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A Comprehensive review on Fast Mouth Dissolving Film as Novel Drug Delivery System

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Abstract

Fast mouth dissolving films are solid dose kind, that dissolve or disintegrate at intervals few seconds once placed in mouth while not manuduction or potable. To eliminate patients, worry of chocking and to beat patient's impediments, fast dissolving films gaining interest as an alternate to quick dissolving tablets. The quick dissolving thin film has emerged as a complicated various to the standard tablets, capsules and liquids typically related to prescription and unlisted medications. Similar in size, form and thickness to an item, thin film strips are generally designed for oral administration, with the person putting the strip on or underneath the tongue or on the within of the cheek. Thin film allows the drug to be delivered to the blood stream either intragastrical, buccally or sublingually. The organ and buccal delivery of a drug via thin film has the potential to enhance the onset of action, lower the dosing, and enhance the effectualness and safety profile of the medication. There is continually increasing demand for patient convenience and compliance connected analysis and a completely unique methodology is that the development of quick dissolving buccal films, that dissolve or disintegrate instantly on the patient buccal membrane.

This quick dissolving drug delivery system is suited to the medicine that endure high first pass metabolism and is employed for up bioavailability with reducing dosing frequency to mouth plasma peak levels that successively minimize adverse/side effects and conjointly create it price effective. within the gift review, recent advancements and literature relating to quick dissolving buccal films is compiled and it suggests that this delivery system may be adopted by varied pharmaceutical corporations within the future at the big scale. There ar presently many comes in development that may deliver pharmaceuticals utilizing the thin film as dose kind.

Keywords: Fast mouth dissolving film, oral strips, Formulation of film, Evaluation of film, Novel drug delivery system, application of oral film

Introduction

Many pharmaceutical dosage forms are administered in the form of granules, liquids, powders, pills. Pill design is for swallowing intact or chewing to deliver a precise dosage of medication to patients. The pills, which include tablets and capsules, however some patients particularly pediatric and geriatric patients have difficulty in swallowing or chewing solid dosage forms. The fear of taking solid tablets and the risk of choking for some patient populations still exist despite their short disintegration time. Hence oral film drug delivery is better alternative in such cases.[1]

Pharmaceutical scientist throughout the world is trying to explore thin film as novel drug delivery tool. It has been identified alternative approach to conventional dosage form. Mouth dissolving films/Fast dissolving films is most advanced solid dosage form due to its flexibility. It improves efficiency of active pharmaceutical ingredients dissolving in short duration oral cavities after contact with saliva as compared to tablet.[1]

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Recently fast dissolving technology has been emerging out as new drug delivery system. It provides a very convenient means of taking medications and supplements. These systems disintegrate in a minute. The delivery system consists of thin film, which is placed under patients tongue or mucosal tissue, instantly wet by saliva, the film is rapidly dissolved then it releases the medication for oral mucosal absorption. They undergo disintegration in salivary fluids of oral cavities, where they release the active ingredient.[2]

By using variety of technologies, including direct compression, wet granulation and freeze-drying Fast dissolving drug delivery systems can be manufactured. In order to dissolve the dosage form rapidly in the mouth, some make use of different disintegrating mechanisms, such as high level of disintegrating or effervescent agents. Because of its easy administration and better compliance, recently fast dissolving drug delivery system have started gaining popularity and acceptance as new drug delivery systems.

Without the need to chew or water to aid in swallowing, these fast dissolving drug delivery systems can be dissolving or disintegrate in the patients mouth within a few seconds or minutes. Oral film drug delivery is a better alternative against oral solid tablets because of its fear of taking and the risk of choking for certain patient populations even it has short disintegration/dissolution times and also the oral availability of many drugs are very poor because of the pH stomach, the presence of enzymes, extensive first-pass metabolism these can also be solved by making oral films. These drugs have been administered as parenteral drug delivery systems, but because of poor patient compliance the pharmaceutical industry look for alternative routes of drug delivery like film drug delivery.

Intraoral fast-dissolving drug delivery system is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption. They also impart unique product differentiation, thus enabling use as line extensions for existing commercial products. This novel drug delivery system can also have an advantage for meeting the current needs of the industry are improved solubility/stability, biological half-life and bioavailability enhancement of drugs.[26]

Benefits of mouth dissolving film

- Films are versatile and therefore they're less fragile than oral dissolving tablets
- Films have larger extent thus it promotes speedy and quick disintegration and dissolution within the Rima.
- There is no risk of chocking.
- Films improves the patients compliance
- For disintegration of film, there's no want of water that has diode to higher satisfactoriness amongst the dysphasic patient.
- Films disintegrate on patients tongue in an exceedingly matter of seconds for quick unleash of active pharmaceutical ingredient.
- Films will be consumed at anywhere at any time as per the convenience of the patient.
- It enhances the oral bioavailability of molecules that endure initial pass result.
- Bypassing the primary pass result ends up in reduction in aspect effects related to the molecule as a result of reduction of the dose.
- Films offer smart mouth feel.
- They are convenient of self-administration.
- Stability for extended period of your time, since the drug remains in solid indefinite quantity kind until it's consumed. So, it has mix advantage of solid indefinite quantity kind in terms of stability and liquid indefinite quantity kind in terms of bioavailability.

