# " Novel approach to drug delivery :A compressive review on rapidly Dissolving oral film."

Jathar Priyanka Dattatraya [1],khose Sakshi Nitin [2], prof.Sushama Lokhande [3].

H.S.B.P .V.T , GOI Faculty of pharmacy , kashti.

## Abstract:

Rapidly dissolving oral films (RDOFs) have emerged as a novel and patient-friendly drug delivery system, offering significant advantages over traditional oral dosage forms, particularly for populations such as pediatrics, geriatrics, and individuals with dysphagia. These thin, flexible films dissolve quickly upon contact with saliva, enabling rapid drug release and absorption without the need for water, which improves patient compliance and enhances therapeutic outcomes. This review provides a comprehensive overview of RDOFs, covering their formulation components, including polymers, plasticizers, and taste-masking agents, as well as their primary manufacturing techniques such as solvent casting and hot-melt extrusion. Key evaluation parameters for quality control, including disintegration time, mechanical properties, and drug content uniformity, are also discussed. Moreover, recent advancements, including 3D printing, nanotechnology integration, and smart film technology, highlight the potential of RDOFs to deliver personalized and controlled therapies. While RDOFs offer considerable benefits, limitations such as drug load capacity and stability remain challenges in formulation. Future research directions focus on overcoming these challenges and advancing RDOFs as an effective platform for innovative drug delivery solutions.

## Key Word:

Mucoadhesive film, Thin-film technology, Polymeric film formulation, Drug release mechanism, Drug-loaded films, Immediate release formulation, Oral bioavailability, targeted drugs delivery .

## Introduction:

Rapidly dissolving films (RDFs), also known as oral thin films (OTFs) or fast-dissolving films, are an innovative dosage form that dissolves quickly upon contact with saliva, making them an effective alternative to traditional tablets, capsules, and

liquids. These thin strips are designed to deliver active pharmaceutical ingredients (APIs) directly to the oral cavity, bypassing the need for water and enabling rapid onset of action. As a result, RDFs are especially beneficial for pediatric, geriatric, and other patient populations who may struggle with swallowing conventional dosage forms. Originally developed for pharmaceutical applications, RDFs have gained traction in various industries, including nutraceuticals, oral care, and even cosmetics. Their convenience, ease of administration, and portability have made them increasingly popular for delivering over-the-counter medications, vitamins, and supplements. In the pharmaceutical sector, RDFs can be used to administer medications for pain relief, allergies, and motion sickness, among other conditions. Moreover, advancements in polymer technology have enabled the formulation of films that dissolve in a matter of seconds to minutes, allowing for quick therapeutic effects.

The appeal of RDFs lies not only in their rapid disintegration but also in their potential to improve patient compliance and provide accurate dosing. Unlike chewable tablets or lozenges, which may be chewed or swallowed inconsistently, RDFs dissolve directly on the tongue, releasing a precise amount of medication. This characteristic is particularly advantageous in the context of personalized medicine, where accurate and convenient dosing is essential.

**Ideal characteristics of film:**

- Have a pleasant mouth feel.
- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Residue free formulation.
- Exhibit low sensitivity to environmental conditions such as temperature and humidity.
- Allow the manufacture of the tablet using conventional processing and packaging equipment’s at low cost .

**Advantages of film:**

- Fast Dissolving Film is flexible so they are not as fragile and incorporated in the FDF. Composition of Film Active need not any kind of special package

for protection during Pharmaceutical agents8transportation and storage as compared to FDT.

- Rapid disintegration and dissolution due to enhance surface area exposure.
- No need of water has led to better satisfactoriness amongst Sr. No Category Percentage the dysphasic patients.amount%
- No fear of chocking as compared to FDT.
- The large surface area available in the film .

