of ODFs to disintegrate and dissolve. By incorporating pyrogens and disintegrating agents, this may be a means through which pore formation increases and consequently quick saliva penetration speeds up film disintegration.

Mechanical Evaluation. [69]
Mechanical properties are fundamental to maintain the satisfactory handling, packing, and storage stability of ODF. Some of the parameters that are usually measured are tensile strength, folding endurance, elongation at break, puncture resistance and flexibility. Tensile test is used texture analysers, etc., or universal test tools in which the force needed was used to break off film is measured and its elasticity and mechanical properties examined. Puncture resistance research evaluates the ability of films to withstand mechanical forces in the course of handling and administration. Optimization of polymer concentration and plasticizer content is necessary to maximize mechanical strength and flexibility as well as to retain rapid disintegration characteristics.

Performance Evaluation. [70]
The performance testing is mainly based on disintegration time, uniformity of drug substance, dissolution, disintegration properties, and release characteristics. Usually, disintegration studies are made in simulated salivary fluid or phosphate buffer under a predetermined scenario to assess the time of the complete film break down. High disintegration rate is regarded as an essential quality factor in ODF formulations such as paediatric and geriatric formulations. Consistency of drug content is assessed for accurate and reproducible dosing of individual films. Methods of dissolution investigations often consist of both pharmacopeially based assays with analytical approaches (HPLC) for drug release profile analyses. Moreover, solid-state characterization methods like DSC, FTIR and XRD are commonly used for studies on drug-polymer compatibility, crystallinity and intermolecular interaction of printed formulations.

In Vitro and In Vivo Evaluation. [71,72]
The 3D-printed ODFs are mainly evaluated in vitro through disintegration studies, dissolution tests, drug release profiles, and the evaluation of mechanical properties. Next-generation analytical processes, such as NIR spectroscopy and imaging techniques, for non-destructive comparison of dose uniformity and print quality have also been investigated. While in vivo evaluation of 3D-printed ODFs is still limited, available studies have reported favourable pharmacokinetic properties, bioavailability and the possibility of patient acceptability. Personal drug dosing capability, fast degradation, and better palatability have resulted in the increased patient adherence, especially in young paediatric and geriatric patients. Clinical potential of 3D-printed ODFs for personalized therapy has also been emphasized by taste-masked and patient-related formulations in clinical studies. However, more long-term studies on stability, safety, large-scale manufacturing, and clinical outcomes are warranted to support the broader use of 3D-printed oral films in the pharmaceutical industry.

Table 5. Evaluation Parameters for 3D-Printed ODFs

Evaluation Parameter	Purpose	Common Techniques
Thickness	Uniformity assessment	Micrometer
Surface morphology	Structural analysis	SEM/Microscopy
Tensile strength	Mechanical integrity	Texture analyser
Folding endurance	Flexibility assessment	Repeated folding
Disintegration time	Rapid breakdown evaluation	Simulated saliva studies
Drug content uniformity	Dose consistency	UV/HPLC
Dissolution studies	Drug release profile	USP dissolution apparatus
Solid-state analysis	Drug-polymer interaction	DSC, FTIR, XRD

IX. CURRENT CHALLENGES IN 3D PRINTED ODF DEVELOPMENT

Despite significant advances in 3D printing technologies, several technical, material-related, and regulatory challenges continue to limit the large-scale pharmaceutical application of 3D-printed oral

disintegrating films (ODFs). Major concerns include material limitations, reproducibility, scalability, and drug stability.

Restrictions upon Formulation and Material [62,73]
The limited availability of pharmaceutically acceptable printable materials remains a major challenge in 3D-printed ODF development. Many film-forming polymers lack suitable rheological and mechanical properties required for specific printing techniques. In addition, incompatibility between active pharmaceutical ingredients (APIs) and polymers may result in poor printability, instability, phase separation, and non-uniform drug distribution. In semi-solid extrusion (SSE) systems, formulation viscosity, shear behaviour, and crosslinking properties must be carefully optimized to ensure uniform layer deposition and structural integrity.

Prints with Resolution and Reproducibility [73]
High print resolution and reproducibility are essential for maintaining dose accuracy, mechanical strength, and uniform drug distribution in 3D-printed ODFs. Printing parameters such as layer thickness, print speed, extrusion pressure, and drying conditions significantly influence product quality. Variations in these factors may lead to structural defects, inconsistent thickness, and irregular drug release profiles. In addition, maintaining batch-to-batch consistency during scale-up remains a major challenge.

Scalability and Production Challenges [75]
Although 3D printing offers significant advantages for personalized medicine, large-scale pharmaceutical manufacturing remains difficult. Most current 3D printers are designed for small-batch production rather than industrial-scale fabrication. Challenges such as process standardization, printing speed, multi-nozzle integration, and quality control continue to restrict commercial implementation. Variations in material flow behaviour, environmental conditions, and printer calibration may also affect dosage accuracy and print quality.

