FAST DISSOLVING ORAL FILM : A REVIEW

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ABSTRACT
Fast-dissolving oral films represent a recent market innovation that offers a practical and user-friendly substitute for traditional dosage forms like orally disintegrating tablets. These rapid-dissolution drug delivery systems provide an effective option for elderly and pediatric patients, serving as an alternative to tablets, capsules, and liquid medications that rapidly break down and dissolve in saliva without requiring water for swallowing. The active pharmaceutical ingredient in these films gets absorbed directly into circulation through the oral cavity. This approach eliminates gastrointestinal complications and avoids first-pass metabolism (the process where the liver metabolizes drugs before reaching systemic circulation). This comprehensive review explores the ingredients utilized in FDOFs, production methods, assessment procedures, and commercially available products.

KEYWORDS: Rapid Dissolution oral films, Used Hydrophilic polymers, Solvent Casting Method etc.

INTRODUCTION

Oral medication forms remain favoured due to their simplicity, patient-friendly nature, minimal hygiene requirements, and versatile design possibilities. Nevertheless, they present difficulties for specific populations including elderly individuals, children, patients with dysphagia, and animals. These delivery systems enable rapid drug dissolution within the oral cavity without water requirements, facilitating quicker absorption into circulation while circumventing hepatic first-pass metabolism. FDOFs must be lightweight, pliable, and maintain stability throughout production, packaging, and shipping. They should provide pleasant taste, comfortable mouthfeel, and rapid dissolution (under 60 seconds).[1]

Given that oral delivery represents more than 52% of the total drug delivery market, considerable focus has been placed on developing modified-release oral formulations. The pharmaceutical sector's approach to identifying drug candidates has undergone substantial transformation in recent years.[Nevertheless, several challenges commonly associated with oral drug administration reduce risks of partial active ingredient loss through tablet or capsule breakage or imprecise liquid dosing, leading to dosage mistakes and either overdosing or inadequate therapeutic outcomes. The evaluation areas of absorption, distribution, metabolism, and elimination follow the principle of extensive chemical space and limited target specificity.[2]

Rapid-dissolving drug delivery platforms are receiving considerable attention as solutions to these challenges. Recently, oral film strips have gained popularity as an innovative approach to breath freshening. These gel-like wafers dissolve rapidly in the mouth to release flavor compounds. Recent technological advances have prompted numerous pharmaceutical companies to explore new opportunities in this field to provide swift, precise dosing expected to enhance compliance, particularly among younger patients. Trans mucosal drug delivery methods have advanced considerably in recent years due to their potential to address oral medication administration challenges. The drug dose dissolves and is swallowed without requiring water or measuring devices. Since oral mucosa is highly vascularized and extremely permeable, drug absorption through this route into systemic circulation represents an attractive approach. Consequently, fast-dissolving films have become popular as an oral dosage form for numerous medications because they provide rapid disintegration through their extensive surface area.[3,4]

Fast-dissolving oral films typically consist of plasticized hydrocolloids or their combinations that can be processed through hot-melt extrusion or solvent casting techniques. Various significant manufacturing challenges may arise depending on the film-forming material characteristics. Common problems include

foaming during film formation caused by material heating or solvent evaporation, flaking during slitting operations, and cracking during cutting processes. The films must demonstrate long-term moisture resistance.[5]

These advantages enhance patient adherence and motivate pharmaceutical companies to invest in developing existing medications for FDOF applications. Considering its rapid plasma half-life and extensive first-pass metabolism, it represents an ideal candidate for immediate-release delivery systems. Therefore, combining buccal/sublingual delivery with oral films appears to be an attractive drug delivery approach for patients. The extensive surface area in film dosage forms enables rapid saliva wetting, leading to quick disintegration and dissolution with direct absorption that can enter systemic circulation without first-pass hepatic metabolism, thereby increasing bioavailability.[6,7]

Swallowing difficulties occur across all age demographics. This condition affects approximately 50% of the population, particularly pediatric and elderly patients, who often avoid oral solid dosage forms due to choking concerns. To address various swallowing-related issues, Fast dissolving films (FDOFs) were initially designed in the early 19th century, gradually leading to further improvements and the development of modern Fast Dissolving oral Films (FDOFs). Rapid-dissolving dosage forms have gained increasing significance due to their distinctive characteristics. They disintegrate and dissolve quickly while being administered without water, making them especially appropriate for pediatric and geriatric populations.[8,9]