Disadvantages of mouth dissolving film

- High doses can't be incorporated
- Dose uniformity is technical challenge

Ideal characteristics of suitable drug candidate

- The drug ought to be stable and soluble in water still as spittle.
- The drug ought to be of smaller or moderate relative molecular mass.
- The drug ought to have pleasant style.
- The dose of the drug ought to be low up to forty milligrams.

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- The drug ought to have ability to permeate in oral tissue layer tissue.
- It ought to be part unionized at the hydrogen ion concentration of Rima.
- It ought to be non nephrotoxic, perishable.
- It ought to have adequate drug loading capability.
- It ought to exhibit low sensitivity to environmental conditions like temperature and wetness.[2]

Structural features of Oral Mucosa

The oral membrane consists of associate outmost layer of stratified squamous epithelial tissue Below this lies a basement membrane, a plate propria followed by the connective tissue because the innermost layer. The epithelial tissue is comparable to stratified squamous epithelia found within the remainder of the body in this it's a mitotically active basal cell layer, advancing through variety of differentiating intermediate layers to the superficial layers, wherever cells area unit shed from the surface of the epithelial tissue .The turnover time for the buccal epithelial tissue has been calculable at 5-6 days and this is often most likely representative of the oral membrane as an entire. The oral membrane thickness varies betting on the site: the buccal membrane measures at 500-800 µm, whereas the membrane thickness of the laborious and soft palates, the ground of the mouth, the ventral tongue and also the gingivae live at regarding 100-200 µm. The composition of the epithelial tissue additionally varies betting on the positioning within the Rima. The mucosae of the gingivae and surface area unit keratinized just like the cuticle that contains ceramides and acyl ceramides (neutral lipids) which are related to the barrier perform. The membrane of the palate, the organ and also the buccal regions, however, aren't keratinized that area unit comparatively water-resistant to water and solely have tiny amounts of ceramide. They additionally contain tiny amounts of neutral however polar lipids, mainly steroid alcohol salt and glucosyl ceramides. The nonkeratinized epithelia are found to be significantly additional leaky to water than keratinized epithelia.

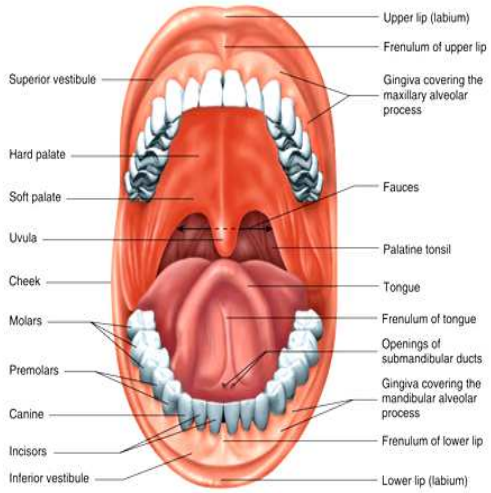

Fig. 1: Anatomy of buccal cavity

Mechanism of absorption through oral mucosa

There are two permeation pathways for passive drug transport across the oral mucosa: paracellular (intercellular, passing round the cell) and transcellular (intracellular, passing through the cell) routes. medication will use these two routes at the same time, however one route is typically most popular over the opposite counting on the chemical science properties of the medication. Since the animate thing areas and protoplasm are unit hydrophilic in character, oleophilic compounds would have low solubility during this atmosphere. The cytomembrane, however, is quite oleophilic in nature and hydrophilic solutes can have problem permeative through the cytomembrane because of an occasional partition constant. Therefore, the animate thing areas are unit the foremost barrier to permeation of oleophilic compounds and also the cytomembrane acts because the major transport barrier for hydrophilic compounds. Since the oral epithelial tissue is stratified, substance permeation might involve a mix of those 2 routes. The route that predominates, however, is mostly the one that has the smallest amount of hindrance to passage.[3]

Classification of Fast Dissolve Technology

Fast-dissolve technologies may be divided in to 3 broad groups:

- Lyophilized systems.
- Compressed tablet-based systems.
- Thin film strips.

The lyophilized systems

This system is that the most undefeated among them in terms of sales worth, sales volume and

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range of worldwide product approvals. Through the utilization of a mound or packing, suspension or resolution of drug with alternative structural excipients can convert into tablet-shaped units. The units or tablets square measure then frozen and lyophilized within the pack or mould. The ensuing units having high consistence square measure to blame for speedy water or spittle penetration and really speedy disintegration. Dose-handling capability for these systems differs reckoning on whether or not the active ingredients square measure soluble or insoluble medicine, with the dose capability being slightly lower for the previous than for a few pills based mostly systems. The units square measure capable of incorporating a spread of taste-masked materials and have a lot of speedy disintegration than tablet-based systems.

