

BEYOND THE TABLET: ORAL THIN FILMS AS A PLATFORM FOR PATIENT-CENTRIC, 3D-PRINTED DRUG DELIVERY**Dr. S. Allimalarkodi M. Pharm. PhD^{1*}, S. Narendhra², K. Arunprasath³, C. Sujan⁴, S. Navin⁵, M. Rajesh⁶**

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ABSTRACT

Oral thin films (OTFs) are flexible drug delivery systems that disintegrate or dissolve quickly in the oral cavity and are convenient to use, without the need for water. The ease of administration and quick onset of drug release, as well as the possibility to enhance patient adherence, has led to growing interest in this new type of dosage form as alternatives to conventional oral dosage forms. This review covers the formulation composition, production methods, assessment criteria and new applications of OTFs. Key formulation excipients like film-forming polymers, plasticisers, sweeteners, flavouring agents, surfactants and permeation enhancers are emphasised. The conventional manufacturing techniques like solvent casting, hot-melt extrusion, rolling, semisolid casting and solid dispersion extrusion as well as the advanced printing technologies like inkjet, flexographic and three-dimensional (3D) printing are reviewed. Other important qualities like thickness of the film, the number of times a film can be folded, the pH value of the surface, the uniformity of the drug, mechanical properties of the film, disintegration and drug release are also discussed. New developments in electrospinning, nanotechnology, multilayer films and customized OTFs illustrate opportunities that may lead to enhanced drug loading, dissolution and therapeutic precision. These improvements, however, have come with their own set of issues, such as a small payload of drugs, moisture sensitivity, stability, scale-up and regulatory standardization. OTFs are an intriguing platform for patient-centred and personalized drug delivery, and additional research is needed to ensure their scale-up and clinical translation.

KEYWORDS: Oral Thin Films, Oral Drug Delivery, Patient-Centric Drug Delivery, Formulation Strategies, 3D Printing, Personalized Medicine, Advanced Drug Delivery Systems.**1. INTRODUCTION**

Oral Thin Films (OTFs) also called as Oral Dissolving Films (ODFs) or Fast Dissolving Films (FDFs) are thin, flexible polymeric dosage form for oral administration. They dissolve quickly or break apart on contact with the tongue, so it doesn't need water to disintegrate, and the drug is absorbed into the mouth or GI tract. The OTFs are typically made with hydrophilic polymers which offer flexibility, suitable mechanical strength, uniform distribution of the drug and rapid disintegration. The advantages of their ease of administration, portability, accurate dosage, and better patient compliance, have made these a popular option over traditional oral dosage forms. For these reasons, oral thin films have been a

topic of great interest as an advanced drug delivery system for patient friendly products.

1.1 Oral Drug Delivery

Oral route is the most favourite method of administration as it is convenient, non-invasive, safe and economical. Oral is the most common route used for marketed therapeutic products, accounting for about 90%, both for systemic and local drug therapy. Oral formulations are very popular and are easily administered and well accepted by patients in the treatment of chronic disease. But there are some drawbacks associated with the conventional oral drug delivery system such as low aqueous solubility, low intestinal permeability, degradation in the gastrointestinal tract, and high first

pass metabolism. The effects of these factors can often decrease the bioavailability and efficacy of drugs, especially biologics like peptides, proteins, nucleic acids and vaccines. Thus, the design of novel oral drug delivery systems is an important research area in the pharmaceutical field.

1.2 Evolution of Oral Thin Films

Oral thin films have been developed as an alternative to the swallowable dosage form in the late 1970s. The first formulations were developed to enhance patient convenience and compliance with polymeric films which are easily dissolved in the mouth. With the passing years, developments in polymer chemistry, formulation methods and taste masking techniques made their way into the oral, buccal, sublingual, ocular and transdermal drug delivery systems. Commercialisation continued to pick up when thin film medications became available for oral use without prescription and later medication used systemically became available. In more recent studies, attention has been paid to new technologies like the 3D printing, multiple layers films, films loaded with nanoparticles and personalized drug delivery systems that can deliver customized dose and improve therapeutic efficacy.

1.3 Market Growth and Future Perspectives

With the growing demand for patient-friendly dosage forms and technological development in the field of pharmaceuticals, the global oral thin film market has witnessed a significant growth in the past few years. The increasing incidence of chronic diseases, growing geriatric population, growing pediatric population, and the growing acceptance of OTC healthcare products are some of the factors contributing to the growth of the market. The formulation design and manufacturing processes and regulatory support are continuously improving, which is expected to further speed up

commercialization. Oral thin film technology has the potential to become more effective in the future with the advent of nanotechnology, personalized medicine and advanced manufacturing processes. Due to their quick drug release, their high patient compliance and versatility, OTFs are expected to become an integral part of next generation oral drug delivery systems.^[1-5]

2. ADVANTAGES AND DISADVANTAGES

2.1 Advantages

- Improved patient convenience.
- Easy self-administration for dysphagia, geriatric, pediatric and bedridden patients, as well as for patients that cannot reach water easily.
- Can be administered by multiple routes orally, buccally, sublingually, ocularly and transdermally.
- Provides instant response, accurate dose and increased bioavailability.
- Beneficial for patients who struggle to swallow pills, especially children and the elderly.

In addition, Mucoadhesive (oromucosal) films are rapidly absorbed and are not metabolized/degraded by the low pH of the stomach.

