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Exploring the Potential of Fast Dissolving oral Film for the Dental Pain Management

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ABSTRACT

In order to improve clinical outcomes, dentists frequently prescribe analgesics since pain management is an essential component of dental practice. In the late 1970s, fast-dissolving medication delivery systems were created as an alternative to tablets, capsules, and syrups for elderly and paediatric patients who had trouble swallowing conventional oral solid dosage forms. They are a multifaceted platform that can offer systemic, local, or immediate solutions. FDF have become a newer method of oral medication administration since they are easier to use and more convenient than previous dosage forms such as buccal, sublingual, and oral disintegrating tablets. As a result, many pharmaceutical industries are becoming interested in FDF. These thin ODS films dissolve in the mouth in a matter of seconds without the need for chewing or water intake. The formulation of FDF will provide a number of difficulties, including API insolubility, API taste, stability problems, and dose consistency. Excellent formulas, superior manufacturing techniques, and optimal storage management can help overcome those obstacles.

FDF is produced in a number of ways, including hot melting extrusion, solvent casting, and other techniques. FDF is made with a number of components, such as plasticizer, saliva stimulants, surfactants, sweeteners, API, hydrophilic polymers, colouring and aromating agents.Examination of the film's mechanical characteristics, disintegration, and dissolution profile is done by authentication tests such the disintegration, dissolution, tensile strength, folding endurance, thickness, and Young's modulus tests. The current review gives an overview of the different formulation techniques and how they are evaluated when creating and using fast-dissolving films for dental pain relief.

KEYWORDS: Fast Dissolving Film, Inflammation, Hot Melt Extrusion method, Dental Pain, Polymer, NSAIDs,Stability Testing, FDA, Plasticizer.

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I. INTRODUCTION

Safe and efficient pain therapy is one of the primary areas of dental practice. One of the primary reasons people see dentists is to manage discomfort related to periodontal or dental disease [1]. Dental soreness is a normal side effect of oral health problems and the associated surgeries. In children, dental discomfort related to oral health problems is 33% common, whereas in adults, it is 25% common [2]. Surgery is commonly used to treat long-term oral health issues, including Root canal therapy (RCT), dental restorations,tooth extractions, and impacted wisdom tooth removal.

Even after the surgery, these intrusive procedures cause excruciating pain and inflammation for a considerable amount of time. In addition to the discomfort, the inflammation makes it difficult to do everyday tasks including speaking, laughing, swallowing, biting, and chewing. The impacted person's quality of life is negatively impacted by the long-lasting impacts. As a result, controlling post-operative pain and inflammation is extremely difficult. Opioids, NSAIDs, and steroids are used in the current therapy regimen to reduce dental procedure-related pain and edema.

Because of the severe adverse effects that come with using opioids and steroids, there are limitations to their use. These drugs are administered parenterally in some situations or orally. Pain occurs during parenteral delivery. Although immediate release tablets provide rapid relief among oral formulations, oral administration is challenging because of the significant inflammation that impairs mandibular joint movement. An effective NSAID administration technique that provides comparable symptomatic relief from pain and inflammation without putting undue strain on the mandibular joint or leading to major side effects including addiction or steroid-induced problems is needed. Because of the need for delivery methods that are tailored to meet the various needs in the treatment of various pain types, such as acute, chronic, sub-chronic, etc., research on pain management has increased throughout time [3].

Only standard pills, injectables, and solutions are included in the various marketed formulations. Severe inflammation is typically linked to dental operations like tooth extraction or root canal therapy. Patients may find it difficult to open their mouths enough to administer a traditional pill due to the discomfort. Because of its flexibility and thinness, a Fast-Dissolving Film (FDF) can be quite helpful in certain situations. An FDF is a more portable and convenient dose form, even when judged against an ODT. It will improve patient cooperation while providing prompt pain relief.Without putting undue strain on the mandibular joint, FDF would offer prompt pain alleviation. Compared to ODTs, it is also easier to carry and store [4,5].

Pharmaceutical technology started to advance in the early 1970s with the development of the Fast melting or Rapid release drug delivery systems. By dissolving quickly in mouth, or OFDFs, are innovative medication delivery methods that do not require chewing or water. There are several benefits of using fast-dissolving medication delivery methods over conventional oral dose forms. Buccal treatment has been more well-known and widely accepted in recent decades due to its enhanced accessibility, excellent blood supply, safety, patient compliance, and lack of a first pass effect. Additionally, the non-invasive delivery of drug active components commonly used in acute treatment is best suited for the buccal route[6].

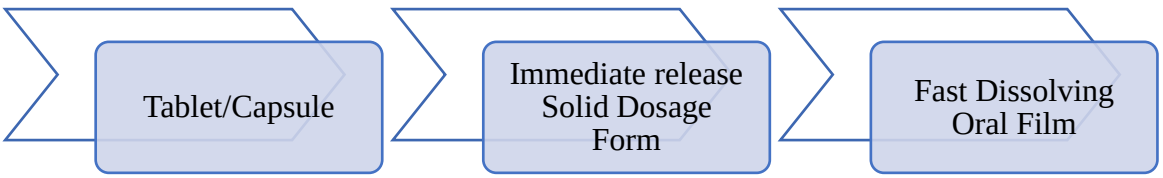

Figure 1. Bioavailability of Fast dissolving oral film.

Anatomical and physiological features of the oral cavity

Understanding the environment that is given for medication dispersion requires an understanding of the anatomy and structure of the mouth cavity. It consists of the floor of the mouth, lips, cheeks, hard palate, and soft palate (figure 2). There are two parts of the oral mouth cavity. The teeth, lips, cheeks, and gingival (gums) comprise the outer oral vestibule.Composed of the hard and soft palate, the roof of the oral moth cavity suitablespreads from the teeth and gums back to the

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fauces, which lead to the throat.Tongue extends to hollow floor[7]. Drugs can Circumvent hepatic first pass and enter the systemic circulation straight through the buccal mucosa. The oral moth cavity's epithelium is actualparallel to the skin's, with only minor variations in keratinization and the mucus that coats its surface for protection and lubrication[8].Typically, saliva has a pH between 6.0 and 7.5, although it can drop as low as ~5.5 in cases of oral, periodontal, and fungal ulcers[9].There is a four to a thousand times more permeability in the oral mucosa than in the skin. There are 170 cm^2 of surface area in the mouth cavity. Depending on the drug and carrier type, mucin, an extra barrier, can either improve or impair drug absorption[10]. Among all the methods that have been studied for the systemic distribution of drugs through various pharmaceutical products with various dosage forms, oral drug delivery has been the most widely utilized method of administration for many years [11].

