REVIEW ARTICLE

An Overview of the Components, Techniques, and Innovation Used for Fast-Dissolving Films

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ABSTRACT

Fast-dissolving films (FDFs) stand as a cornerstone in modern pharmaceutical innovation, heralded for their unrivaled convenience, patient adherence, and the swift onset of action. Within the realm of this paper lies a meticulous exploration of FDFs, delving deep into their intricate formulation intricacies, manufacturing methodologies, and diverse therapeutic applications. The formulation journey traverses the meticulous selection of film-forming polymers, plasticizers, taste-masking agents, and active pharmaceutical ingredients (APIs), each element meticulously calibrated to achieve optimal efficacy. Diverse production techniques, spanning solvent casting, hot melt extrusion, and spray drying, are scrutinized with precision, shedding light on their inherent advantages and nuanced limitations. Beyond the realm of formulation and manufacturing, this review embarks on an expansive voyage into the vast therapeutic landscape that FDFs traverse. From the treatment areas of central nervous system disorders to the realms of cardiovascular diseases, allergies, and pain management, the versatility and adaptability of FDFs emerge as a beacon of hope for patients and practitioners alike. Yet, amidst the brilliance of FDFs, inherent challenges linger, from stability concerns to the intricate dance of bioavailability and the ever-watchful eye of regulatory scrutiny. However, within these challenges lies the fertile ground for future research and development endeavors, beckoning forth a new era of innovation and advancement in the realm of rapidly dissolving films. This study stands as an indispensable compass, guiding researchers, pharmaceutical scientists, and practitioners toward the forefront of FDF development and implementation.

Keywords: Fast-dissolving film, Delivery system, Fast-dissolving technologies.

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INTRODUCTION

The advent of fast dissolving films (FDFs) represents a significant leap forward in pharmaceutical drug delivery, offering a revolutionary approach with numerous advantages over conventional dosage forms. Departing from the realm of traditional pills, capsules, or syrups, FDFs present as ultra-thin, flexible films that swiftly disintegrate upon contact with saliva, facilitating the rapid absorption of the active pharmaceutical ingredient (API) through the oral mucosa.[1] This hallmark characteristic sets FDFs apart by obviating the need for swallowing, rendering them an ideal option for individuals grappling with pill ingestion or liquid intake challenges. Beyond mere convenience, the expeditious disintegration of FDFs not only ensures a prompt onset of action but also enhances usability in manifold ways.[2] FDFs not only revolutionize drug delivery but also redefine patient experience through their unique features. Firstly, by negating the requirement for water or accompanying beverages during administration, FDFs offer unparalleled convenience, particularly in settings where access to water is restricted or cumbersome.[3] This attribute renders FDFs remarkably portable, making them indispensable for on-the-go use or travel scenarios. Secondly, the sleek and pliable nature of FDFs renders them effortlessly manageable and easy to administer. Their thin, flexible form allows for discreet and hassle-free usage sans additional equipment or preparatory steps.[4] This characteristic proves invaluable for individuals needing medication in public settings or seeking privacy. Moreover, FDFs transcend functionality to evoke sensory appeal, thereby enhancing patient compliance. Their innovative design and dissolving mechanism offer a novel tactile experience, fostering patient engagement and acceptance. Thus, by seamlessly integrating convenience, usability, and sensory allure, FDFs emerge as a transformative force in pharmaceutical adherence and patient-centered care.[5] The sensory attributes of FDFs, including their pleasing taste, scent, and mouthfeel, play a pivotal role in enhancing patient acceptability, thereby mitigating the likelihood of aversion or reluctance toward medication intake. This aspect

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Figure 1: Fast dissolving film

assumes paramount significance, especially within pediatric and geriatric populations, characterized by distinct taste preferences or heightened sensory sensitivities. By adeptly addressing these variables, FDFs foster improved adherence to prescribed drug regimens, thereby fostering better treatment outcomes and heightened patient satisfaction. Moreover, the rapid dissolving kinetics inherent in FDFs contribute significantly to their efficacy, facilitating swift entry of the active pharmaceutical ingredient (API) into the bloodstream. This rapid onset of action proves particularly advantageous for treatments necessitating prompt relief or an expedited therapeutic response, such as analgesics, antiemetics, or allergy medications. In essence, the amalgamation of sensory appeal and rapid dissolving kinetics elevates the utility of FDFs, underscoring their pivotal role in optimizing patient experiences and treatment efficacy across diverse therapeutic domains.[6] FDFs offer a transformative approach to medicine administration, efficacy enhancement, and bolstering patient compliance within pharmaceutical drug delivery. By swiftly transporting the drug directly to the systemic circulation through the oral mucosa, FDFs significantly reduce onset time and augment bioavailability, thereby ensuring faster and more effective symptom relief.[7] FDFs emerge as a compelling alternative, poised to revolutionize traditional dosage forms. Their hallmark attributes, including rapid disintegration, convenience, and heightened acceptance, position them as an appealing option for both patients and practitioners alike. Representing a substantial advancement in the pharmaceutical landscape, FDFs hold the promise of fostering improved treatment outcomes and heightened patient satisfaction, ultimately reshaping the paradigm of medicine delivery and patient care (As describe in Figure 1).[8]

Mechanism of Action and Composition

FDFs work on a basic yet effective mechanism, which is essentially determined by their unique composition and design. FDFs work by dissolving quickly when they come into contact with saliva. When an FDF is placed on the tongue or in the buccal cavity, it comes into direct contact with saliva, so initiating the dissolution process. Saliva penetrates the film, causing it to moisten and disintegrate quickly. As the film disintegrates, the active pharmaceutical ingredient (API) within it is liberated and disseminated in saliva. This enables for efficient API absorption via the oral mucosa, where it reaches the circulation directly and bypasses the gastrointestinal tract. FDFs dissolve quickly due to their unique makeup, which typically consists of three major components: polymers, plasticizers, and APIs.[9]