2.2 Disadvantages

The disadvantages are the limited drug-loading capacity, fragility and hygroscopicity.

Stability and to avoid sticking between films require individual packaging of each film.

- Production issues, more specialised production and packaging equipment and costs.
- Only drugs with certain suitable physicochemical properties can be successfully formulated as OTFs.

However, there are certain challenges that still need to be tackled, including moisture sensitivity, low drug loading capacity, and stability.^[17,18]

3. Anatomy and physiology of oral cavity

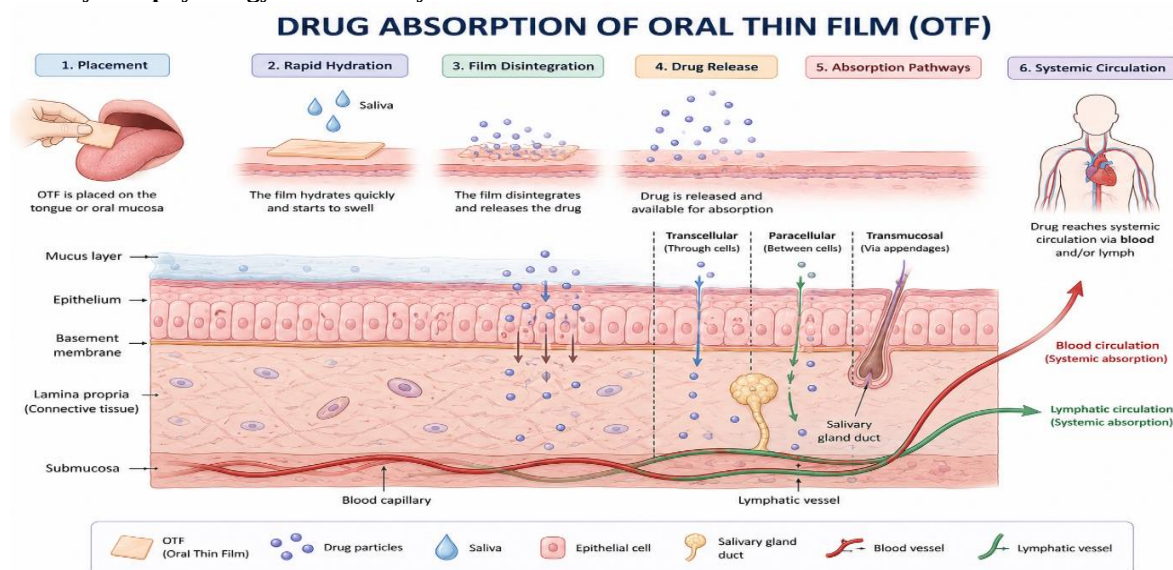


Figure 3: Anatomy and physiology of oral cavity.

4. Need for Patient Centric Drug Delivery

Conventional dosage forms don't always meet the needs of certain patient groups like that of pediatric, geriatric, dysphagic, and psychiatric patients, which can lower adherence, increase medication errors, and negatively affect outcomes, hence the need for patient-centric drug delivery systems. These innovative delivery systems can help lower the burden of dosing, make drugs easier to swallow, customize dosing, and better match the actual patient capability and preference.

4.1 Pediatric Patients

Children require patient-centered drug delivery because they have different dosages, different developmental stage and administration abilities to adults, and many of the traditional drug formulations are not suitable for children. This discrepancy is a source of manipulation, non-compliance and wrong dosage; hence, age-appropriate formulations and devices are required during the development process. Adherence to medications is impeded by taste and swallowability in children. Leading age-appropriate options are ODTs, ODFs, minitabets and multiparticulates, although there are limited dose range and evidence. Pediatric formulation design also should consider the safety of excipients and versatility of dosage.

4.2 Geriatric and dysphagic patient

Patient-centred systems are required for older persons and dysphagic patients due to swallowing difficulties, polypharmacy, comorbidities and loss of function that make it difficult for these patients to take standard tablets and capsules safely. Traditional solid oral products can create the following issues: crushing, splitting, or avoiding medication, leading to altered release, dosing issues, and reduced adherence. Tablets or capsules can be replaced by small particulates or liquids. Doses can be reduced in size, improved film coating, chewable and buccal films can enhance swallowing. Not only is the anatomy important, but so are pill aversion, fear of choking, and enteral tube requirements.

4.3 Psychiatric Patients

For psychiatric patients, adherence complexity, swallowing difficulties and dosage-form acceptability are

more important than age. Three principles for patient-centred design are simplification, burden reduction and product matching: simplify use of the product, reduce treatment burden, and match the product to how patients take medicines. Oral mucosal and rapidly disintegrating systems are particularly important when dysphagia, concealment or reluctance to swallow tablets is a problem. Mentally ill patients tend to implant tablets in their cheek, compromising on the reliability of dosing. ODTs and ODFs have a potential to enhance ease of administration among psychiatric and bedridden population. Buccal systems may provide quicker or more acceptable delivery without the need for first pass metabolism.

4.4 OTFs in Patient-Centric Care

Oral thin films (OTFs) are the dosage form which disintegrates soon in the patient's saliva and may be taken without water, are suitable for patients with difficulties in swallowing. Buccal and sublingual administration can be used for certain drugs to allow them to reach the bloodstream quickly and avoid their first-time metabolism. The features of OTF development that are patient-centric: taste masking; personalization of dosing and formulation. On-demand and personalized drug delivery are possible with advanced technologies like 3D printing and inkjet printing which can provide individualized doses and drug combinations. OTFs can also be used for local or systemic drug delivery via oral, buccal and sublingual routes.