The fundamental concept of oral films originated from the confectionery industry. These films are also referred to as oral strips, mouth-dissolving films, or oral dispersible films. Oral films represent the most sophisticated form of oral solid dosage due to enhanced comfort and flexibility.These films provide immediate bioavailability and rapid drug absorption through oral mucosa permeability. Oral films prove beneficial for elderly patients, those experiencing nausea, children, diarrhoea patients, and others. They are particularly valuable as topical aesthetics for oral ulcers, dental pain, or cold sores.[10]

Traditional oral solid forms such as tablets and capsules are typically favoured by patients compared to liquid medications. Evolving lifestyles and preferences create demand for more user-friendly pharmaceutical formats. Patient reluctance to consume hard-to-swallow medications led to the development of orally disintegrating solid forms in the 1970s. These orally disintegrating solid forms break down within seconds when placed on the tongue, creating a suspension that can be easily swallowed without requiring water.[11,12] Since 2003, North America has launched over 80 oral thin film products, though the market stays restricted compared to FDOFs. Nevertheless, the FDOFs industry shows strong positioning for future expansion. The US market has commercialized OTC films for pain relief and motion sickness management. Significantly, prescription FDOFs have gained approval in the US, EU, and Japan - three key markets. These approved prescription films possess potential to outperform other oral delivery methods for identical medications. The overall oral thin film market value appears set for substantial growth. [13]

FDOFs maintain an established shelf-life spanning 2-3 years based on the active ingredient, yet show extreme sensitivity to environmental humidity. Fast-dissolving delivery systems were initially created as non-bulky oral dose forms offering multiple benefits over conventional oral medications. Oral films are gaining increased attention as an innovative platform for patients. These films represent a preferred dosage format due to their superior durability.[14,15]

Special Features Of Fast dissolving oral films

- Available in multiple shapes and sizes
- Non-obstructive
- Superior quality
- Quick disintegration
- Swift release
- Sleek elegant film

The Ideal Characteristics of A Drug To Be Selected

- The medication should possess pleasant flavour
- The incorporated drug should maintain low dosage up to 40 mg
- Drugs with smaller to moderate molecular weights work best
- The medication should demonstrate good stability and water solubility as well as saliva solubility
- It should remain partially unionized at oral cavity pH levels
- It should possess capability to penetrate oral mucosal tissues

Advantage of fast dissolving oral film

- Water not required for administration
- Suitable for pediatric, elderly and dysphasic patients experiencing swallowing difficulties.
- Quick breakdown and dissolution in oral cavity due to expanded surface area of films
- Swift action onset with enhanced bioavailability through bypassing hepatic first pass metabolism
- Lower dosage requirements, improving drug efficacy and safety while minimizing adverse effects.
- Flexible and portable characteristics providing easy handling, transport and storage
- Simple administration for mentally impaired, disabled, uncooperative patients and those on restricted fluid intake or experiencing nausea
- Valuable for conditions like motion sickness, acute pain, sudden allergic reactions, asthma attacks and coughing, requiring extremely rapid action onset
- Extended stability duration, as the medication remains in solid form until consumption
- Dosage precision compared to liquid preparations
- Pleasant oral sensation, leaving minimal or no residue following administration [16,17]

Disadvantage Of Fast Dissolving Oral Film

- Hygroscopic nature requires storage in dry environments
- Exhibits fragile, granular characteristics
- Requires specialized packaging for product stability and protection
- Medications unstable at oral pH cannot be delivered through this method
- Drugs causing mucosal irritation are unsuitable for this delivery route [18]

Classification of Fast Dissolving Oral Films (FDOFs)

Fast dissolving oral films can be broadly classified based on their release behavior, mucoadhesive characteristics, and intended therapeutic application. Each category is designed to meet specific clinical needs, ranging from immediate drug action to prolonged and sustained delivery within the oral cavity.

Flash Release Films:

Flash release films are formulated to disintegrate rapidly and release the drug almost immediately upon contact with saliva. These films are primarily composed of highly hydrophilic polymers, which enable quick wetting and dissolution.Release profileThe defining feature of flash release films is their very fast disintegration, resulting in immediate drug release and a rapid onset of action.Absorption site of these films are generally placed on the tongue, where they dissolve within second. Drug delivery the active pharmaceutical ingredient may be absorbed systemically through the sublingual mucosa or act locally to treat conditions affecting the oral cavity or throat. Applications of the Flash release films are particularly useful for drugs that require quick therapeutic action, such as analgesics, antiemetics, and emergency medications where time to onset is critical.