- Polymer: Polymers are the basic building blocks of FDFs, ensuring structural integrity and allowing for the development of a thin, flexible film. These polymers are carefully selected for their ability to dissolve quickly in saliva while preserving film integrity during storage and handling. HPMC, PVA, and pullulan are common polymers utilized in FDF formulations.
- Plasticizers: These additives improve the flexibility and elasticity of polymer films. Plasticizers improve the film's capacity to conform to the contours of the mouth cavity and dissolve quickly when it comes into contact with saliva by lowering intermolecular pressures within the polymer chain. Glycerine, propylene glycol, and polyethylene glycol are common plasticizers used in FDF formulations.
- Active Pharmaceutical Ingredients: The API is the therapeutic agent in the FDF that produces the desired pharmacological effect. The API is typically mixed into the polymer matrix as a solid dispersion or solution to ensure even distribution throughout the film. The API used is determined by the therapeutic indication and desired pharmacokinetic profile.[10]

Applications of Fast Dissolving Film

FDFs have a wide range of uses in numerous therapeutic fields, catering to both over-the-counter (OTC) and prescription pharmaceuticals. Their fast dissolving, convenience, and increased patient compliance make them ideal for treating a wide range of medical disorders. Here's an investigation into the applications of FDFs in many therapeutic areas.[11]

OTC medications

FDFs provide pain relief by delivering analgesics, including ibuprofen, acetaminophen, and aspirin. These drugs offer quick relief for headaches, muscle aches, and mild ailments. FDF formulations of antitussives, expectorants, and decongestants provide fast relief from cough and cold symptoms, including congestion, coughing, and sore throat. FDF-formulated antihistamines and decongestants relieve allergy symptoms such as sneezing, itching, and nasal congestion.

Prescription drug

FDFs can be used for cardiovascular medications, including antiplatelet, antihypertensive, and lipid-lowering therapies. These formulations provide quick onset of action, which is critical for addressing acute cardiovascular problems. FDFs are used for drugs that affect the central nervous system, such as sedatives, hypnotics, antiepileptics, and antidepressants. They provide immediate relief from symptoms associated with neurological diseases while also promoting patient compliance. FDF formulations of PPIs, antacids, and antiemetics can effectively treat gastrointestinal diseases such as acid reflux, ulcers, and nausea. Their fast disintegration gives immediate relief from symptoms and improves patient comfort.[12]

Pediatrics and geriatric formulations

FDFs are easy to administer and have a nice flavor, making them ideal for children. Antipyretics, antihistamines, and antibiotics can all be designed as FDFs to help children comply and achieve better treatment results. For elderly adults who struggle to swallow pills or capsules, FDFs are a favored method of medicine delivery. Formulations for illnesses such as hypertension, diabetes, and osteoarthritis can be customized to the unique needs of the elderly, guaranteeing effective therapy while reducing suffering.

Examples of drug formulated as FDFs

- Zolmitriptan is a migraine drug available in FDF form that provides quick relief without the need for water or swallowing.
- Ondansetron is a fast-acting antiemetic used to treat nausea and vomiting. It is especially effective for chemotherapy-induced nausea.
- Loratadine, an antihistamine used to treat allergic rhinitis and urticaria, is available as FDFs for easy administration, particularly for pediatric patients.
- Aripiprazole is an FDF-formulated antipsychotic drug used to treat schizophrenia and biopolar disorder, with increased compliance and dosing.[11]

Advantages of Fast-Dissolving Films

- Fast-dissolving films have numerous benefits, making them a minor but powerful advance in pharmaceutical drug delivery.
- Rapid onset of action: FDFs break down fast in saliva, allowing for speedy absorption of APIs through the oral mucosa. This results in a speedier onset of therapeutic benefits compared to typical dosage forms such as tablets or capsules, making FDFs ideal for drugs that require instant relief or a quick treatment response.
- Convenience and Ease of Administration: FDFs are compact and thin, making them easy to transport and administer. They are easily portable in pockets or bags and may be used discreetly in a variety of locations without the need for water or additional equipment. This convenience not only increases patient compliance but also provides a hassle-free option for people who have difficulties swallowing pills or drinking liquids.[12]
- Improved Patient Compliance and Acceptability: FDFs are designed for a pleasing flavor and texture, leading to increased patient acceptance and compliance. This is especially good for children and the elderly, as well as people who dislike taking medicines. By addressing these sensory preferences, FDFs improve drug adherence, resulting in greater treatment outcomes and patient satisfaction.
- Customisable Dosing and Combination Therapies: FDFs enable precision pharmaceutical dosing and the inclusion of numerous APIs in a single film. This allows for the creation of individualized therapeutic regimens to fit the needs of individual patients, as well as the development of combination medications to more effectively address complicated medical diseases. Furthermore, FDFs allow for easy dose adjustment, making them ideal for personalised medicine approaches.[13]

Challenge and Consideration

FDFs involve a number of issues and factors that must be addressed to ensure their efficacy, safety, and regulatory compliance. These challenges include:

- Stability and shelf-life Issues: FDFs are susceptible to degradation due to factors such as moisture, temperature, and exposure to light, which can compromise their stability and shelf life. Formulation ingredients, such as polymers and plasticizers, may interact with the API or degrade over time, leading to changes in film properties and drug release kinetics. Ensuring adequate packaging and storage conditions is crucial to mitigate stability issues and maintain the integrity of FDFs throughout their shelf life.
- Bioavailability and Drug Release Profiles: FDFs might have inconsistent and unpredictable drug release profiles due to formulation, manufacturing, and environmental factors. Film thickness, polymer type, and API solubility can effect drug dissolution and bioavailability, impacting therapeutic efficacy. Novel excipients, formulation adjustments, and controlled-release technologies can improve drug release kinetics and bioavailability.
- Regulatory Requirements and Compliance: FDFs must adhere to strict quality standards for patient safety and efficacy. Regulatory agencies, including the FDA and EMA, require detailed data on product quality, stability, bioequivalence, and manufacturing processes for approval and marketing authorization. FDFs must adhere to GMP and other guidelines during development, manufacturing, and distribution.[14]

