JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue

JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)

An International Scholarly Open Access, Peer-reviewed, Refereed Journal

Advances in Oral Thin Films: Modern Strategies for Patient-Centric Drug Delivery and Global Regulatory Perspectives

Samruddhi S. Khonde*, Rohini Vishnu Bhojane, Rashmi Ramesh Lokhande,

Priti Dinesh Barange, Puja Gajananrao Khante, Rasika Surendra Shelke,

Assistant Professor*, Student of Bachelor of Pharmacy (4th year)

P. R. PATIL INSTITUTE OF PHARMACY, Talegaon (S.P.), Wardha

Dr. Koshish Gabhane, Dr. Vikrant Salode

Associate Professor

P. R. PATIL INSTITUTE OF PHARMACY, Talegaon (S.P.), Wardha

Abstract-

Oral thin films (OTFs) have emerged as a cutting-edge drug delivery platform designed for enhanced patient-centric care. These thin, rapidly dissolving films provide a convenient alternative to traditional oral dosage forms, enabling fast drug release and absorption through the oral mucosa, which bypasses first-pass metabolism and improves bioavailability. OTFs are particularly beneficial for pediatric, geriatric, and dysphagic patients who face difficulties swallowing tablets or capsules. Advances in manufacturing techniques, such as solvent casting, hot melt extrusion, and novel printing technologies including inkjet and 3D printing, have enabled precise dosing, personalized therapies, and rapid onset of action. The films can also incorporate taste masking and controlled release features, further improving patient compliance and therapeutic efficacy. On the regulatory front, global agencies are evolving guidelines to ensure safe, effective OTF quality control and manufacturing standards, fostering wider adoption. The OTF market is rapidly growing, reflecting the increasing demand for user-friendly, efficient drug delivery systems. Future directions explore multilayer films and multi-drug combinations, positioning OTFs as transformative solutions in modern pharmacotherapy and nutraceutical applications. This review elucidates these advances and regulatory perspectives underpinning the OTF landscape today and beyond.

Keywords- Oral thin films (OTF), Patients-Centric Drug Delivery, Fast-Dissolving Films, Regulatory Guidelines, Global Market

1. Introduction

Oral drug delivery is generally convenient, but it can pose difficulties for specific groups, such as pediatric, older adults, and individuals with swallowing disorders (dysphagia). These populations may struggle to swallow conventional dosage forms like tablets and capsules. Even fast-dissolving tablets may present a choking hazard and are not always well accepted by all patients. To overcome these challenges, oral fast-dissolving films (OFDFs) have been developed as a novel solution. These thin, polymer-based films rapidly dissolve upon contact with the tongue, allowing for easy administration without water or chewing. This approach improves patient adherence, especially in elderly individuals taking multiple medications and those affected by conditions such as Alzheimer's disease, Parkinson's disease, and schizophrenia. OFDFs also offer a practical and safe alternative for pediatric patients compared to traditional dosage forms.[1-2]

1.1 Oral Thin Film:

Oral fast-dissolving films or strips are drug delivery systems designed to quickly release the active ingredient by dissolving or attaching to the mucosal surface with the aid of saliva, usually within seconds of being placed in the mouth or on the tongue. The concept of oral thin films was introduced in the 1970s as an innovative dosage form. They were officially introduced to the market in 2004 for systemic drug delivery and have since become widely accepted.[3-5]

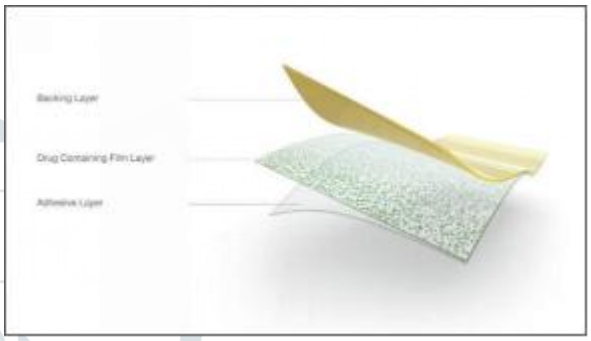

Figure 1: Oral Thin Film

Oral disintegrating or dissolving films (ODFs) are drug delivery systems designed to release the active ingredient rapidly by dissolving or adhering to the oral mucosa with the help of saliva within seconds, owing to the presence of water-soluble polymers, when placed in the mouth or on the tongue. The sublingual mucosa has a thin membrane and is highly vascularized, which allows for rapid absorption and excellent bioavailability. Oromucosal films are considered patient-friendly dosage forms due to their high level of patient acceptance. According to the European Medicines Agency, patient acceptability refers to the ability and willingness to use a medicinal product as intended. This is particularly relevant for populations such as the elderly with swallowing difficulties, infants, young children, and patients who are uncooperative or prone to nausea and vomiting. Although oral solid dosage forms make up around 60% of all dosage types, they present several challenges that can be mitigated through alternative systems like fast-dissolving oral films (FDOFs).The development of fast-dissolving drug delivery systems originated from the need to provide patients with a more convenient way to take medications. FDOFs are ultra-thin films, generally ranging from 5–20 cm^2 in size, containing an active pharmaceutical ingredient. Among the available administration routes, the buccal cavity is especially advantageous for systemic FDOF delivery because of its superior bioavailability, quick onset of therapeutic action, and high treatment adherence, resulting from the rich vascular supply and permeability of the oral mucosa. These films are particularly useful for pediatric and geriatric patients who struggle with swallowing, as well as bedridden patients, those suffering from nausea, diarrhea, allergic reactions, or cough, and individuals with active lifestyles. In addition, FDOFs are effective for achieving localized therapeutic effects, for example, as local anesthetics for toothaches, oral ulcers, cold sores, or teething discomfort.[6-17]

This dosage form consists of an ultra-thin oral strip that quickly disintegrates and dissolves in the mouth, enabling rapid medication release for oromucosal absorption. It offers a shelf life of 2–3 years, depending on the nature of the active pharmaceutical ingredients. Recognized as one of the most advanced solid oral dosage forms, it combines flexibility with patient comfort and enhances the effectiveness of APIs by dissolving within seconds upon contact with saliva, eliminating the need for chewing. Drugs commonly formulated as FDOFs include selective serotonin reuptake inhibitors (such as Fluoxetine and Sertraline), antiemetics (e.g., Ondansetron, Granisetron), 5HT3antagonists (such as Alosetron, Ondansetron, Granisetron, Palonosetron), antiepileptics (including Carbamazepine, Clonazepam, Phenytoin), antimigraine agents (like Almotriptan, Zolmitriptan), and dopamine D1/D2 receptor antagonists (including Bromperidol and Domperidone) Chlorpromazine (CPZ), an antipsychotic and antiemetic used to treat schizophrenia, has not yet been

formulated as an FDOF according to existing literature. Hence, the present study aims to develop and evaluate fast-dissolving oral films for the oro-buccal delivery of chlorpromazine. It's formulated and evaluated but not in marketed.[18-22]