**Disadvantages of film:**

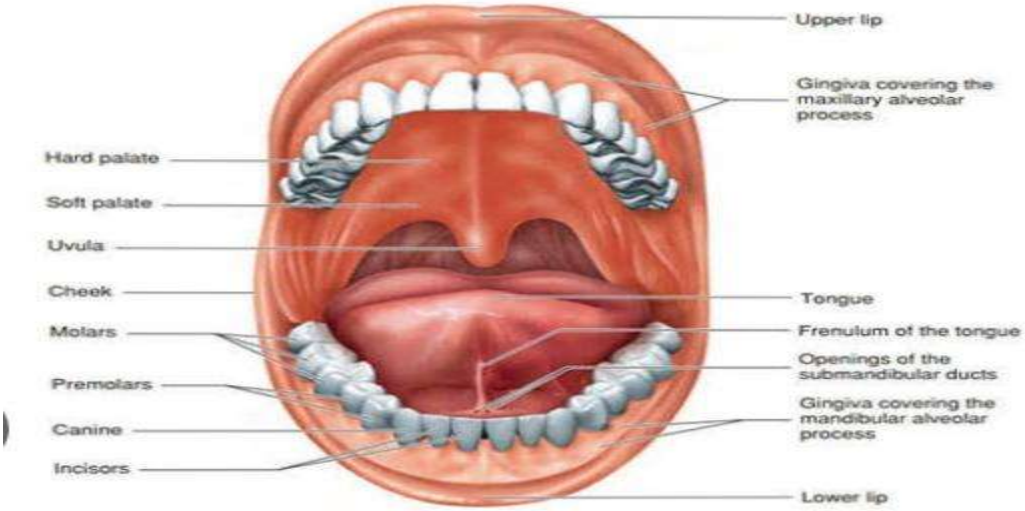
- Dose uniformity is technical challenge.
- Hygroscopic in nature.
- High dose can not incorporated.
- Required special packaging for stability and efficacy.
- Mechanism of absorption through oral mucosa:

**Mechanism of absorption through oral mucosa:**

Passive drug transport over the oral mucosa, there are two permeation routes: transcellular (passing inside the cell) and Para cellular (passing around the cell). Dual action mechanism, however depending on the chemical scientific features of the drug, one route is usually preferred over the other. Hydrophillic cellular environments hinder oleophilic chemical solubility. However, due to a rare partition constant, the cytomembrane’s oleophilic composition might make it difficult for hydrophilic solutes to pass through it. Cytomembrane and tissue selectively restrict hydrophilic and oleophilic substance passaage. Since the oral epithelial epithelium is stratified, a combination of those 2 pathways may be used for substance penetration. But often, the path with the fewest obstructions to passage is the one that prevails.

**Structural features of Oral Mucosa:**

The oral mucosa comprises stratified squamous epithelium, supported by




basement membrane, lamina propria and underlying connective tissue. The epithelial tissue progresses from a mitotically active basal cell layer through several differentiating intermediate layers to the superficial layers, where cells are shed from the epithelial tissue's surface. Similar to the lining in other body part. The mouth lining epithelial layer renovates every 5 to 6 days. The buccal membrane measures at 500-800 m, but the membrane thickness of the hard and soft palates, the floor of the mouth, the ventral tongue, and also the gingivae live at around 100-200 m. Depending on where it is located inside the Rima, the epithelial tissue's composition also changes. The gingival and oral mucosa exhibit keratinization, analogous to cuticle with ceramides and acylceramide facilating barrier function. However, the membranes of the palate, organ, and buccal areas aren't keratinized, which are rather water-resistant to water and contain only very little levels of ceramide. They also include trace quantities of neutral yet polar lipids, primarily glucosyl ceramides and steroid alcohol salt. It is discovered that the nonkeratinized epithelia are substantially more keratinized epithelia. Water-leaky than the the keratized epithelium.

**Classification of Fast Dissolve Technology :**

technologies may be classified into the three groups:

- Lyophilized systems.
- Compressed tablet-based systems.

- Thin film strips.

**The lyophilized systems:**

This method leads globally in sales, volume and product diversity. Drugs in suspension or resolution with different structural excipients.whether the active components are soluble or insoluble, these systems have different dose- handling capacities, with the former having slightly lower capacities than systems based on a few tablets. The devices are able to incorporate a variety of flavor-masked ingredients and disintegrate much more quickly than tablet-based solution.

**Compressed tablet-based systems:**

This technique utilizes conventional tableting technology, compressing excipients to produce pills with variable hardness and friability. The formulation of fast-dissolve tablets uses water soluble excipients, or superdisintegrant or effervescent portions, to enable rapid penetration of water into the pill's core, resulting in a faster rate of disintegration than a conventional tablet. Biovail's Fuisz technology uses the Shearform process to create a cotton candy-like matrix loaded with the drug, which is then combined with excipients to produce tablets. This method supports relatively high API concentrations and can incorporate taste-masked particles, though the resulting tablets may dissolve more slowly compared to thin-film or freeze-dried forms.

Additionally, the loose compression tablet technique has gained traction among branded and generic pharmaceutical companies for developing fast-dissolving tablets, especially in line extensions and generic products.