To overcome these challenges, ongoing research efforts are focused on several areas:

- Formulation Optimisation: Researchers are testing new excipients, polymer blends, and manufacturing procedures to improve the stability, bioavailability, and drug release patterns of FDFs. Advanced formulation technologies, such as nanoencapsulation and solid dispersion, are being researched to improve the solubility and dissolution properties of poorly soluble pharmaceuticals.
- Innovative Drug Delivery Technologies: Nanotechnology, microneedle patches, and Innovative Drug Delivery Technologies. Nanotechnology, microneedle patches, and mucoadhesive formulations are being investigated to improve the efficacy and functionality of FDFs. These technologies allow for targeted delivery, prolonged release, and site-specific drug administration, which addresses specific treatment demands and improves patient outcomes.
- Quality Control and Regulatory Compliance: Improved analytical techniques, process monitoring, and quality

control systems ensure FDFs meet quality, safety, and regulatory requirements. The use of modern analytical instruments, such as spectroscopic and chromatographic approaches, provides full characterisation of FDFs and improves batch-to-batch consistency.[15]

Future Direction and Potential Development

The future of FDFs holds enormous promise for revolutionary advances in medication delivery. Here are some expected directions and possible developments:

- New materials and formulation strategies: Novel materials like biodegradable polymers, natural gums, and nanomaterials can stimulate innovation in FDF formulation. These materials have benefits in terms of biocompatibility, controlled release, and increased drug stability. To broaden the variety of medications acceptable for FDF delivery, we will examine formulation strategies such as solid dispersion, lipid-based formulations, and nanoencapsulation to improve their solubility and bioavailability.
- Advanced Drug Delivery Technologies: Nanotechnology and microneedle patches can improve the functioning and performance of FDFs. Nanoparticle-loaded FDFs increase drug transport, release, and efficacy by increasing solubility and permeability. Embedding FDFs in microneedle patches allows for painless and controlled transdermal medication delivery, making FDFs more suitable for a variety of therapeutic purposes.[16]
- Personalized and Targeted Therapies: Advancements in personalized medicine and targeted therapies will lead to the creation of FDFs that meet individual patient needs. Targeted FDF formulations with ligands or nanoparticles for specific tissue or cell targeting can improve therapeutic outcomes and minimize negative effects. Personalized FDFs tailored to patients' age, genetics, and illness features can enhance therapy efficacy, adherence, and satisfaction.

These Advances have Far-reaching Consequences for the Pharmaceutical and Healthcare Industries

- Improved Therapeutic Efficacy: New materials, sophisticated drug delivery technologies, and personalized techniques can lead to more effective FDFs, improving treatment outcomes and patient care.
- Expanded Treatment Options: As formulation and delivery technologies improve, FDFs will be used for a greater range of medications and therapeutic indications, providing healthcare practitioners and patients with more treatment options.
- Improved Patient Experience: Targeted and personalized FDFs, together with innovative medication delivery technologies, offer convenient, effective, and personalized treatment options. This will improve patient satisfaction and adherence to treatment regimes.
- Improved Efficiency and Cost-effectiveness: Advancements in FDF formulation and manufacturing techniques will lead to more efficient and scalable manufacture and distribution of FDF-based pharmaceuticals. This will help healthcare systems, pharmaceutical businesses, and people alike.[17]

Disadvantages of Fast-Dissolving Films

- It is hygroscopic and should be stored in a dry place; it also has a fragile, granular texture.
- Products must be packaged in a specific manner for safety and security.
- High doses are not permitted on oral films.[18]

Special Feature

- Available in many sizes and shapes
- Tinny and elegant film
- No problem breaks down or dissolves quickly
- Releases quickly

Classification of Fast Dissolving Technology

For ease of explanation, Fast Dissolving Technology is divided into three categories:

Desiccants

The technology behind these machines involves a suspension or solution in tablets, such as molds or blisters, along with other additives. Freeze-dried products or tablets are stored in packages or molds. The resulting product is porous and can be rapidly penetrated and degraded by water or saliva.

Compressed tablet

This system is based on the direct compression of excipients using tablet technology. The hardness and friability of the tablet machine are determined by the manufacturing method. Rapid tablets dissolve faster than standard tablets because they contain water-soluble excipients, super disintegrants, or effervescent ingredients that allow water to penetrate the tablet's core.

Film strips

In recent years, food and oral care products have developed oral film or oral wafers, which have become a new and widely recognized product by consumers to provide different types of vitamins and personal care goods. FDF is currently a proven and widely used system for the delivery of over-the-counter (OTC) medicinal products APIs and is in early to mid-stage development for pharmaceuticals.[19]

Aspects of Fast-Dissolving Film Formulation

- Classification of drugs
- Film-forming polymers
- Polymers
- Flavouring agents
- Saliva stimulating agents
- Cooling agents
- Aroma
- Colorants
- Surfactants
- Stabilizers and thickeners

FDF's design is characterized by facial taste, rapid burst, body shape, mouth, etc. It should be beautiful and functional. From a regulatory perspective, all excipients used in OS formulations should be recognized as safe (GRAS) and approved for oral use. Table 1 lists the components in a combination.[20]

Drug classes

FDFs have the capability to host a wide array of APIs spanning various therapeutic classes. However, the thin nature of FDFs limits the amount of drug that can be incorporated, posing a challenge when formulating drugs requiring higher dosages. Despite this limitation, FDFs have shown versatility in accommodating antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), antihistamines, and more, promising a diverse range of applications.