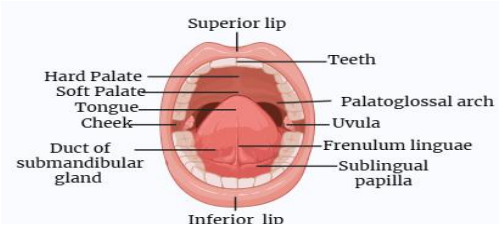

Figure 2. An illustration of the mouth cavity's anatomy and key components.

In order to ease a variety of pain symptoms, adults and elderly patients frequently turn to nonsteroidal anti-inflammatory medicines (NSAIDs). There are many different NSAIDs on the market, and because they are widely accessible and widely used by people, it is crucial to understand their pharmacology in order to utilize them safely and effectively. NSAIDs can be used as analgesics, antipyretics, and anti-inflammatory medications, according to FDA approval [12].

How NSAIDs works on dental pain management

Their main MOA is the inhibition of the COX enzyme by NSAIDs. Arachidonic acid must be converted by cyclooxygenase into prostacyclins, prostaglandins, and thromboxane. effectiveness of NSAIDs is believed to be due to the lack of these eicosanoids. Prostaglandins, in instance, Cause vasoexpansion, risein hypothalamus thermal level set-point, &help prevent nociception, whereas thromboxane promotes thrombocyte adhesion.

Two cyclooxygenase isoenzymes are COX-1 and COX-2. The body continuously expresses COX-1, which is important in maintenance of the lining of the gastrointestinal system, renal function, and platelet aggregation. However, COX-2 does not express itself constantly; it does so only follow an inflammatory reaction. A majority of non-selective NSAIDs block both COX-1 and COX-2 pathways. A unique side effect profile is provided by celecoxib and other COX-2 selective NSAIDs, which target COX-2 exclusively. These selective NSAIDs are believed to reduce inflammation without harming the gastric mucosa because COX-1 is essential for preserving the integrity of the stomach lining, whereas COX-2 is mainly engaged in inflammation. some analgesics are given in Table 1.

Opioid painkillers	Codeine, tramadol, oxycodone, and hydrocodone
Non-opioid pain relievers (NSAIDs)	Etodolac, diclofenac sodium , ketrol, piroxicam, meloxicam, mefenamic acid, nabumetone, indomethacin, sulindac, ibuprofen, naproxe, ketoprofen.
COX-2inhibitors	Celecoxib , Etoricoxib
Medication neuropathic pain	Duloxetine, pregabalin

Table 1. Analgesics used in dentistry [14]

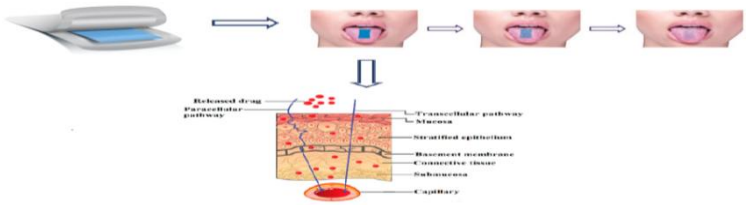

Figure 3. The breakdown and dissolution of fast dissolving film (FDF) are shown schematically. Natural swallowing of dissolved FDF with saliva allows it to enter capillaries through a transport mechanism.

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Advantages of oral film [15]

1) Administration simplicity for individuals with mental illness who are not cooperative.
2) Helpful in circumstances requiring a quick response.
3) Without the need for water or chewing, oral thin films typically melt or disintegrate inminute.
4) Saliva increases the bioavailability of several drugs by absorbing them from the mouth, pharynx,and oesophagus and then flowing down into the stomach.
5) Since it dissolves and disintegrates quickly, its wide surface area may provide better bioavailability for medications that are poorly soluble in water.
6) After ingestion, it leaves little to no residue in the mouth.

Limitations of fast dissolving oral films [16]

1) Limited drug loading capacity: The film's ability to contain a certain amount of medication is restricted.
2) Eating and drinking may become restricted.
3) Potential for inconsistent dosing: Variability in film thickness and drug distribution.
4) Potential for oral irritation: Localized irritation or allergic reactions.
5) Difficulty in incorporating multiple active ingredients: Compatibility issues.
6) This method is unable to deliver medications that cause irritation to the mucosa, have a disagreeable taste, or have an offensive odor.

CLASSIFICATION OF FDF[17]

Mainly 3 types of oral FDFs

- Instant release film.
- Mucoadhesive meltaway film.
- Mucoadhesive prolonged release film.

Property /sub /type	**Instant Release Film**	**Mucoadhesive Melt Away Film**	**Mucoadhesive Prolonged Release Film**
Area	2-8	2-7	2-4
Thickness	20-70	50-500	50-250
structure	One layer	One/more layers	one or more layers
Excipients	Hydrophilic soluble polymers	Hydrophilic soluble polymers	Non-soluble or low-Soluble polymers
Dissolution	60 s	It takes a few minutes for the gel to form.	Max. 8-10 h
Phase of drugs	Solid Solution	Particles of a suspended drug / solid solution	Suspension / solid solution
Location for activity	Local / systemic	Local or systemic	Local or systemic
Implement ation	Tonge	The buccal area or gingival layer	The gingival layer or another appropriate mouth cavity area

Table 2. Categorization of fast dissolving film

COMPOSITION OF THE FORMULATION

Active pharmaceutical ingredients (APIs)

The most important factors in choosing a medication candidate to formulate as an FDF are, first and foremost, drug solubility and permeability. For the drug formulation to work, the dose should be in mgs (fewer than 20 mg/day). The ideal candidates designed for inclusion in fast-dissolving films are strong medications. In addition to being crucial to the creation of FDF, taste also ensures end user compliance and acceptability. Other methods were also used to hide the bitter flavor.FDFs are medications that fall within BCS classes I, II, and III. It is challenging to put large doses of molecules into a film [18].

