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A REVIEW ON ORAL DISINTEGRATING TABLETS AND ORAL SOLUBLE FILMS

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ABSTRACT

Oral drug delivery is the most prominent route of adminstation,Fast disintegrating tablets and fast dissolving filims are gaining importance now a days due to their rapid and effective drug release.Fast disintegrating tablets avoids some prolems like pediatric and geriatric patients, have difficulty swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking. For example, a very elderly patient may not be able to swallow a daily dose of antidepressant in the form of a Caplet shaped Tablet. Orally disintegrating tablets (ODTs) are a perfect fit for all of these patients. Fast-dissolving drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology. Mouth dissolving film becomes a novel approach to oral drug delivery system as it provides convenience and ease of use over other dosage forms such as orally disintegrating tablets buccal tablets and sublingual tablets, so mouth dissolving films are gaining the interest of large number of pharmaceutical industries. Mouth dissolving film was developed on the basis of technology of transdermal patch. Mouth dissolving films are thin solid dosage forms which when placed in the oral cavity; dissolve within few seconds without chewing and intake of water. The oral buccal mucosa being highly vascularized, drugs can absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism. This advantage can be exploited in preparing products with improved oral bioavailability of molecules that undergo first pass effect. These films offer convenient way of dosing medication to pediatric, geriatric and bedridden patients. Present review provides an account of various formulation methods

and their evaluation used in film formulations and applications of Fast dissolving tablets and Oral soluble filims.

KEYWORDS: Oral disintegrating tablets, Oral soluble filims, Preperation techniques, Applications.

FAST DISINTEGRATING TABLETS are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. Upon introduction into the mouth, these tablets dissolve or disintegrate in the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. FDTs or orally disintegrating tablets provide an advantage particularly for paediatric and geriatric populations who have difficulty in swallowing conventional tablets and capsules.

The concept of Fast Dissolving Drug Delivery System emerged from the desire to provide patient with conventional means of taking their medication. Because of physiological changes associated with, especially, elderly and paediatrics are quite unable to swallow (Dysphagia); rather, this is a common problem of all age groups patients. Solid dosage forms that can be disintegrated, dissolved, or suspended by saliva in the mouth resulting in easy swallowing can provide significant benefits to the paediatric and geriatric population, as well as other patients who prefer the convenience of easily swallow-able dosage forms. This tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva.

A tablet which can rapidly disintegrate in saliva (rapidly disintegrating tablet) is an attractive dosage form and a patient-oriented pharmaceutical preparation. The mouth-dissolving tablets have attracted the interest of many researchers. Many elderly patients have difficulty swallowing tablets, capsules, or powders. To alleviate this problem, these tablets are expected to dissolve or disintegrate in the oral cavity without drinking water. The disintegrated mass can slide down smoothly along the oesophagus with the help of saliva, so even people who have swallowing or chewing difficulties can take it with ease.

DESIRED CRITERIA FOR MOUTH DISSOLVING DRUG DELIVERY SYSTEM

The tablets should

i. Not require water to swallow, but is should dissolve or disintegrate in the mouth in matter of seconds.

ii. Be compatible with taste masking.
iii. Be portable with taste masking.
iv. Have a pleasing mouth feel.
v. Leave minimal or no residue in the mouth after oral administration.
vi. Exhibit low sensitivity to environmental conditions as humidity and temperature.
vii. Allow the manufacture of tablet using conventional processing and packaging equipment at low cost.

SALIENT FEATURES OF MOUTH DISSOLVING TABLET

a) Ease of administration to patient who refuses to swallow tablets, such as paediatric, geriatric and psychiatric patients.
b) No need of water to swallow the dosage form, which is highly convenient feature for patients who are travelling and do not have immediate access to water.
c) Rapid dissolution and absorption of drug, which will produce quick onset of action.
d) Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.
e) Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.

Formulation aspects in developing FDT

Orally disintegrating tablets are formulated by utilizing several processes, which differ in their methodologies and the FDTs formed vary in various properties such as

i. Mechanical strength of tablets
ii. Taste and mouth feel
iii. Swallow-ability
iv. Drug dissolution in saliva
v. Bioavailability
vi. Stability

The major advantages with effervescent formulation approach that it is a well established, easy to implement and mask the bitter taste of drug.[9] The effervescent system is generally composed of dry acid and dry base, which when react facilitate a mild effervescent reaction when the tablet contacts saliva. The effervescent reaction accelerates the disintegration of tablet through the release of carbon dioxide, water and salt. Due to evolution of carbon dioxide, the bitter taste of drug is also masked and a pleasant mouth feel is felt.