Film-forming polymer

The choice of film-forming polymers is critical in FDF formulation, as they determine the film's mechanical properties, disintegration characteristics, and overall performance. Water-soluble polymers are preferred for their ability to rapidly dissolve in saliva, ensuring quick drug release and improved patient compliance. Commonly employed polymers include Rubralin, gelatin, and Hypromellose, each offering unique advantages in terms of film strength, adhesion to the buccal mucosa, and drug delivery kinetics. The proportion of polymer in the formulation significantly influences the film's properties, with a minimum polymer content of around 45% w/w typically recommended for optimal performance.[21]

Plasticizer

Plasticizers play a crucial role in enhancing the flexibility and elasticity of FDFs, thereby preventing brittleness and improving handling characteristics. The choice of plasticizer depends on its compatibility with the selected polymer and solvent system. By lowering the glass transition temperature of the polymer, plasticizers facilitate greater mobility of polymer chains, resulting in improved film flexibility and drug release kinetics. Commonly used plasticizers include glycerin, propylene glycol, low molecular weight polyethylene glycol, and various citric acid derivatives, each offering unique benefits in terms of plasticization efficiency and compatibility with other formulation components.

Sweeteners

Sweeteners are integral to FDF formulations, serving to improve palatability and patient acceptance, particularly in pediatric and geriatric populations. Both natural and artificial sweeteners are utilized to enhance the taste of FDFs, catering to a wide range of consumer preferences. Natural sweeteners such as xylose, ribose, and sucrose provide a familiar taste profile, while artificial sweeteners such as sodium saccharin and acesulfame potassium offer sweetness without added calories. The selection of sweeteners is guided by considerations of taste, solubility, and regulatory approval for use in pharmaceutical formulations.[22]

Acid stimulants

Saliva stimulants are employed in FDF formulations to promote rapid disintegration and dissolution in the oral cavity. By increasing saliva production, these agents facilitate faster drug release and absorption, leading to more rapid onset of action. Commonly used saliva stimulants include citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid, each exerting its effects through different mechanisms. The incorporation of saliva stimulants enhances the overall performance of FDFs, particularly in terms of bioavailability and therapeutic efficacy.

Coolants

They are added to FDF formulations to improve the sensory experience upon administration, providing a refreshing sensation and masking any unpleasant tastes or odors. Monomethyl succinate and other cooling agents such as WS3, WS23, and Utracoll II are commonly used to impart a cooling effect to FDFs, enhancing their palatability and overall consumer appeal. By enhancing the flavor and mouth feel of FDFs, coolants contribute to better patient acceptance and compliance, particularly in populations with sensory sensitivities or aversions to oral medications.

Aroma

Aroma plays a crucial role in determining the overall sensory experience of FDFs, influencing taste perception and consumer acceptance. A wide range of flavoring agents, including synthetic flavoring oils, oleoresins, and extracts from various plants, are utilized to impart distinct flavors and aromas to FDFs. Fruity oils such as vanilla, cocoa, and citrus are commonly used to enhance sweetness and palatability, while aromatic oils such as peppermint and cinnamon provide a refreshing and invigorating sensory experience. The selection and concentration of aroma compounds are tailored to meet consumer preferences and regulatory requirements, ensuring optimal taste and aroma profiles in FDF formulations.

Colorants

Colorants are added to FDF formulations to enhance visual appeal and differentiate products from one another. Titanium dioxide and approved FD&C colorants are commonly used to impart color to FDFs, with concentrations typically not exceeding 1% w/w to comply with regulatory guidelines. The choice of colorants is guided by considerations of safety, stability, and compatibility with other formulation components, ensuring that FDFs meet stringent quality standards while appealing to consumer preferences.

Surfactants

Surfactants are incorporated into FDF formulations to improve solubility, wetting, and dispersion of active ingredients, thereby facilitating rapid dissolution and drug release. Surfactants such as Poloxamer 407, sodium lauryl sulfate, and various Tween and Span derivatives are utilized to enhance the absorption of poorly soluble drugs and improve overall bioavailability. By promoting uniform distribution of active ingredients

Table 1: Composition for fast-dissolving films

S. No	*Ingredient*	*Amount*
1	Film-forming polymer	40–50
2	Drug	1–30
3	Saliva stimulation agent	2–6
4	Plasticizer	0–20
5	Sweetening agent	3–6
6	Color, filler	q.s
7	Surfactant	q.s
8	Flavoring agent	q.s

within the film matrix, surfactants contribute to consistent and predictable drug delivery, ensuring optimal therapeutic outcomes for patients.

Stabilizers and thickeners

Stabilizers and thickeners are employed in FDF formulations to enhance viscosity, consistency, and processability during manufacturing. Natural gums such as xanthan gum, locust bean gum, carrageenan, and cellulose derivatives are commonly used as stabilizers and thickeners, providing texture and structural integrity to FDFs. These ingredients help to improve film homogeneity, prevent sedimentation or phase separation, and ensure uniform drug distribution throughout the formulation. By optimizing formulation rheology and flow properties, stabilizers and thickeners contribute to the overall quality and performance of FDFs, ensuring reproducible manufacturing processes and consistent product characteristics.[23] As mention in Table 1.

Methods of Manufacturing Fast-Dissolving Films

Manufacturing films is a diverse process that encompasses a wide range of types, including thin films, packaging films, and specialized pharmaceutical films like fast-dissolving films. The methods employed for manufacturing these films vary significantly based on the specific type of film being produced and its intended application. Here, we delve into a detailed exploration of some common methods used for manufacturing films:

Extrusion

Extrusion is a prevalent method utilized in film manufacturing, particularly for producing packaging films. This process involves feeding raw material, typically in the form of pellets or granules, into an extruder. Within the extruder, the material is melted and then forced through a die to form a continuous film. There are several variations of extrusion methods, including blown film extrusion and cast film extrusion. In blown film extrusion, the molten material is inflated into a bubble using air, which is then flattened to create a film. Cast film extrusion, on the other hand, involves cooling the molten material on a chilled roller to form a flat film. Both methods offer advantages in terms of efficiency and scalability.