Figure 2 : Fast Dissolving Oral Thin Film

The oral mucosal epithelium is a multilayered structure, about 40–50 cells thick, consisting primarily of carbohydrates and proteins. The mucosa's thickness in regions such as the mouth base, tongue, and gums typically ranges between 100 and 200 µm. Beneath this layer, the submucosa secretes a small quantity of gel-like mucus composed mainly of water (90%–99%) and water-insoluble glycoproteins (1%–5%), along with proteins, enzymes, electrolytes, and nucleic acids. The salivary glands are made up of lobules that produce saliva and parotid secretions, which are delivered through ducts located near the sublingual canals and submandibular teeth. Numerous minor salivary glands are distributed within the lip and cheek mucosa. On average, about 1–2 mL of saliva is secreted each minute. This fluid contains mucus, water, the enzyme amylase, lysozyme, mineral salts, immunoglobulins, and blood-clotting components. Together, mucin and saliva provide a protective barrier for the oral mucosa.[23-24]

The mucosal epithelium consists of two distinct zones: a lipophilic stratified epithelial membrane and hydrophilic intercellular spaces. The oral absorption of many drugs is restricted by enzymatic degradation, first-pass metabolism, and the stomach's acidic environment. Traditionally, these drugs have been delivered through parenteral routes, which often lead to poor patient compliance. To overcome these limitations, the pharmaceutical industry has developed innovative drug delivery systems, including thin, rapidly dispersing or dissolving oral films. Fear of choking, commonly associated with orally disintegrating tablets (ODTs), poses a challenge for some patients. In contrast, oral thin films (OTFs) that dissolves quickly in the mouth offer a more suitable alternative. Once placed on the tongue, OTFs are rapidly hydrated by saliva, resulting in their disintegration or dissolution and facilitating drug release for systemic or local absorption. Additionally, because ODTs are fragile and can break during transport, fast-dissolving OTF systems have emerged as a more durable and patient-friendly option.[25-28]

1.2 Types of Oral Thin Films:

OTFs are classified into 3 types

i. Flash Release
ii. Mucoadhesive Melt Away Wafers
iii. Mucoadhesive Sustained Release Wafers. [29]

- **Advantages**

1. Rapid breakdown within seconds, ensuring a swift therapeutic effect.
2. Simple and convenient to administer.
3. Enhances patient adherence, especially for children, elderly individuals, bedridden patients, and those with psychiatric conditions who are unwilling to swallow tablets.

4. Can be taken without the need for water or chewing.
5. Eliminates the risk of choking.
6. Offers a pleasant taste and texture in the mouth.
7. Requires no specialized training for proper use.
8. Avoids the first-pass metabolism, allowing for a lower dosage and reducing the likelihood of side effects from the active ingredient [30-36]

- **Disadvantages**

1. Requires specialized packaging equipment.
2. Unsuitable for drugs that are unstable or cause irritation at oral pH.
3. Allows administration of only small medication doses, although studies indicate that API content can be increased by up to 50% of the film's weight (for instance, each Gas-X® film strip from Novartis Consumer Health contains 62.5 mg of Simethicone).
4. Being hygroscopic, they pose challenges for long-term storage and protection.
5. Applicable only to drugs that are absorbed through passive diffusion
6. Due to their rapid dissolution, discontinuing the dose once administered is not possible.
7. Not currently recognized in any pharmacopoeia.
8. Manufacturing is more costly compared to orally dissolving tablets.[37 -39]

2. Overview and Mechanism of Oral Thin Film:

Drug absorption in the buccal cavity occurs mainly through passive diffusion of non-ionized molecules via epithelial intercellular spaces, driven by a concentration gradient. The primary pathway involves passive transport of non-ionic compounds across the lipid membrane of the buccal cavity. Similar to other mucosal membranes, the buccal mucosa functions as a lipid-rich barrier, and drugs with higher lipophilicity tend to be absorbed more rapidly. The absorption process in this region can be effectively described by first-order kinetics. Various factors can impede buccal drug absorption. Dearden and Tomlinson (1971) reported that salivary secretion changes the drug concentration within the oral cavity, which subsequently impacts the absorption kinetics from a drug solution. The relationship between salivary secretion and time can be expressed as a linear equation

$$[- dm / dt = Kc/ViVt]$$

Where,
m - Mass of drug in mouth at time
K - Proportionality constant
c - Concentration of drug in the mouth at time
Vi - The volume of the solution put into mouth cavity and
Vt - Salivary secretion rate.[40-42]

2.1 Comparison Between Fast Dissolving Oral Films and Conventional Tablets: [43-45]

Table 1: Comparison between Fast dissolving oral films and Conventional Tablets

Oral dissolving film	Oral disintegrating tablets
It is a film	It is a tablet
Greater dissolution due to greater surface area	lesser dissolution due to less surface area
Better durable as compared to disintegrating tablet	Less durable as compared to oral film
More patient compliance	Less patient compliance as compared to film
Low dose can only be incorporated in film	Higher dose can be incorporated in tablet
No fear of choking	It has fear of choking

3. Preparation Techniques and Technological Innovation:

3.1 Solvent Casting Methods

The solvent casting method is an efficient and straightforward approach for developing fast-dissolving oral thin films. In this technique, water-soluble polymers, active pharmaceutical ingredients, and excipients are mixed to form a viscous solution, which is subsequently spread and dried to obtain thin films with a thickness range of 12–100 µm. Researchers have emphasized that this method is economical, suitable for thermo labile drugs, and yields films with adequate mechanical strength and rapid drug release. Nonetheless, careful control of the solvent selection and solution viscosity is essential to maintain the uniformity and quality of the films.[46]