4.5 Challenges and Patient-Centric Drug Delivery

Poor drug absorption, low solubility, gastrointestinal barriers and first-pass metabolism are factors that can restrict the use of conventional oral dosage forms. Tablets and capsules can also be difficult to administer to pediatric, geriatric and dysphagic patients. These are some of the drawbacks that OTFs overcome with their smaller size, portability, waterless administration, rapid disintegration and improved patient acceptability. They are also easy to use for children and the elderly with taste masking and flexibility in dosage. However, issues like drug loading, stability and commercialization are important factors that should be considered for broader clinical applications.^[28,29]

5. Drug absorpti...

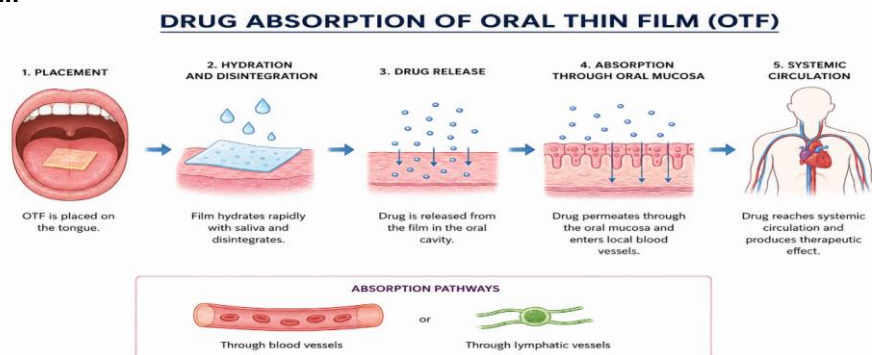


Figure 5: Drug absorption.

6. Oral Thin Film Formulation Components

The oral thin film formulations consist of a polymer matrix used for its film-forming properties and functional excipients (flexibility, taste, wetting, disintegration and stability) in addition to the API. The most common frequency of occurrence of the various categories of excipients identified within the reviews and formulation studies is with respect to Polymers, Plasticizers, Sweeteners, Flavorings, Surfactants, Saliva Stimulants, Coloring Agents (including some stabilizers), Permeation Enhancers and Mucoadhesive Agents.

The component of the film, usually the largest in terms of dry weight, is the film forming polymer, which is typically 40-65% of the total dry weight. HPMC, gelatin, pullulan, PVA, starch, sodium alginate, pectin, chitosan, MC, CMC and xanthan gum are common polymers used. The API is typically a low dose drug and is generally 1-30% of the formulation, depending on the

size and thickness of the film that can be loaded with the drug. Other excipients such as plasticizers, sweeteners, flavors and surfactants are added to aid handling and patient acceptability; additives like salivary stimulants and colour are also occasionally used, and sometimes blended to control film integrity and thickness, tensile behaviour, disintegration, mouth feel and drug release.

The most widely used water soluble hydrophilic polymers are those that promote disintegration and good mouthfeel and are generally acceptable with respect to mechanical strength, such as glycerin, propylene glycol, sorbitol, mannitol, citric acid esters (PEG/macrogol) and related citric acid esters (tributyl citrate). Permeability and solubilisation and sometimes wetting are improved with the use of surfactants, for example, sodium lauryl sulfate, benzalkonium chloride, polysorbates, poloxamer 407 and poloxamer as a solubiliser in curcumin films.^[6-8]

Respective components

Table 6: Formulation of Oral thin film.

Component Class	Main Role	Examples
Polymer	Forms matrix, controls strength and release	HPMC, gelatin, pullulan, PVA
Plasticizer	Improves flexibility and handling	Glycerin, propylene glycol, triethyl citrate
Taste-masking/palatability	Improves acceptability	Sweeteners, flavors
Wetting/solubilizing agent	Enhances dissolution or dispersion	Polysorbates, poloxamer, SLS
Special-function excipient	Modifies absorption or adhesion	Permeation enhancers, mucoadhesive agents

