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Review Article

EXPLORING THE POTENTIAL OF FAST DISSOLVING ORAL FILMS

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Abstract

The introduction of oral fast dissolving films (OFDFs) has revolutionized drug delivery by offering rapid dissolution, enhanced patient compliance, and versatility in medication administration. OFDFs provide advantages over traditional dosage forms, including improved bioavailability, site-specific targeting, and non-invasiveness. However, challenges in formulation, stability, and manufacturing exist, such as solubility issues and the selection of suitable drug characteristics. OFDFs are classified into flash release, mucoadhesive melt-away wafers, and mucoadhesive sustained-release wafers, each serving specific purposes. The composition of OFDFs involves water-soluble polymers, active pharmaceutical ingredients (APIs), plasticizers, and other excipients to ensure stability and efficacy. Polymers play a crucial role in film formation and disintegration, impacting mechanical properties and water absorption. The solubility and compatibility of APIs in OFDFs are essential for uniform drug distribution. Formulation development focuses on selecting appropriate components and employing various techniques to enhance drug delivery. Manufacturing techniques vary, and characteristic analysis is conducted to ensure quality and performance. Regulatory guidelines for OFDFs differ across regions, influencing packaging and distribution. OFDFs find applications in various therapeutic areas, offering a promising future for personalized medicine and improved patient outcomes.

Keywords: Oral fast dissolving films (OFDFs); Sustained-release; Active pharmaceutical ingredients; Polymer; Regulatory guidelines.

Introduction:

Oral drug delivery is a widely used and convenient approach for administering medications, offering various options such as tablets, capsules, liquids, powders, chewable tablets, effervescent tablets, controlled-release formulations, sublingual and buccal administration, orally disintegrating tablets (ODTs), gastrointestinal coatings, and sustained-release and extended-release formulations [1]. Each method has its unique advantages and considerations, ensuring flexibility in catering to patients' needs. The ease of administration, patient compliance, and cost-effectiveness make oral drug delivery appealing. However, the effectiveness of these methods depends on factors like drug properties, patient characteristics, and interactions with food in the digestive system. Healthcare providers carefully assess these factors when selecting the most suitable oral drug delivery method for a specific medication and individual patient, ensuring optimal therapeutic outcomes [2].

Innovative drug delivery forms called oral fast dissolving films (OFDFs) break down quickly within the mouth, making it easy to provide medication without the need for water or chewing [3]. They offer numerous advantages, including enhanced bioavailability, precise dosing, improved patient compliance, versatility in drug formulation, discreet administration, suitability for diverse patient populations, stability, and portability. Pharmaceutical companies are now conducting research and development on OFDFs because they offer a patient-friendly substitute for conventional oral dosage

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forms and have the potential to completely transform medication administration [4]. Oral fast-dissolving films (OFDFs) have gained substantial significance in contemporary pharmaceutical research for several compelling reasons. OFDFs excel in enhancing patient compliance, particularly among populations such as children and the elderly, due to their user-friendly nature, rapid dissolution, and pleasant taste [5]. This leads to improved treatment outcomes by promoting adherence to prescribed therapies.

Moreover, OFDFs address the unique challenges posed by paediatric and geriatric patients who often struggle with swallowing difficulties, offering an effective and convenient medication administration solution. OFDFs also hold promise in improving drug bioavailability by enabling direct absorption through the oral mucosa, circumventing first-pass hepatic metabolism [6]. In contrast to conventional oral dose forms, this may lead to a quicker start of action and more effective drug delivery.

The potential uses of OFDFs are expanded by their adaptability in handling various drug classes, such as small molecules, biologics, and combination treatments. Researchers have the flexibility to tailor drug release profiles, providing precise control over drug release kinetics to meet specific therapeutic needs. Additionally, OFDFs afford discreet and convenient administration, making them suitable for various settings, including social or public environments, which is particularly relevant for medications with social stigma or frequent dosing requirements [7].

OFDFs open doors to personalized medicine approaches, enabling customized drug delivery based on individual patient preferences and needs. Their stability at room temperature and portability makes them adaptable for both clinical and non-clinical settings, including emergency situations, travel, and remote healthcare settings [8].

Furthermore, OFDFs represent a dynamic field of research and development within the pharmaceutical industry. Ongoing investigations explore novel materials, formulation techniques, and drug delivery strategies to expand the scope of OFDF applications and enhance their performance [1]. In conclusion, OFDFs have emerged as a valuable asset in contemporary pharmaceutical research, offering innovative solutions to critical challenges related to patient adherence, drug bioavailability, and personalized medicine. Their adaptability and benefits for the patient make them a viable platform for the creation of cutting-edge medication delivery systems.