**Oral thin film strips:**

Oral films, or wafers, originally developed from the confectionery and oral care markets, where breath strips became popular, have now become an innovative and consumer-friendly way to deliver vitamins and personal care products. This delivery method—Fast-Dissolving Films (FDFs)—is now established and widely accepted for over-the-counter (OTC) medications and is currently in early to mid-development phases for prescription drugs. This acceptance is largely due to the success of breath-freshening products, like Listerine PocketPaks, in the U.S. market, which demonstrated consumer demand for convenient, quick-dissolving dosage forms.

**Composition of film:**

Fast dissolving film is a thin film with an area of 2-8 $cm^2$ containing an active ingredient Immediate dissolution in water or saliva is achieved in oral films through a specialized matrix made from water-soluble polymers, allowing drugs to be incorporated up to a single dose of 30 mg. The formulation of these fast-dissolving films is complex, as the choice of excipients can significantly impact the films' mechanical properties, such as flexibility and durability. From a regulatory standpoint, all excipients used must be recognized as Generally Regarded as Safe (GRAS) and approved for oral pharmaceutical use, ensuring consumer safety and compliance with regulatory standards.

Fast Dissolving Films (FDFs) can incorporate active pharmaceutical ingredients (APIs) from diverse therapeutic classes that are suitable for oral or buccal delivery. These include medications for conditions such as ulcers, asthma, cough, allergies, epilepsy, chest congestion, and angina. To achieve effective delivery in FDFs, the ideal drug dosage is typically low—preferably less than 20 mg per day. This low-dose requirement aligns with the capabilities of FDFs, enhancing both the practicality of formulation and the potential for rapid absorption.

**The ideal characteristics of a drug :**

- The drug should have pleasant taste.
- The drug to be incorporated should have low dose less than 30mg.
- The drugs with smaller and moderate molecular weight are preferable.
- The drug has stability and solubility in water as well as in saliva.
- It should be partially unionized at the pH of oral cavity.
- It should have the ability to permeate oral mucosal tissue

**Water-soluble polymers :**

Film-forming polymers have gained significant interest in medical and nutraceutical dissolvable films due to their ability to provide rapid disintegration, a pleasant mouthfeel, and adequate mechanical strength. These water-soluble polymers allow films to break down quickly when in contact with saliva. Notably, as the molecular weight of these polymer bases increases, the disintegration rate tends to slow. Common water-soluble polymers used in film formation include Hydroxypropyl

Methylcellulose (HPMC) types E-3 and K-3, methylcellulose, pectin, gelatin, sodium alginate, hydroxypropyl cellulose, polyvinyl alcohol, and maltodextrins.

**Plasticizers**:

Formulation factors, such as the inclusion of plasticizers, play a crucial role in determining the mechanical properties of dissolvable films. Plasticizers help improve the films' flexibility and enhance characteristics like tensile strength and elongation. Adjusting the concentration of plasticizers can significantly impact these properties. Commonly used plasticizers in film formulations include glycerol, di-butyl phthalate, and polyethylene glycol, all of which contribute to optimizing the film's performance and durability.

**Saliva stimulating agent:**

Saliva-stimulating agents are included in rapid dissolving film formulations to enhance the rate of saliva production, which facilitates quicker disintegration of the film. Typically, food-grade acids are employed as salivary stimulants, such as citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid. These agents are usually incorporated into the film formulation in concentrations ranging from 2% to 6% w/w of the film's total weight, either alone or in combination, to optimize the disintegration process.

**Surfactants:**

Surfactants are incorporated into rapid dissolving films to function as solubilizing, wetting, or dispersing agents, ensuring that the film dissolves rapidly and releases the active ingredient immediately. Commonly used surfactants include sodium lauryl sulfate, benzalkonium chloride, benzethonium chloride, and various Tweens. Among these, Poloxamer 407 is particularly significant, as it serves multiple roles: it acts as a solubilizing, wetting, and dispersing agent, aiding in the efficient dissolution and release of the active pharmaceutical ingredient in the formulation.

**Sweeting agent:**

Sweeteners play a crucial role in the formulation of pharmaceutical products, particularly those intended for disintegration or dissolution in the oral cavity. The classical sweeteners, including sucrose, dextrose, fructose, glucose, liquid glucose, and isomaltose, are commonly used in oral dosage forms. Among these, fructose is

perceived as sweeter than sucrose and dextrose, providing a rapid onset of sweetness upon consumption. This makes it a preferred option in many formulations.

