ORAL FAST DISSOLVING FILMS: A DETAILED REVIEW

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ABSTRACT

Oral fast dissolving films (ofdfs) are innovative drug delivery systems that rapidly disintegrate when placed on the tongue, eliminating the need for water. They provide a convenient alternative to tablets and capsules, particularly for children, elderly patients, and individuals with swallowing difficulties. Ofdfs enable quick therapeutic action, improved patient adherence, and easy portability, making them suitable for medications such as antiemetics, analgesics, and antiallergics. This review discusses the historical development, formulation approaches, manufacturing techniques, evaluation methods, marketed products, and recent advancements in ofdfs. Special focus is given to excipient selection, drug loading criteria, and modern technologies including electrospinning and 3D printing. Challenges like limited drug loading, taste masking, and moisture sensitivity are highlighted. Current trends aim at personalized therapies, biologics delivery, and continuous manufacturing, indicating that ofdfs are likely to become a widely accepted patient-centered dosage form.

INTRODUCTION

History

Oral fast dissolving dosage forms emerged in the late 1970s with orally disintegrating tablets (odts). While odts improved swallowing convenience, they often lacked sufficient strength and disintegrated slower than films. In the 1990s, thin-film consumer products such as breath strips demonstrated practical rapid-dissolving technology. Pharmaceutical research adapted these films to deliver active drugs, leading to the development of ofdfs. Over the last two decades, ofdfs have evolved from novelty forms into viable drug delivery platforms for both pharmaceuticals and nutraceuticals.

Advantages

1. No water required for administration.
2. Convenient for pediatric, geriatric, and dysphagic patients.
3. Reduced risk of choking compared to odts.
4. Rapid disintegration and faster onset of therapeutic effect.
5. Potential for transmucosal drug absorption, bypassing first-pass metabolism.
6. Improved patient compliance through better taste and mouthfeel.
7. Portable and discreet for on-the-go use.

Disadvantages

1. Difficulty in masking bitter taste of some drugs.
2. Complex manufacturing process requiring precise control.
3. Lack of globally harmonized regulatory guidelines.
4. Low drug-loading capacity (usually ≤ 30 mg).
5. Sensitive to moisture and environmental conditions.

Ideal Characteristics

1. Thin, flexible, and non-brittle film structure.
2. Disintegration within 30–60 seconds without water.
3. Pleasant taste and acceptable mouthfeel.
4. Adequate mechanical strength for handling and packaging.
5. Sufficient drug loading while maintaining film integrity.
6. Stability under standard storage conditions.
7. Safe and biocompatible excipients.

COMPOSITION OF ORAL FAST DISSOLVING FILMS

The formulation design of OFDFs significantly influences their mechanical and dissolution performance.

Film-forming polymers

Polymers act as the backbone of OFDFS, providing structure and controlling disintegration and drug release.

Table 1.1 Types of polymer

Polymer	Type	Key Properties	Advantages	Limitations
HPMC	Semi-synthetic	Strong films, good stability	Widely used, good handling	May slow disintegration
Pullulan	Natural	Transparent, fast dissolving	Excellent taste masking	Expensive
PVA	Synthetic	Flexible, stable	Good shelf life	Slower dissolution
PVP	Synthetic	Hydrophilic, enhances solubility	Improves api dispersion	Hygroscopic
Sodium alginate, CMC	Natural	Biocompatible, swellable	Eco-friendly	Weak mechanical strength

Plasticizers

Plasticizers such as triethyl citrate, polyethylene glycol (PEG), and glycerol improve film flexibility and reduce brittleness. Insufficient plasticizer results in brittle, fragile films. Excessive plasticizer produces sticky films that dissolve more slowly.

Taste-masking agents, flavors, and sweeteners

These excipients are essential to ensure patient compliance:

Sweeteners: aspartame, sucralose Flavors: fruit, mint

Microencapsulation or cyclodextrin complexes for bitter drugs

Permeation enhancers and pH modifiers

Fatty acids, surfactants, and bile salts improve transmucosal absorption. Local pH can be adjusted with sodium bicarbonate or citric acid to enhance solubility.