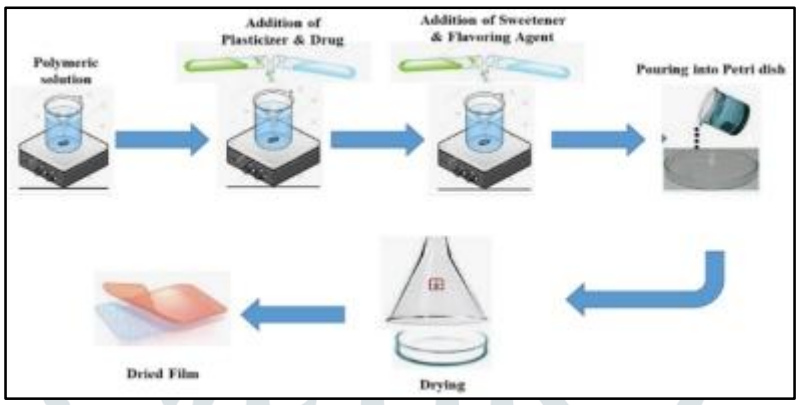

Figure 3: Diagrammatic Representative Solvent Casting Methods

3.2 Hot Melt Extrusion:

The hot melt extrusion technique is a widely used method for producing oral thin films, involving the melting of polymers under controlled heat and pressure to create films. In this process, all components are mixed in their dry form, heated to generate a molten mass, and subsequently cast, cooled, and cut into the desired film shapes. One key advantage of this approach is its ability to produce uniform films without requiring solvents; however, its main drawback is the risk of thermal degradation or loss of activity in heat-sensitive drugs due to elevated processing temperatures. According to Patel et al., while hot melt extrusion is an effective manufacturing method, the solvent casting technique is often favored for oral thin film formulation, as it better accommodates temperature-sensitive compounds and achieves improved film uniformity.[47]

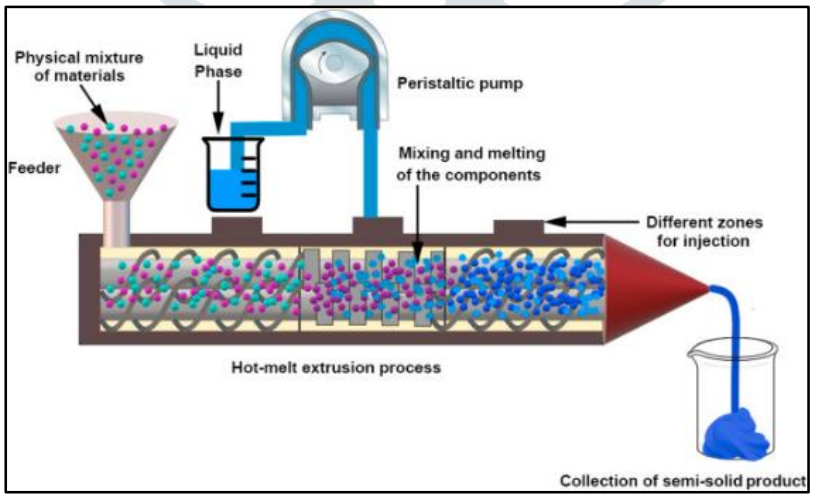

Figure 4: Diagrammatic Representative Hot Melt Extrusion Methods

3.3 Inkjet and 3D Printing:

The study described printing technologies such as 3D printing and inkjet printing as advanced and versatile techniques for producing oral thin films. It was noted that these methods offer precise and individualized drug dosing by depositing drug-containing inks onto appropriate substrates, enabling the creation of patient-specific formulations. In inkjet printing, the active pharmaceutical ingredient is directly printed, whereas flexographic printing applies a polymeric thin film coating onto the substrate. The researchers highlighted that these approaches ensure excellent uniformity, accurate dose control, cost efficiency, and enhanced film stability, making printing technology a valuable tool for developing fast-dissolving oral films.[48]

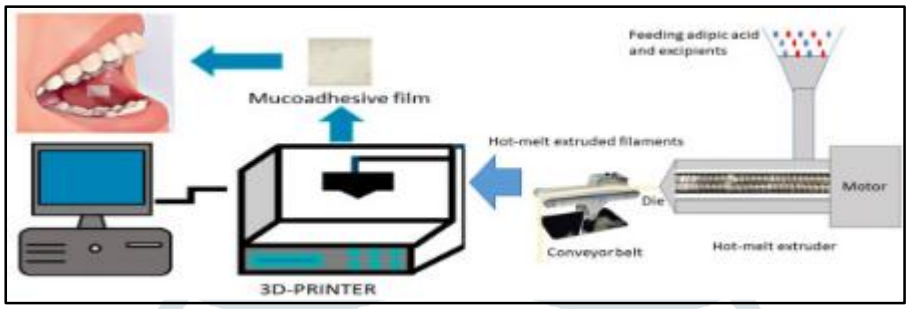

Figure 5: Diagrammatic Representative 3D Printing Technology

3.4 Slot-Die Coating

The slot-die casting technique, employing a doctor blade setup, is a highly effective method for producing thin polymeric films. In this process, a hydrogel is dispensed through a slot-die nozzle onto a plasma-treated PET substrate positioned on a heated platform, resulting in the formation of a uniform film layer. The system comprises rollers, a regulated syringe pump, and an adjustable nozzle that together ensure accurate control of film thickness and coating smoothness. The study indicated that regulating parameters such as deposition rate, temperature, and substrate movement enables the fabrication of transparent films with uniform thickness and high consistency. The authors concluded that slot-die casting is a reliable and scalable technique for producing polymeric thin films suitable for pharmaceutical and biomedical.[49]

4. Polymer and Film Forming Agent:

- Classification Of Polymers Used In Mouth Dissolving Film
- Natural Polymer
- Synthetic Polymer

  Polymer selection plays a vital role in ensuring the successful formulation of oral films, as tensile strength is directly influenced by the type and proportion of polymer used. For optimal performance, the dry film composition should contain at least 45% polymer by weight, with 60%–65% being ideal to achieve the desired mechanical and functional properties. Polymers may be utilized alone or blended to tailor specific film characteristics.

  Given that oral thin films (OTFs) are intended to quickly dissolve and disperse in the oral cavity, film-forming polymers should exhibit water solubility. Additionally, the films must possess enough strength to withstand handling, transportation, and storage without sustaining damage.[51-53]

Table 2: Common Polymers Utilized In Otfs [51-54]

Component	Class	Example
Natural	carbohydrate	Pectin, pullulan , mallodextrin, sodium alginate, and sodium starch glycollate
	protein	gelatin
	resin	Polymerized (new film forming)
Synthetic	Cellulose derivatives	Hydroxy propyl methylcellulose (K50, K3, K15, E5, E3, and E15), carboxy methylcellulose, methylcellulose (A3, A15, and A6), sodium carboxymethyl cellulose, croscarmellose sodium, and microcrystalline cellulose
	Vinyl polymer	Polyvinylpyrrolidone (K90 and K30), polyvinyl alcohol, and polyethylene oxide
	Acrylic polymer	Eudragit (RL-100, 9, 10, 11, 12, and RD-100)