Fructose is sweeter than polyhydric alcohols such as sorbitol and mannitol. However, polyhydric alcohols are still widely used in combination with other sweeteners because they offer benefits such as a pleasant mouth-feel and a cooling sensation, which can improve patient experience. Additionally, these polyhydric alcohols, including sorbitol, mannitol, and isomalt, are less likely to cause tooth decay and do not have the bitter aftertaste that some sweeteners exhibit, making them valuable in formulating oral pharmaceutical products. Their lower cariogenic potential and smoother taste profile are significant advantages, especially in oral care products and chewables.

**Flavoring agents :**

Flavoring agents are selected from a variety of sources, including synthetic flavor oils, oleoresins, and plant-derived extracts from leaves, fruits, and flowers. These flavors can be used individually or in combination to enhance the taste of the product. A wide range of flavors is available, such as essential oils or water-soluble extracts of menthol, mint varieties (peppermint, spearmint, wintergreen), spices like cinnamon and clove, sour fruit flavors (lemon, orange), or sweet flavors like vanillin, chocolate, and fruit essences (apple, raspberry, cherry, pineapple). The quantity of flavor required to mask the taste of active ingredients depends on the flavor's type and intensity.voring agents :

**Coloring Agent:**

A wide variety of color options are available for pharmaceutical formulations, including FD&C colors, EU-approved colors, natural colors, and custom Pantone-matched shades. To promote rapid disintegration and enhance the release of the active ingredient, saliva-stimulating agents can also be incorporated into the formulation. These include acids such as citric acid, tartaric acid, malic acid, ascorbic acid, and succinic acid, which help accelerate the disintegration process.

**Methods of manufacture of fast dissolving films:**

Mnufacturing processes of oral films:

- Solvent casting
- Hot-melt extrusion
- Semisolid casting
- Solid dispersion extrusion
- Rolling.

**Solvent Casting:**

Fast-dissolving buccal films are commonly formulated using the solvent casting method. In this process, water-soluble ingredients are dissolved to form a clear, viscous solution. The active drug and other excipients are then dissolved in a suitable solvent. Both solutions are mixed and stirred, and the final mixture is cast onto a Petri dish and dried to form the film.

**Semisolid Casting:**

A solution of water-soluble film-forming polymer is prepared, and then an acid-insoluble polymer, such as cellulose acetate phthalate or cellulose acetate butyrate, is added. A plasticizer is incorporated to form a gel-like mass. This gel is then cast into films or ribbons using heat-controlled drums. The desired thickness of the film is about 0.015-0.05 inches, and the ratio of the acid-insoluble polymer to the film-forming polymer is typically 1:4.

**Solid Dispersion Extrusion:**

Solid dispersion refers to the process where one or more active ingredients are dispersed in an inert carrier in a solid state, using amorphous hydrophilic polymers. The drug is dissolved in a suitable solvent, and the solution is mixed into a melt of polyethylene glycol (PEG), typically at temperatures below 70°C. The resulting solid dispersion is then shaped into films using dies.

**Rolling Method:**

In the rolling method, a pre-mix is prepared by combining the film-forming polymer, polar solvent, and other additives (excluding the drug). This pre-mix

is added to a master batch feed tank, from which it is pumped into one or more mixers. The drug is then introduced into the mixer and blended to form a uniform matrix. The uniform matrix is fed to a pan where the film is formed on a substrate, carried by a support roller. The wet film is dried through controlled bottom drying, completing the process.

**Patented technology:**

**1) XGel:**

XGel is a core technology developed by BioProgress, integrated into Meldex International's film systems and ingestible delivery technologies. This innovative film technology is revolutionizing pharmaceutical product formulations and manufacturing methods. XGel films likely increase product stability and have been developed for various non-ingestible applications, such as cosmetics, ostomy pouches, sanitary products, and healthcare devices. The XGel film is produced using a technique called "solution casting.

**2)Soluleaves Technology**

Soluleaves is an advanced drug delivery system that uses thin, dissolvable films to release active ingredients upon contact with saliva. This system is primarily used for flavor-release products such as mouth fresheners, confectionery, and nutritional supplements, including vitamins. Soluleaves is an efficient delivery system designed for easy portability, providing a convenient way to administer drugs or other active ingredients to the oral cavity. Additionally, the system can be used to deliver therapeutic agents for conditions like cough, cold, gastrointestinal disorders, and pain relief.

The unique feature of Soluleaves is its ability to adhere to mucous membranes and release the active ingredients over a prolonged period, typically around 15 minutes. This extended release profile ensures that the therapeutic effects are sustained, providing an alternative to traditional fast-dissolving or immediate-release dosage forms. As a result, Soluleaves technology is suitable for both rapid and controlled-release applications in various pharmaceutical and nutraceutical markets.