Other excipients

1. Surfactants: improve wetting of the film
2. Fillers: ensure uniform drug dosing
3. Preservatives: prevent microbial contamination

TYPES OF ORAL FAST DISSOLVING FILMS

Table 1.2 Types of oral fast dissolving film

Type	Description	Example/notes
Rapid dissolving films	Dissolve quickly in the oral cavity without water	Commonly used for pain relief, anti-allergic drugs
Effervescent films	Contain effervescent agents to enhance disintegration	Used for vitamins and minerals
Mucoadhesive films	Adhere to oral mucosa for localized effect	Suitable for oral ulcers, local anesthetics

Layered films	Multi-layered for sequential release of drugs	Can combine immediate and sustained release
OralThinFilms with Nanoparticles	Incorporate nanoparticles to improve solubility	Used for poorly water-soluble drugs

APPLICATIONS OF ORAL FAST DISSOLVING FILMS

- Pain management: Analgesics and anti-inflammatory drugs
- Allergy and cold treatments: Antihistamines and decongestants
- Nutraceuticals and vitamins: Quick delivery of vitamins, minerals, and dietary supplements
- Oral local therapy: Mucoadhesive films for treating oral ulcers, infections, and localized pain
- Systemic drug delivery: Drugs requiring fast onset such as antiemetics, cardiovascular drugs, and CNS-active agents

DRUG SELECTION CRITERIA FOR ORAL FAST DISSOLVING FILMS

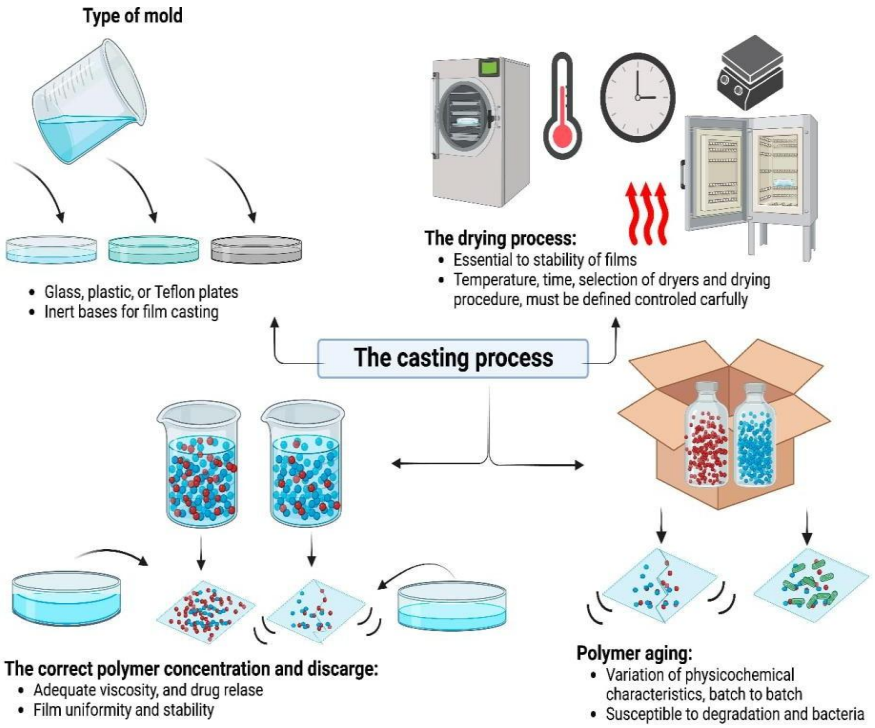
- Dose: Low-dose drugs (typically ≤ 20 mg) are preferred due to limitations in film thickness and drug-loading capacity.
- Solubility: Water-soluble drugs are ideal as they dissolve quickly in saliva; poorly soluble drugs may require solubilizers or nanoparticles.
- Stability: Drugs must remain stable in the film matrix and during storage, resisting moisture and temperature variations.
- Taste: Drugs with a bitter taste may require taste-masking techniques to ensure patient compliance.
- Permeability and absorption: Drugs with high permeability and suitable bioavailability in the oral cavity are preferred for systemic effect.
- Safety: Drugs with a wide therapeutic index and minimal local irritation are ideal candidates.
- Compatibility with excipients: Drugs should be compatible with film-forming polymers, plasticizers, and other excipients to maintain film integrity and performance.