5. Innovation in Drug Loading and Release:

The innovation of micropellet-loaded oral films designed to achieve rapid disintegration along with controlled drug release. The authors highlighted that embedding coated, drug-loaded micropellets within the film matrix helps maintain prolonged drug release and reduces dose dumping. Speer incorporated diclofenac-loaded micropellets using the spheronization technique to enhance the solubility of poorly soluble drugs such as indomethacin. The study emphasized that such films improve stability, safety, and patient compliance. Additionally, the development of pH- and sugar-sensitive layer-by-layer thin films was discussed as a promising approach for controlled drug release, in which environmental pH or sugar concentration regulates drug permeability and release behavior .[55]

6. Mechanical and Physiochemical Characterization:

Mechanical and physicochemical characterization, including thickness, folding endurance, weight uniformity, and moisture sensitivity, are essential for evaluating oral thin films reported that film thickness directly affects drug content and patient comfort, with an optimal range of 50–1000 µm. Flexibility, assessed through folding endurance, reflects the film's mechanical strength, with values above 300 folds indicating high flexibility. Uniform film weight ensures an even distribution of the active drug, while moisture absorption measurements help determine stability under humid conditions. The study concluded that these characteristics are critical for maintaining the quality, durability, and overall performance of oral thin films .[56]

7. Clinical and Therapeutic Application:

Discussed the clinical and therapeutic uses of oral thin films, emphasizing their increasing role in modern healthcare. The researchers noted that oral film technology provides a convenient, patient-friendly, and effective way to administer medication, thereby improving adherence. The study highlighted that these films are successfully used to deliver drugs such as antipsychotics, antihistamines, and analgesics. When formulated with nano-sized particles, oral films further enhance drug dissolution, bioavailability, and therapeutic performance. The authors also proposed that applying this technology to other drug categories, such as antihypertensive and antiulcer agents, could lead to better outcomes for chronic diseases. Overall, the study

identified oral thin films as a promising innovation for advancing drug delivery and promoting patient compliance .[57]

8. Market Trends:

Oral thin film (OTF) drug delivery systems have demonstrated high market acceptance due to ease of patient use and effectiveness, drawing investment from both established and startup pharmaceutical companies. The OTF drug products market grew from around $7.3 billion in 2015 to an estimated $16 billion by 2024, reflecting more than 100% growth within ten years. Although only about 10 prescription OTF products existed by 2015, the number has steadily increased, with ongoing clinical trials and regulatory approvals.

North America remains the leading manufacturer of oral thin films, accounting for approximately 85% market share as of 2015, with notable companies including Pfizer, Novartis, Solvay, Allergan, Sumitomo Dainippon Pharma, and IntelGenx Corp, alongside emerging startups such as FFT Medicals and Cynapsus Therapeutics. Technologies such as MonoSol's PharmFilm and Applied Pharma Research/Labtec's Rapid Film account for nearly 38% of marketed products. The Asia Pacific region, led by India, Japan, and China, is projected to be the fastest-growing area for OTF manufacturing.

In India, investor interest in OTF technology is rising, exemplified by new companies like Aavishkar Oral Strips Pvt. Ltd., NU Therapeutics, ZYM Laboratories, and major manufacturers such as Cipla, Mankind, and Dr. Reddy's Laboratories.[58]

Table 3: Market Comparison

Year	Global OTF Market Value ($ million)	CAGR (2016–2024)	# Prescription Products (2015)	Regional Market Leader	Tech Usage Share (%)	Fastest Growth Region
2007	500	—	—	—	—	—
2010	2,000	—	—	—	—	—
2015	7,338	18.3	10	North America (85.3%)	MonoSol/APR-Labtec (38)	Asia Pacific
2024	15,984	18.3	—	North America, Asia-Pacific rising	—	Asia Pacific (India, Japan, China)

9. Regulatory Guidelines For Oral Thin Film Is Different Regions:

9.1 Regulatory Perspectives:

All industries in the pharmaceutical sector must undertake an initial experimental phase in product design to develop goods that are both acceptable and sustainable. Applying ideas through a structured process ensures that the resulting products meet established quality standards. The manufacture and development of pharmaceutical products are governed by various compendial requirements and are subject to regulations set by national authorities, which are formed after extensive testing. Almost every country has its own regulatory agency that enforces laws, guidelines, and standards concerning drug development, registration, licensing, manufacturing, classification, and marketing. Alongside national agencies, international organizations also work to enhance drug safety by creating guidelines for product approval, distribution, production, pricing control, marketing, advertising, and the protection of intellectual property rights (Franco, 2013). Table 1 offers a detailed reference to regulatory bodies from different nations. Drug regulation entails numerous measures

to safeguard the safety, efficacy, and quality of medications (Wirthumer-Hoche and Bloechl-Daum, 2016). To meet regulatory requirements, pharmaceutical companies must establish a regulatory affairs department that engages in all stages of drug development—from clinical trials through marketing and post-marketing surveillance. This department functions as the connection between regulatory authorities and the pharmaceutical industry (De Frutos, 2013).[59]

Table 4: Regulatory Bodies and Function:

Regulatory bodies	**Function**
International Council for Harmonization**(ICH)**	Technical Requirements for Pharmaceuticals for Human Use: Issues guidelines defining quality, safety, efficacy, and related aspects for developing and registering new medicinal products in Europe, Japan, and the United States.
Central Drugs Standard Control Organization **(CDSCO)**	Ministry of Health & Family Welfare, Government of India: Provides drug regulatory requirements in India.
European Medicines Agency **(EMA)**	Decentralized body of the European Union headquartered in London prescribes guidelines for inspections and general reporting and all aspects of human and veterinary medicines.
US Food and Drug Administration **(FDA)**	Issues regulations, guidelines, notification, news, and other communications
Medicines and Healthcare Products Regulatory Agency **(MHRA)**	Responsible for ensuring efficacy and safety of medicines and medical devices in the United Kingdom; produces news, warnings, information, and publications.
Japanese Pharmaceutical and Medical Devices Agency (**PMDA)**	An Independent Administrative Institution responsible for ensuring the safety, efficacy, and quality of pharmaceuticals and medical devices in Japan.
Health Canada	The federal department responsible for health-related issues in Canada; issues advisories warnings, recalls, reports, publications, activities, legislation, and guidelines

9.2 Regulatory Guidelines for Ofdfs in Different Regions: [60]

Table 5: Regulatory guidelines for OFDFs Region

Regulatory Authority	**Region**	**Key Guidelines and Regulations**	**Functions**
Central Drugs Standard Control Organization (CDSCO)	India	-CDSCO's Schedule M for Good Manufacturing Practices (GMP) -CDSCO's requirements for registration and marketing approval -Indian Pharmacopoeia standards for pharmaceutical products	Provides drug regulatory requirements in India.
Therapeutic Goods Administration(TGA)	Australia	-TGA's Good Manufacturing Practice(GMP) requirements -TGA's guidelines for the registration of therapeutic goods	Assessing new medicines and medical devices before they can be sold.