Direct compression is the easiest method to manufacture mouth dissolving tablets (MDTs). The great advantage of direct compression is its low manufacturing cost. It uses conventional equipment, commonly available excipients and a limited number of processing steps. In many cases the disintegrants used have a major role in the disintegration and dissolution process of fast disintegrating tablets made by direct compression method. The choice of a suitable type and an optimal amount of disintegrate is important for ensuring a high disintegration rate. The addition of other formulation components such as water-soluble excipients or effervescent agents can further enhance dissolution or disintegration properties.

The various processes employed in formulating FDTs are as follows-

1. Freeze drying or lyophilization

A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze-dried forms offer more rapid dissolution than other available solid products. The lyophilization process imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristics of the formulation.

2. Molding

Tablets produced by molding are solid dispersions. Physical form of the drug in the tablets depends whether and to what extent, it dissolves in the molten carrier. The drug can exist as discrete particles or microparticles dispersed in the matrix. It can dissolve totally in the molten carrier to form solid solution or dissolve partially in the molten carrier and the remaining particles stay undissolved and dispersed in the matrix. Disintegration time, drug dissolution rate and mouth feel will depend on the type of dispersion or dissolution.

3. Cotton candy process

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy flos matrix is then milled and blended with active ingredients and exipients and subsequently compressed to FDT.

4. Spray drying

Spray drying is a process by which highly porous, fine powders can be produced. The composition contains a bulking agent (mannitol and lactose), a disintegrant (sodium starch glycolate and croscarmellose sodium), an acidic ingredient (citric acid) and/ or alkaline

ingredients (sodium bicarbonate), which when compressed into tablets show fast disintegration and enhanced dissolution.

5. Mass extrusion

This technology involves softening the active blend using the solvent, mixture of water soluble polyethylene glycol using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product and cutting into even segments upon heated blade to form tablets.

6. Sublimation

This method includes the addition of a sublime salt to the tableting components, compressing the blend and removing the salt by the process of sublimation. The active ingredient, a diluent, a sublime salt (camphor/ ammonium bicarbonate), a binder and other excipients are blended and tablets are prepared. The tablets dissolve within 10-20 seconds and exhibit sufficient mechanical strength.

7. Sugar based excipient

Sorbitol, mannitol, dextrose, xylitol, fructose, maltose and polydextrose have been used as bulking agents. Because of their high aqueous solubility and sweetness, which impart a pleasing mouth feel and good taste masking, nearly all formulations for rapidly dissolving tablets contain sugar-based materials.

8. Direct compression

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Directly compressed tablets disintegration and solubilization depends on single or combined action of disintegrants, water soluble excipients and effervescent agents. Disintegrant efficacy is strongly affected by tablet size and hardness. Large and hard tablets have disintegration time more than that usually required. As a consequence, products with optimal disintegration properties often have medium to small size and /or high friability and low hardness. The breakage of tablet edges, during handling and tablet rupture during the opening of blister alveolus, all result from insufficient physical resistance. Disintegrants have major role in the disintegration and dissolution process of mouth dissolving tablets made by direct compression. To ensure a high disintegration rate, choice of suitable type and an optimal amount of disintegrant is important. Other formulation components such as water soluble excipients or effervescent agents can further enhance dissolution or disintegration properties.

ADVANTAGES OF FAST DISINTEGRATING TABLETS

Fast disintegrating tablets (FDTs) are meant for administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure, and patients who refuse to swallow, such as paediatric, geriatric, and psychiatric patients.

By the use of FDTs, rapid drug therapy intervention can be achieved, achieve increased bioavailability/rapid absorption through pregastric absorption of drugs from mouth, pharynx, and oesophagus as saliva passes down.

FDTs are convenient for administration and patient compliant for disabled, bedridden patients, and for travellers and busy people who do not always have access to water.
Their good mouth feel property helps to change the perception of medication as bitter pill, particularly in paediatric patients.

The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
The new business opportunity like product differentiation, product promotion, patent extension, and life cycle management become easy after the intervention of FDTs. The FDTs are often formulated for existing drugs with an intention to extend the patent life of the drug through product differentiation.