TECHNIQUES FOR MAKING ORAL FAST-DISSOLVING FILMS

Oral fast-dissolving films (ofdfs) can be manufactured using multiple techniques. The choice of method depends on the drug's properties, desired film characteristics, and scalability. Commonly used methods include solvent casting, hot-melt extrusion, electrospinning, 3D printing, and other modified approaches.

Solvent casting method Principle:

This method involves preparing a polymer solution containing the drug and excipients, casting it onto a flat surface, and drying it to obtain thin films.



fFg.1.1 Solvent casting method

Process steps:

1. **Selection of solvent**: Typically water, ethanol, or hydroalcoholic mixtures.
2. **Preparation of polymer solution:** Film-forming polymer is dissolved in the chosen solvent with continuous stirring.
3. **Addition of excipients**: Plasticizers (e.g., glycerol, PEG) enhance flexibility; sweeteners, flavors, or permeation enhancers can also be included.
4. **Drug incorporation**: The active pharmaceutical ingredient (API) is dissolved or uniformly dispersed in the solution.
5. **Degassing:** Air bubbles are removed using sonication or vacuum.

Limitations:

1. Time-consuming drying process.
2. Possibility of residual solvent in the final film.
3. Limited scalability compared to extrusion methods.

Example: Hydroxypropyl methylcellulose (HPMC) is often used to prepare ondansetron oral films.

Hot-melt extrusion (HME) Principle:

This technique involves melting or softening a mixture of drug and polymer and then extruding it through a die to form films.

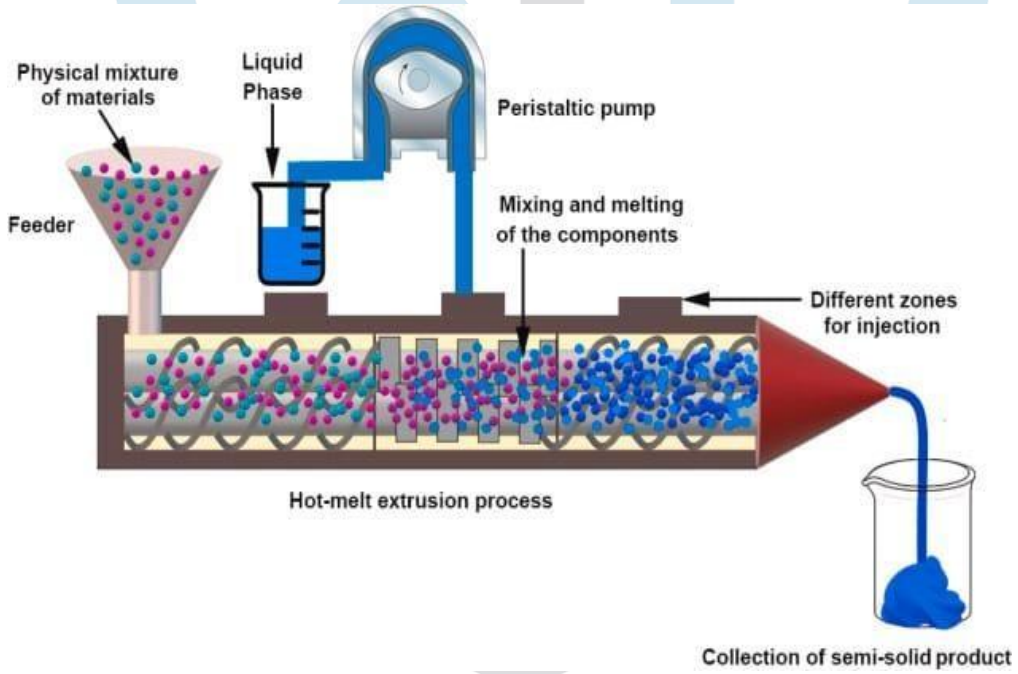


Fig.1.2 Hot melt extrusion

Process Steps:

1. **Dry mixing**: Blend polymer, excipients, and API.
2. **Extrusion**: Feed the mixture into a hot-melt extruder.
3. **Melting and mixing:** Heat and mechanical shear ensure uniform distribution of the drug.
4. **Shaping**: Molten mixture is pushed through a flat die to form films.
5. **Cooling:** Films are cooled and solidified.
6. **Cutting:** Films are trimmed into uniform strips

Benefits:

1. Solvent-free (green) process.
2. Continuous and scalable production.
3. Good compatibility between drug and polymer.

Limitations:

1. Not suitable for heat-sensitive drugs.
2. Requires specialized, costly equipment.

Example: Nicotine oral films have been successfully produced using HME.