		-TGA's requirements for complementary medicines	
National Medical Products Administration (NMPA)	China	-NMPA's Good Manufacturing Practice(GMP) regulations -NMPA's guidelines for drug registration and approval -NMPA's technical guidelines for pharmaceutical products	Drafting laws, regulations, and policies related to supervision of drugs, medical devices, cosmetics, and health food, and developing plans for food and drug safety.
National Health Surveillance Agency(ANVISA)	Brazil	-ANVISA's Good Manufacturing Practices(GMP) requirements -ANVISA's regulations for registration and approval of drugs -ANVISA's requirements for labeling and package inserts	Promote public health by regulating, monitoring, and controlling the production, marketing, and use of products and services that impact health, including food, drugs, cosmetics, medical devices, and health services.
South African Health Products Regulatory Authority (SAHPRA)	South Africa	-SAHPRA's Good Manufacturing Practice(GMP) standards -SAHPRA's guidelines for the registration of medicines -SAHPRA's requirements for labeling and package inserts	The national regulatory body for health products, ensuring their quality, safety, and efficacy by monitoring, evaluating, investigating, inspecting, and registering all health-related products, including medicines, medical devices, and clinical trials

9.3 Indian Regulatory Framework (CDSCO):

India’s pharmaceutical regulatory system plays a crucial role in ensuring the safety, efficacy, and quality of medicinal products, thereby contributing significantly to public health protection. This section provides an overview of the organizational structure, functions, and regulatory responsibilities of the Central Drugs Standard Control Organization (CDSCO), the national regulatory authority of India, and the Drug Controller General of India (DCGI), who governs drug approval and regulatory enforcement in the country.[61]

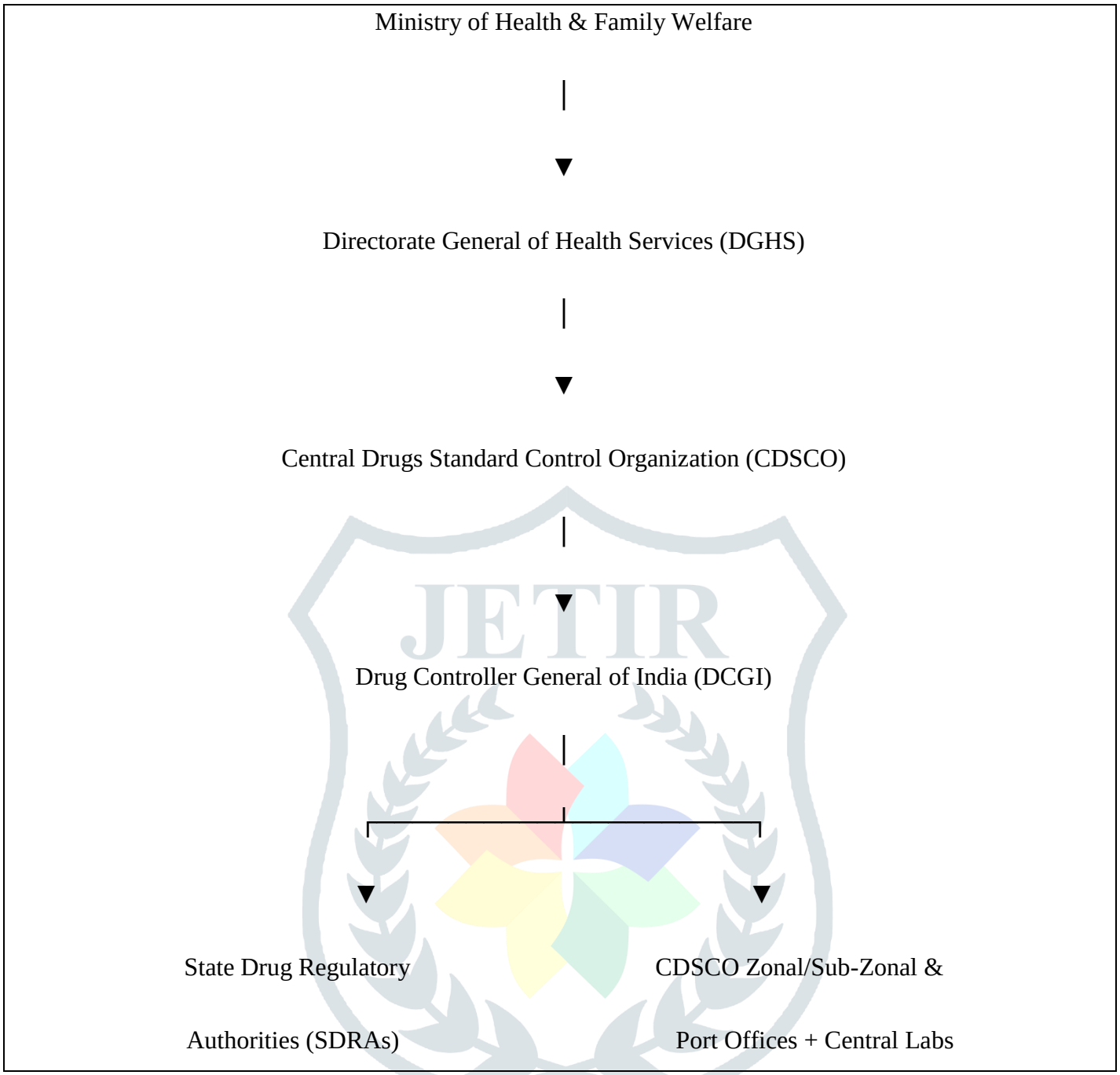

Figure 6: Organizational Hierarchy of Drug Regulation in India

The Central Drugs Standard Control Organization (CDSCO)

The Central Drugs Standard Control Organization (CDSCO) operates under the Directorate General of Health Services, Ministry of Health & Family Welfare, Government of India, and serves as the nation's National Regulatory Authority (NRA). Its headquarters is located at FDA Bhawan, New Delhi, with an extensive network of zonal and sub-zonal offices, port offices, and central laboratories across the country. CDSCO functions under the Drugs and Cosmetics Act, 1940 and the Drugs and Cosmetics Rules, 1945, regulating critical areas including new drug approval, clinical trial authorization, import control, and establishment of drug quality standards. In coordination with State Drug Regulatory Authorities, CDSCO ensures uniform regulatory enforcement nationwide. Additionally, it is responsible for licensing and monitoring high-priority and sensitive biological products such as blood and blood-derived products, vaccines, and intravenous fluids.[62]