Compressed tablet-based systems

This system is created exploitation customary pill technology by direct compression of excipients. The pill technologies have totally different levels of hardness and break ableness reckoning on the strategy of manufacture. The speed of disintegration for fast-dissolve pills compared with a customary tablet is achieved by formulating exploitation water soluble excipients, or superdisintegrant or effervescent parts, to permit speedy penetration of water into the core of the pill. The one exception to the present approach for tablets is Biovail.s Fuisz technology. It uses the proprietary Shear kind system to supply drug-loaded candy floss, that is then used for tableting with alternative excipients. These systems will in theory accommodate comparatively high doses of drug material, together with style disguised coated particles. The potential disadvantage is that they take longer to disintegrate than the thin-film or lyophilized dose forms. The loose compression pill approach has progressively been employed by some technology homes, branded firms and generic pharmaceutical firms, for in-house development of line extension and generic fast dissolve dose forms.[30]

Oral thin film strips

Oral films, conjointly known as oral wafers within the connected literature, square measure a gaggle of flat films that square measure administered into the Rima. though oral film systems, the third category, are living for variety of years, they have recently become the new space of interest in fast-dissolve pharmaceutical drug delivery. dissoluble oral thin films or oral strip evolved over the past few years from the confection and oral care markets within the sort of breath strips and have become a unique and wide accepted kind by customers for delivering vitamins and private care product. Firms with expertise within the formulation of chemical compound coatings containing active pharmaceutical ingredients for stratum drug delivery capitalized on the chance to transition this technology to oral thin film formats. Today, oral thin films square measure a proved and accepted technology for the general delivery of arthropod genus for over-the-counter medications and square measure within the early- to middle development stages for pharmaceuticals .This is mostly as a results of the success of client the buyer the patron} breath thing product like Listerine Pocket parks within the United States of America consumer market. Such systems use a range of deliquescent polymers to supply a 50-200 millimeter film of fabric. This film will reportedly incorporate soluble, insoluble or taste-masked drug substances. The film is factory-made as an oversized sheet then take away individual dose units for packaging in an exceedingly vary of pharmaceutically acceptable formats.[30]

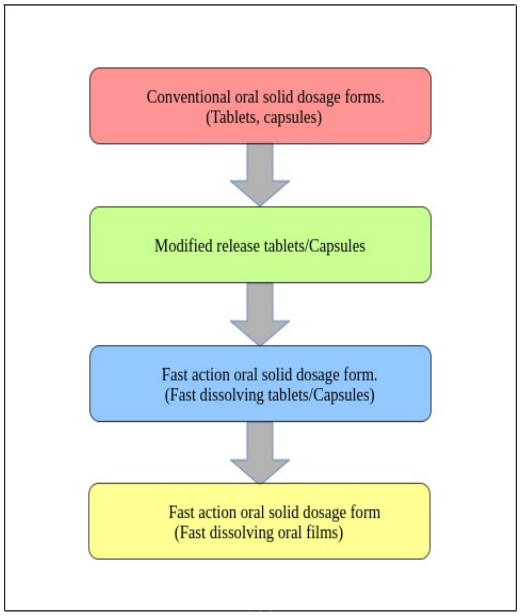

Fig. 2: Development of fast dissolving oral film

Formulation consideration

- Active pharmaceutical ingredient.
- Film forming polymer.
- Plasticizers.
- Disintegrating agent.
- Solubilizing agent.
- Sweetening agent.
- Saliva stimulating agent.
- Flavoring agent.
- Coloring agent.

Active pharmaceutical ingredients

A typical composition of the film contains 1-25% w/w of the drug. A variety of active Pharmaceutical ingredients may be delivered through quick dissolving films. Little dose molecules square measure the simplest candidates to be incorporated in mouth dissolving film. Various classes of medication like medicament neuroleptics, vessel agents, analgesics, anti allergic, anti epileptics, anxiolytics, sedatives, hypnotics, diuretics, ant parkinsonism agents, anti-bacterial agents and medicines used for dysfunction, antialzheimers, expectorants square measure appropriate for mouth dissolving film.[5,6] List of the drug molecule which will be incorporated in mouth film:[48]

Table 2: Pharmaceutical ingredients incorporated in mouth film

Drug	Dose	Therapeutic category
Loratadine	10 mg	Anti histaminic
Chlorpheniramine maleate	4 mg	Anti allergic
Famotidine	10 mg	Antacid
Azatadine maleate	1 mg	Anti histaminic
Sumatriptan succinate	35-70 mg	Anti migraine
Ketoprofen	12.5 mg	Analgesic
Ondansetron	2.5 mg	Antiemetic
Nicotine	2 mg	Smoking cessation
Acrivastine	8 mg	Anti histaminic