7. Methods of Oral thin film

SOLVENT CASTING METHOD FOR ORAL THIN FILMS

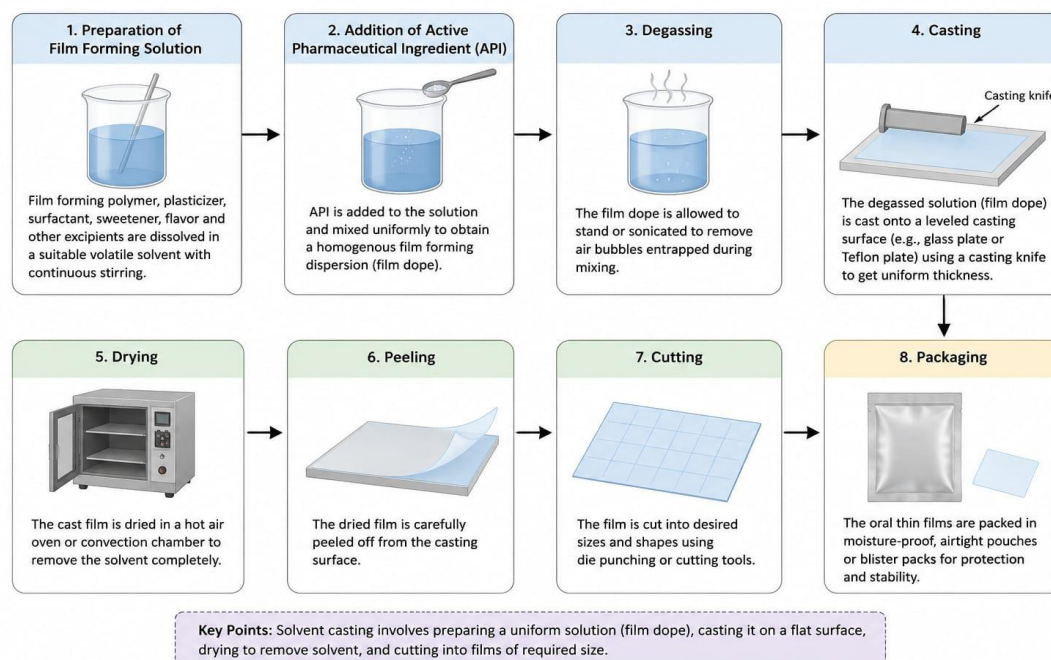


Figure 7.1 Solvent casting method.

7.1 Solvent casting method

One of the most used techniques for the preparation of oral thin films is solvent casting. The drug, polymer and

excipients are dissolved or dispersed in an appropriate solvent to make a film forming solution. It is uniformly deposited on a smooth surface and dried under controlled

conditions. The dried film is cut and packed to desired size. To achieve uniform films, viscosity and film thickness and the drying conditions need to be properly controlled.^[3]

7.2 Hot melt extrusion method

Hot melt extrusion is a solventless process that involves feeding the drug, polymer and plasticizer into a hot

extruder, where they are melted and mixed by mechanical shear. The molten material is extruded through a die to be formed to a desired thickness and then cooled and cut. It minimizes solvent issues and can affect the heat sensitive drugs due to the processing temperatures.^[19]

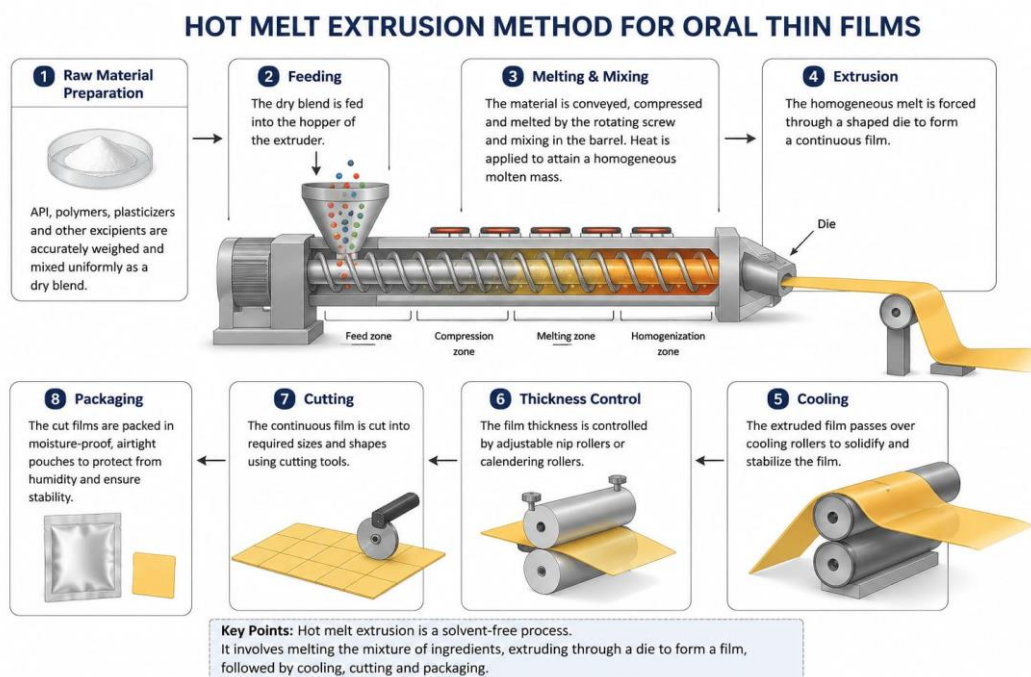


Figure 7.2: Hot melt extrusion method.

7.3. Rolling method

The rolling method involves preparing a solution or suspension of the drug, polymer and excipients and rolling it uniformly onto rotating rollers to create a thin

layer. The film is dried in a controlled environment and then cut to proper size. The appropriate rheological characteristics are crucial for achieving uniform film formation.^[4]