Electrospinning method Principle:

A high-voltage electric field is applied to a drug-polymer solution, producing ultrafine fibers that form a nanofiber mat, which acts as a fast-dissolving film.

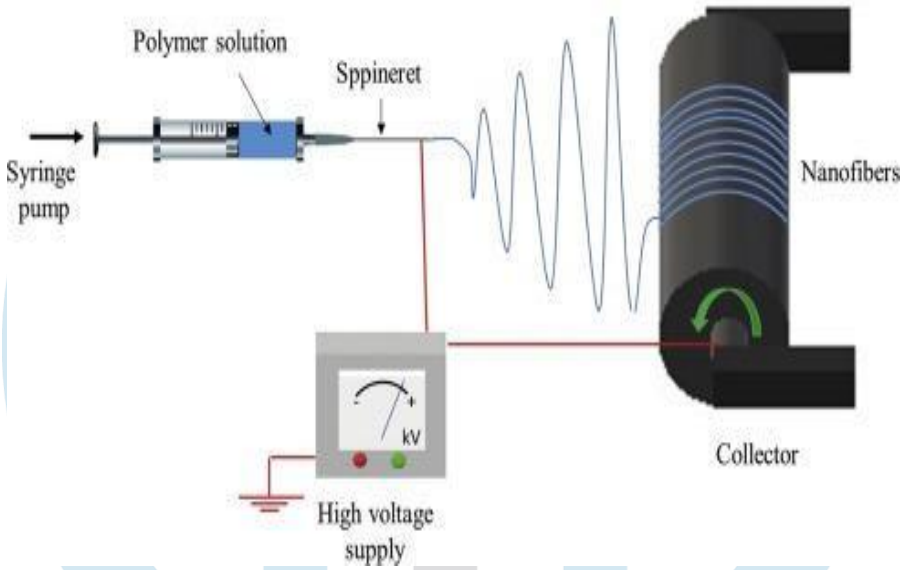


Fig.1.3 Electrospinning method

Process steps:

1. **Preparation of solution:** Dissolve polymer and API in an appropriate solvent.
2. **Setup:** Load the solution into a syringe with a needle.
3. **Voltage application**: Apply 10–30 kv between the needle and collector.
4. **Fiber formation**: Electrostatic forces produce fine fibers collected on a flat surface or rotating drum.
5. **Drying**: Residual solvent evaporates, leaving a fibrous film.

Benefits:

1. Produces high surface area nanofibrous films that dissolve rapidly.
2. Potential for improved solubility and taste masking.

Limitations:

1. Difficult to scale up.
2. High-voltage equipment is expensive; organic solvents pose safety concerns.

Example: Ciprofloxacin nanofiber films have been fabricated using electrospinning.

Additive manufacturing (3d printing) Principle:

Custom oral films with precise dosages are created using digital printing technologies, such as inkjet printing or fused deposition modeling (FDM).