Coating

Coating is a versatile method employed for manufacturing films by applying a thin layer of material onto a substrate. This technique is commonly used in the production of pharmaceutical films, where a drug solution or suspension is coated onto a substrate and then dried to form a thin film. The coating offers flexibility in terms of material selection and can be tailored to achieve specific properties such as controlled release or taste masking.

Solvent casting

Solvent casting is a method commonly used for manufacturing thin films, including pharmaceutical films like oral fast-dissolving films. This process involves dissolving the film-forming material in a solvent to create a solution, which is then spread onto a substrate. The solvent is subsequently evaporated, leaving behind a thin film. Solvent casting enables precise control over film thickness and uniformity and is suitable for producing films with delicate or heat-sensitive ingredients.

Compression molding

Compression molding is a technique used for producing thermoplastic films by placing a powdered material in a mold and applying pressure and heat to form a solid film. While less common than other methods, compression molding offers advantages in terms of material versatility and cost-effectiveness for certain applications.

Stretching

Stretching is a process employed to improve the mechanical properties of films by orienting the molecules in one or more directions. This method is commonly used for manufacturing packaging films like biaxially oriented polypropylene (BOPP) films, which exhibit enhanced strength, clarity, and barrier properties. Stretching can be achieved through various techniques such as tentering or sequential stretching, depending on the desired film properties.[24]

Objectives of FDFS Formulations

Current research endeavors to develop and characterize oro-soluble oral film formulations of selected drug candidates with the following key objectives:

Enhance patient compliance

By formulating drugs into oro-soluble oral films, the aim is to improve patient compliance by providing a convenient and user-friendly dosage form. Fast-dissolving films eliminate the need for swallowing tablets or capsules, catering to individuals who may have difficulty swallowing or prefer alternative administration methods. This approach encourages better adherence to prescribed medication regimens, ultimately enhancing treatment outcomes.

Mitigate first-pass metabolism

The development of oro-soluble oral films seeks to reduce the first-pass metabolism of drugs by delivering them directly into the bloodstream via the oral mucosa. By bypassing the liver's first-pass effect, the bioavailability of the drug can be significantly increased, leading to more efficient drug delivery and potentially lower doses required for therapeutic efficacy.

Minimize side effects

Oro-soluble oral films aim to optimize drug dosing to minimize potential side effects. By formulating drugs into fast-dissolving films, it may be possible to achieve more controlled and sustained drug release profiles, reducing the likelihood of adverse reactions associated with peak plasma concentrations. Additionally, by enhancing bioavailability and targeting specific absorption sites, lower doses of the drug may be sufficient to achieve therapeutic effects, thereby reducing the risk of side effects.

Augment oral bioavailability

The formulation of drugs into oro-soluble oral films is geared towards enhancing the oral bioavailability of the active pharmaceutical ingredient (API). By utilizing innovative formulation techniques and excipients, researchers aim to improve the solubility and permeability of the drug, facilitating its absorption through the oral mucosa and into the systemic circulation. This approach can lead to more predictable and consistent drug absorption kinetics, ultimately optimizing therapeutic outcomes.[25]

Enhance onset of action

Oro-soluble oral films offer the potential to enhance the onset of action of drugs by facilitating rapid absorption and onset of therapeutic effects. The quick dissolution of the film upon contact with saliva enables the rapid release and absorption of the drug molecules through the oral mucosa, bypassing the gastrointestinal tract and potentially reducing the onset time compared to traditional dosage forms. This can be particularly advantageous for medications requiring fast relief, such as analgesics or antiemetics.

Improve convenience and portability

Oro-soluble oral films are designed to offer convenience and portability to patients, allowing for discreet and hassle-free administration without the need for water or additional accessories. The compact and easily transportable nature of the films makes them suitable for use in various settings, including on-the-go or during travel, thereby enhancing patient convenience and compliance.

Enable tailored dosing

The flexibility of oro-soluble oral films allows for precise dosing adjustments to meet individual patient needs. By formulating drugs into films, researchers can tailor the dosage strength and composition to optimize therapeutic efficacy while minimizing the risk of under- or overdosing. This personalized approach to dosing enhances patient safety and ensures optimal treatment outcomes.[26]

Evaluation of Fast-Dissolving Films

- Test approval
- Mechanical properties
    - Thickness
    - *Drying Test/Adhesion Test*
- Transparency
- Contact Angle
- Content/Content Uniformity
- Disintegration Time
- In Vitro Dissolution Test

Evaluation Test

Products undergo evaluation through meticulously controlled human taste panels to assess their palatability and sensory characteristics. In this process, in vitro methods employing taste test products are employed, providing a robust platform for taste analysis targeted at oral membranes. These in vitro taste testing equipment and methodologies are ideally tailored for high-throughput taste assessment, ensuring efficient and accurate evaluation of product taste profiles without the need for extensive human intervention. By leveraging these innovative techniques, researchers can gain valuable insights into the taste properties of oral formulations, facilitating the development of palatable and consumer-friendly products that enhance patient acceptance and adherence.[27]

Mechanical Properties

Thickness

Spiral micrometers serve as invaluable tools for measuring tape thickness at crucial points, ensuring consistency and uniformity throughout the film. This meticulous measurement process is pivotal in maintaining precise control over film thickness, as it directly correlates with the dosage exposure in the strip. By meticulously assessing thickness at various critical points, manufacturers can guarantee uniform distribution of active ingredients, enhancing dosage accuracy and therapeutic efficacy. Consequently, the use of spiral micrometers plays a pivotal role in quality assurance protocols, safeguarding product integrity and patient safety in the production of fast-dissolving films.[28]

Dryness test/adhesion test

The adhesion strength of a fast-dissolving film to an auxiliary surface, such as a piece of paper, upon being pressed into contact with the film, is termed adhesion. This crucial property measures the ability of the film to adhere firmly to the auxiliary surface, reflecting its cohesion and integrity. High adhesion strength ensures proper handling and administration of the film, preventing detachment or loss during storage, transportation, or use. Therefore, assessing adhesion is essential in evaluating the performance and reliability of fast-dissolving films, ensuring their efficacy and user-friendliness in pharmaceutical applications.