Mucoadhesive Melt-Away Wafers

Mucoadhesive melt-away wafers are developed using single-layered or multilayered water-soluble polymers that adhere to the buccal mucosa, specifically the inner lining of the cheek. Release profile these wafers dissolve at a moderate rate, enabling a more sustained and prolonged release of the drug compared to flash

release films. Absorption site they are designed to attach to the gingival or buccal region, allowing the drug to be absorbed either locally or systemically through the oral mucosa. Drug delivery Due to their mucoadhesive nature, these films remain in place for an extended period, which enhances residence time and ensures a controlled and extended drug delivery profile.Applications: Mucoadhesive melt-away wafers are well suited for chronic conditions that require consistent therapeutic levels over time rather than immediate drug release.

Mucoadhesive Sustained-Release Wafers

Among the three categories, mucoadhesive sustained-release wafers exhibit the longest drug release profile. These films are specifically engineered to remain in the oral cavity for several hours.

Release profile and mechanism Sustained-release wafers continuously deliver the drug over an extended duration. This is achieved by incorporating polymers that precisely control the drug release rate. Mucoadhesive properties These wafers possess very strong mucoadhesive characteristics, ensuring long-term retention at the site of application within the oral cavity.Drug distribution typically, these systems are multilayered and composed of low-solubility polymers containing drug suspensions and/or solid solutions, which further contribute to prolonged drug release Applications They are commonly used in therapies that require maintenance of therapeutic drug concentrations for longer periods, such as in the management of chronic pain or diabetes.[19]

Methods of Preparation of FDOFs

Fast dissolving oral films can be manufactured using several well-established techniques, including solvent casting, hot-melt extrusion, semisolid casting, solid dispersion extrusion, and rolling. Each method has distinct advantages and is selected based on the nature of the drug, polymers used, and desired film characteristics. Below is an overview of the commonly employed preparation methods and their key process parameters.

Solvent Casting Method

The solvent casting method, illustrated in Figure 1, is one of the most widely preferred techniques for preparing fast dissolving oral films. In this approach, two separate solutions are initially prepared using suitable solvents. First, water-soluble polymers are dissolved in water to form a clear and viscous polymeric solution. In parallel, the drug along with other excipients is dissolved in an appropriate solvent. These two solutions are then combined and stirred thoroughly, typically at around 1000 rpm, to obtain a homogeneous mixture.

The resulting solution undergoes vacuum treatment to remove entrapped air, ensuring uniformity and preventing bubble formation in the final film. The degassed solution is then cast onto a Petri plate and allowed to dry under controlled conditions. Once dried, the film is carefully cut into pieces of the desired size and shape.[20]

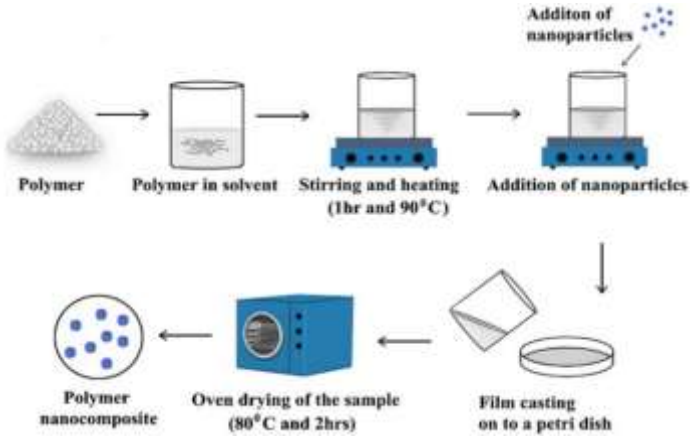

Fig1: Solvent Casting Method

Hot Melt Extrusion Method

In the hot melt extrusion method, as shown in Figure 2, the drug is first mixed with suitable carriers to obtain a dried solid mass. This mass is then fed into an extruder, which is typically divided into multiple zones, each maintained at different temperature settings. For example, zone 1 may be maintained at around 80°C, zone 2 at 150°C, zone 3 at 100°C, and zone 4 at 65°C.The extruder speed is generally set at approximately 15 rpm, allowing the granules to be processed within the barrel for about 3–4 minutes. The extruded material is then pressed through a cylindrical calendar to form a uniform film.