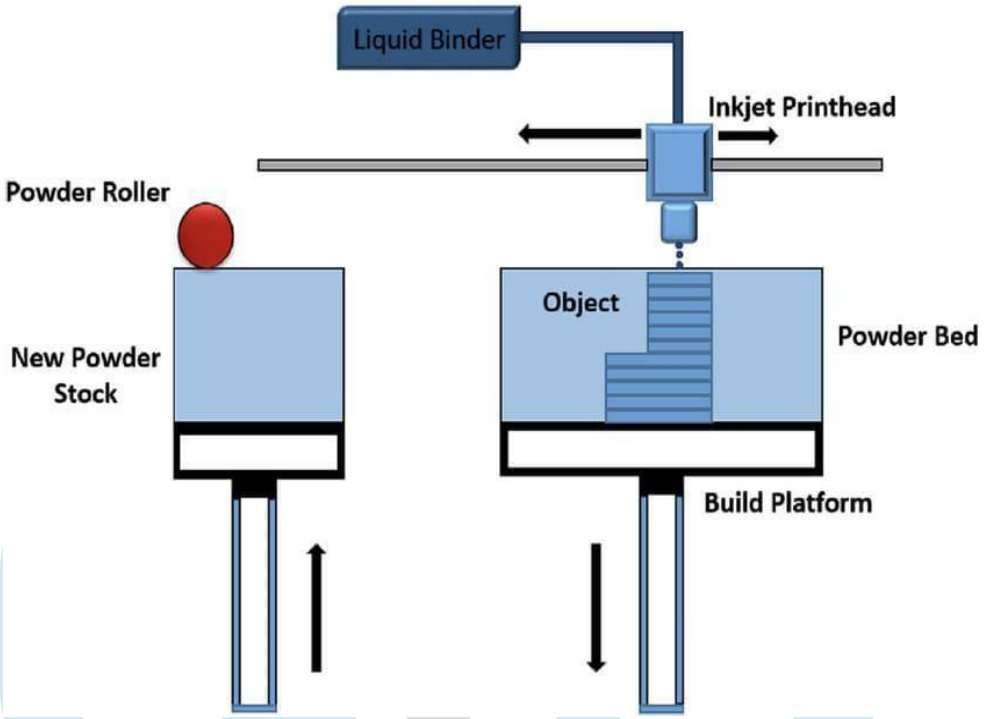


Fig .1.4 Additive manufacturing (3d printing)

Process steps:

1. **Design:** cad software is used to define the film geometry.
2. **Material loading:** drug-polymer filaments (fdm) or liquid inks (inkjet) are prepared.
3. **Printing**: layer-by-layer deposition forms the film.
4. **Post-processing**: films may require coating, drying, or curing.

Benefits:

1. Enables personalized medicine with adjustable dosages.
2. Supports multilayer films and complex designs.
3. Useful for rapid prototyping in research and clinical trials.

Constraints:

1. Regulatory guidelines are still evolving.
2. Equipment is costly.
3. Limited large-scale production potential.

Example: 3d printed oral films of levothyroxine and paracetamol have been reported for customized dosages.

Additional techniques

Rolling method: the drug-polymer mixture is rolled between rollers to form thin films. Drying is faster than solvent casting.

Spray deposition method: the formulation is sprayed onto a substrate and dried immediately. Suitable for multilayer films.

Freeze Drying (Lyophilization): Produces porous films that disintegrate rapidly, though less commonly used for ofdfs.

Table 1.2: Comparison of oral fast-dissolving film manufacturing techniques

Technique	Principle	Process Steps	Advantages	Limitations	Example
Solvent casting	Dissolve polymer and drug in solvent, cast and dry to form film	1. Select solvent 2. Prepare polymer solution 3. Add excipients 4. Incorporate drug 5. Degassing	Simple, widely used, suitable for water-soluble drugs	Long drying time, residual solvent, limited scalability	HPMC ondansetron films
Hot-melt extrusion (HME)	Melt drug-polymer mixture and extrude through die	1. Drymix 2. Extrusion 3. Melting & mixing 4. Shaping 5. Cooling 6. Cutting	Solvent-free, continuous, scalable, good miscibility	Not for heat-sensitive drugs, expensive equipment	Nicotine oral films
Electrospinning	High-voltage electric field produces nanofibers from drug-polymer solution	1. Prepare solution 2. Set up syringe 3. Apply voltage 4. Collect fibers 5. Dry	High surface area, rapid disintegration, enhanced solubility	Difficult scale-up, expensive equipment, solvent safety	Ciprofloxacin nanofiber films
3d printing	Layer-by-layer deposition of drug-polymer material	1. Design geometry 2. Load material 3. Print layer-by-layer 4. Post-processing	Personalized dosing, complex designs, rapid prototyping	Costly, regulatory issues, limited large-scale production	Levothyroxine, paracetamol films
Rolling method	Compress drug-polymer mixture between rollers	Rolling, drying	Faster drying than solvent casting	Limited to thin, uniform films	-
Spray deposition	Spray formulation onto substrate and dry	Spraying, drying	Supports multilayer films	Requires precise spraying equipment	-
Freeze drying	Lyophilize drug-polymer solution to make porous films	Freezing, drying under vacuum	Rapid disintegration	Lesscommon, expensive	-