Clarity

The clarity of fast-dissolving films can be quantitatively assessed using a straightforward method involving a UV spectrophotometer. In this method, the film sample is prepared by cutting it into rectangles and placing it in the spectrophotometer cell. The spectrophotometer is then set to measure the transmittance of light through the film at a specific wavelength, typically 600 nm**.** By measuring the transmittance at this wavelength, the extent to which light passes through the film can be determined. Higher transmittance values indicate greater clarity, suggesting that the film is more transparent and free from impurities or defects that could obstruct light transmission. This simple and reliable method allows for objective evaluation of the clarity of fast-dissolving films, providing valuable insights into their visual quality and suitability for pharmaceutical applications.

Contact angle

A goniometer is employed to measure angles at room temperature, providing precise and accurate measurements of contact angles. In the context of fast-dissolving films, this instrument is utilized to assess the wettability of the film surface. The procedure involves pouring double-distilled water onto the dry film and capturing images of the resulting water droplets using a digital camera. Subsequently, specialized software such as Image 1.28v is employed to analyze these digital images. The software facilitates the measurement of contact angles formed between the water droplets and the surface of the film. By quantifying these contact angles, researchers can gain insights into the surface properties of the fast-dissolving film, including its hydrophilicity or hydrophobicity. This information is crucial for understanding how the film interacts with aqueous environments, which in turn influences its dissolution behavior and suitability for pharmaceutical applications. Overall, the use of a goniometer and digital imaging software enables precise characterization of the wetting behavior of fast-dissolving films, contributing to their development and optimization for various pharmaceutical formulations.[29]

Test/content uniformity

To verify the content of the active pharmaceutical ingredient (API) in fast-dissolving films, a test method described in the standard pharmacopeia for the specific API can be employed. This method typically involves estimating the quantity of the API present on each film line and determining the relevant content. The percentage difference between the measured content and the expected content should fall within the range of 85 to 115% to meet the pharmacopoeial standards for API content uniformity. This test ensures that the fast-dissolving films contain the specified amount of the API, guaranteeing consistency and reliability in dosage delivery. Any deviations from the specified range may indicate issues with formulation, manufacturing, or quality control processes, requiring further investigation and corrective measures to ensure product efficacy and safety.

Disintegration time

The Center for Drug Evaluation and Research (CDER) guidelines stipulate that the disintegration time of oral tablets should not exceed 30 seconds, ensuring rapid dissolution and absorption for efficient drug delivery. While these guidelines specifically pertain to tablets, they can serve as a valuable reference for assessing the disintegration time of fast-dissolving films during quality assurance (QA) or development processes. Fast-dissolving films are designed for swift administration, and their disintegration time typically falls within the range of 5 to 30 seconds. This rapid disintegration allows for quick dosing, making them an attractive option for patients who have difficulty swallowing tablets or liquids. During QA or development, monitoring the disintegration time of fast-dissolving films ensures adherence to performance standards and regulatory requirements. Any deviations from the expected disintegration time may indicate formulation issues, variability in manufacturing processes, or degradation of active ingredients. By comparing disintegration times against CDER guidelines for oral tablets, manufacturers can ensure the quality, efficacy, and patient acceptability of fast-dissolving films in pharmaceutical applications. Additionally, assessing the presence of antibiotic degradation products further enhances the understanding of film stability and integrity, contributing to overall product quality and safety.[30]

In-vitro dissolution test

In the Pharmacopoeia, dissolution testing for fast-dissolving films can be conducted using either basket or paddle attachments. The choice of dissolution medium is influenced by factors such as API solubility and maximum dosage. However, a common challenge arises when using the paddle apparatus, as the film strips may float on the dissolution medium, complicating separation and potentially compromising test accuracy. To address this, adjustments to the dissolution medium, pre-wetting techniques, and the use of sinkers can aid in submerging the strips effectively. Optimizing agitation parameters and considering specialized equipment can further enhance dissolution testing reliability. Overcoming these challenges ensures accurate assessment of fast-dissolving film dissolution, which is crucial for quality assurance and regulatory compliance in pharmaceutical manufacturing.[31]

Storage and Packaging of Films

Effective storage and packaging protocols are paramount to preserving the integrity and potency of FDFs, ensuring they maintain their quality throughout their shelf life. These meticulous procedures are fundamental for pharmaceutical manufacturers, guaranteeing that FDFs reach consumers in optimal condition, ready to deliver their therapeutic benefits reliably. At the core of storage and packaging considerations is the need to control environmental factors that could compromise the stability of FDFs. Temperature regulation is critical, with storage areas maintained within specified ranges typically between 15 and 25°C, safeguarding against extreme heat or cold, which could lead to degradation of the films or their constituents.[32] Humidity control is equally vital; excess moisture can trigger chemical reactions, jeopardizing the integrity of FDFs. Therefore, environments with controlled humidity levels are essential, protecting against moisture-induced degradation. Light exposure poses another significant risk to FDFs, particularly ultraviolet (UV) radiation, which can catalyze photochemical reactions, causing degradation of active ingredients and excipients. Hence, FDFs should be shielded from direct sunlight and artificial light sources and stored in opaque packaging materials designed to minimize light transmission. Moisture barrier properties are paramount in packaging materials to prevent moisture ingress, ensuring the films retain their structural integrity and drug content. Materials such as aluminum foil or laminated films provide effective moisture protection, minimizing the risk of degradation. Additionally, airtight packaging is crucial to limit exposure to oxygen, which can accelerate oxidation reactions, compromising the efficacy of FDFs. To prevent contamination, packaging materials must be sterile and free from impurities, safeguarding against microbial growth or chemical contamination. Tamper-evident seals and child-resistant closures enhance safety, preventing unauthorized access and ensuring product integrity. Proper labelling is essential for clear identification and user guidance, providing vital information such as product name, strength, dosage form, batch number, expiration date, and storage instructions. This facilitates accurate traceability and ensures compliance with regulatory requirements. During transportation and distribution, FDFs must be handled with care to avoid physical damage and maintain optimal storage conditions. Shipping containers should provide adequate insulation and protection against environmental fluctuations, safeguarding the integrity of the products until they reach their destination. By adhering to stringent storage and packaging protocols, pharmaceutical manufacturers can uphold the quality, stability, and efficacy of FDFs, ensuring they deliver consistent therapeutic benefits to patients while meeting regulatory standards and industry best practices.[33]