Film forming polymer

The physical and mechanical properties of the mouth dissolving film rely on the characteristics of film-forming compound, that forms 20-75 % (w/w) of total dry wt. of the mouth dissolving film. the choice of compound, therefore, is one in every of the foremost necessary and demanding parameter for the successful development of the formulation. The polymers used ought to have smart hydrophilicity, fast disintegration, smart mouth feel, and appropriate mechanical properties. at the side of its smart solubility, the compound ought to have spare mechanical, chemical science and porousness properties. so as to stay intact against the interior and external stresses developed throughout storage and particularly once exposed to environ-mental conditions, a movie ought to have high mechanical strength with spare elongation and physical property properties.[4,5]

Ideal properties of the film forming polymers

1) It ought to have smart wetting and spreading properties
2) It ought to be void of leachable impurities.
3) It shouldn't be expensive.
5) It ought to have a decent period of time
6) It ought to have smart mouth feel property
7) The compound ought to exhibit spare peel shear and strength List of polymers employed in twin films.[4,5]

Table 3: Film forming polymer used in mouth film

Group	Class	Example
Natural	Protein	Polymerized resin
	Resin	Pullulan, Pectin, Sodium alginate ,Maltodextrin,
	Carbohydrate	Sodium starch glycolate
Synthetic	Cellulose Derivative	Hydroxypropyl methyl cellulose[E3,E5,E15,K3,K15,K50] Methyl cellulose [A3,A6,A15], carboxy methyl cellulose, secekol-30, Sodium Carboxy methyl cellulose, Croscarmellose Sodium
	Vinyl	Polyvinyl Pyrrolidone(K-

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	Polymer	90,K-30) Polyvinyl alcohol
		Poly ethylene oxide
	Acrylic Polymer	Eudragit (RD-100,9,10,11,12 and RL-100

Plasticizer

Plasticizers are used to reduce the glass transition temperature and improves flow of the polymer. It helps to improve flexibility of the strip and reduce the brittleness of the strip. It also effects the absorption rate of the drug. Various effects associated with the appropriate use of the plasticizers are [6]cracking, blooming, pilling, spitting of the strip.

Different types of polymers which get plasticized with different polymers like,

1]Cellulose hydrophilic polymers were easily plasticized with hydroxyl containing plasticizers like glycerol, polyols, propylene glycol, PEG.

2]Less hydrophilic cellulose polymers were plasticized with esters of phthalic acid, citric acid. [6] Examples of drugs with type of plasticizers used given in following table.

Table 3: Plasticizer used in mouth film

oral film	Plasticizer
Montelukast sodium	Glycerine
Triclosan	Propylene Glycol
Sertraline	Propylene Glycol or PEG-400
Telmisartan	Propylene Glycol
Amlodipine Besylate	Glycerol
Levocetirizine Dihydrochloride	Glycerine, Dibutyle Phthalate

Saliva stimulating Agent

This agent will increase the assembly of saliva that may help within the quicker disintegration of the oral thin film. Example: water-soluble vitamin, Mallic acid, Tartaric acid, Citric acid, Lactic acid. These agents will be used alone or together between 2 and 6 w/w of the strip.[7]

Flavoring agent

Selection of flavor is counting on which kind of drug is to be incorporated within the formulation. The number of flavors needed to mask the task relies on the flavor kind and its strength. Any flavor that is US FDA approved will be accustomed to mask the bitter style of the formulation. Example: Essential oils, menthol, intense mints like to pepper mint, sweet mint, spearmint, wintergreen, cinnamon, clove sour fruit like lemon, orange, sweet confectionary flavor like vanillium, chocolate.[2,8]

Sweetening Agent:

Generally, sweeteners are used to mask the bitter style of bound drug. Each natural and artificial sweeteners will used alone or together.[9]

Table 4: sweetening agents used in mouth film.

Sweeteners	Example
Natural	Xylose, Glucose, Mannose, Fructose, Dextrose, Sucrose, Maltose, Comsyrup solids
Artificial	1st generation: Saccharin, aspartame, Cyclamate 2nd generation: Sucralose, alitame, neotame

Surfactant

Surfactants are used as solubilizing or wetting agent in the formulation so that film get dissolved within few second and releases active ingredient.

Example: Sodium Lauryl sulfate, Benzalkonium Chloride, Tweens

Manufacturing methods

Various approaches to manufacturing of rapid dissolving film are classified as follow: [8]

1. Solvent casting
2. Semisolid casting
3. Hot melt extrusion
4.Solid dispersion extrusion
5. Rolling

A Method of preparation of film:

Solvent casting method

In solvent casting method excipients are dissolved in water, then water soluble polymers and in last drug is added and stirred to form homogeneous solution. Finally, solution is casted in to the Petri plate and dried.[11]

Advantages:

1.More flexibility.
2.Better physical properties.
3.Finished film thickness is 12-100um.
4.great clarity then extrusion.
5.great uniformity of thickness.