Thermal and Stability Issues [36]
Thermal degradation of active pharmaceutical ingredients (APIs) and excipients is another important limitation, particularly in thermal extrusion-based techniques such as fused deposition modelling (FDM) and selective laser sintering (SLS). Exposure to elevated temperatures may reduce drug stability and bioactivity. Although semi-solid extrusion (SSE) is more suitable for thermosensitive formulations because of its low-temperature processing, stability issues may still occur if formulation parameters are not properly optimized.

Future Considerations
To overcome these challenges, future research should focus on the development of pharmaceutical-grade printable materials, advanced rheological optimization strategies, real-time process monitoring systems, and scalable manufacturing platforms. In addition, integration of quality-by-design (QbD) principles, artificial intelligence-assisted optimization, and automated quality control systems may improve reproducibility and facilitate broader pharmaceutical adoption of 3D-printed ODF technologies.[65, 67]

Table 6. Major Challenges Associated with 3D-Printed ODF Development

Challenge	Impact on ODFs	Possible Solution
Limited printable polymers	Poor printability and stability	Development of pharmaceutical-grade printable materials
Thermal degradation	API instability	Use of low-temperature techniques such as SSE
Reproducibility issues	Dose variability	Process standardization and QbD
Scalability limitations	Reduced industrial feasibility	Multi-nozzle and automated systems
Mechanical fragility	Poor handling properties	Polymer and plasticizer optimization
Regulatory uncertainty	Delayed commercialization	Development of harmonized guidelines

X. REGULATORY CONSIDERATIONS

The regulatory framework for three-dimensional (3D) printed pharmaceutical products is still evolving because of the complexity and novelty of additive

manufacturing technologies. Regulatory agencies such as the U.S. Food and Drug Administration (FDA), European Medicines Agency (EMA), and other national authorities have shown increasing interest in pharmaceutical 3D printing, although specific guidelines for oral disintegrating films (ODFs) remain limited.

U.S. Food and Drug Administration (FDA) [6,75]

The FDA has played a major role in regulating additive manufacturing technologies. In 2017, the agency released the guidance document "Technical Considerations for Additive Manufactured Medical Devices," focusing on design control, manufacturing processes, device testing, and quality assurance systems. Although primarily intended for medical devices, the guidance established important principles relevant to pharmaceutical 3D printing.

A major milestone was the FDA approval of Spritam® (levetiracetam) in 2015, the first commercially approved 3D-printed drug product, demonstrating the feasibility of additive manufacturing for rapidly disintegrating dosage forms with accurate dose uniformity. In addition, the FDA Emerging Technology Program (ETP) supports innovation in advanced pharmaceutical manufacturing, including personalized and point-of-care 3D-printed medicines.

European Medicines Agency (EMA) and European Regulatory Framework [75]

In the European Union, additive manufacturing technologies are regulated under broader medicinal product and medical device regulations, including the Medical Device Regulation (MDR 2017/745). The Medical Device Coordination Group (MDCG) has also provided guidance on quality management systems, risk assessment, process validation, and technical documentation for 3D-printed healthcare products.

Although the EMA has not yet issued specific guidelines for pharmaceutical 3D printing, existing Good Manufacturing Practice (GMP) standards and medicinal product regulations are applied to additive manufacturing processes. Regulatory authorities emphasize product reproducibility, process control, material safety, and dosage accuracy.

National regulatory agencies such as the Therapeutic Goods Administration (TGA, Australia), Medicines and Healthcare products Regulatory Agency (MHRA, UK), and Pharmaceuticals and Medical Devices Agency (PMDA, Japan) are also actively exploring regulatory frameworks for additive manufacturing technologies. Current discussions particularly focus on process validation, quality assurance, software control, and patient safety.

Regulatory Challenges at Present

Despite growing regulatory interest, several challenges continue to limit the pharmaceutical application of 3D printing technologies. These include the lack of harmonized international guidelines, limited availability of pharmaceutically approved printable materials, batch-to-batch variability, and difficulties in validating personalized dosage forms.[6,75]

In addition, regulatory pathways for individualized therapy and on-demand manufacturing are still under development. Future regulatory strategies are expected to emphasize quality-by-design (QbD), real-time process monitoring, automated quality control systems, and standardized validation procedures to support the safe commercialization of 3D-printed pharmaceutical products.

XI. FUTURE PROSPECTS

Three-dimensional (3D) printing technologies are expected to play an important role in advancing personalized oral drug delivery systems, particularly oral disintegrating films (ODFs). The ability to customize dosage forms according to patient requirements offers significant potential for improving therapeutic outcomes, patient compliance, and precision medicine approaches.