Qualitiesto choose drug

1. It need to have a pleasant flavor and miniaturized molecule andsmall mass compound.
2. Medication should infuse the oral mucous membrane.

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3. It must solvable and constant in saliva and water.
4. It needs to be partially dissociated at the pH of the oral cavity
5. API must less susceptible to environmental factors[19].

Plasticizers

It's a necessary component of oral films. Type of solvent used to cast the film and the plasticizer's compatibility with the polymer determine which one is best. The film becomes more flexible and less brittle as a result. Their weight percentage of dry polymer is between 1 and 20%. If plasticizer is used improperly, the film may peel, shatter, and split. Castor oil, glycerol, propylene glycol, low molecular weight polyethylene glycols [20].

Polymer

FDFs are primarily made of a hydrophilic or Water-miscible polymer materialthat acts as the film's foundation. Film forming polymer selection is one of the most vital and serious elements in the effective growth of film preparation. In, commonly used polymers are arranged by on their classification and FDF applications [21].

The following polymers should be utilized to formulate oral films

1.Needs enough tensile, peel, and shear strength.
2.Must not contribute to the development of subsequent oral mucosal infections.
3.It should be tasteless.
4.It should be readily available and inexpensive.
5.The disintegration time of the film shouldn't be prolonged

Category of polymers	Examples
Natural polymers	Sodium alginate, Chitosan, Pullulan, Gelatin Xanthan gum, Guar gum
Cellulosic Polymers	Hydroxyethyl cellulose (HEC) Methyl cellulose, Ethyl cellulose Microcrystalline cellulose Hydroxypropyl methylcellulose (HPMC)
Combination Polymers	Unification of HPC and HEC Combinations of PVP and HPMC HPMC and PVA combinations
Synthetic Polymers	PVA, or polyvinyl alcohol PVP, or polyvinylpyrrolidone PEG, or polyethylene glycol Polymers of the Eudragit® brand (such as Eudragit® E, RS, RL, S, and L) PVA, or polyvinyl acetate Copolymers of methacrylic acid (such as Eudragit® Eudragit® RS, RL, and RLPO)

Table 3. Various examples of polymers

Surfactants

The addition of surfactants could help the film dissolve quickly in the oral cavity and act as a wetting, dispersing, or solubilizing agent[22]. They improve the bioavailability of the API. Common examples of surfactants include tweens, spans, poloxamer 407.

Saliva stimulating agent

By increasing salivary flow, saliva-stimulating chemicals hasten the dissolution of films that dissolve quickly. Usually, dietary acids such as citric, Hydroxybutanedioic,lactic, vit.c, and wine acids are the source of these stimulants [23].

Sweetening agents

Unpleasant tastes in some medications may cause patients to stop taking them. In order to increase patient acceptance and compliance, sweeteners can be applied to cover up an unpleasant or bitter taste.of the medication by forming a barrier between the taste buds and the drug molecules. According to Regulatory Considerations, sweeteners must adhere to EU rules (Regulation (EC) No 1333/2008) on food additives and FDA standards (21 CFR 184) requiring their approval for use in pharmaceuticals. contrasted to table sugar and glucose or corn sugar, fructose's sourness is absorbed by the mouth more quickly. Aspartame, cyclamate, and saccharin are examples sweetening agents [24].

Colouring agents

For films that dissolve quickly, FD & C-

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approved coloring chemicals are utilized. Depending on the specific Color and application, approved Color concentrations typically fall between 0.01 to 5.0% w/w of the final product.

Examples of FDA-approved oral films with colours:
1. Zuplenz (Ondansetron) - Yellow
2. Nitro Mist (Nitro-glycerine) - Red

Flavoring agent

The quality of the Flavors that are noted in the first few minutes after ingestion&composition aftertaste, which lingers for at least ten minutes, determine whether or not a person approves an oral break down or dissolving formulation. The kind of medication that will be included in the formulation determines the Flavors choice. Flavors can be combined or used separately. FDA Regulation 21 CFR 101.22 (Food Labelling: Flavoring), EU Regulation (EC) No 1334/2008 (Flavoring's and Food Ingredients), and ICH Q6A (Guideline for Pharmaceutical Flavoring) are the regulatory guidelines for Flavoring agents.

Oral film-specific considerations
1. Flavour stability and release
2. Compatibility with film-forming polymers
3. Impact on film texture and mouthfeel
4. Masking unpleasant tastes (e.g., bitter, metallic)

Fast Dissolving Tablet	Fast Dissolving Oral Film
A tablet that releases the active component quickly by dissolving or disintegrating quickly in water, usually in a matter of seconds.	The active pharmaceutical component or ingredients are released for oral absorption through a thin, transparent, flexible film that dissolves quickly in saliva.
The greater the surface area, the greater the disintegration.	A smaller surface area results in less dissolution.
Tablets that dissolve quickly are the same size as regular tablets.	Thickness of FDFs ranges from 0.015 to.05 inches.
Compared to oral films, it is not as durable.	Possess a longer shelf life than a pill that dissolves orally.
When compared to oral film, patients are less compliant.	Patients are more inclined to take a medication that dissolves quickly.
It is possible to combine high doses.	Only little doses are allowed.
It was afraid of choking.	Choking is unlikely.

Table 4. A table comparing films and tablets [25].

METHODS OF PREPARATION

Solvent casting method

While the active pharmaceutical ingredient (API) and other excipients are dissolved in a suitable solvent, water-soluble polymers are dissolved in water in the solvent casting process. The liquid is heated to between 50°C and 60°C, swirled, and then poured into a Petri dish. It is then dried and cut into 2-by-2 pieces of uniform size [26].