Table 6: Comparison of Major Global Drug Regulatory Authorities

Parameter	**CDSCO (India)**	**FDA (United States)**	**EMA (European Union)**
Governing Ministry/Body	Ministry of Health & Family Welfare	U.S. Department of Health & Human Services	European Commission
Key Lead Authority	DCGI (Drug Controller General of India)	Commissioner of Food and Drugs	EMA Executive Director + CHMP
Establishment Year	1940 Act / 1945 Rules	1906 Pure Food & Drugs Act	1995
Primary Responsibilities	New drug approval, clinical trials, import regulation, GMP, pharmacovigilance	Review & approval of drugs/devices, manufacturing oversight, post-market surveillance	Scientific evaluation and supervision of medicinal products within EU
GMP Regulation	Schedule M	21 CFR Parts 210 & 211	EU GMP Guidelines (EudraLex Vol. 4)
Clinical Trial Oversight	Under NDCT Rules (2019) via CDSCO + Ethics Committees	Investigational New Drug (IND) & Institutional Review Boards (IRB)	Clinical Trials Regulation (EU No. 536/2014)
Territory Covered	India	United States	27 EU member states
Marketing Authorization Validity	India-specific	US-specific	EU-wide centralized approval

9.4 Regulatory Challenges: [59]

10. Oral Fast Dissolving Film Packaging:

In the pharmaceutical industry, packaging serves as a vital component in maintaining the stability and therapeutic effectiveness of a product. The protection of rapidly dissolving formulations during manufacturing and storage demands precise processing, careful handling, and frequently, high-cost packaging methods. Several packaging approaches are available for fast-dissolving films (FDFs). These drug delivery systems are typically packaged as single units, with aluminum pouches being one of the most widely used options. A notable innovation in this field is the Rapid Card, an exclusive packaging solution created by APR-Labtec for Rapid films. This credit card-sized system accommodates three films on each side, allowing users to separate and access individual doses with ease. The materials selected for packaging fast-dissolving films must meet

essential criteria, as highlighted in earlier research: Packaging materials should effectively shield the product from environmental factors such as moisture, light, and air, preserving its quality and potency. In compliance with FDA guidelines, all materials used in pharmaceutical and food packaging must be certified for safety and suitability. Tamper-evident features are mandatory to assure product authenticity and safeguard consumers. Packaging substances should undergo stringent safety assessments to confirm they are non-toxic and suitable for use. There must be no physical or chemical interaction between the material and the product throughout storage or distribution. Packaging components must not transfer odors or tastes to the product, maintaining its sensory characteristics.[63-65]

Blister Packs:

Blister packs remain one of the most common formats for oral fast-dissolving films (OFDFs). Each strip contains individual cavities that isolate and protect each dose from environmental exposure. This design enhances dosing accuracy, facilitates easy handling, and guarantees tamper evidence.

Aluminium Foil Pouches:

Aluminium pouches are another excellent option for OFDF packaging, offering superior barriers against moisture, oxygen, and light. Each pouch securely encloses the film units, ensuring long-term stability and product protection. They are especially suitable for storing or distributing multiple OFDF units together.[66-67]

Application of Oral Thin Film:

- Orally dissolving films are used to treat localized discomfort, allergies, sleeping problems, and CNS issues.
- Soluble films are appropriate for topical administration as analgesics or antibacterial agents in wound treatment.
- Orally disintegrating films can be used to improve the bioavailability of medications that are poorly bioavailable.
- Topical application of dissolvable films as analgesics or antibacterial agents for wound treatment is possible.
- Unpleasant medications are hidden in the taste.[68-71]

11. Discussion:

Oral thin films (OTFs) represent a significant advancement in drug delivery systems, offering a patient-friendly alternative to conventional oral dosage forms. Their rapid disintegration, ease of administration without water, and potential for enhanced bioavailability make them particularly suitable for pediatric, geriatric, and dysphagic patients. Recent developments in film-forming polymers, plasticizers, and taste-masking agents have improved OTFs' mechanical strength, flexibility, palatability, drug loading, and stability. Natural and synthetic polymers such as hydroxypropyl methylcellulose (HPMC), pullulan, and polyvinyl alcohol (PVA) are widely used, while nanotechnology-based approaches—including nanoemulsions, solid dispersions, and microneedle-assisted films—enable controlled and targeted drug release.

Regulatory alignment across the US FDA, EMA, and CDSCO is key to ensuring quality, safety, and efficacy. Although classified as oral solid dosage forms, OTFs require specific testing for tensile strength, disintegration time, folding endurance, and dissolution. However, variations in global regulatory standards remain a challenge. Market adoption of OTFs is growing across indications such as migraine, schizophrenia, nausea, and allergy management, with pharmaceutical companies focusing on convenience, adherence, and user experience. Persistent challenges include dose uniformity, limited drug loading capacity, and moisture sensitivity.

Overall, the integration of formulation innovation, regulatory harmonization, and market growth positions OTFs as a promising platform for systemic and local drug delivery. Future research will likely prioritize enhancing drug stability, expanding eligible drug categories and leveraging smart polymer technologies for personalized therapies.

12. Conclusion:

Oral thin film (OTF) technology marks a major advancement in pharmaceutical drug delivery, offering rapid disintegration, improved absorption, and enhanced bioavailability. Its water-free, easy-to-use design benefits pediatric, geriatric, and dysphagic populations, boosting comfort and adherence. Innovations in polymer science and manufacturing methods ensure dose precision, mechanical stability, and scalability. The integration of mucoadhesive and biodegradable polymers improves retention and therapeutic efficiency, while novel designs enable controlled release and stability. Regulatory authorities like the FDA, EMA, and ICH emphasize quality-by-design and bioequivalence to guarantee safety and consistency. These combined developments make OTFs a next-generation platform that blends scientific progress with global regulatory alignment, paving the way for personalized and universally accepted drug delivery systems.

13. Future Scope:

The future of oral thin films (OTFs) is promising, with personalized formulations using advanced 3D printing and inkjet printing technologies enabling tailored doses and drug combinations. Integration of nanotechnology is expected to improve bioavailability and enable targeted delivery. The use of OTFs is also expanding in nutraceuticals and vaccine delivery. The global oral thin film market is projected to grow significantly, driven by increasing patient demand for convenient and effective drug delivery systems.