Patient-Specific Personalized ODFs for Paediatric and Geriatric Patients [72]

Paediatric and geriatric patients often experience challenges such as swallowing difficulties, dose adjustment requirements, reduced compliance, and polypharmacy-related complications. In this context, 3D-printed ODFs provide a promising platform for developing patient-specific formulations with adjustable doses, rapid disintegration, and improved palatability.

Future research is expected to focus on age- and weight-based dosing, taste-masking strategies, and patient-friendly dosage form designs. Customized film

sizes, shapes, flavors, and multilayered structures may further improve patient acceptance and therapeutic adherence. In geriatric patients, personalized ODFs may help overcome dysphagia, reduced saliva production, and medication burden through optimized disintegration profiles and multi-drug loading approaches.

On-Demand Manufacturing and Digital Pharmacies [73]

On-demand pharmaceutical manufacturing represents another promising application of 3D-printed ODFs. Decentralized production systems within hospitals or pharmacies may enable rapid fabrication of patient-specific dosage forms directly from electronic prescriptions, thereby reducing drug wastage and improving supply chain flexibility.

Digital pharmacy systems integrated with automated dispensing and computerized prescription processing may further support personalized therapy through precise dose customization and efficient medication management. In addition, pharmaceutical polypills containing multiple active ingredients may improve adherence in patients receiving complex therapeutic regimens.

Integration with Smart Healthcare Tools [67]

The integration of smart technologies with 3D printing is expected to further expand personalized drug delivery systems. Advances in artificial intelligence (AI), machine learning, biosensors, and Internet of Things (IoT)-based systems may support automated formulation optimization, real-time monitoring, and patient-specific therapeutic adjustments.[75]

AI-assisted computational tools may also improve formulation design, printability prediction, and process reproducibility in pharmaceutical 3D printing. Despite these promising developments, further progress in material development, process standardization, large-scale manufacturing, regulatory harmonization, and long-term safety evaluation is still required for broader clinical adoption of 3D-printed ODFs.

Table 7. Future Opportunities and Emerging Trends in 3D-Printed ODFs

Emerging Area	Potential Advantage
Personalized paediatric dosing	Improved dose accuracy and compliance
Geriatric polypharmacy management	Reduced pill burden
On-demand manufacturing	Reduced wastage and faster therapy
Digital pharmacies	Automated prescription processing
AI-assisted optimization	Improved formulation design
Smart healthcare integration	Real-time therapeutic monitoring

XII. CONCLUSIONS AND RESEARCH GAPS

Three-dimensional (3D) printing technologies have also been regarded as promising platforms for tailoring custom designed oral disintegrating films (ODFs) for enhanced dose accuracy, rapid disintegration and patient compliance. There have been many emerging methods of additive manufacturing such as fused deposition modelling (FDM), semi-solid extrusion (SSE), inkjet printing, stereolithography (SLA), binder jetting, and selective laser sintering (SLS), which have brought forward large scope of design flexibility and application capabilities for oral films. Of these technologies, SSE and inkjet printing seem to be suited for ODF manufacturing due to their compatibility with thermosensitive drugs, accurate deposition of individual drugs and potential for design and dosage customization based on patients. With the advancement of computer-aided design (CAD), quality-by-design (QbD) and advanced formulation strategy and tools, ODFs have been developed in a controlled manner, in a multilayer architecture, and with tailored drug release behaviour and dosing profile. Those technological achievements offer great promise for enhancing medication compliance in children and elderly patients suffering from swallowing problems, dose modifications and polypharmacy-related comorbidities. Though these developments have been made, multiple demand areas and implementation constraints remain to restrict the use in the wider clinical and industrial use of 3D-printed ODFs. Challenges are there is limited access to high-quality printables appropriate for pharmaceutical production, process reproducibility issues, scalability, thermal instability of active pharmaceutical ingredients and heterogeneity in standardized control guidelines. Moreover, there was an absence of long-term clinical safety data, large-scale manufacturing

validation and healthcare training for the workforce. Future developments in pharmaceutical 3D printing will likely hinge on collaboration among pharmaceutical scientists; materials engineers and computational researchers; physicians and their clinicians; regulators; and digital healthcare practitioners. New technologies including AI-supported formula designing, predictive modelling, digital simulation platforms, and automated quality control systems for example, might be used to accelerate the formulation optimization and manufacture reproducibility. In addition, the innovation of sustainable manufacturing systems, decentralized drug manufacturing models, and smart drug delivery systems integrating healthcare would likely broaden the use of 3D printing for personalized medicine. However, numerous unsolved scientific, regulatory and economic problems, although advancing in the printable biomaterial, process engineering and digital pharmaceutical technology would help to accelerate the future clinical translation and commercialization of 3D-printed oral disintegrating films in the future.

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