Hot melt extrusion offers several advantages, including a reduced number of processing steps, minimal waste generation, and elimination of solvents or water, making it an anhydrous process. Additionally, the intense mixing and agitation during extrusion ensure excellent content uniformity.[21]

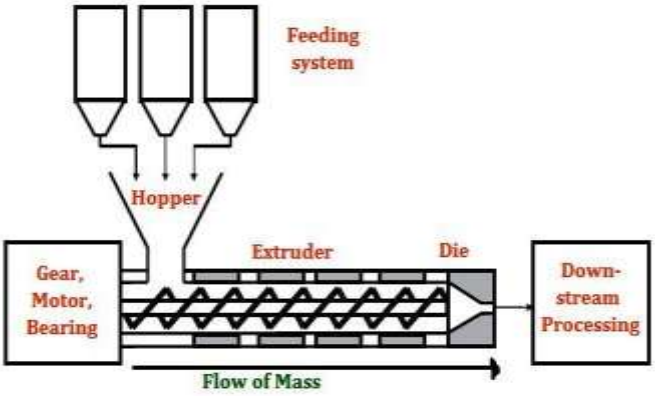

Figure 2: Hot Melt Extrusion Method

Rolling Method

The rolling method involves combining the drug solution with a film-forming polymer solution and mixing thoroughly to ensure homogeneity. The prepared mixture must exhibit appropriate flow properties before further processing. Once ready, the solution is passed through a set of rollers to form a thin, uniform film. The film is then dried directly on the rollers, after which it is cut into the required shapes and sizes.[22]

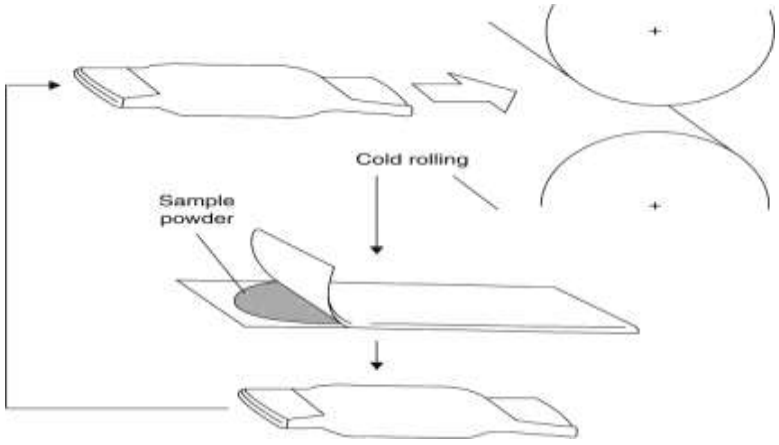

Figure 3: Rolling Method

Solid Dispersion Extraction Method

The primary objective of the solid dispersion extraction technique is to disperse the drug uniformly within a melted polymer matrix, thereby enhancing drug loading and solubility. In this method, one or more active pharmaceutical ingredients are dissolved in a suitable liquid solvent that acts as an inert carrier. This process is carried out in the presence of an amorphous hydrophilic polymer at temperatures below 70°C, without removing the liquid solvent. The result is a solid dispersion system, which is then shaped into films using suitable dies. It is important to note that the selected solvent or dissolved drug may sometimes be immiscible with the polymer melt, which requires careful optimization of formulation parameters.[23]