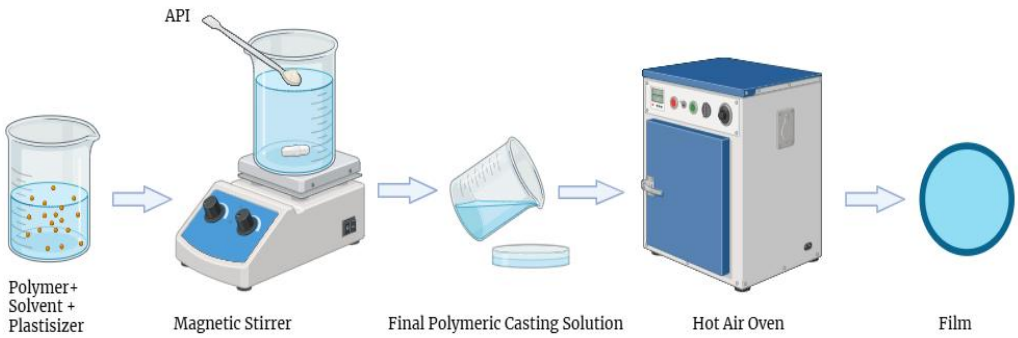

Figure 4. Solvent casting method.

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Hot melt extrusion method (HME)

To make a film, the HME process entails melting the polymer, adding the API, and then extruding the mixture via a die. This process of creation is ongoing [27,28] melting the plasticizer and polymer. combining the molten polymer with the API. Examining the Potential of Oral Film That Dissolves Quickly When creating an oral film, the spray drying procedure is used. extruding the mixture through a die to produce a thin layer. cooling the film and making it solid. slicing the film to the appropriate dimensions.

Printing Technology (PT)

The most recent approach is to prepare FDFs utilizing printing technology[29].Preparing a API solution in ink, choosing a substrate, jetting the drug-containing ink over the substrate, and then drying the printed FDF are the general procedures for creating FDFs. They can be made by printing onto a substrate using ink-jet or thermal ink-jet technology[30]. Although these technologies are often called 2D printing technologies, FDFs can also be made using 3D printing (3DP) techniques.

Rolling Method

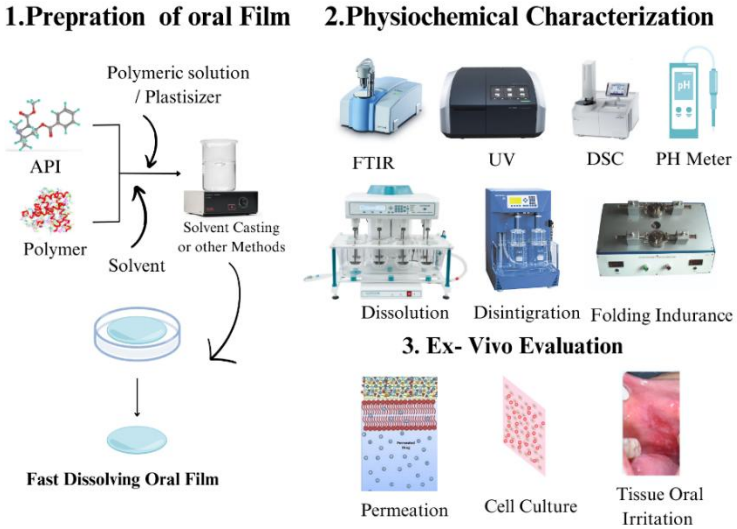
Following steps are taken for rolling method [31].

- Make a pre-mix using a polar solvent, a film-forming polymer, and additional ingredients (apart from a medication).
- Pour premix into the master batch feed tank.
- It was fed to either or both of the first and second mixers through a control valve and initial metering pumps.
- To the preferred mixer, add the necessary amount of medication.
- Blend the preparation with the mainset premix to get a reliablemedium.
- The pan is subsequently supplied with a predetermined quantity of homogeneous matrix via the second metering pumps. Finally, the support roller is used to force the film onto the substrate and remove it.
- Afterwards, the wet film is dried.

Solid Dispersion Extrusion

Anappropriate liquid solvent is used to dissolve the drug. The solution is mixed with polyethylene glycol that has been melted below 70°C. The final step is to shape the solid dispersions into the films using dies [32].

EVALUATION PARAMETERS



Organoleptic evaluation

Many pharmaceutical medicines must be identified by their colour, which is also crucial for consumer approval. Within a dose form, the product's colour must be consistent. The smell of oral films can be used to assess their quality because a batch's presence of an odor may indicate a stability problem. For oral dosage forms to be accepted by customers, odor is also essential. Taste is another important factor in customer approval. Taste preference is subjective, and the development of oral soluble films depends on whether a particular taste is present or absent [33].

Weigh variation of films

The typical weight of the films wasmeasured by weighing them using an analytical balance. The ideal weight of films should be almost

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equal. It is convenient to sanction that the precisequantity of excipients and API are present in a film [34].

Surface pH

First Prepared films were put into a petri plate for 20 seconds containing some distilled water, pH wasrecordedwith digital pH meter. Three results were averaged for each formulation [35].

Swelling index of film

This study set out to determine how well the selected polymer absorbed water or how hydrated it was for use in filmmaking. 10 ml of 6.8 pH PBS were combined through pre-weighed formulations in petri plates. Water absorption and patch swelling caused weight changes that were recorded at regular intervals over a period of six hours.

DS (%) = ((Ww - Wd) / Wd) × 100

Where; Ww = Weight ofthe swollen film, Wd = Weight of the dry film[36].

Thickness of film

Five measurements of the film's thickness were made with a micrometre screw gauge, and the average of the three measurements was calculated. The homogeneity of the FDFs which is straightcorrelated to the film's dosing accuracy[37].

Folding endurance

It can be done by prepared films are folded number of times repeatedlyon same place until it broke[38].

In vitro disintegration

After adding 10 ml of water, the 4.15 cm2 film (unit dose) was placed in a petri plate. Keep track of how long it takes for film to break [39].

Percentage elongation

Strain is the term for the stretching that occurs when a sample is subjected to stress; typically, the film elongates in proportion to the plasticizer concentration. The elongation percentage is calculated using the formula below, which quantifies increase in film length once tensile strength is measured [40].