15. Reference

1) Bhaskar R, Ola M, Khade S, et al. 2025. Oral Thin Films: A Modern Frontier in Drug Delivery Systems, Journal of Drug Delivery and Therapeutics, 15(4):150-164.
2) Reddy TUK, Reddy KSK, Manogna K, et al. 2018. A detailed review on fast dissolving oral films. Journal of Pharmaceutical Research, 8(06).
3) Parashar AK, Kakde D, Chadhar V, et al. 2011. A review on solid lipid nanoparticles (SLN) for controlled and targeted delivery of medicinal agents. Curr Res Pharm Sci, 1(2): 37-47.
4) Sloboda M, Barnhart S. et al. 2011. Formulation Flexibility Broadens the Scope for Oral Thin Film Technology; Adhesives Research, 22-24.
5) Liew K.B, Tan Y.T, Pen K.K.et al. 2012. Characterization of orally disentrigating film containing donepezil for Alzheimer disease; AAPS Pharm Sci Tech, 13(1); 134-142.
6) Hussain MW, Kushwaha P, Rahman MA, et al. 2017. Development and Evaluation of Fast Dissolving Film for Oro-Buccal Drug Delivery of Chlorpromazine. Indian Journal of Pharmaceutical Education and Research, 51:S539–S547.
7) Mahboob MBH, Riaz T, Jamshaid M, et al. 2016. Oral Films: A Comprehensive Review. International Current Pharmaceutical Journal, 5:111–117.
8) Krampe R, Visser JC, Frijlink HW, et al. 2016. Oromucosal film preparations: points to consider for patient centricity and manufacturing processes. Expert Opin Drug Deliv, 13:493–506.
9) European Medicines Agency. Guideline on pharmaceutical development of medicines for pediatric use, EMA/CHMP/QWP/805880/2012. (2013).
10) Orlu M, Ranmal SR, Sheng Y, et al. 2017. Acceptability of or dispersible films for delivery of medicines to infants and preschool children. Drug Deliv, 24:1243–1248.
11) 11. Slavkova M, Breitkreutz J. et al. 2015. Or dispersible drug formulations for children and elderly. Int J Pharm, 75:2–9.
12) Wong E, Pulenzas N, Bedard G, et al. 2015 Ondansetron rapidly dissolving film for the prophylactic treatment of radiation-induced nausea and vomiting-a pilot study. Curr Oncol, 22:199–210.
13) Singh S, Gangwar S, Garg G, et al. 2010 Formulation and evaluation of rapidly disintegrating film of Levocetrizine Hydrochloride. Der Pharmacia Letter, 2(2):434-9.
14) Kushwaha V, Akhtar J, Usmani S, et al. 2015. A review on fast dissolving formulation technologies. World Journal of Pharmacy and Pharmaceutical Science, 4(7):574-85.

15) Prabhu P, Malli R, Koland M, et al. 2011. Formulation and evaluation of fast dissolving films of levocitirizine dihydrochloride. Int J Pharm Investin, 1(2):99-4.
16) Rathi V, Senthil V, Kammili L, et al. 2011.A brief review on oral film technology. International Journal of Research in Ayurveda and Pharmacy, 2(4):1138-47.
17) Vondrak B, Barnhart, Scott. 2008. Dissolvable films: dissolvable films for flexible product format in drug delivery. Pharmatech, (1):1-5.
18) BN Nalluri, B Sravani, VSAnusha, et al. 2013. Development and evaluation of mouth dissolving films of sumatriptan succinate for better therapeutic efficacy. Journal of Applied Pharmaceutical Science, 3(8):161-6.
19) 19. Banarjee T, Ansari VA, Singh S, et al. 2015. A review on fast dissolving films for buccal delivery of low dose drugs. International Journal of Life Sciences and Review, 1(4):117-23.
20) 20. DK Vishwkarma,AK Tripathi,P Yogesh, et al. 2011. Review article on mouth dissolving film. Journal of Global Pharma Technology, 3(1):1-8.
21) Bhyan B, Jangra S, Kaur M and Singh H. 2011. Orally fast dissolving films: innovations in formulation and technology. International Journal of Pharmaceutical Sciences Review and Research, 9(2):9-15.
22) Mishra R, Amin A. 2011. Formulation and characterization of rapidly dissolving films of cetirizine hydrochloride using pullulan as a film forming agent. Ind J Pharm Edu Res, 45(1):71-7.
23) Sharma D, Kaur D, Verma S, et al. 2015. Fast dissolving oral films technology: A recent trend for an innovative oral drug delivery system. Int. J. Drug Deliv, 7:60–75.
24) Siddiqui MDN, Garg G, Sharma PK. 2011. A Short Review on "A Novel Approach in Oral Fast Dissolving Drug Delivery System and Their Patents". Advan Biol Res, 5:291–303.
25) Chan R. 2016. Oral thin films: Realms of Possibility. Frederick Furness Publishing Ltd., 12–17.
26) Malke S, Shidhaye S, Desai J, et al. 2009. Oral films: Patient compliant dosage form for pediatrics. The Internet Journal of Pediatrics and Neonatology, 11:1–7.
27) Ghodake PP, Karande MK, Osmani RA, et al. 2013. Mouth dissolving films: Innovative vehicle for oral drug delivery. International Journal of Pharma Research & Review, 2:41–47
28) Niyaz USH, Elango K. 2018. Oral fast dissolving films: An innovative drug delivery system. World Journal of Pharmacy and Pharmaceutical Sciences, 7:881–907.
29) M. Irfan, S. Rabel, Q. Bukhtar, et al. 2016. Orallydisintegration films: A modern expansion in drug delivery system, Saudi Pharmaceutical Journal, 537-546.
30) Bhaskar R, Ola M, Khade S, et al. 2025. Oral Thin Films: A Modern Frontier in Drug Delivery Systems, Journal of Drug Delivery and Therapeutics, 15(4):150-164.
31) Yildiz ZI, Uyar T. 2019. Fast-dissolving electrospun nanofibrous films of Science, 492:626-33.
32) Patil S L, Mahaparale P L, Tiwari S S, et al. 2012. Fast Dissolving Oral Films: An Innovative Drug Delivery System; International Journal of Research and Reviews in Pharmacy and Applied Science, 2(3); 482-496.
33) Thakur N, Bansal M, Sharma N, et al. 2013. Overview A Novel Approach of Fast Dissolving Films and Their Patients; Advances in Biological Research, 7(2); 50-58.
34) Aggarwal J, Singh G, Saini S, et al. 2011.Fast Dissolving Films: A Novel Approach to Oral Drug Delivery; International Research Journal of Pharmacy, 2(12); 69-71.
35) Radhakisan U R, Chavan V, Tribhuvan N. 2012. Mouth Dissolving Film and Their Patent: An Overview; International Research Journal of Pharmacy, 3(9); 39-42.
36) Arya A, Chandra A, Sharma V, et al. 2010. Fast Dissolving Oral Films: An Innovative Drug Delivery System and dosage Form; International journal of Chem Tech Research, 2(1); 576-5.
37) Sharma D, Kaur D, Verma S, et.al. 2015. Fast dissolving oral films technology: A recent trend for an innovative oral drug delivery system. Int. J. Drug Deliv, 7:60–75.
38) Kathpalia H, Gupte A. 2013. An Introduction to Fast Dissolving Oral Thin Film Drug Delivery Systems: A Review. Current Drug Delivery, 10:667–684.
39) Karki S, Kim H, Na SJ, Shin D, Jo K, Lee J. 2016. Thin films as an emerging platform for drug delivery. Asian Journal of Pharmaceutical Sciences, 11:559–574.