Advantages of OFDFs over traditional dosage forms

1. **Bioavailability:** Oral fast-dissolving films offer improved drug bioavailability and site-specific targeting, leading to enhanced therapeutic efficacy [9].
2. **Passive Drug Diffusion:** These films utilize two penetration pathways: route paracellular and passive drug diffusion over the oral mucosa [10].
3. **Patient Compliance and Convenience:** As OFDFs are non-invasive and convenient to use, they are patient-friendly [11].
4. **Non-Invasiveness:** OFDFs are non-invasive, which makes them a preferred route over other oral dosage forms [11].
5. **Site-Specific Drug Delivery:** Drug delivery to certain locations in the mouth is possible with OFDFs, which improves the therapeutic effect of the medication [12].
6. **Durable and Fragile:** While traditional tablets and capsules are durable, OFDFs are fragile but still maintain their integrity until they reach the stomach [13].
7. **Overcoming Resistance:** OFDFs can be designed to release drugs at the back of the mouth, which can help in overcoming drug resistance [14].
8. **Overcoming Physical Barriers:** OFDFs can be designed to release drugs at the back of the mouth, which can help in overcoming physical barriers [14].

Challenges in formulation, stability, and manufacturing of OFDFs

1. Solubility: About 80% of new chemical entities (NCEs) in the pipeline face solubility challenges, leading to the production of poorly soluble OFDFs [15].
2. Nanosuspension: Because of the instability of nanosuspensions, it is difficult to formulate OFDFs loaded with them in order to increase the bioavailability of paroxetine [15].
3. Nanoemulsion: The development of fast-dissolving nano-emulsion-based sublingual films is hampered by the instability of nano-emulsions [15].
4. Nano-emulsion-in-oil: The replacement of microplastics in capsules with oil- dispersions is a challenge due to the instability of oil dispersions [16].
5. Fast-dissolving films loaded with active ingredients: Challenges include maintaining the stability of the active ingredients in the film and overcoming the limitations of oil dispersions [17].
6. Fast-dissolving films loaded with microplastics: The replacement of microplastics in capsules with oil-dispersions is a challenge due to the instability of oil-dispersions [16].
7. Fast-dissolving films loaded with polymers: Challenges include maintaining the stability of the polymers in the film and overcoming the limitations of oil dispersions [17].

The perfect characteristic of drug to choose [16, 18].

1. It should taste nice. Low molecular weight and tiny molecular size are desirable for the drug.
2. It has to be stable and soluble in both water and saliva.
3. It should be partially unionized at the oral cavity's pH.
4. The drug has to be less sensitive to environmental conditions.
5. The drug should penetrate mucosal tissue of the mouth.
6. The drug's therapeutic dose shouldn't exceed 40 mg.

Oral FILM's classifications

Three distinct subcategories of oral film are: [19].
i. Flash release
ii. Mucoadhesive melt-away wafer
iii. Mucoadhesive sustained-release wafers

Table 1 represents the types of oral films and their properties.

Table 1: Types of Oral Films and their Properties

Sl. No	Property/Sub/Type	Flash Release Water	Mucoadhesive Melt-Away Wafer	Mucoadhesive Sustained Release Wafer
1	Area (cm2)	2-8	2-7	2-4
2	Thickness (µm)	20-70	50-500	50-250
3	Structure	Single layer	Single or multilayer System	Multi-layer system
4	Excipients	Soluble, highly hydrophilic polymers	Soluble, hydrophilic Polymers	Low/Non-soluble Polymers
5	Drug phase	Solid solution	Solid solutionor suspended drug particles	Suspension and/or solid Solution
6	Application	Tongue (upper palate)	Gingival or buccal Region	Gingival, (another region in the oral cavity
7	Dissolution	Maximum 60 sec	Disintegration in a few mins, forming gel	Maximum 8-10 hrs

Composition of OFDFs:

The composition of OFDFs is carefully formulated to achieve these characteristics while ensuring the stability and efficacy of the active pharmaceutical ingredients (APIs). Typically, OFDFs consist of the following essential elements [20–23].:

Polymer Matrix: The primary structural component of OFDFs is a water-soluble or water-dispersible polymer matrix, which forms the film's backbone. Common polymers used include hydroxypropylcellulose (HPC), hydroxypropylmethylcellulose (HPMC), polyvinyl alcohol (PVA), and pullulan. The necessary characteristics of the film, such as mechanical strength, disintegration rate, and API compatibility, dictate the choice of polymer.