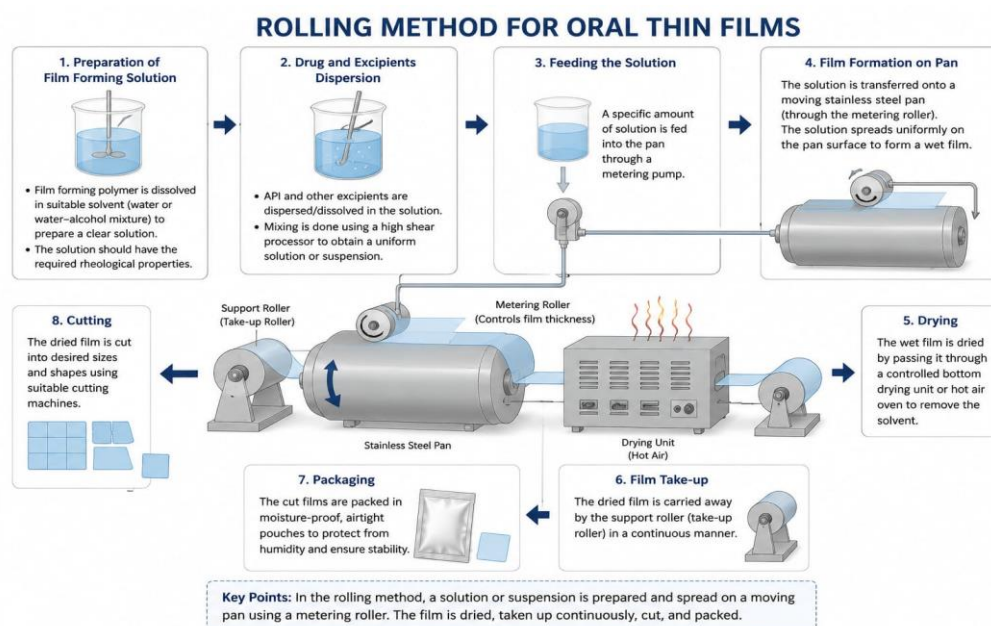


Figure 7.3: Rolling method.

7.4 Semisolid Casting Method

Semisolid casting is mainly used for films containing water-insoluble polymers. The polymer is dissolved in an alkaline solution and then added to a film-forming

polymer and plasticizer to give a gel-like consistency. The mixture is poured onto hot drums, and the thin films are dried. Polymer is often either cellulose acetate phthalate or cellulose acetate butyrate.^[3]

SEMISOLID CASTING METHOD FOR ORAL THIN FILMS

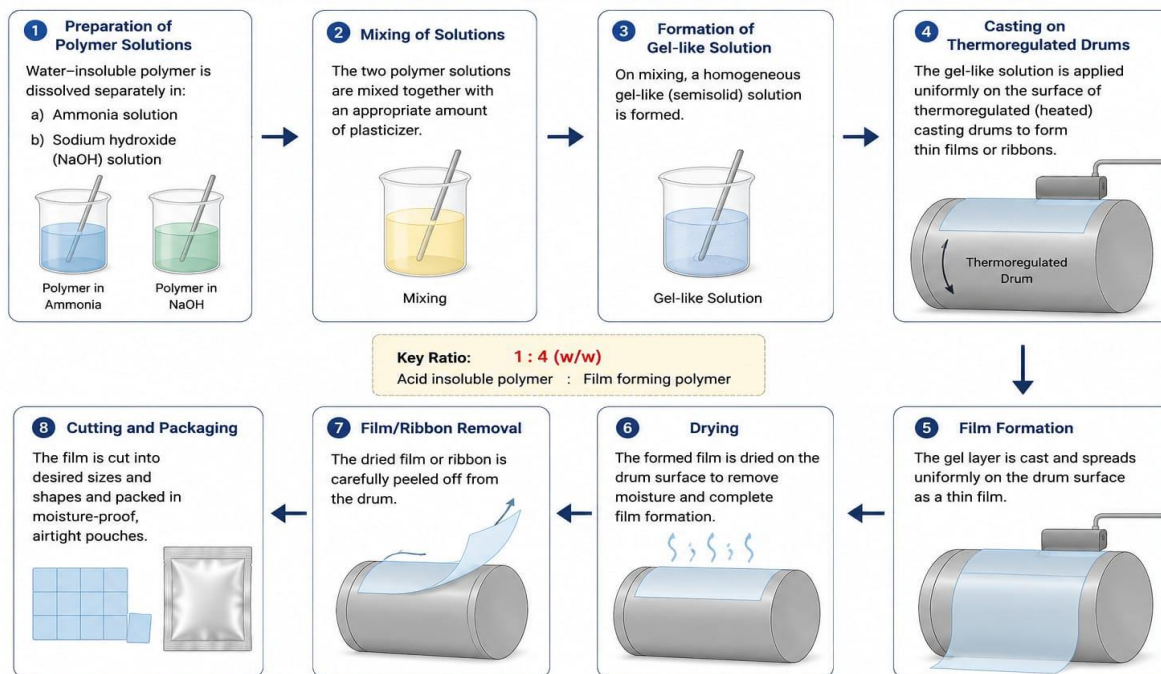


Figure 7.4: Semisolid Casting Method.