**3)WAFERTAB Technology**

WAFERTAB is a patented drug delivery system that incorporates pharmaceutical actives into thin, dissolvable films. The system involves a specialized process to prepare drug-loaded films, which can be used for both topical and oral applications. Unlike traditional drug delivery systems, WAFERTAB films are cast with active ingredients embedded into them after the film is formed, ensuring a uniform distribution of the drug.

This innovative delivery system offers numerous possibilities for developing multi-functional and customizable dosage forms. WAFERTAB technology enables the creation of films with varying release profiles, where different films may contain different active ingredients or have distinct release rates. This makes it a versatile platform for innovative drug design, catering to a wide range of therapeutic areas, including pain management, cough and cold treatment, and gastrointestinal health.

WAFERTAB's ability to deliver active ingredients through a thin, portable, and discreet film makes it an attractive option for both over-the-counter and prescription drugs. Furthermore, this system can be tailored to meet the needs of specific patient populations, offering improved patient compliance, ease of use, and effective drug delivery.

**4) Foamburst:**

FOAMBURST, patented in September 2004, involves capsules made from foamed films. During production, gas is infused into the film, creating a honeycombed structure. These voids in the film can be filled with gas, air, or other materials to achieve specific taste bursts or deliver active ingredients. The honeycombed structure results in capsules that dissolve quickly, providing a melt-in-the-mouth

sensation. FOAMBURST has gained attention from the confectionery and flavor industries for its unique ability to carry and release flavor Evaluation of Fast Dissolving Oral Films (FDFs)

**Evaluation of Fast Dissolving Oral Films (FDFs)**

**1. Organoleptic Evaluation:**

The fast dissolving oral films undergo sensory evaluation for properties like color, odor, and shape. Visual inspection ensures uniformity in color and shape, which is critical for both aesthetic quality and consumer acceptance.

**2. Folding Endurance:**

The folding endurance is assessed by repeatedly folding the film at the same location until it fractures. The number of folds the film can undergo before breaking indicates its flexibility and mechanical strength, helping assess the film’s ability to withstand handling.

**3. Thickness:**

The thickness of the film is determined using a calibrated vernier caliper at several spots on the film's surface to ensure uniformity. The average thickness is then calculated to ensure consistent film quality and drug dose delivery.

**4. Weight Variation:**

Weight variation is measured by weighing 10 randomly selected films. The average weight is calculated to verify that the film weight is consistent across all units, which is crucial for uniform drug delivery.

**5. Surface pH:**

The surface pH is determined by moistening the film with phosphate buffer (pH 6.8) for 30 seconds and measuring the pH using a pH meter. This ensures that the film's pH is compatible with oral mucosa and minimizes irritation.

**6. Tensile Strength:**

Tensile strength is measured using a Texture Analyzer (TAXT Plus), which determines the maximum stress the film can endure before breaking. This is calculated using the formula:

Tensile strength = Load at rupture / (Strip thickness × Strip width), providing an indication of the film's mechanical strength.

**7. Percentage Elongation:**

Percentage elongation is calculated by dividing the elongation at rupture by the initial length of the film, and multiplying by 100. This measures the flexibility and stretchability of the film, ensuring it can handle mechanical stress without tearing.

**8. Drug Content Uniformity:**

To assess drug uniformity, 10 individual films are assayed. Each film is dissolved in methanol, filtered, and diluteds.

**Ex Vivo Permeation Study:**

An ex vivo permeation study was conducted using goat buccal mucosa in a Franz diffusion cell setup. The mucosa was mounted between the donor and receptor compartments. The receptor compartment was filled with an isotonic phosphate buffer (pH 6.8) maintained at 37 ± 0.2°C, with continuous stirring by a magnetic stirrer to ensure uniform conditions. A 2 cm x 2 cm film, pre-moistened with a few drops of phosphate buffer, was placed in the donor compartment. The donor chamber

was filled with 1 mL of pH 6.8 phosphate buffer. Samples were withdrawn from the receptor compartment at regular intervals, and replaced with an equal amount of fresh phosphate buffer. The drug content in the receptor compartment was determined by measuring the absorbance at specified wavelengths.