Active Pharmaceutical Ingredient (API): The API is the therapeutic agent intended to provide the desired pharmacological effect. It is incorporated into the OFDF formulation in a finely dispersed or molecularly dispersed form, ensuring uniform distribution within the film matrix.

Plasticizers: To increase the film's elasticity and flexibility, plasticizers are added to the mixture, making it more comfortable for patients to handle and ensuring proper film formation. Common plasticizers include polyethylene glycol (PEG), glycerine, and sorbitol.

Sweeteners and Flavouring agent: To improve the palatability and patient acceptance of OFDFs, sweeteners (e.g., sucralose, mannitol) and flavouring agent (e.g., mint, fruit flavours) may be included. These additives mask the taste of the API and provide a pleasant sensory experience during administration.

Disintegrants: Disintegrants are used to facilitate the rapid disintegration of the film upon contact with saliva. Common disintegrants in OFDFs include crospovidone and croscarmellose sodium.

Surfactants: In order to facilitate the film's wetting and quick disintegration in the oral cavity, surfactants could be added. They increase the API's bioavailability. Common surfactants include polysorbates and sodium lauryl sulphate.

Antioxidants and Preservatives: These additives are used to protect the stability of the API and prevent degradation due to exposure to light, oxygen, or moisture.

Colorants: Colorants are optional and are added for aesthetic purposes, allowing for differentiation between different OFDF formulations.

Role of polymers in film formation and disintegration

The disintegration and film creation processes of oral fast-dissolving films (OFDFs) are significantly influenced by the polymer selection used in the formulation. Firstly, polymers act as the structural backbone of the film, ensuring its integrity and shape while encapsulating the active pharmaceutical ingredient (API) and other components. Water-soluble or water-dispersible polymers like hydroxypropylcellulose(HPC) and hydroxypropylmethylcellulose(HPMC) lend flexibility to the film, making it suitable for handling and oral administration [24]. These polymers also contribute to the uniform dispersion of the API within the film matrix, ensuring consistent dosing and therapeutic efficacy.

Moreover, some polymers possess mucoadhesive properties, enabling the film to adhere to the oral mucosa. This adhesion enhances API absorption and prolongs contact time with the mucosal surface. In terms of disintegration, polymers readily absorb saliva's moisture upon contact, causing them to swell and disrupt the film matrix, thereby promoting rapid disintegration [25]. Polymers like crospovidone and croscarmellose sodium, utilized as disintegrants, absorb water quickly, creating internal pressure that breaks the film into smaller particles. Additionally, polymers may enhance film solubility in saliva by dispersing and dissolving within the oral cavity, facilitating swift API release and dissolution. Some polymers can even contribute to taste masking by encapsulating the API's bitter

or unpleasant taste, improving patient acceptance during the disintegration process [26]. Consequently, selecting the right polymers with optimal mechanical properties, water absorption, and disintegration characteristics is imperative for achieving the desired performance of OFDFs, ensuring their rapid and uniform disintegration in the oral cavity for swift API release and absorption.

Impact of Plasticizers

Plasticizers are essential for improving the mechanical and flexible qualities of materials made of polymers. They achieve this by increasing polymer chain mobility, improving elongation and tensile strength, enhancing impact resistance, and reducing the modulus of elasticity. These properties are particularly valuable in industries like packaging, automotive, construction, and textiles [27].

However, it's essential to consider the potential impact of plasticizers on thermal stability and the environment, especially concerning health concerns related to specific plasticizers like phthalates [28]. This has prompted the exploration of eco- friendly alternatives and a growing emphasis on sustainable material development.

A comprehensive understanding of plasticizers' effects on material properties, coupled with environmental and health considerations, is essential for responsible material design and application [16] [29]. This comprehensive overview underscores the multifaceted role of plasticizers in tailoring polymer properties, with relevance across diverse industrial sectors.