7.5. Solid dispersion extrusion method

The solid dispersion extrusion technique consists of dispersing the drug in a hydrophilic polymer and then extruding through an extruder to produce thin films. This

technique is effective in enhancing dispersion and dissolution of drugs and is especially beneficial for poorly water-soluble drugs.^[3]

SOLID DISPERSION EXTRUSION METHOD FOR ORAL THIN FILMS

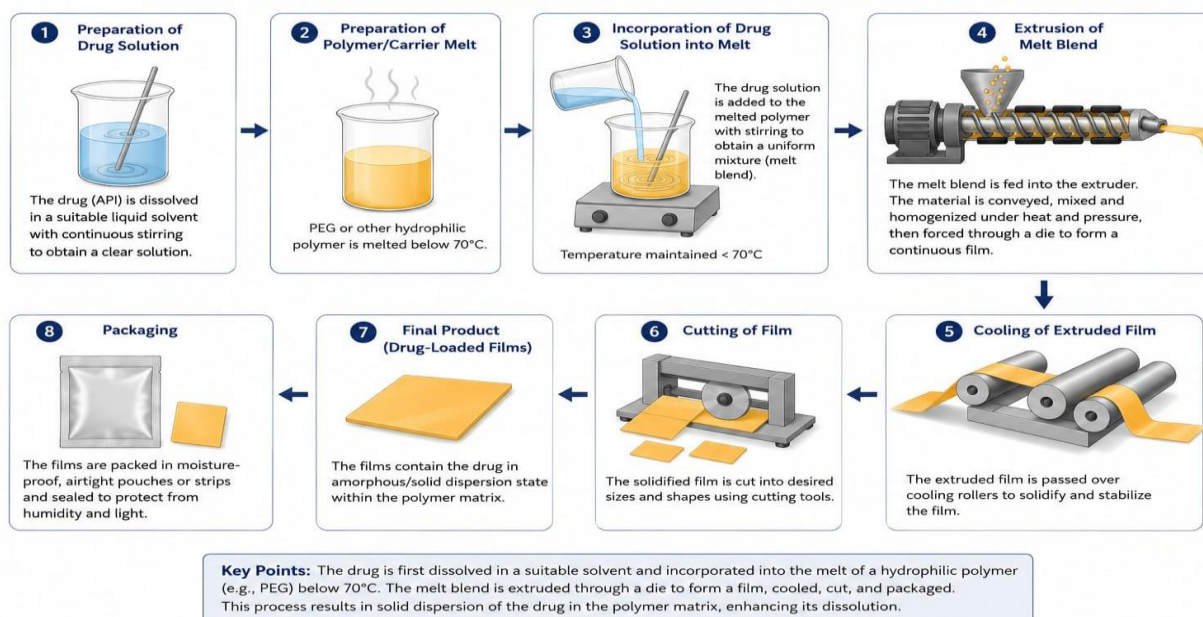


Figure 7.5: Solid dispersion extrusion method.

7.6 Printing Technologies

Printing technologies are advanced techniques for manufacturing oral thin films. These methods provide accurate drug loading and superior content uniformity as compared to the conventional methods.

7.6.1. Inkjet Printing

Inkjet printing is the technology for depositing a formulation containing the drug on a film substrate with a very small droplet that enables the accurate and controlled delivery of the drug. It is especially helpful for strong or low dose medications.

7.6.2. Flexographic Printing

Drug containing ink is applied to a pre-formed polymer film via a flexible printing plate and rollers in flexographic printing. It offers a uniform distribution of drug, correct dosage and quick production speed, and it does not expose the drug to high processing temperatures, and it is easy to scale up. But it needs special equipment.

7.6.3. 3D Printing

Three-dimensional (3D) printing has become a robust platform for the manufacture of oral thin films (OTFs), offering advantages such as customization of dose delivery, multi-layer construction, and solvent-free processing that are difficult to achieve using conventional solvent casting methods. Several 3D printing methods are available for OTF production, each with distinct materials, processes and trade-offs.

➤ Fused Deposition Modeling (FDM)

FDM is the most extensively studied 3D printing technique for pharmaceutical oral films; it extrudes thermoplastic polymer filaments into structured films. In vitro studies loading acetaminophen into HPC/Soluplus matrices showed that FDM-printed films had more uniform drug distribution and better drug release than melt-cast and hot-melt-extruded films. The method enables multilayered films with taste-masking and drug layers separated from each other, with disintegration as fast as 42 seconds for single-layer mesh designs and allows incompatible drugs to be delivered in separate layers within the same buccal film. A key drawback is the high printing temperature (typically 165–190°C), which may degrade heat-sensitive APIs, along with comparatively poorer printing accuracy and surface roughness.

➤ Semi-Solid Extrusion (SSE) and Direct Powder Extrusion (DPE)

Semi-solid extrusion (SSE) prints viscous gels or pastes at or near room temperature, making it suitable for thermolabile drugs. SSE-printed dental films containing diclofenac sodium achieved an initial burst release of 50–70% within 20 minutes, with sustained release maintained for 150 minutes, while SSE-printed apigenin-loaded mucoadhesive films demonstrated

chemopreventive efficacy in a rat model of oral carcinogenesis.

➤ Vat Photopolymerization – LCD and SLA Printing

Liquid Crystal Display (LCD) printing and Stereolithography (SLA) printing are vat photopolymerization-based 3D printing methods that build dosage forms by selectively curing a photosensitive resin with UV light. Both operate at room temperature, unlike thermal extrusion methods, making them attractive for thermolabile actives. LCD printing uses a UV LED light source with a liquid crystal display mask to cure an entire layer at once, giving high printing speed, dimensional accuracy and smooth surface characteristics; bilayer mucoadhesive oral films fabricated from polyethylene glycol diacrylate (PEGDA) and hydroxypropyl methylcellulose (HPMC) showed uniform size, good mechanical properties, strong mucoadhesion and good in vivo therapeutic performance, with PEG 300 used as a plasticiser/pore-forming agent to increase flexibility and drug release. SLA selectively cross-links liquid photopolymer resin using a focused UV laser scanned layer by layer, producing highly accurate structures with excellent surface finish; although its use in oral thin film manufacturing remains limited, its ability to create complex geometries under mild processing conditions gives it strong potential for future personalized OTFs. Overall, LCD and SLA are promising room-temperature alternatives to conventional manufacturing for heat-sensitive drug formulations.