EVALUATION TESTS FOR PURITY OF ORAL FAST DISSOLVING FILMS

The purity of oral fast dissolving films (OFDFS) is a critical quality parameter that ensures the drug remains chemically stable, uniformly distributed, and free from undesirable impurities or degradation products. Several tests are routinely employed to assess the purity of OFDF formulations:

Assay and Drug Content Analysis

1. **Purpose**: To confirm that each film contains the intended amount of the active pharmaceutical ingredient (API).
2. **Method**: Commonly performed using validated techniques such as UV–Visible spectrophotometry or High-Performance Liquid Chromatography (HPLC).
3. **Indicator of Purity:** A drug content close to 100% of the label claim, with minimal variation, indicates chemical purity and absence of degradation

Content Uniformity

1. **Purpose:** To ensure that the API is evenly distributed throughout the entire film.
2. **Method:** Multiple strips are cut from different parts of the film and assayed individually.
3. **Indicator of Purity:** Uniform results (usually within ±5–10% of the declared dose) confirm homogeneous distribution without segregation or crystallization.

Spectroscopic compatibility studies (FT-IR)

1. **Purpose:** To detect potential chemical interactions between the drug and excipients that may compromise purity.
2. **Method:** Fourier-Transform Infrared (FT-IR) spectroscopy is used to check for new or shifted functional groups.
3. **Indicator of Purity**: Retention of characteristic API peaks without additional signals indicates chemical integrity.

Thermal and Solid-State Analysis (DSC and XRD)

1. **Purpose:** To verify the physical form of the drug and detect unwanted polymorphic or crystalline changes.
2. **Methods:**
3. Differential Scanning Calorimetry (DSC): Identifies melting point changes, which may suggest drug–excipient interactions or degradation.
4. X-ray Diffraction (XRD): Differentiates crystalline versus amorphous states of the drug in the film.
5. **Indicator of Purity:** Absence of unexpected thermal transitions or crystalline peaks ensures physical purity.

Chromatographic Impurity Profiling

1. **Purpose**: To quantify degradation products or related impurities.
2. **Method**: High-Performance Liquid Chromatography (HPLC) or Liquid Chromatography–Mass Spectrometry (LC–MS).
3. **Indicator of Purity**: Impurities should remain within International Council for Harmonisation (ICH) limits (Q3A/Q3B guidelines).

Residual solvent analysis

1. **Purpose**: To confirm complete removal of organic solvents used in the solvent casting method.
2. **Method**: Gas Chromatography (GC) or headspace GC analysis.
3. **Indicator of Purity:** Residual solvent levels must comply with ICH Q3C guidelines.

Moisture Content and Water Uptake

1. **Purpose:** To assess the susceptibility of films to degradation and microbial contamination caused by excess moisture.
2. **Method:** Gravimetric moisture analysis or Karl Fischer titration.
3. **Indicator of Purity**: Low and consistent moisture levels maintain chemical and microbial purity.

Microbial Limit Tests

1. **Purpose:** To ensure the film is free from microbial contamination, which can compromise safety and purity.
2. **Method:** Total viable count (bacteria, fungi) and absence of specific pathogens (e.g., E. Coli, Salmonella).
3. **Indicator of Purity:** Compliance with pharmacopeial microbial limits.

Stability Studies

1. **Purpose:** To evaluate whether purity is maintained during storage under various conditions.
2. **Method:** Films are stored at accelerated conditions (40 °C / 75% RH) and periodically analyzed for drug content, impurities, and physical appearance.
3. **Indicator of Purity:** Stable drug assay and absence of new degradation peaks confirm long- term purity.