40) Onkar Raje, Prof. Prashant Khade, Dr. Ashok Bhosale, et al. 2021. A Review on Fast Dissolving Oral Films: Recent Trend of Drug Delivery, International Journal of Creative Research Thoughts, 9(7): e336- e350.
41) Siddiqui N, Garg G and Sharma PK. 2011. A short review on a novel approach in oral fast dissolving drug delivery system and their patents. Advances in Biological Research, 5(6): 291-303.
42) Patil D, Ahmed AH, Awais M, et al. 2018. Design and development of fast dissolving film of telmisartan .pharma science monitor, 9(1):171-87.
43) Kshirsaga Tatwashil, Jaiswal Naresh ,Chavan Gitanjali , et al. 2021. Formulation & Evaluation of Fast Dissolving Oral Film, World Journal of Pharmaceutical Research, 10(9): 503-561.18.
44) Sunil Kumar Reddy et al. 2018. A Detailed Review on Fast Dissolving Oral Films. Indo American Journal of Pharmaceutical Research, 8(06), 1315-1326.
45) Bhyan Bhupinder,Jangra Sarita, Kaur Mandeep, et al. 2011. Orally Fast Dissolving Films: Innovations in Formulation and Technology, International Journal of Pharmaceutical Sciences Review and Research, 9(2): 50-57.
46) Manasa Chandramouli, Rajendra Prasad Shivalingappa, Vrushabendra Basavanna et al. 2023. Oral Thin-films from Design to Delivery: A Pharmaceutical ViewpointVolume 13, Issue 2, 177.
47) Suripeddi Muralidhar, Ramya.K, et.al. 2023. Oral dissolving films: a review. International Journal of Research and Review, 10(9):450-468.
48) Dhanashree P. Sanap, Uddhav S. Mhatre, et al. 2022. Oral Thin Films: A Multi – Faceted Drug Delivery System Int. J. Pharm. Sci. Rev. Res., 72(1).
49) Oliver J. Pemble, Maria bardosova, Ian m. povey et al. 2021. A Slot-Die Technique for the Preparation of Continuous, High-Area, Chitosan-Based Thin Films; Polymers, 13(10), 1566.
50) Choudhury A. 2019. Floating drug delivery system: an outlook. J Appl Pharm Res, 7(3):1–8.
51) Sharma D, Kaur D, Verma S. et al. Fast dissolving oral films technology: A recent trend for an innovative oral drug delivery system. Int.
52) Kathpalia H, Gupte A. 2013. An Introduction to Fast Dissolving Oral Thin Film Drug Delivery Systems: A Review. Current Drug Delivery, 10:667–684.
53) Saini P, Kumar A, Sharma P, et al. 2012. Fast disintegrating oral films: A recent trend of drug delivery. Int J Drug Dev Res, 4:80–94.
54) Akeuchi H, Yamakawa R, et al. 2013. Design of rapidly disintegrating drug delivery films for oral doses with hydoxypropyl methylcellulose. Journal of Drug Delivery Science and Technology, 23:471–475.
55) Bhaskar R, Ota M, Pawar A, et al. 2025. Oral Thin Films: A Modern Frontier in Drug Delivery Systems, Journal of Drug Delivery and Therapeutics, 15(4):150-104.
56) Rukiye SEVİNÇ ÖZAKAR , Emrah ÖZAKAR. 2021. Current Overview of Oral Thin Films; Turk J Pharm Sci. 18(1):111–121.
57) Effiong DE, Umoh RA, Akpabio AE, et al.The oral film delivery- Application of nanotechnology and potential in medication adherence. GSC Biological and Pharmaceutical Sciences, 11(3), 34-51.
58) Apurva G., Rushikesh J., Mrunal S. 2018. ORAL THIN FILM TECHNOLOGY- CURRENT CHALLENGES AND FUTURE SCOPE; Vol. 7 | No. 2| ISSN: 2278-6252.
59) Faraat A., Leo N. 2024. Global Regulations of Medicinal, Pharmaceutical, and Food Products; Edition: 1.
60) Paul D, Ray P. 2023. Exploring the potential of fast dissolving oral films, Curr Trends Pharm Res, 10 (2): 20-35.
61) Mohd.W. Piyush Y. et al. 2025. An Overview of Regulatory Authorities in India: Rules, Functions, and Impact; Volume 10, Issue 2 Mar–Apr, pp: 2665-2670.
62) https://cdsco.gov.in/opencms/opencms/en/Home/?utm_source=perplexity
63) Joshua JM, Hari R, Jyothish FK, et al. 2016. fast dissolving oral thin films: An effective dosage form for quick releases. Int J Pharm Sci Rev Res, 38(1):282–9.

64) Irfan M, Rabel S, Bukhtar Q, et al. 2016. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharm J. 24(5):537–46.
65) Pawar R, Sharma R, Sharma P, et al. 2019 A Review on Mouth Dissolving Film. J Drug Deliv Ther, 9(6):206–10.
66) Sevinç Özakar R, Özakar E. 2021. Current Overview of Oral Thin Films. Turkish J Pharm Sci, 18(1):111–21.
67) Hemavathy S, Sinha P, Ubaidulla U, et al. 2022. A Detailed Account on Novel Oral Fast Dissolving Strips : Application and Future Prospects. Dep Pharm, 10(4):773–87.
68) Zajicek A, Fossler MJ, Barrett JS, et al. 2013. A report from the pediatric formulations task force: perspectives on the state of child-friendly oral dosage forms. The AAPS journal, 15:1072-81.
69) Pravin S. 2022. Formulation and Evaluation of Mouth Dissolving Films of Amlodipine Besylate by using Natural and Synthetic Polymers. Research Journal of Pharmacy and Technology, 15(11):5154-5161.
70) Dixit RP, Puthli SP. 2009. Oral strip technology: Overview and future potential. Journal of controlled release, 139(2):94-107.
71) Bhupinder B, Sarita J. 2012. Formulation and evaluation of fast dissolving sublingual films of Rizatriptan Benzoate. International Journal of Drug Development and Research, 4(1).