Elongation as a Percentage = [L-L0] ×100/L0

Where; L0 was the starting length, while L was the final length

Strength

It can be measured of a strip specimen is the greatest strain placed on it before it breaks. Determining the formulation strength and flexibility is the goal of the tensile testerand it can be measured by following formula [41].

TS = F / A

Where: F = Breaking Force, A = Cross-Sectional Area

Transparency

It is conceivable to measure the transparency of the films using UV spectrophotometers. Formerly being located into the spectrophotometer cell, the film samples were divided into rectangular pieces. The films' transmittance at 600 nm was determined. To assess the transparency of the films, the following methodology was employed:

$Transparency$ = ($logT600$) /b = – €c ($logT600$)

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

In vitro dissolution studies

Using USP basket type dissolution apparatus in 600 ml of PBS at6.8 pH (artificial saliva solution) as media, while maintaining temperature of 37 ± 2°C. The film that had been created was placed inside the tester. Then every five minute, five ml of the sample was extracted and same medium is substitutedeach time for adjusting volume of medium. A spectrophotometer from the Shimadzu UV-1800 series was used for evaluation [42].

Ex-vivo diffusion study

For in vitro release tests, pbs (pH 6.8) is utilized as the medium and barrier membrane made of goat buccal mucosa is employed. Franz diffusion cell is used for drug release. A buccal mucosa membrane separates the donor and receptor compartments. The film is placed on the mucosal membrane. Diffusion cell temperature in saliva simulation is maintained at 37±2°C. To maintain the hydrodynamic conditions, 50 mL of pbs (pH 6.8) is placed in the receptor chamber and stirred at 50 rpm using a magnetic bead. To keep the sink condition, 1 ml of the sample is taken out and exchanged with one milliliter of new medium.Samples are examined at a certain wavelength using UV spectrophotometer[43].

Stability testing

In accordance with ICH requirements, oral strips are stored in a stability chamber for 12 months at controlled temperatures of 40°/75% & 25ºC/60% RH in order to measure stability. During

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storage, a number of assessment factors are looked at, including thickness, morphological traits, tensile strength, water content, and dissolving Behavior [44].

QUALITY BY DESIGN PRINCIPLES IN DEVELOPMENT OF FDF

A methodical approach to product development is called Pharmaceutical QbD. ICH standards define it as a systematic strategy to expansion that starts with desired outcomes and places a powerful importance on process control and understanding of both the product and the development. It is predicated on sound risk management and science.Determining the product's CQAsand QTPPis typically the first step. After determining developmentconstraints (CMAs and CPPs, singly) through risk assessment in line with ICH Q9, it creates a control plan that integrates novelty and continuous upgrading across the product's life cycle and conducts designs experiments (DOEs) to regulate design space [45]. It is the first and most crucial stage in the QbD process to determine the QTPP, which is basically a projected overview of the ideally feasible quality features of safe and effective FDFs, as per the ICH Q8 criteria. This prospective summary is created using input from both external (physician, pharmacist, and patient) and internal (a pharmaceutical company's manufacturer, regulator, quality assurance, and formulator) sources. A general graphical depiction of customer voice that includes customer types and expectations together with QTPP for FDFs is shown in Table No: 5

QTPP Component	Goal	CQAs	Explanation
Nature	Fast dissolving Film	-	-
Design of dosage Form	Immediate Release	-	-
Route of Delivery	Oral	-	-
Formulation Strength	% w/w	-	-
Drug product quality attributes	Appearance	-	**Note:** There is no formal compendia limit, thus the values must correspond to the relevant reference standard and/or published values in the literature. **Dimension:** It must fit into the mouth cavity and be of a size that is appropriate. **Peel adhesion:** Film must be smoothly removed. **Assay:** To ensure that the medication produces the intended therapeutic effect. **Disintegration:** Rapid disintegration makes it easier to get patient cooperation. If the quick breakdown fails, the person will either spit or choke. **Dissolution:** Aids in comprehending the medication release profile in order to demonstrate the desired therapeutic outcome.
	Disintegration time	Yes	
	Peel adhesion	Yes	
	Uniformity of content	Yes	
	Dimensions	Yes	
	Water content	Yes	
	Assay	Yes	
	Tensile strength	Yes	
Primary packaging	Compatibility is a must.	Yes	Plastic packaging and an aluminium sachet are used to shield against light, moisture, and microbiological destruction.
Pharmacokinetics Profile (ADME)	Bioequivalence is required.	Yes	Plasma protein binding, Vd, main metabolite, half-life of elimination, Cmax, Tmax, and

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			AUC
Storage, stability Distribution and shelf life	Shelf life needs to be high.	Yes	Stable in the face of light, moisture from the atmosphere, and microbes.
Patient compliance and acceptance	Aid in obtaining cooperation and acceptance so that pharmacotherapy Do not SPIT the ODF.	Yes	To be accepted, taste must be disguised. Dysphagia patients may benefit from this. Avoid chewing the FDF. Since it requires no water to ingest, it may be taken on the move. delivered directly to the tongue, where it quickly dissolves.

Table 5. Quality Target Product Profile of FDF

REGULATORY AND CLINICAL ASPECTS

If a product is therapeutically equivalent to an existing oral drug, the USFDAwill employ the ANDA process. Clinical investigations are not related to this generic approval process (Food, Drug, and Cosmetic Act, section 505(j)). A comparative bioequivalence between an oral fast-dissolving film (OFDF) product and an oral disintegrating tablet (ODT) formulation would be an illustration of such a situation.

However, film pharmacokinetic profile may not be the same as the one that is currently on the market. Since the OFDF is classified as a "new dosage form," the approval procedure outlined in section 505(b)(2) must be followed. A fresh clinical investigation would be necessary in this situation. One benefit of the new clinical research is that it gives the product exclusive marketing rights for three years. According to the guidelines established by the European Medicine Evaluation Agency, marketing authorization clearance is crucial in Europe. One of two approaches the mutual recognition process or the decentralization process can be used. Product approval in Japan is the responsibility of the Ministry of Health, Labor, and Welfare.