MARKETED EXAMPLES

Table 1.4 Marketed oral fast dissolving films (global + india)

Brand name	Company	Strength(s)	Approx. Cost
Zuplenz	Par pharmaceutical / monosol rx (usa)	4 mg, 8 mg	Higher cost than odt; premium pricing in us
Setofilm	Bioalliance pharma (eu)	4 mg, 8 mg	Price details not publicly available
Zolmitriptan rapidfilm®	Labtec / apr (eu)	2.5 mg, 5 mg	Not officially published
Suboxone film	Indivior / generic manufacturers	2/0.5 mg, 4/1 mg, 8/2 mg, 12/3 mg	Approx. Us$ 30–35 per strip (branded); generics lower
Molshil	Shilpa medicare (india)	60 mg, 120 mg	Cost not published
Montelukast + levocetirizine otf	Zim laboratories (india)	Fixed dose	Similar to tablet formulations
Emefilm+ strips	Kerom (india, apollo pharmacy)	—	Around ₹300 per 30 strips
Dsr strips	Drs biopharma (india)	60,000 iu	About ₹290 per 10 strips
Other otfs (nicotine, tadalafil, simethicone, ondansetron)	Relyon sutures (india)	2–20 mg depending on drug	Price varies (bulk and retail supply)

RECENT RESEARCH / ADVANCES

Here are recent developments and research trends in the field of oral fast-dissolving / thin films, summarized under major themes.

New Formulation Methods / Manufacturing Technologies

Traditional solvent casting remains common, but newer techniques such as hot-melt extrusion, solid dispersion extrusion, electrospun nanofibrous films, and semisolid casting are being increasingly explored to improve mechanical strength, reduce drying time, better control drug release. Composite or co-amorphous film systems have been investigated, for example in co-administration of two natural products via an oral fast dissolving film with moderate drug load (~14%) while retaining good dissolution.

Polymers & excipients innovations

Use of new polymers or blends to allow better flexibility, faster disintegration, improved taste masking, and moisture stability. Hydrophilic polymers with good film-forming ability (e.g. Pullulan, maltodextrin) are under investigation. Plasticizers, saliva-stimulating agents, flavors, stabilizers being

optimized to enhance user acceptability. Studies are focusing not just on rapid dissolution but sensory properties.

Drug candidates / applications expanded

Beyond small molecules for nausea or opioid dependence (e.g., ondansetron, buprenorphine/naloxone), oral films are being studied for poorly soluble drugs (BCS class II/IV), nutraceuticals, and even herbal extracts. Local action in the oral cavity (e.g. Local anesthetics, antimicrobials) as well as systemic delivery via lingual / buccal absorption.

Quality control, disintegration & dissolution performance

Researchers are refining in vitro and in vivo methods to measure disintegration time, dissolution, bioavailability. Optimizing thickness, surface area, weight of strip to balance strength vs fast disintegration. Example: zuplenz films dissolve in ~4-21 seconds depending on strength. Addressing issues of moisture sensitivity, mechanical fragility, and packaging challenges. Better barrier packaging, inclusion of stabilizers.

Regulatory / market trends

There is growing regulatory interest in approving oral thin films; first major fda approval for films like zuplenz (ondansetron) in 2010, and for suboxone film etc. Market size is growing; research reviews indicate increasing publications, patent filings. Surveys show greater attention to films vs odts due to patient compliance, portability, ease of manufacturing in some contexts.

Challenges under investigation

Drug loading capacity: films often limited to low or moderate dose, as adding more drug can affect flexibility, disintegration. Taste masking, stability under humid conditions, cost of film formulation and packaging.Ensuring consistent performance (dissolution, bioavailability) especially under different conditions (with/without water, fed/fasted, etc.).

CONCLUSION

Oral fast-dissolving / thin film technologies represent a promising and increasingly mature platform for delivering drugs and active ingredients, especially where rapid onset, ease of administration, and patient compliance are priorities (e.g. Pediatric, geriatric, or patients with swallowing difficulty). Marketed products like Zuplenz and Suboxone demonstrate that films can deliver therapeutically meaningful doses and gain regulatory approval, although at a higher cost compared to conventional oral tablets. Recent research continues to push boundaries in manufacturing methods (e.g. Hot-melt extrusion, nanofiber electrospinning), formulation science (polymers, co-amorphous systems, taste masking), and performance (faster disintegration, better stability). Key challenges remain: achieving higher drug loading without compromising film properties, ensuring stability (especially to moisture and temperature), controlling cost of production and packaging, and maintaining consistent bioavailability across different use conditions. Overall, the potential for oral fast dissolving films is high, particularly in niches where their advantages outweigh costs. With ongoing innovations and broader adoption, their role may expand both in prescription therapeutics and over-the-counter / nutraceutical spaces.

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