Solubility and compatibility of API’s in OFDFS

Regarding Oral Fast Dissolving Films (OFDFs), addressing the solubility and compatibility of Active Pharmaceutical Ingredients (APIs) presents multifaceted challenges and opportunities [30]. API solubility, often hindered by poor water solubility, necessitates inventive approaches like co-solvents, complexation techniques, and nanoparticle formulations to ensure uniform distribution within the film matrix. Achieving compatibility between APIs and film materials is paramount for maintaining film integrity and bioavailability. This requires careful material selection and comprehensive compatibility studies [31]. Moreover, API solubility and compatibility exert a significant influence on essential film properties, including thickness, mechanical strength, flexibility, and disintegration time. Striking a delicate balance while accommodating the API's specific requirements is pivotal in OFDF development. Researchers employ various strategies, including solid dispersion techniques and particle size reduction, to surmount these challenges [32]. Regulatory compliance is crucial, involving the rigorous demonstration of API solubility and compatibility, along with stringent stability testing. Emerging technologies such as nanotechnology and hot melt extrusion offer innovative pathways to enhance API solubility and compatibility, potentially expanding the scope of OFDFs to a broader range of APIs [33]. Table 2 represent list of some APIs.

Table 2: List of drugs that can be incorporated in fast dissolving film

Sl. No.	**Drug**	**Dose**	**Therapeutic action**
1	Azatadine Maleate	1mg	Anti histaminic
2	Nicotine	2mg	Smoking cessation
3	Loperamide	2mg	Anti diarrhoeal
4	Ondensetron	2.5mg	Anti emetic
5	Triprolidine hydrochloride	2.5mg	Anti histaminic
6	Zolmitritpan	2.5mg	Anti migraine
7	Salbutamol	4mg	Anti histaminic
8	Chlorpheniramine Maleate	4mg	Anti allergic

9	Cetirizine	5-10mg	Anti histaminic
10	Acrivastine	8mg	Anti histaminic
11	Loratadine	10mg	Anti histaminic
12	Omeprazole	10-20mg	Proton pump inhibitor
13	Famotidine	10mg	Antacid
14	Ketoprofen	12.5mg	Analgesic
15	Dicyclomine hydrochloride	25mg	Muscle relaxant
16	Diphenhydramine hydrochloride	25mg	Anti allergic
17	Sumatriptan succinate	35-70mg	Anti migraine

Formulation Development

1. Selection of Suitable Polymers and Excipients: The formulation of OFDFs begins with the careful selection of polymers and excipients. Polymers should possess film-forming properties, such as hydroxypropylmethylcellulose(HPMC), polyvinyl alcohol(PVA), and pullulan. Excipients, including plasticizers (e.g., glycerine, propylene glycol), stabilizers, and bulking agents, are chosen to fine-tune film characteristics such as flexibility, stability, and disintegration [34]. Table 3 represents list of some film forming polymers.

Table 3: List of Film Forming Polymers [41].

Natural polymer	**Synthetic polymer**
Starch	Hydroxy propyl methyl cellulose
Pectin	Poly vinyl pyrolidone (PVP)
Gelatin	Polyvinyl alcohol (PVA)
Sodium alginate	Sodium Carboxy methyl cellulose
Maltodextrin	Poly ethylene oxide (PEO)
Pullulan	Kollicoat IR
Xanthan	Hydroxy propyl cellulose (HPC)
Polymerized rosin	Hydroxy ethyl cellulose (HEC)
Gum acacia	Methyl cellulose (MC)

2. Techniques for Preparing OFDF Formulations: Several techniques are employed for OFDF formulation preparation, each with its advantages. Solvent casting involves dissolving polymers and excipients in a solvent, casting the solution, and allowing it to dry. Hot melt extrusion uses elevated temperatures to melt the polymer and blend it with other components before forming films [35]. Spray drying and inkjet printing are also emerging techniques. The required film properties and the heat sensitivity of the API are two important considerations when selecting a technique.

3. Incorporation of Taste-Masking Agents and Sweeteners: To enhance patient acceptability, taste-masking agents and sweeteners are often incorporated into OFDF formulations. Bitter APIs can be masked with compounds like cyclodextrins, while sweeteners like mannitol and sucralose improve palatability. These additives ensure that the OFDFs not only deliver the medication effectively but also provide a pleasant taste experience [36].

4. Role of Surfactants in Enhancing Dissolution: Surfactants significantly improve the dissolution rate of poorly water-soluble active pharmaceutical ingredients (APIs) in oral fast dissolving films (OFDFs) by reducing the interfacial tension between the dissolving medium and the API, thereby facilitating faster drug release. Commonly used surfactants include Tween® and sodium lauryl sulphate (SLS) [18]. Careful selection and optimization of surfactant concentrations are necessary to achieve the desired dissolution profile.