Taste and palatability are given particular weight by many regulatory bodies, particularly when a product is meant for a younger audience. Testing for oral mucosal irritation is done on people and animal models. The best model for animal research is the hamster cheek pouch because it can precisely estimate the level of discomfort needed prior to human testing. The clinical endpoint is important in clinical trials. It is important to highlight both primary and secondary outcome measures. The goal is to show how the recently created OS is better and more advantageous than the current conventional dose forms.

The ICH has created guidelines for the creation of new products. ICH Q8 guideline on pharmaceutical development allows companies to selectbetween additionalorderlymethod to product development and an empirical one. This paper is an essential component of the regulations for Japan, the EU, and the USA. A clear objective should be specified in the clinical trial protocol; Investigating various issues should be done in distinct, well-defined methods. The intended investigation should have enough resolved power to identify and explain serious negative health effects. The type of examination (e.g., impacts on soft tissues) determines the size of the study or sizes. Specifications should be developed for each endpoint. If there are one or more applications, describe the usage pattern or patterns. After treatment, it is appropriate to bring up follow-up at a pertinent moment (e.g., follow-up intervals of one, three, six, and twelve months, or several applications with extended follow-up).

Confounders and outcomeschangers should be mentioned, together withaccount of the methodology, collectionnorms,& subject source or sources, all of which should contain relevant analytical information. Compared to traditional dose forms, the therapeutic impact and medicine bioavailability may diverge significantly because to the changed drug dissolving properties. The clinical profile may be altered by the first-pass impact, which is mostly avoided by this non-invasive administration technique.

If the medicine is mostly absorbed by the buccal mucosa, the reduction of noxious metabolites consequential from hepatic metabolism

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can boost safety features. Its quicker commencement of action, which results in quicker clinical end-point indicators, is another feature. Each strip should ideally contain particular dosage quantitiesof dose, and the dosage form is not impacted by the physiological unpredictability of theGIT, therefore intersubject unpredictability in scientificfeedback is noticeably contracted. Possibility of dosage dumping exists, however the ingestion of medications over the mouth oral mucosa would happen far more quickly than with their conventional counterparts, which must first break down and then solubilize the active ingredient. Research on its clinical implications is necessary. It is important to frequently monitor the safety aspects of the dose form because of this rapid reaction characteristic[46].

PACKAGING OF FAST DISSOLVING FILM

The pharmaceutical sector depends on packaging to preserve the product's authenticity. Additional care during production and storage, specific processing, and expensive packaging are required to maintain the dosage of other FDF forms. There are several packing options for films that dissolve quickly. Films, which are pharmaceuticals, must be packaged in a single container; aluminium pouches are the most popular type. For the Rapid films, APR-Labtech developed a special and proprietary packaging solution called the Rapid card. Similar in size to a credit card, the fast card has the capacity to hold three raid videos on each side. Separate removal of each dose is possible[47].

The following qualities must be present in the chosen material:

- They have to shield the preparation from the elements.
- They need FDA approval.
- They have to fulfil the relevant tamper-resistant requirements.
- They must not be harmful.
- They shouldn't react negatively to the merchandise.
- They must not add Flavors or smells to the product.

MARKETED PRODUCT OF FDF

There are several marketed products of fast dissolving films (FDFs) available in the market. Here are a few examples:

Drug	Dosage Form	Disease	References
Telmisartan	Fast Dissolving Film	Hypertension	[48]
Rizatriptan	Oral Disintegrating Film	Migraine headaches	[49]
Caffeine	Fast Dissolving Film	CNS stimulant	[50]
Cetirizine and dextromethorphan	Fast Dissolving Film	Allergic asthma and throat infection	[51]
Propranolol HCL	Sublingual film	Hypertension, migraine prophylaxis	[52]
Dicyclomine	Fast Dissolving Film	Stomach pain, muscle spasm.	[53]
Tramadol hydrochloride	Orally disintegrating film	Pain	[54]

Table: 6 Marketed product of Fast dissolving Films.

II. CONCLUSION

According to this evaluation, it is now crucial for formulators to simultaneously bring forth innovation and satisfy customers in the current environment. Therefore, OFDs have thus been recognized as one of the novel and promising approaches for enhancing patient compliance and maximizing the medication's therapeutic efficacy. Additionally, it is a pharmaceutical dosage form that is patient-centric and falls under the category of customized medications with particular attributes. Because they are portable and do not

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require water to swallow or ingest, they offer enormous potential to increase patient compliance in groups with special needs. When FDFs are applied to the tongue, the active pharmaceutical ingredient is released instantly. This ingredient can either be eaten with saliva or, in the presence of permeation enhancers, can pass through the buccal mucosa to increase bioavailability. They are among the best options for patients with needle fear in general, paediatrics in particular, and specific patient populations in general. The caregiver can administer straight to the patient's tongue in cases where the patient has particular needs and is unable to administer themselves.

FDFs can be produced using a variety of fabrication techniques, the most widely used and widely accepted of which being solvent casting. Although the HME method is also used, it should be used with caution when handling medications that are heat sensitive. Under the right regulatory guidance, which is currently lacking, ODFs could be created in a pharmacy using contemporary printing methods like additive manufacturing, inkjet printing and 3DP. There are even more options for producing personalized dose forms when printing procedures are used. On the other hand, FDFs are ideal for administering potent drugs in little amounts, as those used to treat diseases of the central nervous system and post-operative dental pain.

REFERENCES

[1]. Kim SJ, Seo JT. Selection of analgesics for the management of acute and postoperative dental pain: a mini-review. Journal of Periodontal & Implant Science.2020Apr;50(2):68.doi: 10.5051/jpis.2020.50.2.68

[2]. Peres MA, Macpherson LM, Weyant RJ, Daly B, Venturelli R, Mathur MR, Listl S, Celeste RK, Guarnizo-Herreño CC, Kearns C, Benzian H. Oral diseases: a global public health challenge. The Lancet. 2019 Jul 20;394(10194):249-60.