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Disadvantage: polymer must be soluble in a volatile solvent or water viscosity should be formed.[2]

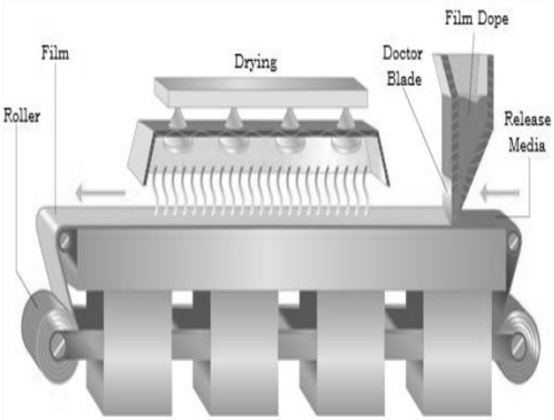

Fig. 3: Solvent casting method for preparation of mouth films.

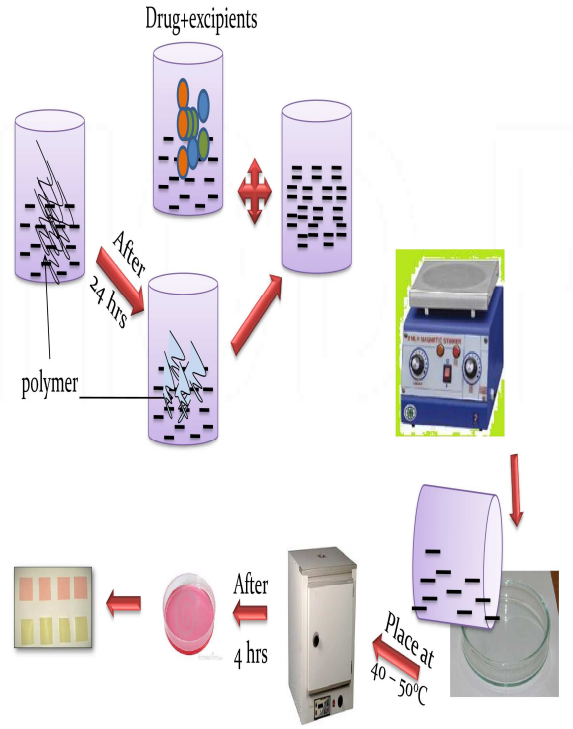

Fig. 4: Solvent casting method for preparation of film at laboratory

Semisolid casting

This method is preferably adopted when acid insoluble polymers are to be used in the preparation of the films. In Semisolid casting method gel mass is casted in to the films or ribbons using heat controlled drums. Gel mass is obtained by adding solution of film forming to a solution of acid insoluble polymer in ammonium or sodium hydroxide. Acid-insoluble polymers used to prepare films include: cellulose acetate phthalate, cellulose acetate butyrate. Acid insoluble polymer and film forming polymer should be used in the ratio of 1:4.[12]

Hot melt extrusion

In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then dried granular material is introduced into the extruder. The screw speed should set at 15 rpm in order to process the granules inside the barrel of the extruder for approximately 3–4 min. The processing temperatures should be 800 C (zone 1), 1150 C (zone 2), 1000 C (zone 3) and 650 C (zone 4). The extrudate (T = 650 C) then pressed into a cylindrical calendar in order to obtain a film. There are certain benefits of hot melt extrusion28, 29 . -Fewer operation units -Better content uniformity -An anhydrous process Solid dispersion extrusion In this method immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.[12]

Advantages:

1.Cost effective process with reduced production time and reduced number of unit operation.

2.Improved bioavailability of poorly soluble compounds.

3.Capability of sustained, modified and targeted release.

4.Have stability at varying pH and moisture levels.

Rolling Method

In rolling method, a solution or suspension of drug with film forming polymer is prepared and subjected to the roller. The solution or suspension should have specific rheological consideration. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cutted in to desired shapes and sizes.[12]

Application of oral strip in drug delivery

Oral mucosal delivery via Buccal, sublingual, and mucosal route by use of OTFs could become a preferential delivery method for therapies in which rapid absorption is desired, including those used to manage pain, allergies, sleep difficulties, and central nervous system disorders. Dissolvable oral thin films evolved over the past few years

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from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers for delivering vitamins and personal care products.[28]

Topical applications: The use of dissolvable films may be feasible in the delivery of active agents such as analgesics or antimicrobial ingredients for wound care and other applications.