**Stability Study:**The stability of the formulation was assessed according to ICH guidelines, using an accelerated stability study conducted over six months. The formulation was stored in a stability chamber at 40 ± 2°C and 75 ± 5% relative humidity to simulate real-world storage conditions**.**

## Conclusion:

Fast dissolving films (FDFs) offer multiple advantages over traditional dosage forms. They provide rapid disintegration and improved dissolution profiles, combining the stability of solid dosage forms with the convenience of liquids. This unique blend makes them an effective and elegant drug delivery system. FDFs are particularly beneficial in emergency situations, such as allergic reactions or asthma attacks, where immediate action is necessary. The technology is advancing quickly, prompting many pharmaceutical companies to develop oral films for a variety of active pharmaceutical ingredients.

Compared to conventional dosage forms, FDFs offer better patient compliance and are safer for populations that might have difficulty swallowing pills, such as children, the elderly, and individuals with cognitive impairments. FDFs are widely used for conditions like pain, acidity, allergies, and cardiovascular diseases, which highlights their growing significance in modern healthcare. Key benefits include the ability to administer medication without water, which is particularly beneficial for patients in challenging situations. Additionally, they avoid first-pass metabolism in the liver, leading to potentially enhanced therapeutic effects. The widespread use of FDFs in treating various conditions—such as flatulence, allergies, sore throat, mouth ulcers, anxiety, and mouth fresheners—demonstrates their value in improving drug delivery.

**References :**


1. Raghavendra, P., et al. (2013). “Formulation and evaluation of rapidly dissolving films of ketorolac tromethamine.” *International Journal of Pharmacy and Pharmaceutical Sciences*, 5(1), 404-410.
2. Choudhury, P., et al. (2014). “Formulation and characterization of oral dissolving films of ondansetron.” *Asian Journal of Pharmaceutics*, 8(2), 107-113.
3. Goal for the delivery of drugs.” *Journal of Pharmaceutical Sciences and Research*, 7(6), 350-355.
4. Mura, P., et al. (2015). “Formulation and evaluation of orodispersible films based on drug-polymer interactions.” *Drug Development and Industrial Pharmacy*, 41(7), 1066-1075.
5. Desai, S., et al. (2017). “Rapidly dissolving films: An overview.” *Journal of Advanced Pharmaceutical Technology & Research*, 8(2), 40-45.
6. Hussain, A., et al. (2014). “Formulation and characterization of fast dissolving oral films of metoclopramide hydrochloride.” *World Journal of Pharmacy and Pharmaceutical Sciences*, 3(10), 1523-1535.
7. Kazi.M., et al. (2018). “Recent advances in formulation and characterization of fast dissolving oral films.” *Journal of Drug Delivery and Therapeutics*, 8(2), 112-120.
8. Tiwari, G., et al. (2011). “Formulation and evaluation of taste masked orodispersible films of ondansetron.” *American Journal of PharmTech Research*, 1(2), 108-117.
9. Jain, S., et al. (2012). “Formulation and evaluation of oral dissolving films of buprenorphine.” *International Journal of Current Pharmaceutical Research*, 4(3), 66-70.
10. Muthusamy, K., et al. (2018). “Development of rapidly dissolving oral films of metformin hydrochloride.” *Journal of Drug Delivery and Therapeutics*, 8(5), 67-75.
11. Prajapati, V., et al. (2014). “Formulation and evaluation of oral dissolving film of chlorpheniramine maleate.” *International Journal of PharmTech Research*, 6(4), 1173-1178.
12. Akhgari, A., et al. (2015). “Development of a fast dissolving film [3]containing lamotrigine.” *Journal of Pharmaceutical Innovation*, 10(2), 175-182.

13. Ghosh, A., et al. (2019). “Characterization of rapidly dissolving films for delivery of antiviral drugs.” *Current Drug Delivery*, 16(5), 472-480.
14. Gupta, R., et al. (2016). “Development and evaluation of oral dissolving films of the antiemetic drug granisetron.” *International Journal of Applied Pharmaceutics*, 8(2), 28-34.
15. Shukla, S., et al. (2015). “Preparation and evaluation of orodispersible films of domperidone.” *Asian Journal of Pharmaceutics*, 9(4), 226-233.
16. Raghav, S., et al. (2012). “Formulation and characterization of fast dissolving films of acyclovir.” *International Journal of Research in Pharmaceutical Sciences*, 3(2), 112-118.
17. Soni, P., et al. (2017). “An overview of rapidly dissolving oral films.” *International Journal of Pharmaceutical Sciences Review and Research*, 44(1), 66-71.
18. Alshaikh, M., et al. (2021). “Recent advances in oral dissolving film technology: A review.” *Saudi Pharmaceutical Journ**al*.**