Manufacturing Techniques

There are several manufacturing methods for OFDFs, each with its own advantages and limitations. Here's a detailed explanation of different manufacturing methods for OFDFs:

1. Solvent Casting Method:

For the production of OFDFs, this is one of the most used methods. To create a homogenous solution, the active pharmaceutical ingredients (APIs) and a suitable solvent is used to dissolve the film-forming polymers. After that, a thin layer of the solution is dried and cast onto a level surface [19,37].

- Steps:

1. Selection of film-forming polymers and plasticizers.
2. Dissolving the polymer, plasticizer, and API in a volatile solvent (e.g., ethanol).
3. Casting the solution onto a flat surface (e.g., glass) using a casting machine or a spreader.
4. Drying the cast film to remove the solvent, leaving behind a thin, flexible film (Figure 1).
5. Cutting the film into the desired dosage forms.

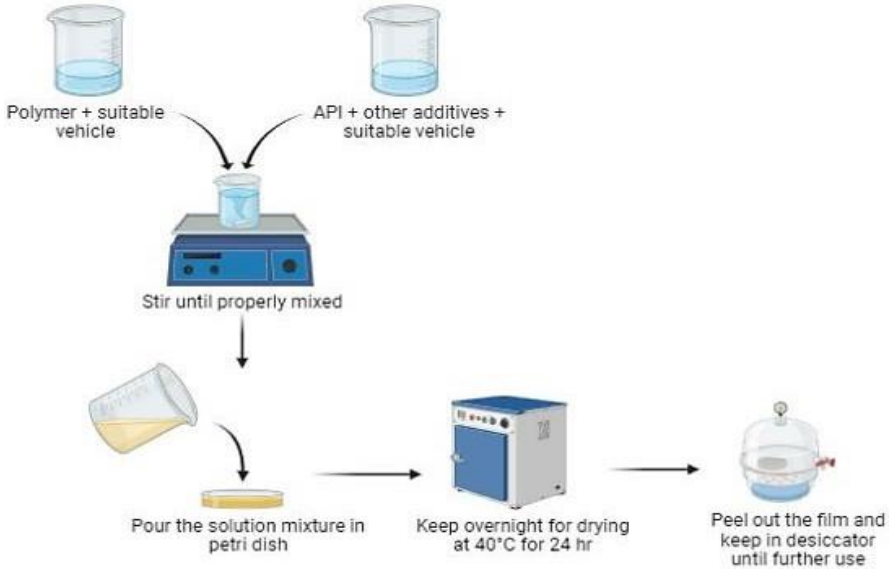

Fig. 1: Solvent casting method (Created with BioRender.com)

2. Hot Melt Extrusion method (HME):

In HME, the polymer is melted, the API is added, and the mixture is then extruded through a die to create a film. This is a continuous production procedure [38] [39].

- Steps:

1. Melting the polymer and plasticizer.
2. Mixing the API into the molten polymer.

3. Creating a thin film by extruding the mixture through a die.
4. Cooling and solidifying the film.
5. Cutting the film into the desired shape and size (Figure 2).

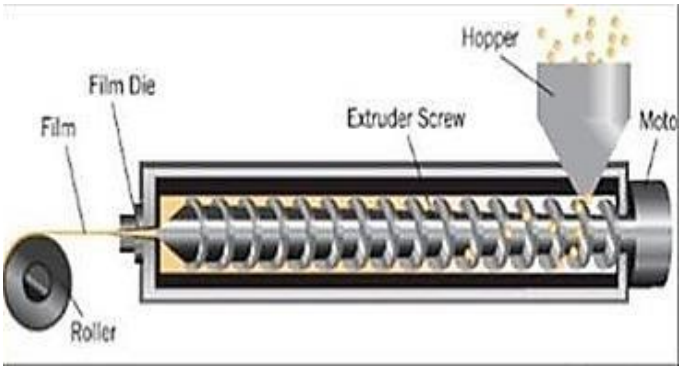

Fig. 2: Hot Melt Extrusion method (HME) [40].

3. Spray Drying Method:

This method involves atomizing a solution or suspension of the polymer and API into fine droplets and drying them using hot air, resulting in the formation of solid film particles [41].

- Steps:

1. Preparing a solution or suspension of the polymer and API.
2. Atomizing the solution/suspension into droplets in a spray dryer.
3. Drying the droplets to form solid film particles.
4. Collecting and further processing the particles into the desired dosage forms (Figure 3).