Retentive dosage systems: Dissolvable films are being considered in dosage forms for which water-soluble and poorly soluble molecules of various molecular weights are contained in a filmformat Dissolution of the films could be triggered by the pH or enzyme secretions of the gastrointestinal tract, and could potentially used to treat gastrointestinal disorders. [29]

Diagnostic device : Dissolvable films may be loaded with sensitive reagents to allow controlled release when exposed to a biological fluid or to create isolation barriers for separating multiple reagents to enable a timed reaction within a diagnostic device.[28,29]

Evaluation Parameters

Weight variation test

A random study of films is performed from each formulation batch. The weight of each film strip was taken on digital analytical balance and the weight variation as well as mean deviation of films is calculated and recorded.[1]

Fig. 5: Digital analytical balance

Thickness

Methods like dial gauge or Vernier calipers or screw gauge or microscope were used to measure the thickness. Thickness at different points is measured to find out the average thickness of film. By using Vernier caliper the thickness can be measured as sample equivalent to dose of the drug was taken Anvil of the thickness gage was lifted and the film was inserted after making sure that pointer was set to zero, then the film was held on the anvil and the reading on the dial was noted.The average of three readings was taken. This is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of dose in the strip.[18]

Fig. 6: Electronic digital caliper

Folding endurance:

The number of times the film is folded without breaking is computed as the folding endurance value. The folding is performed at the same place for a number of times that is 300 in some cases, the number of folds required to form cracks gives the value of folding endurance.[1,11]

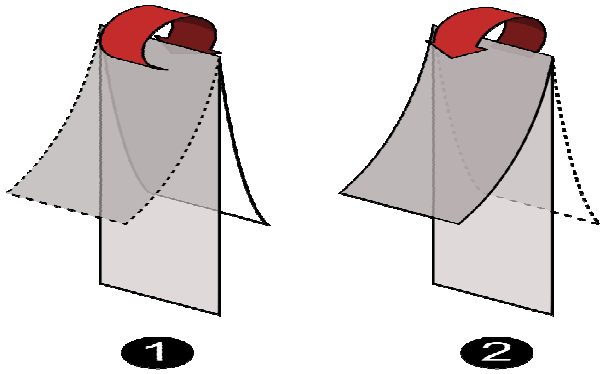

Fig. 7: Folding endurance test

Tensile strength

stress required to break the film is considered as tensile strength. It is calculated by the load at rupture divided by the cross-sectional area of the film as given below.[22]

$$\text{Tensile strength} = \frac{\text{load at failure} \times 100}{\text{Film thickness} \times \text{Film width}}$$

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A film which is free from any physical imperfections is to be selected to get proper results. The film is placed between two clamps at a distance of 10mm, the film was pulled at the rate of 5mm to 10mm/min. The whole experiment is repeated three times.[2,13]

Fig. 8: Tensile strength detector

Percent elongation

After exerting stress on the film, the film stretches which is referred as strain. Strain is defined as change in length of film divided by its original/initial length of the film which is used. Percent elongation is related quantitatively to the amount of plasticizer used while formulating the film. More amount of plasticizer in the preparation results in the film which has more elongation properties. It is determined by the following[23]

$$\text{Percentage elongation} = \frac{\text{change in length} \times 100.}{\text{Initial length}}$$

Drug uniformity

Test is performed to find out whether there is a drug uniformity in all the films that are produced it is determined by any selected assay method described for that particular API in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual strip. Limit of content uniformity is 85-115%. In case of loperamide each film is dissolved in 50 ml of volumetric flask containing methanol. Which is later filtered through what Mann filter paper No.41.Aliquot of 1ml of filter solution taken into 25ml of volumetric flask made up to 25 ml with 6. Phosphate buffer. The solution is analyzed in U.V spectrophotometer at 223nm against in phosphate buffer pH 6.8 solution as blank.[1,4,13]

Surface pH

pH of film was determine to investigate side effect. The acidic or alkaline pH causes irritation to oral mucosa hence it is necessary the film having the surface pH close to neutral. The film allowed for swelling in Petri dish at room temperature for 30 minutes, In that 1ml of solution placed under the digital pH meter to find out the surface pH of film. [1,15]

Fig. 9: Digital pH meter

Swelling test

Take a Petri dish containing 40 ml of 6.8 phosphate buffer, then submerge the wire mesh into it. Then the increase in weight of film was determined at regular time interval till the constant weight is obtained. The hydration ratio of the film was calculated by using the following formula:[25,1]

Swelling index (SI) = (Wt-Wo)/Wo

Where,

Wt=weight of film at 't' time.

Wo=weight of film at '0' time.

In vitro disintegration test

When a film starts to break or disintegrate it is called as disintegration time. The disintegration test for fast mouth dissolving film was carried out using single unit disintegration apparatus containing 900 ml of 6.8 phosphate buffer. The temperature setted to 37.5±0.5°C. After reaching, the temperature film is placed on disintegration apparatus time required to start breaking film is noted as disintegration time of of particular film.[26,16]

There are another two methods for determining disintegration time.[39,40,41]

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Slide frame method: A drop of distilled water is poured onto the film clamped into slide frames placed on petri dish. Time taken by the film to dissolves noted as disintegration time.39,41

Petri dish method: A film is placed into 2 ml distilled water taken in Petri dish. Time taken by the film to dissolve completely is considered as the disintegrating time.[39,42]

Fig. 10: Disintegration apparatus

In vitro dissolution study

In vitro dissolution of fast dissolving film was studied in USP paddle dissolution test apparatus using 900 ml phosphate buffer at pH 6.8 as the dissolution medium. The temperature was maintained at 50 rpm and 37±0.5°C throughout the experiment. 5 ml sample was withdrawn for 5 minutes. and the same quantity was replaced with phosphate buffer of pH 6.8. The percentage of drug released was determined using UV visible spectrophotometer.[14.]