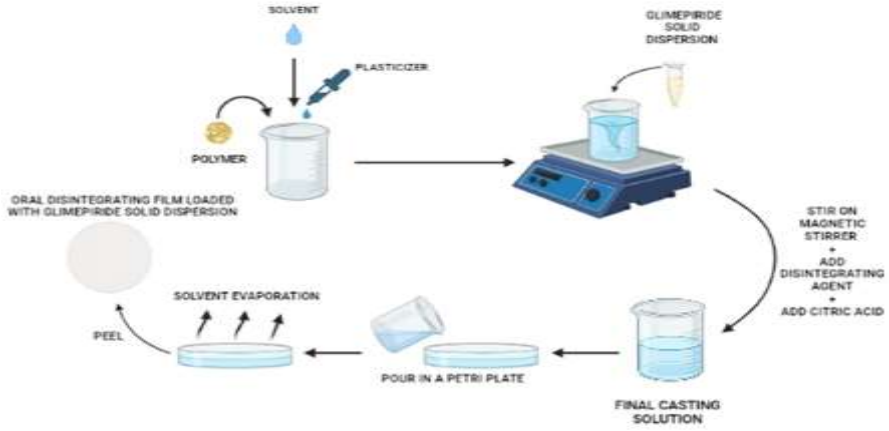

Figure 4: Solid Dispersion Extraction Method

Semi-Solid Casting Method

Semi-solid casting is a more complex technique compared to solvent casting and is commonly employed when acid-insoluble polymers are used. Initially, a water-soluble polymer solution is prepared. Separately, an acid-insoluble polymer, such as cellulose acetate phthalate, is dissolved in a solution containing ammonium or sodium hydroxide. These two polymer solutions are then combined, and a plasticizer is added to obtain a gel-like mass. This semi-solid gel is cast into a film or ribbon using a heat-controlled drum. Films produced by this method are generally thicker than those prepared by other techniques, with thickness typically ranging from 0.015 to 0.05 inches.

Formulation Consideration:

The drug loaded FDOFs should have a surface area of 1-20 cm2. The single dose of the drug can be up to 2× 30mg and fill.

All these properties were related to the formulation characteristics, as observed by several other studies. All the excipients used in the fast dissolving oral film should be GRAS-listed and approved for use in drug delivery oral strip. [24]

A Typical Formulation Composition

Sr.no	Component	Quantity (w\w)
1	API	1-30%
2	Film Forming polymer	40-50%
3	Plasticizing agent	0-20%
4	Saliva Stimulating excipient	2-6%
5	Sweetening agent	3-6%
6	Flavouring substance	q.s
7	Surfactant	q.s
8	Colouring agent	q.s

1.API :

A standard film composition typically includes 1-25% w/w of active pharmaceutical ingredient. Multiple types of APIs can be delivered using fast-dissolving film technology. Low-dose compounds represent the most suitable candidates for incorporation into OFDFs. These thin film strips find primary application in delivering consumer vitamins, dietary supplements, and over-the-counter medications. Appropriate active components for these films encompass vitamins, melatonin, CoQ10, along with various OTC substances. Different categories of medications, including treatments for coughs, colds, and throat discomfort, can be integrated into these film strips.[25]

The Following a variety of therapeutic agent can be successfully formulated into fast dissolving oral films.

Active pharmaceutical ingredient	**Dose (mg)**	**Therapeutic Action**
Levocetrizine	75	Antihistaminic
Ondensteron	2.5	Anti emetic
Ketoprofen	12.5	Analgesic
Salbutamol	4	Anti-histamic
Omeperazole	10-20	Antacid

2. Polymer:

Polymers serve a crucial function in oral film development. The manufacturing process utilizes hydrophilic polymers to ensure rapid dissolution within the oral cavity, allowing medication delivery to the bloodstream through dissolution upon contact with saliva at the mucous membrane interface. Water-soluble polymeric materials function as film-forming agents, delivering rapid disintegration, pleasant oral sensation, and excellent mechanical properties. These polymers may be used individually or combined with others to achieve desired film characteristics including hydrophilic behavior, flexibility, palatability, and dissolution properties.[26]

3. Plasticizer:

Plasticizers play a crucial role in oral film production. They enhance the film's flexibility while reducing brittleness. The selection of an appropriate plasticizer relies on its compatibility with both the polymer (primary film component) and the processing solvent. These additives improve strip characteristics by reducing the polymer's glass transition temperature. Typical usage ranges from 1% to 20% based on the dry polymer weight.

4. Saliva stimulating agents:

These compounds boost saliva production, enabling faster breakdown and dissolution of oral films in the mouth. Food-grade acids frequently serve as saliva stimulants. Such agents may be used individually or combined at concentrations of 2-6% by weight of the oral strip. Common salivating compounds include citric, malic, lactic, ascorbic, and tartaric acids.

5.Sweetening agent:

Sweeteners serve as essential components in oral films, primarily for taste enhancement, and prove especially valuable in pediatric formulations. They typically comprise 3% to 6% of the overall weight. Both natural and synthetic sweeteners help improve the palatability of mouth-dissolving medications.

6. Flavouring agent

Flavoring compounds are incorporated to enhance patient acceptance. Concentrations reach up to 10% w/w of added flavors. The selection of flavoring agents depends on the specific drug being used. Patient age

significantly influences flavor choice. Children prefer chocolate and fruit varieties, while elderly patients favor orange and mint options.