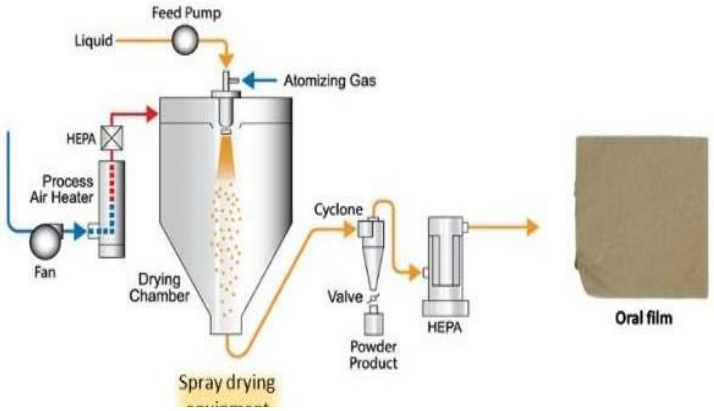

Fig. 3: Spray drying method in formulation of oralfilm.

4. Compression Molding:

In this method, a mixture of powdered polymers, plasticizers, and API is compressed into a solid film using a mold and a hydraulic press [16].

- Steps:

1. Mixing the polymer, plasticizer, and API powders to achieve a homogeneous blend.

2. Placing the mixture into a Mold cavity.
3. Applying pressure and heat to the Mold to form a solid film.
4. Cooling and demoulding the film.
5. Trimming the film to the desired size and shape (Figure 4).

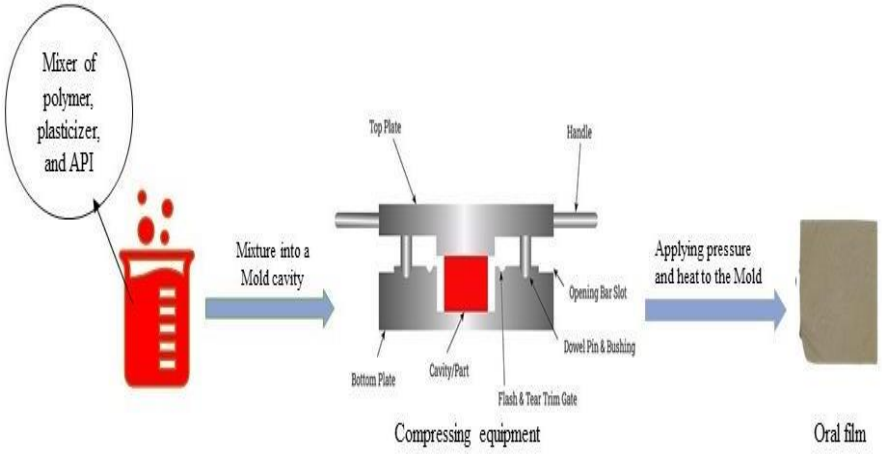

Fig. 4: Compression molding method

5. Rolling Method:

This method involves rolling out a mixture of polymer, plasticizer, and API between two rollers to form a thin film (Figure 5) [42].

- Steps:

1. Mixing the polymer, plasticizer, and API to form a uniform dough-like mass.
2. Feeding the dough between two closely spaced rollers.
3. Adjusting the gap between the rollers to achieve the desired film thickness.
4. Cutting the film into individual doses.

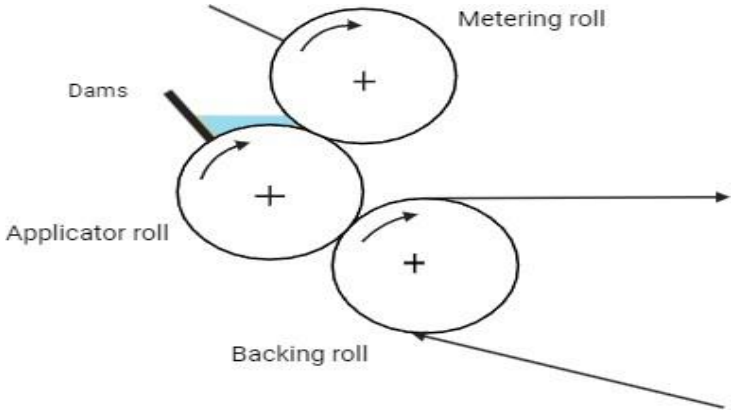

Fig. 5: Rolling method for manufacturing of oral films (Created with BioRender.com)

Characteristic Analysis of Oral Fast-dissolving Films

The different tests for characteristic analysis of the oral fast-dissolving films are: [32, 43, 44].