Fig. 11: Dissolution apparatus

Technologies[44]

SOLULEAVES

This is applied to flavor-release merchandise like mouth fresheners, confectionery and victuals merchandise. SOLULEAVES technologies are often wont to deliver active ingredients to mouth expeditiously and during a pleasant and simply moveable type. SOLULEAVES films are often designed to dissolve apace on contact with saliva, quickly cathartic the active ingredients and flavors. This quality makes edible films a superb delivery technique for an outsized vary of merchandise requiring quick unharness within the mouth. For pharmaceutical uses this technique of administration is particularly helpful for pediatric medicine or old patients UN agency could have problem swallowing ancient tablets or capsules. The delivery systems are often used for the cough/cold, gastrointestinal and pain therapeutic areas additionally as delivering organic process merchandise. SOLULEAVES films also can be designed to stick to mucosa membranes and to unharness the active ingredient slowly over quarter-hour.

WAFERTAB

It could be a proprietary delivery system that uses a novel method to arrange drug-loaded thin films which may be employed in topical or oral application .Active ingredients are incorporated into the film when casting could be a drug delivery system that comes with pharmaceutical actives into an ingestible filmstrip. The system provides fast dissolution and unharness of actives once the strip comes into contact with saliva within the mouth. The WAFERTAB filmstrip are often tasteful for to boot improved style masking. The active ingredient is exactly treated and integrated into the body of a pre-manufactured XGEL film, so preventing exposure to uncalled-for heat and wetness and probably enhancing product stability. The WAFERTAB system lends itself to several prospects for innovative product style, enabling multiple films with completely different actives to be secure along. WAFERTAB are often ready during a sort of shapes and sizes and is a perfect technique for delivery of medicines, that need quick release, or to be used by patients who have problem swallowing.

FOAMBURS

It is a special variant of the SOLULEAVES technology wherever an chemical element is passed into the film throughout production. This ends up in a movie with a pitted structure, that dissolves apace giving a unique mouth sensation. FOAMBURST has attracted interest from food and confectionary makers as a way of carrying and releasing flavors.

XGEL

This film is at the guts of Meldex International's holding, employed in all its film systems and its ingestible indefinite quantity delivery technologies. XGEL film provides distinctive product advantages for care and pharmaceutical products: it's nonanimal- derived, approved on spiritual grounds and is appropriate for vegetarians; the film is GMO free and continuous production process provides an economic and competitive producing platform. XGEL film are often style disguised, colored, layered, and capable of being enteric properties while additionally having the flexibility to include active pharmaceutical ingredients. The XGEL film systems are often created to encapsulate any oral indefinite quantity type, and may be soluble in either cold or quandary. XGEL film is comprised of a variety of various soluble polymers, specifically optimized for the supposed use. All of the XGEL ingredients square measure documented and usually considered safe. X Gel film Technology developed by Bio Progress is inflicting a revolution within the product offerings and producing ways currently out there to the pharmaceutical trade.

Storage and Packaging[45]

The changing and packaging stage conjointly provides product flexibility to drug makers. The rolled film may be die-cut into any form or size or slit into narrower rolls as required for the appliance. For stigmatization functions and to fulfill trade laws, converters might favor to print info directly onto the film unit doses before packaging. Criteria that will be taken into thought embrace the necessity for unit-dose packaging, barcode labeling, and therefore the content in directions to be used, child-resistant seals, and senior-friendly packaging.[27]

In the pharmaceutical trade it's important that the package chosen adequately preserve the integrity of the merchandise. costly packaging, specific process, and special care are needed throughout producing and storage to shield the dose of alternative quick dissolving dose forms. a range of packaging choices are offered for quick dissolving films. Single packaging is necessary for films, that are pharmaceutical products; associate degree metallic element pouch is that the most typically used packaging format. APR- Labtech has developed the speedy card, a proprietary and proprietary packaging system, that is specially designed for the speedy films. The speedy card has same size as a Mastercard and holds 3 raid films on all sides. each dose may be taken out singly. the fabric chosen should have the subsequent characteristics:

- They have to defend the preparation from environmental conditions.
- They have to be Food and Drug Administration approved.
- They have to meet applicable tamper-resistant demand.
- They have to be non-toxic.
- They have to not be reactive with the merchandise.
- They have to not impart to the merchandise tastes or odors.[31]

Foil, paper or plastic pouches

The versatile pouch may be a packaging idea capable of providing not solely a package that's temper- resistance, however conjointly by the right choice of fabric, a package with a high degree of environmental protection. a versatile pouch is typically shaped throughout the merchandise filling operation by either vertical or horizontal forming, filling, or waterproofing instrumentality. The pouches may be single pouches or metallic element pouches. Single pouch and metallic element pouch: Soluble film drug delivery pouch may be a peel able pouch for “quick dissolve” soluble films with high barrier properties. The pouch is clear for product show. employing a a pair of structure combination permits for one facet to be clear and therefore the alternative to use a cheap foil lamination. The foil lamination has primarily zero transmission of each gas and wetness. The package provides a versatile skinny film different for nutraceutical and pharmaceutical applications. the only dose pouch

provides each product and dose protection. metallic element pouch is that the most typically used pouch.