[3]. Phadke A, Amin P. A recent update on drug delivery systems for pain management. Journal of Pain & Palliative Care Pharmacotherapy. 2021 Jul 3;35(3):175214.doi.org/10.1080/15360288.2021.1925386

[4]. Jani R, Patel D. Hot melt extrusion: An industrially feasible approach for casting Orodispersible film. Asian journal of pharmaceutical sciences. 2015 Jul 1;10(4):292305.https://doi.org/10.1016/j.ajps.2015.03.002

[5]. Sinha S, Dutt R. Oral soluble films: attributes of the polymeric material and critical process parameters for designing good quality films. Current Applied Polymer Science. 2020;3: 167-88.DOI: 10.2174/2452271603666191210121944

[6]. Paul D, Ray P. Exploring the potential of fast dissolving oral films. Current Trends in Pharmaceutical Research. 2023;10(2).

[7]. Mishra S, Kumar G, Kothiyal P. A review article: Recent advances in buccal patches.2012;1(7):78-82DOI: 10.52711/0974-360X.2022.00930

[8]. Frenkel ES, Ribbeck K. Salivary mucins in host defense and disease prevention. Journal of oral microbiology. 2015 Jan 1;7(1):29759.https://doi.org/10.3402/jom.v7.29759

[9]. Aframian DJ, Davidowitz T, Benoliel R. The distribution of oral mucosal pH values in healthy saliva secretors. Oral diseases. 2006Jul;12(4):4203. https://doi.org/10.1111/j.1601-0825.2005.01217.x

[10]. Patel VF, Liu F, Brown MB. Advances in oral transmucosal drug delivery. Journal of controlled release. 2011 Jul 30;153(2):106-16.https://doi.org/10.1016/j.jconrel.2011.01.027

[11]. Gandhi SD, Pandya PR, Umbarkar R, Tambawala T, Shah MA. Mucoadhesive drug delivery systems-An unusual maneuver for site specific drug delivery system. Int J Pharm Sci. 2011 Jul;2(3):132-52.

[12]. Phillips WJ, Currier BL. Analgesic pharmacology: II. Specific analgesics. JAAOS-Journal of the American Academy of Orthopaedic Surgeons. 2004 Jul 1;12(4):221-33.

[13]. Chaiamnuay S, Allison JJ, Curtis JR. Risks versus benefits of cyclooxygenase-2-selective nonsteroidal anti-inflammatory drugs. American journal of health-system pharmacy. 2006 Oct 1;63(19):1837-51.https://doi.org/10.2146/ajhp050519

[14]. Kim SJ, Seo JT. Selection of analgesics for the management of acute and postoperative

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dental pain: a mini-review. Journal of Periodontal & Implant Science.2020Apr;50(2):68.https://doi.org/10.5051/jpis.2020.50.2.68

[15]. Meher A, Dighe NS. An overview of fast dissolving oral film. Journal of Drug delivery and Therapeutics. 2019 Aug 29;9(4-s):822-5. http://dx.doi.org/10.22270/jddt.v9i4-s.3428

[16]. Patil BS, Tate SS, Kulkarni U, Hari Prasanna RC, Wadageri GV. Development and in-vitro evaluation of mucoadhesive buccal tablets of Tizanidine hydrochloride using natural polymer xanthan gum. Int J Pharm Sci. 2011;8(2):140-6.

[17]. Meher A, Dighe NS. An overview of fast dissolving oral film. Journal of Drug delivery and Therapeutics. 2019 Aug 29;9(4-s):822-5.

[18]. Shinde P, Salunkhe V, Magdum C. Buccal film: An Innovative Dosage form designed to improve patient compliance. IJPCS. 2012;1(4):1262-78.

[19]. Alsofany JM, Hamza MY, Abdelbary AA. Fabrication of nanosuspension directly loaded fast-dissolving films for enhanced oral bioavailability of Olmesartan medoxomil: in vitro characterization and pharmacokinetic evaluation in healthy human volunteers. AAPS Pharm SciTech. 2018 Jul;19: 2118-32.DOI https://doi.org/10.1208/s12249-018-1015-2

[20]. Arunachalam A, Karthikeyan M, Kumar SA, Konam K, Prasad PH, Sethuraman S, Manidipa S. Fast dissolving drug delivery system: A review. Journal of global trends in pharmaceutical sciences. 2010 Oct;1(1):92-110.

[21]. Nagansurkar SB, Bais SK, Khilare SK. Review on polymers used in oral dissolving film. International journal of pharmacy and herbal technology. 2023; 1:132-42.

[22]. Mundhe B, Kadam V, Jadhav S. A short review on fast dissolving oral film. World Journal of Pharmacy and Pharmaceutical Sciences. 2014;3(3):463-75.

[23]. Nagendra R, Sheetal P, Nanditha VV, Venkatesh K. Oral Disintegrating Film: A Review. DOI:10.5281/zenodo.10640441

[24]. Nautiyal U, Saini M. Fast dissolving Buccal film: A comprehensive Review. Asian Pacific Journal of Nursing and Health Sciences. 2023 Jul 20;6(1):11-22.

[25]. Heer D, Aggarwal G, Kumar SH. Recent trends of fast dissolving drug delivery system-an overview of formulation technology. Pharmacophore. 2013;4(1-2013):1-9.

[26]. Ghodake PP, Karande KM, Osmani RA, Bhosale RR, Harkare BR, Kale BB. Mouth dissolving films: Innovative vehicle for oral drug delivery. polymer. 2013; 9:20.

[27]. Speer I, Preis M, Breitkreutz J. Prolonged drug release properties for Orodispersible films by combining hot-melt extrusion and solvent casting methods. Eur J Pharm Biopharm. 2018; 129:66–73. 39.https://doi.org/10.1016/j.ejpb.2018.05.023

[28]. Jain A, Ahirwar HC, Tayal S, Mohanty PK. Fast dissolving oral films: a tabular update. Journal of Drug Delivery and Therapeutics. 2018 Jul 14;8(4): 10-9.DOI: http://dx.doi.org/10.22270/jddt.v8i4.1724

[29]. Alomari M, Mohamed FH, Basit AW, Gaisford S. Personalised dosing: Printing a dose of one's own medicine. International journal of pharmaceutics. 2015Oct30;494(2):56877.https://doi.org/10.1016/j.ijpharm.2014.12.006

[30]. Buanz AB, Saunders MH, Basit AW, Gaisford S. Preparation of personalized-dose salbutamol sulphate oral films with thermal ink-jet printing. Pharmaceutical research. 2011 Oct; 28:2386-92.https://doi.org/10.1007/s11095-011-0450-5

[31]. Mundhe B, Kadam V, Jadhav S. A short review on fast dissolving oral film. World Journal of Pharmacy and Pharmaceutical Sciences. 2014;3(3):463-75.