CONCLUSION

FDFs are a remarkable improvement in pharmaceutical dosage forms, providing unsurpassed ease and a quick beginning of action. This analysis delves into the complexities of FDFs, including formulation, production procedures, applications, problems, and future opportunities. To attain desired properties like as quick dissolution and flavour masking, FDFs must be carefully formulated using a variety of components. Manufacturing technologies such as solvent casting and hot melt extrusion offer versatile ways to efficiently make FDFs. FDFs have a wide range of therapeutic uses, with the potential for enhanced drug administration and patient compliance. Nonetheless, obstacles remain, including stability issues, bioavailability concerns, and regulatory barriers. Overcoming these problems necessitates ongoing research and development activities targeted at improving formulations and manufacturing methods while adhering to regulatory norms. Looking ahead, collaboration among researchers, pharmaceutical experts, and regulatory agencies will be critical in realizing FDFs' full potential and providing creative solutions to patients. This evaluation serves as a guiding beacon for future efforts to advance FDF technology, with the ultimate goal of improving patient outcomes and healthcare accessibility.

REFERENCES

1. Akhade B, Chatap V, Jain P, Bhat M. Design, Development and Characterization of Ropinirole Mouth Dissolving Film by using Spin Coating Technique. Int J Drug Deliv Technol. 2023;13(2):516–21. doi: 10.33263/BRIAC132.177.
2. Bidkar SJ, Rao MEB, Dama GY, Bidkar JS, Dighe AD. Design of Fast Dissolving Oral Film of Lamivudine using Ion Exchange Resins Indion 204, Tulsion 335 and Doshion P551. Int J Drug Deliv Technol. 2022;12(4):1774–82. doi: 10.3389/fphar.2021.618411.
3. Grilc, B.; Planinšek, O. Evaluation of Monolayer and Bilayer Buccal Films Containing Metoclopramide. *Pharmaceutics* **2024**, *16*, 354. https://doi.org/10.3390/pharmaceutics16030354
4. Hong TD, Edgington S, Ellis RH. Saturated salt solutions for humidity control and the survival of dry powder and oil formulations of Beauveria bassiana conidia Saturated salt solutions for humidity control and the survival of dry powder and oil formulations of Beauveria bassiana conidia. 2017;(June 2005).doi: 10.1016/j.jip.2005.03.007.
5. Thakare MM, Karole S. Formulation, Statistical Optimization and Stability Study of Ondansetron Films. Int J Pharm Qual Assur. 2022;13(4):377–84. doi: 10.25258/ijpqa.13.4.06.
6. Hariharan G, Shanmugamsundaram S, Narayanasamy D. Formulation and Ex-vivo Permeation Study of Tamoxifen Citrate Loaded Transfersomal Gel. Int J Pharm Qual Assur. 2022;13(4):354–7. doi: 10.25258/ijpqa.13.4.02.
7. Chotiyarnwong P, McCloskey EV, Harvey NC, Lorentzon M, Prieto-Alhambra D, Abrahamsen B, Adachi JD, Borgström F, Bruyere O, Carey JJ, Clark P, Cooper C, Curtis EM, Dennison E, Diaz-Curiel M, Dimai HP, Grigorie D, Hiligsmann M, Khashayar P, Lewiecki EM, Lips P, Lorenc RS, Ortolani S, Papaioannou A, Silverman S, Sosa M, Szulc P, Ward KA, Yoshimura N, Kanis JA. Is it time to consider population screening for fracture risk in postmenopausal women? A position paper from the International Osteoporosis Foundation Epidemiology/Quality of Life Working Group. Arch Osteoporos. 2022 Jun 28;17(1):87. doi: 10.1007/s11657-022-01117-6.
8. Sriram P, Suttee A, Marasakatla Z. Formulation and taste masking of metronidazole oral disintegrating tablets by a novel approach. Int J Pharm Qual Assur. 2020;11(3):399–403. doi: 10.25258/ijpqa.11.3.15.
9. Kawale KA, Neha B Autade, Narhare H s, Mhetrea RL. a Review on Fast-Dissolving Oral Film. Asian J Pharm Clin Res. 2023;16(10):7–17. doi: 10.22159/ajpcr.2023.v16i10.48099.
10. Pote AB, Zarad SB, Dalimbe A. , A Review On : Fast Dissolving Oral Thin Film, Int. J. in Pharm. Sci., 2023, Vol 1, Issue 12, 474-481. https://doi.org/10.5281/zenodo.10401691
11. Jain A, Ahirwar H, Tayal S, Mohanty P. FAST DISSOLVING ORAL FILMS: A TABULAR UPDATE. JDDT [Internet]. 14Jul.2018;8(4):10-9. Available from: https://jddtonline.info/index.php/jddt/article/view/1724
12. Irfan M, Rabel S, Bukhtar Q, Qadir MI, Jabeen F, Khan A. Orally disintegrating films: A modern expansion in drug delivery system. Saudi Pharm J. 2016 Sep;24(5):537-546. doi: 10.1016/j.jsps.2015.02.024.
13. Sharma D, Vishwakarma MDK, Mishra DJN. Comparative Study on Mouth Dissolving Film and Mouth Dissolving Tablet for Etoricoxib Drug. J Popul Ther Clin Pharmacol. 2023;30(4):741–53. doi: 10.53555/jptcp.v30i3.2846.
14. Avhad PS, Nikam SD, Chaudhari AA, Wagh S V., Rayjade MS, Gosavi PY. Review on: Recent advances in mouth dissolving film. Int J Pharm Chem Anal. 2023;9(4):163–8. doi: 10.18231/j.ijpca.2022.030.