➤ Direct Powder Extrusion (DPE) and Pneumatic Pressure Extrusion

DPE avoids the filament preparation process and directly extrudes powder blends to simplify manufacturing processes. Partial amorphization and cyclodextrin complexation were found to improve the solubility of the drug in the DPE films containing clobetasol propionate to be used in pediatric oral lichen planus. Formulation containing chitosan improved the mucoadhesion property, and the study on porcine mucosa showed that the drug was retained inside the epithelial layer and there was low systemic absorption.

Pneumatic pressure extrusion uses compressed air to push ink through a nozzle, enabling deposition of viscous or paste-type formulations. Hybrid pullulan-HPMC films fabricated by pressure-assisted microsyringe printing showed tensile strength increases from 8.9 to 14.5 MPa depending on spatial deposition control, while fenofibrate-loaded films printed at 60 kPa using sodium starch glycolate inks achieved 44% drug loading with approximately 77% dissolution within 30 minutes.

Advantages of 3D Printing in Oral Thin Films

➤ An individual patient's needs can be met by adjusting film size, shape, thickness, geometry and drug dose.

- High dose uniformity and reproducibility, eliminating inter-film variability through accurate digital dosing.
- Complex film designs – multilayer, bilayer, compartmentalized and multi-drug OTFs – can be produced in a single manufacturing process.
- Film architecture, infill density, porosity and polymer composition can be tailored for immediate, sustained or biphasic drug release.
- Rapid dissolution and ease of administration are especially useful for dysphagia, pediatric and geriatric patients.
- Material waste is minimised, as additive manufacturing deposits material only where needed.
- Formulation and film design can be developed, optimized and modified quickly, accelerating R&D.
- LCD and SLA are non-thermal processes suitable for thermolabile drugs.
- Printing parameters can be optimized for film thickness, flexibility, tensile strength and mucoadhesion.
- On-demand, decentralized manufacturing of customized OTFs is possible in hospitals, pharmacies or clinics.

Table 7.6.3: Comparison of 3D printing techniques used for oral thin film fabrication.

3D Printing Technique	Working Principle	Common Polymers Used	Advantages	Limitations
Fused Deposition Modeling (FDM)	Extrudes thermoplastic filament layer-by-layer.	PEO, PVA, HPC, Soluplus	Better dose uniformity; multilayer film fabrication; personalized dosing.	High processing temperature may cause drug degradation; surface roughness.
Semi-Solid Extrusion (SSE)	Extrudes a viscous gel or paste through a syringe/nozzle.	HPMC, Carbopol, Sodium Alginate, CMC	Low-temperature process; suitable for heat-sensitive drugs.	Ink rheology must be carefully controlled.
Liquid Crystal Display (LCD) / Stereolithography (SLA)	UV light cures liquid photopolymer resin layer-by-layer.	PEGDA, UV photoinitiators, photoabsorbers	High printing precision; smooth surface finish.	Limited to UV-curable resins; potential phototoxicity.
Direct Powder Extrusion (DPE)	Powder is directly fed into a heated extrusion print head.	HPMC, PEO, Chitosan, Cyclodextrins	Solvent-free process; enables partial drug amorphization.	Requires thermoplastic-compatible polymers and optimized processing conditions.
Pneumatic Pressure Extrusion	Deposits polymer inks using pneumatic pressure.	Pullulan, HPMC, Beeswax, PVA	Prevents polymer immiscibility; mechanical properties can be tailored.	Requires optimization of ink viscosity and printing pressure.

Current Challenges and Future Perspectives of 3D Printing in OTFs

- Thermal constraints: FDM operates at high temperatures, which can preclude the use of thermosensitive drugs; plasticised polymers and alternative extrusion techniques are being explored as solutions.
- Commercial scalability: appropriate materials, equipment, quality control testing and process analytical technology (PAT) are needed before industrial-scale adoption.
- Regulatory pathway: health regulatory agency involvement and quality-by-design frameworks are required to facilitate clinical approval.
- Market entry barriers: the current thin film market exceeds \$1.3 billion per year, and 3D printing must demonstrate clear benefits over solvent casting to become a significant market player.