7. Colouring agents

Coloring compounds provide visual appeal to the film and are generally selected to complement the chosen flavor. These substances typically require FD&C approval. Titanium dioxide stands as the most frequently used coloring agent in fast-dissolving oral films. Coloring additives must not exceed 1% of the film's total weight.

EVALUATION PARAMETERS:

Fast-dissolving oral films undergo assessment for the following criteria:

1.Weight variation of Films:

The mouth-dissolving oral films undergo weighing using an analytical balance, with the mean weight of each film being determined. Maintaining consistent weight across films is crucial. This ensures each film delivers the correct amount of components, including the active pharmaceutical ingredient (API) and other essential materials.[27]

2.Thickness test:

Film thickness gets measured using a calibrated digital micrometer, followed by mean average calculation. Typically, three measurements from all batches are taken and averaged. Weight variation of films is assessed in triplicate by cutting the film and measuring each piece's weight. Maintaining thickness uniformity is essential since it directly relates to the film's dose precision[28].

3.Tensile strength:

Tensile strength represents the maximum stress level at which film breakage occurs. This evaluation measures the mechanical durability of films. The calculation involves dividing the applied load at rupture by the strip's cross-sectional area using the following equation.

Tensile strength = Load at breakage/ Strip thickness × Strip Width

4.Percentage elongation:

When sample films experience tensile stress, film deformation happens, causing sample stretching or elongation. This procedure helps predict polymer ductility using texture analysis equipment.

The calculation formula is: % Elongation = Increase in length ×100 / Original length

5.Folding Endurance:

Folding endurance gets evaluated by repeatedly bending the film at the same location until breakage occurs. The folding endurance measurement represents how many times the film withstands folding before failure.

6.Content uniformity:

Film contents are analyzed using standard assay procedures specified for individual drugs in various pharmacopoeia. This evaluation involves testing 20 samples through analytical methods. The acceptable value should be under 15% according to Japanese pharmacopoeia standards. Per USP27 guidelines, contents must range between 85% to 115% with standard deviation at or below 6%. Content uniformity assessment estimates drug quantity in individual films.

7.Wetting time:

For wetting time evaluation, a circular paper gets positioned in a petri dish with 6 ml of 0.1% amaranth dye solution added. A 2x2 cm film strip is positioned over the tissue paper. Wetting time measures how long the dye takes to reach the film's surface.

8.Surface pH:

The test film is positioned in a petri dish and dampened with 0.5 ml of distilled water for 30 seconds. Subsequently, the pH meter electrode contacts the film surface, with pH measurement taken after 1 minute. Each film undergoes pH testing three times, and the mean value is determined.

9.Transparency:

Film transparency can be assessed using a basic UV spectrophotometer. Film samples are cut into rectangular shapes and positioned on the spectrophotometer cell's internal surface. Film transmittance is measured at 600 nm. Transparency calculation follows this formula:

$$\text{Transparency} = (\log T600)/b = - €c$$

Where,

T600 represents transmittance at 600 nm,
b indicates film thickness (mm)
c shows concentration.

10.Disintegration Time:

The 30-second or less disintegration time limit for orally disintegrating tablets outlined in CDER guidance applies to fast dissolving oral strips (44). While no official guidance exists for oral fast disintegrating films/strips, this serves as a qualitative benchmark for quality control testing or development phases. Pharmacopoeia disintegrating test equipment may be utilized for this evaluation. Standard disintegration time for strips ranges from 5–30 seconds.

11.In-vitro Dissolution Test:

Dissolution evaluation uses standard basket or paddle equipment as outlined in pharmacopeia. The testing medium selection depends on drug dissolution requirements and maximum API dosage. The test can present challenges since film strips may float on the medium surface when using paddle equipment.

Conclusion

Among various drug delivery pathways, the oral route stands as the most preferred and widely accepted by both patients and healthcare providers. This innovative drug delivery system benefits all patient populations experiencing swallowing difficulties, including pediatric and geriatric groups. It offers numerous benefits compared to other dosage forms, such as enhanced drug bioavailability and accelerated action onset. These systems combine solid dosage form stability with liquid form applicability, creating a bridge between both concepts while incorporating favorable aspects from solid and liquid formulations into an refined, stable and efficient delivery method. They prove particularly valuable during emergency situations like allergic reactions and asthmatic episodes when rapid action onset is required. Consequently, fast dissolving orally disintegrating films with superior patient compliance and multiple benefits present extensive future possibilities.

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