[32]. Singh SG, Singh RP, Gupta SK, Kalyanwat R, Yadav S. Buccal mucosa as a route for drug delivery: mechanism, design and evaluation. Research journal of Pharmaceutical, Biological and chemical sciences. 2011;2(3):358-72.

[33]. Malke S, Shidhaye S, Kadam VJ. Formulation and Evaluation of Oxcarbazepine Fast Dissolve Tablets. Indian journal of pharmaceutical sciences. 2007 Mar 1;69(2).

[34]. Nair AB, Kumria R, Harsha S, Attimarad M, Al-Dhubiab BE, Alhaider IA. In vitro techniques to evaluate buccal films. Journal of Controlled Release. 2013 Feb 28;166(1):10-21.https://doi.org/10.1016/j.jconrel.2012.11.019

[35]. John AS, Sathesh BP, Divakar G, Jangid MK, Purohit KK. Development and evaluation of Bucco adhesive drug delivery system for Atorvastatin calcium. journal of current pharmaceutical research. 2010; 1:31-8.

[36]. Bose A, Abraham S, Steffy PR, Ullas N, Pillai CS, Abraham E, Mohanty D. Formulation and evaluation of sitagliptin buccal patch. Research Journal of Pharmacy and Technology. 2020;13(10):4883-7. Available from: Doi:10.5958/0974-360X.2020.00859.8

[37]. Verma N, Ghosh AK, Chattopadhyay P. Preparation and in vitro assessment of mucoadhesive buccal patches containing Carvedilol. Int. J of Pharmacy and Pharmaceutical Sciences. 2011;3(3):218-20.

[38]. Alam M, Tasneem F, Pathan MS. Formulation and evaluation of swellable oral thin film of metoclopramide hydrochloride. Bangladesh Pharmaceutical Journal. 2014;17(1): 102-12.DOI: https://doi.org/10.3329/bpj.v17i1.22325

[39]. Dinge A, Nagarsenker M. Formulation and evaluation of fast dissolving films for delivery of triclosan to the oral cavity. Aaps Pharmscitech. 2008 Jun;9: 349-56.DOIhttps://doi.org/10.1208/s12249-008-9047-7

[40]. Nishimura M, Matsuura K, Tsukioka T, Yamashita H, Inagaki N, Sugiyama T, Itoh Y. In vitro and in vivo characteristics of prochlorperazine oral disintegrating film. International journal of pharmaceutics. 2009 Feb 23;368(1-2): 98-102.DOI: 10.1016/j.ijpharm.2008.10.002

[41]. Costa P, Lobo JM. Modelling and comparison of dissolution profiles. European journal of pharmaceutical sciences. 2001 May 1;13(2):123-33.https://doi.org/10.1016/S0928-0987(01)00095-1

[42]. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: an innovative drug delivery system and dosage form. International Journal of Chemtech Research. 2010 Jan 1;2(1):576-83.

[43]. Kshirasagar NA, Thamada NA, Naik VN, GOPAL MS. Design and evaluation of chitosan containing mucoadhesive buccal patch of Fluoxetine HCL. Int J Sci Res. 2012; 2:1-5.

[44]. Arya A, Chandra A, Sharma V, Pathak K. Fast dissolving oral films: an innovative drug delivery system and dosage form. Int J ChemTech Res. 2010; 2:576-83.

[45]. International Conference on Harmonization. Q8 ICH. International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. ICH Harmonised Tripartite Q8 (R2) Guideline: Pharmaceutical Development. Geneva, Switzerland: ICH; 2009. Guideline.pdf, Accessed on 9 th April 2021. https://doi.org/10.1016/B978-0-12-822211-9.00008-3.

[46]. Mahaveer Singh and Hemant R. Jadhav: "Fast Dissolving Oral Films', book chapter in 'Current Advances in Drug Delivery Through Fast Dissolving/Disintegrating Dosage Forms', Edited by Prof. Vikas A Saharan, Bentham Science, 318-356. (2017)

[47]. Rowe RC, Forse SF. The effect of polymer molecular weight on the incidence of film cracking and splitting on film coated tablets. Journal of Pharmacy and Pharmacology. 1980 Sep;32(1):583-4. https://doi.org/10.1111/j.2042-7158.1980.tb13003.x

[48]. Tomar A, Sharma K, Chauhan NS, Mittal A, Bajaj U. Formulation and evaluation of fast dissolving oral film of dicyclomine as potential route of buccal delivery. Int J Drug Dev Res 2012; 4:402.

[49]. Nautiyal U, Saini M. Fast dissolving Buccal film: A comprehensive Review. Asian Pacific Journal of Nursing and Health Sciences. 2023 Jul 20;6(1):11-22.

[50]. Bala R, Pawar P, Khanna S, Arora S. Orally dissolving strips: A new approach to oral drug delivery system. International journal of pharmaceutical investigation. 2013 Apr;3(2):67. Doi: 10.4103/2230-973X.114897

[51]. VS L, MENON RB, RAJU K, MU A, NAIR SC. Formulation and evaluation of lorazepam encapsulated collagen/pectin buccal patch. Int J App Pharm. 2019;11(5): 200-9.DOI: http://dx.doi.org/10.22159/ijap.2019v11i5.34366

[52]. Kathpalia H, Sule B, Gupte A. Development and evaluation of orally disintegrating film of tramadol hydrochloride. Asian J Biomed Pharm Sci 2013; 3:27-32.

[53]. Deepthi A, Reddy BV, Navaneetha K. Formulation and evaluation of fast

dissolving oral films of zolmitriptan. American journal of advanced drug delivery. 2014;2(2):153-63.

[54]. Singh H, Kaur M, Verma H. Optimization and evaluation of desloratadine oral strip: an innovation in paediatric medication. The Scientific World Journal. 2013;2013(1):395681. http://dx.doi.org/10.1155/2013/395681