Blister card with multiple units

The blister instrumentation consists of 2 components: the blister, that is that the shaped cavity that holds the merchandise, and therefore the lid stock, that is that the material that seals to the blister. The blister package is made by heat – softening a sheet of thermoplastic rosin and vaccum-drawing the softened sheet of plastic into a contoured mildew. when cooling the sheet is free from the mildew and payoff to the gas station of the packaging machine. The semi –rigid blister antecedently shaped is full of the merchandise and lidded with the warmth sealable material. The film choice ought to be based mostly upon the degree of protection needed. usually the lid stock is created of tin foil. the fabric wont to kind the cavity is usually a plastic, which might be designed to shield the dose kind from wetness.[31]

Barrier Films

Many drug preparations area unit extraordinarily sensitive to wetness and thus need high barrier films. many materials is also wont to offer wetness protection like Polychlorotrifluoroethylene (PCTFE) film, plastic. plastic doesn't stress crack beneath any conditions. it's a superb gas and vapor barrier. Lack of clarity continues to be a disadvantage.

Applications of quick dissolving buccal films[46]

Vaccines

Quick dissolving buccal films film may be delivered within the style of vaccine that is stable at temperature therefore it's quickly dissolved in mouth and in spittle. reovirus vaccine ready in united states could be a temperature stable fast-dissolving buccal film delivery system for vaccines which will build vaccinations nearly as easy as freshening your breath. This delivery system exhibits several blessings that include: improved patient compliance, improved bioavailability, reduction within the prices related to storage and distribution, handling and administration.[46,49]

Controlled and Sustained release film

Sustained release buccal film is applicable in hospital preparations and numerous polymers like polyose and chitosan derivatives are used as excipients. They contribute to enlargement of application, decrease toxicity, wound dressings, oral mucoadhesive and water-resisting adhesive by virtue of their release characteristics and adhesion.[32,35]

Taste masking

Taste masking is an important demand for quick dissolving tablets for industrial success. quick dissolving buccal films dissolve or disintegrate in patient's mouth, so releasing the active ingredients that are available in contact with the style buds and thence this property becomes important for the patient compliance. In style masking, medicine with unacceptable bitter style may be microencapsulated into pH scale sensitive acrylic polymers by solvent evaporation and solvent extraction techniques. These polymers microspheres showed economical style masking and complete dissolution in an exceedingly short amount.[33,35]

Orally disintegrating films

Fast dissolving buccal films are supported a soluble chemical compound. The film has the flexibility to dissolve quickly while not the necessity for water provides an alternate to the patients with swallowing disorders and to patient tormented by nausea, like those patients receiving therapy. Various formulations of quick dissolving films area unit accessible commercially area unit given in table no.5[36,37,38]

Table 5: Marketed Films available in market.[43]

Brand name	Manufacturer /Distributer	API(strength)	Uses
Gas-X	Novartis	Simethicone (62.5 mg)	Anti Flatulating
Benadryl	Pfizer	Diphenhydramine HCL (12.5mgor 25mg)	Anti allergic
Chlorase ptic	Prestige	Benzocaine/menthol (3 mg/3 mg)	Sore throat
Orajel	Del	Menthol/pectin(2mg/ 30 mg)	Mouth ulcer
Triaminic	Novartis	Diphenhydramine HCL (12.5 mg)	Anti allergic
Listerine Cool Mint Pocket Paks	Pfizer, Inc.	Cool mint	Mouth fresheners
Klonopin Wafers	Solvay Pharmaceuticals	Clonazepam In five strength (0.125mg,0.25 mg, 0.5 mg, 1 mg and 2 mg.)	Treatment of anxiety

Conclusion

The present review shows that oral quick disintegrating films are one amongst the novel approaches within the field of pharmaceutical sciences. They need improved acceptance and patient compliance with no risk of choking related to higher safety and effectiveness compared with standard indefinite quantity forms. The most plan behind formulation of oral disintegrating film was to deal with the issue in swallowing standard oral indefinite quantity forms among paediatric, geriatric and psychiatrical patients with upset. Presently, oral disintegrating films are wide obtainable for cardiovascular disease, acidity, allergy, pain, etc. reflective their importance. Major benefits of such indefinite quantity kind ar their administration while not employment of water fulfilling the requirement of target population seeking convenience in drug administration along side bypassing the internal organ metabolism, consequently, resulting in improved therapeutic response.

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