15. Patil SD, Ambekar SS, Tadavi SA, Pawar SP., Review On Mouth Dissolving Film: The Advancement In Oral Drug Delivery, Int. J. of Pharm. Sci., 2024, Vol 2, Issue 3, 559-568. https://doi.org/10.5281/zenodo.10824195
16. B. Sontakke Patil S, Daswadkar DS. A Comprehensive Review: Natural Polymers Used for Fast Dissolving Mouth Film. Int J Pharm Sci Rev Res. 2020;65(2):14–21. doi: 10.47583/ijpsrr.2020.v65i02.003.
17. Chandramouli M, Shivalingappa RP, Basavanna V, Doddamani S, Shanthakumar DC, Nagarajaiah SR, et al. Oral Thin-films from Design to Delivery: A Pharmaceutical Viewpoint. Biointerface Res Appl Chem. 2023;13(2):1–23. doi: 10.33263/BRIAC132.177.
18. Alqahtani MS, Kazi M, Alsenaidy MA, Ahmad MZ. Advances in Oral Drug Delivery. 2021;12(February). doi: 10.3389/fphar.2021.618411.
19. Dangre, Pankaj & Phad, Ram & Surana, Sanjay & Chalikwar, Dr. Shailesh. (2019). Quality by Design (QbD) Assisted Fabrication of Fast Dissolving Buccal Film for Clonidine Hydrochloride: Exploring the Quality Attributes. Advances in Polymer Technology. 2019. 1-13. 10.1155/2019/3682402.
20. Brown CK, Friedel HD, Barker AR, Buhse LF, Keitel S, Cecil TL, et al. Meeting Report FIP / AAPS Joint Workshop Report : Dissolution / In Vitro Release Testing of Novel / Special Dosage Forms. 2011;12(2):782–94. doi: 10.1208/s12249-011-9634-x.
21. Abbas IK, Rajab NA, Hussein AA. Formulation and in-vitro evaluation of darifenacin hydrobromide as buccal films. Iraqi J Pharm Sci. 2019;28(2):83–94. doi: 10.31351/vol28iss2pp83-94.
22. Pengse Po1, Erin Delaney1, Howard Gamper2, Miklos Szanti-Kis3, Lee Speight3, LiWei Tu1, Andrey Kosolapov1, E. James Petersson3, Ya-Ming Hou2 and CD, Das C, Lucia MS HK and TJ. 乳鼠心肌提取 HHS Public Access. Physiol Behav. 2017;176(3):139–48. doi: 10.1016/j.jacc.2016.11.034.
23. Shen J, Liang X, Lei H. Hydrogen Bonding Study on the Solubilities of Metoprolol Succinate in Organic Solvents. 2018; doi: 10.3390/molecules23102469.
24. Cheng KL, Road R, City K. On Calibration of pH Meters. 2005;209–19.
25. Eugênio C, Teixeira F, Rebechi IDA, Fontaneli RS, Engenharia M, Ifsul M, et al. Digital Micrometer Used in Thickness Measurement of Plastic Film Compared to Standardized Instrument. 2017;577–83. doi: 10.4236/msa.2017.87040.
26. Quinten T, Andrews GP, Beer T De, Saerens L, Bouquet W, Jones DS, et al. Preparation and Evaluation of Sustained-Release Matrix Tablets Based on Metoprolol and an Acrylic Carrier Using Injection Moulding Preparation and Evaluation of Sustained-Release Matrix Tablets Based on Metoprolol and an Acrylic Carrier Using Injection Mo. 2012;(September). doi: 10.1208/s12249-012-9848-6.
27. Gonz O, Ramirez IO, Ramirez BI, Connell PO, Ballesteros MP, Jos J, et al. Drug Stability : ICH versus Accelerated Predictive Stability Studies. 2022,Oct 28;14(11):2324. doi: 10.3390/pharmaceutics14112324.
28. Junmahasathien T, Panraksa P, Protiarn P, Hormdee D, Noisombut R, Kantrong N, et al. Preparation and evaluation of metronidazole-loaded pectin films for potentially targeting a microbial infection associated with periodontal disease. Polymers (Basel). 2018;10(9). doi: 10.3390/polym10091021.
29. Mankar J, Biyani DD, Umekar DM. Oral Thin Film: Advanced Oral Dosage Form. Glob J Pharma Allied Sci. 2020;1(5):1–7. doi: 10.47583/gjfpas.2020.v01i05.001.
30. Dinge A, Nagarsenker M. Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity. AAPS PharmSciTech. 2008;9(2):349–56. doi: 10.1208/s12249-008-9047-7.
31. Papadopoulos DP, Papademetriou V. Metoprolol Succinate Combination in the Treatment of Hypertension. *Angiology*. 2009;60(5):608-613. doi:10.1177/0003319708326450
32. Basile JN. Systolic blood pressure. Br Med J. 2002;325(7370):917–8. doi: 10.1136/bmj.325.7370.917.
33. MS A, C V. Formulation and Evaluation of Fast Dissolving Oral Films of Diazepam. J Pharmacovigil. 2016;4(3). doi: 10.4172/2329-6887.1000210.