Thickness: To maintain consistency in drug content, it is crucial to ensure uniform film thickness, which can be measured using a micrometer screw gauge or calibrated digital Vernier calipers at specific strategic locations.

Dryness test/tack tests: The adhesive property of a material to maintain contact with a surface after being pressed against it is referred to as tack, and this characteristic will be examined in this study using specialized equipment.

Tensile strength: Tensile strength, defined as the maximum stress experienced by a material at the point of rupture, is calculated as the applied load at failure divided by the cross-sectional area of the strip specimen, as outlined in the formula provided.

$$Tensile\ strength\ = \frac{load\ at\ failure\ \times\ 100}{\text{strip thickness}\ \times \text{strip width}}$$

Percent elongation: Strain, defined as the ratio of deformation to initial dimension, describes the stretching that occurs in a strip under stress, with greater plasticizer content leading to increased elongation.

$$\%\ elongation\ =\ \frac{increase\ in\ length\ \times 100}{original\ length}$$

Young's modulus: Young's modulus, commonly referred to as elastic modulus, quantifies the stiffness of a material by defining it as the ratio of applied stress to corresponding strain in the elastic deformation range.

$$Young's\ modulus\ = \frac{Force\ at\ corresponding\ strain}{\text{cross sectional area}}\ \times \frac{1}{corresponding\ strain}$$

Hard and brittle materials with minimal elongation exhibit a high Young's modulus and tensile strength in their rigid, unyielding strip forms.

Tear resistance: Tear resistance, measured as the maximum stress required for initiation of tearing at a low loading rate of 51 mm/min, provides a metric for evaluating the final barrier property of plastic films and sheets against rupture.

Weight Variation: A study on weight variability in films involved the random selection of 10 films for individual weight assessments, resulting in the calculation of an average weight.

Folding endurance: The folding endurance of a material is determined by repeatedly folding it in the same location until it fractures, with the number of folds required for breakage serving as the measure of its folding endurance.

Surface pH of film: To mitigate potential in vivo negative effects and maintain a neutral surface pH, a mixed pH electrode was utilized to measure the pH of the rapidly dissolving film's surface, as an acidic or alkaline pH may irritate the oral mucosa.

Swelling property: Salivary simulators are used in studies on film swelling. Each film sample is weighed, placed within a previously weighed stainless-steel wire mesh, and then submerged in 15 ml of medium within a plastic container. The weight of the film was raised periodically until a constant weight was observed. These parameters were used to calculate the extent of swelling.

$$\propto = \frac{wt\ -\ w0}{w0}$$

The symbol wt indicates the weight of the film at time t, and at time zero by w0.

Transparency: The transparency of the films may be assessed using UV spectrophotometers. After being divided into rectangles, the film samples were placed inside the spectrophotometer cell. the transmittance of films measured at 600 nm. This is how the films' transparency was determined:

$$Transparency = \frac{(logT600)}{\mathrm{b}} = -€c\ (logT600)$$

where T600 is the transmittance at 600 nm, b is the film thickness (mm), and c is the concentration.

Assay/ Content uniformity: This will be ascertained by any standard pharmacopoeia, using any standard test process that is defined for the particular API. Content consistency is determined by analysing the API content in every single strip. The maximum content homogeneity ranges from 85–115%.

Disintegration time: The demand for US disintegration equipment is increasing for the dissolution of oral fast-dissolving films, particularly for oral fast-disintegrating film strips that lack established guidelines for disintegration times, which typically range from five to thirty seconds in accordance with Center for Drug Evaluation and Research (CDER) guidelines for oral disintegrating tablets with a disintegration time restriction of 30 seconds or less.

Dissolution test: The choice of dissolving medium and equipment (standard basket or paddle gear) for conducting dissolution tests is influenced by the maximal dosage of the active pharmaceutical ingredient (API) and sink conditions, with consideration given to the potential for strip floating in paddle equipment.

Stability studies: It is necessary to conduct stability experiments in the humidity chamber under accelerated conditions (65% relative humidity and 35 ºC temperature).

Regulatory guidelines for OFDFs in different regions

Like other dosage forms there are regulatory guidelines for manufacturing and sales of oral fast dissolving films as well. regulatory guidelines of different are mentioned in table 4 [45,46]..