Sustainable ink development from agro-food wastes and natural biopolymers (e.g., CMC from durian rind, κ -carrageenan-starch systems) and hybrid printing approaches combining two or more techniques (e.g., SSE and FDM) are emerging trends that could enable multi-drug, multi-release-profile therapies.^[24-27]

8. Evaluation test

Table 8: Evaluation test. ^[3,20-23]

S. No.	Evaluation Test	Procedure
8.1	Physical Examination	Films were visually checked for colour, transparency, smoothness, flexibility and observable defects.
8.2	Film Thickness	Thickness was measured at different positions using a vernier caliper/micrometer, and the mean thickness was calculated.
8.3	Weight Variation	Ten films of 2 × 2 cm were individually weighed, and the mean weight and percentage variation were calculated.
8.4	Folding Endurance	A 2 × 2 cm film was repeatedly folded at the same place until breakage, and the number of folds was recorded.
8.5	Surface pH	The film was moistened, allowed to swell for 1 minute, and the surface pH was measured using a calibrated pH meter.
8.6	Drug Content Uniformity	A known amount of film was dissolved, diluted and analysed using UV-Visible spectrophotometry/HPLC.
8.7	Tensile Strength & Percentage Elongation	The film was stretched until breakage, and tensile strength and percentage elongation were determined.
8.8	Disintegration Time	The film was placed in a suitable medium at 37 ± 0.5°C, and the disintegration time was recorded.
8.9	<i>In vitro</i> Drug Release	Drug release was studied in phosphate buffer pH 6.8 at 37 ± 0.5°C and 50 rpm, with samples withdrawn at predetermined intervals.

9. Therapeutic applications

OTFs are used for local oral therapy, rapid systemic delivery, and increasingly for vaccines, probiotics, and nutraceuticals. They are especially positioned for patients who need easy administration without water, including pediatric, geriatric, dysphagic, Parkinson's, schizophrenia, and oral cancer populations.

9.1 Current Uses

OTFs can be used for oral and throat problems such as local anesthetic for dental purposes, fungal or bacterial infections, sore throat, oral ulcers, pharyngitis and tonsillitis. They also have marketing and/or research for use in cough, cold, allergic reactions, asthma, gastrointestinal disturbance, pain, sleep disturbances, and erectile dysfunction.

Its uses range from commercial to developmental such as antiemetics, migraine, seizure therapy, smoking cessation, and addiction treatment. Examples of reported products and/or candidates are ondansetron, zolmitriptan, clobazam, buprenorphine/naloxone, nicotine films, sildenafil, and cytosin.^[9,10]

9.2 Emerging Uses

The research into growing OTFs with other than conventional drugs, like vaccines, probiotics, herbal

products and nutraceuticals. Some nutraceutical films have been manufactured or suggested using strategies such as the incorporation of plant extracts, vitamins and minerals, proteins or peptides, probiotics, and vitamin D3 supplementation, with one such film resulting in a 25% increase in vitamin D3 absorption when compared to an oral solution. The pathway is also being looked at for personalised medicine films and products which can be tailored to children's dosing requirements, created in a pharmacy or a print shop. There is more evidence for broad therapeutic versatility and applications to special populations, but newer applications like vaccine, probiotic and personalized printed films are promising but less mature. Hence, OTFs have acute and chronic; local and systemic; therapeutic applications and are most promising at this time in situations where the delivery of the drug is required to be fast and compliance is high. Showcase of emerging OTF applications for the field of Biologics, Vaccines and Personalization. These areas of evidence include anti-diabetic/peptide delivery, vaccine and other biologics, and personalized medicine. The most advanced area for OTFs is the patient friendly small molecule delivery area while the other areas biologics, vaccines and individualized products are more nascent.^[11-14]

10. Recent advance techniques^[15,16]

Table 10: Recent advance techniques of Oral thin films.

Recent Advance	Recent Developments	Limitation
3D-Printed Oral Thin Films (OTFs)	Enables personalized medicine through customized doses, multilayer films, and multi-drug combinations.	Printability depends on the rheological properties of the printing ink and the mechanical strength of the film.
Hot-Melt Extrusion (HME)-Based OTFs	Provides a solvent-free manufacturing process and produces amorphous films with improved drug dissolution.	High processing temperatures may not be suitable for heat-sensitive (thermolabile) drugs.
Electrospun OTFs	Produces ultra-thin nanofiber films with very rapid disintegration and excellent drug release.	Long-term storage stability and moisture sensitivity remain concerns.
Nano-Enabled OTFs	Enhances drug solubility, bioavailability, targeted delivery, and drug loading capacity.	Large-scale manufacturing and clinical translation are still under development.
Personalized OTFs	Advanced printing technologies allow patient-specific dosing, controlled drug release, and combination therapies.	Maintaining dose uniformity and meeting regulatory requirements are major challenges.

11. CONCLUSIONS

Oral thin films (OTFs) have been proposed as promising patient-centric drug delivery systems due to their rapid disintegration, water-free administration, user-friendly application and the potential to enhance the patient's compliance. They are versatile and can be used to deliver drugs either locally or systemically via oral, buccal and sublingual routes and are ideal for patients who cannot swallow, such as children, geriatrics, and patients with dysphagia. Their therapeutic potential has been further enhanced by the development of formulation strategies (such as mucoadhesive polymers, taste-masking strategies, permeation enhancers, nanotechnology and multilayer systems). Although OTFs are typically manufactured using conventional methods such as solvent casting and hot-melt extrusion, new methods, such as inkjet printing, flexographic printing, 3D printing and electrospinning, are increasing the possibilities for designing drug-loaded OTFs, providing customized dosing and personalized therapy. But some limitations like low drug-loading capacity, moisture sensitivity, mechanical instability, formulation stability, scale-up difficulty and limited regulation standardization remain major barriers to their wider commercial use. Thus, future studies should emphasize the formulation stability, drug loading, and the reproducible and standardized methods of evaluation of the formulation. Integration of advanced manufacturing and personalized medicine approaches may further establish OTFs as a versatile platform for next-generation, patient-centred and precision drug delivery.

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