Table 4: Regulatory guidelines for OFDFs

Region	Regulatory Authority	Key Guidelines and Regulations
India	Central Drugs Standard Control Organization (CDSCO)	- CDSCO's Schedule M for Good Manufacturing Practices (GMP)
		- CDSCO's requirements for registration and marketing approval
		- Indian Pharmacopoeia standards for pharmaceutical products
Australia	Therapeutic Goods Administration (TGA)	- TGA's Good Manufacturing Practice (GMP) requirements
		- TGA's guidelines for the registration of therapeutic goods
		- TGA's requirements for complementary medicines
China	National Medical Products Administration (NMPA)	- NMPA's Good Manufacturing Practice (GMP) regulations
		- NMPA's guidelines for drug registration and approval
		- NMPA's technical guidelines for pharmaceutical products

Brazil	National Health Surveillance Agency (ANVISA)	- ANVISA's Good Manufacturing Practices (GMP) requirements
		- ANVISA's regulations for registration and approval of drugs
		- ANVISA's requirements for labeling and package inserts
South Africa	South African Health Products Regulatory Authority (SAHPRA)	- SAHPRA's Good Manufacturing Practice (GMP) standards
		- SAHPRA's guidelines for the registration of medicines
		- SAHPRA's requirements for labeling and package inserts

Oral Fast Dissolving film packaging

In the pharmaceutical industry, the packaging must preserve the product's efficacy and stability to ensure its therapeutic integrity. Safeguarding the dose of other rapidly dissolving dosage forms during production and storage necessitates costly packaging, particular processing, and extra caution. For fast-dissolving films, there are several packaging choices. Films are medicinal items that must be packaged in singles; the most popular package type is an aluminium bag. The Rapid card is a unique and exclusive packaging solution created by APR-Labtec that is specifically made for the Rapid films. Three raid videos are stored on each side of the credit card-sized quick card. Each dosage can be removed on its own. The chosen material must possess distinct properties as outlined in our thorough investigation [25, 47, 48].

- Packaging materials must provide barrier protection against external environmental factors to preserve the integrity of the product inside.
- In accordance with regulatory requirements set forth by the Food and Drug Administration (FDA), packaging materials utilized in the food industry must obtain approval for their safety and suitability.
- Packaging materials should conform to established tamper-evident standards in accordance with relevant regulatory requirements.
- To ensure safe packaging, materials must adhere to stringent safety standards and be deemed harmless by rigorous scientific evaluation.
- The selected packaging materials should not elicit any adverse chemical or physical interactions with the product during storage or transportation.
- Packaging materials should not impart flavors or odors to the product to maintain its sensory integrity.

Blister Packs: Blister packs are a popular choice for packaging OFDFs. Each OFDF unit is placed in an individual blister cavity, which provides protection against environmental factors, ensures dosing accuracy, and facilitates easy removal of each unit. Blister packs are also tamper-evident [49].

Aluminium Foil Pouches: Aluminium foil pouches provide excellent moisture and light barrier properties. The OFDF units are sealed within the pouch, protecting them from external factors. These pouches are often used for larger quantities of OFDF units [50].

Application of oral fast dissolving films

The application of fast dissolving oral films are as follows: [26, 36, 51]

1. **Buccal Drug Delivery:** OFDFs are commonly used for buccal drug delivery, where they rapidly hydrate and adhere to the oral mucosal tissue. This method is ideal for drugs that need to reach the bloodstream quickly, such as certain pain relievers or vaccines.
2. **Gastroretentive Delivery:** OFDFs can also be used in gastroretentive delivery systems, which involve creating a reservoir of drug in the stomach that is released slowly over time. This can be beneficial for drugs that need to be absorbed over a prolonged period or have a high therapeutic index.
3. **Sublingual Delivery:** OFDFs can also be used for sublingual delivery, where they are placed under the tongue. This method is effective for rapid absorption of drugs into the bloodstream.
4. **Drug Coating:** OFDFs can be used to coat other drugs, improving their solubility and bioavailability. For example, they can be used to coat buccal films that are less soluble.

Conclusion

Oral fast-dissolving films (OFDFs) have revolutionized pharmaceutical research and drug delivery. They offer rapid dissolution, enhanced patient compliance, and versatility in delivering medications, making them a compelling alternative to conventional dosage forms. Despite formulation and manufacturing challenges, OFDFs have gained a foothold in the market, driven by patient preferences for convenience and specialized drug delivery. The future holds promising innovations, including nanotechnology and 3D printing, which will further expand their potential. Overall, OFDFs represent a commitment to improving medication delivery, catering to diverse patient needs, and advancing pharmaceutical science, promising a brighter future for both healthcare providers and patients.

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Conflict of Interest

The authors declare no conflicting interests.

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