PATENTED TECHNOLOGIES

1. Zydis technology

Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast-dissolving carrier material. When zydis units are put into the mouth, the freeze dried structure disintegrates instantaneously and does not require water to aid swallowing. The zydis matrix is composed of many materials designed to achieve a number of objectives. To impart strength during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength. To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration. Various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of zydis unit during freeze drying process or long-term storage. Zydis

products are packed in blister packs to protect the formulation from moisture in the environment.

2. Lyoc

Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Non-homogeneity during freeze drying is avoided by incorporating inert filler to increase the viscosity.

3. Quick solv

This technology uses two solvents in formulating a matrix, which disintegrates instantly. Methodology includes dissolving matrix components in water and the solution or dispersion is frozen. Then dry the matrix by removing water using excess of alcohol (solvent extraction). Thus the product formed has uniform porosity and adequate strength for handling.

4. Nano-crystal technology

Nano-crystal technology includes lyophilization of colloidal dispersions of drug substances and water soluble ingredients filled into blister pockets. This method avoids manufacturing process such as granulation, blending and tableting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drugs.

5. FlashTab technology

This technology involves the preparation of rapidly disintegrating tablet, which consists of an active ingredient in the form of microcrystals. Drug microgranules may be prepared by using the conventional techniques like coacervation, microencapsulation, extrusion-spheronization or simple pan coating method. The microcrystals or microgranules of the active ingredients are added to the granulated mixture of excipients prepared by wet or dry granulation and compressed into tablets.

6. Durasolv technology

The tablets made by this technology consist of a drug, fillers and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for products requiring low amounts of active ingredients.

7. OraSolv

The system essentially makes tablets that contain the taste masked active ingredients and an effervescent disintegrating agent, which on contact with saliva, rapidly disintegrates and releases the active ingredient. The tablets are made by direct compression at very low

compression forces in order to minimize oral dissolution time. The tablets produced are soft and friable.

8. WOW tab

WOW means without water. These processes use a combination of low mouldability saccharide (rapid dissolution) and high mouldability saccharide (good binding property) to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide (lactose, mannitol) and granulated with a high mouldability saccharide (maltose, sorbitol) and compressed into tablets.

9. Dispersible tablet technology

It offers development of ODT with improved dissolution rate by incorporating 8-10% of organic acids and disintegrating agents. Disintegants include starch, modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose and cyclodextrins.

10. Pharma burst technology

It utilizes the co-processed excipients to develop ODT, which dissolves within 30-40s.This technology involves dry blending of dug, flavor, lubricant followed by compession into tablets.

11. Frosta technology

It utilizes the concept of formulating plastic granules and compressing at low pressure to produce strong tablets with high porosity. The process involves usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15-30s depending on size of tablets.

12. Oraquick

It utilizes taste masking microspheres technology called as micromask, which provides superior mouth feel, significant mechanical strength, and quick disintegration/dissolution of product. This form of matrix that protects drug, which can be compressed with sufficient mechanical strength. Oraquick product dissolves within few seconds.

13. Ziplets/Advatab

It utilizes water-insoluble ingredient combined with one or more effective disintegrants to produce FDT with improved mechanical strength and optimal disintegration time at low compression force.

14. Flash Dose technology

Flash dose technology has been patented by Fuisz. Nurofen meltlet, a new form of Ibuprofen as melt-in-mouth tablets. Flash dose tablets consist of self binding shearform matrix termed as "floss". Shearform matrices are prepared by flash heat processing.

ORAL SOLUBLE FILIMS

The oral route is one of the most preferred routes of drug administration as it is more convenient, cost effective, and ease of administration lead to high level of patient compliance. The oral route is problematic because of the swallowing difficulty for pediatric and geriatric patients who have fear of choking. Patient convenience and compliance oriented research has resulted in bringing out safer and newer drug delivery systems. Recently, fast dissolving drug delivery systems have started gaining popularity and acceptance as one such example with increased consumer choice, for the reason of rapid disintegration or dissolution, self-administration even without water or chewing. Fast dissolving drug delivery systems were first invented in the late 1970s as to overcome swallowing difficulties associated with tablets and capsules for pediatric and geriatric patients. Buccal drug delivery has lately become an important route of drug administration. Various bioadhesive mucosal dosage forms have been developed, which includes adhesive tablets, gels, ointments, patches, and more recently the use of polymeric films for buccal delivery, also known as mouth dissolving films. The surface of buccal cavity comprises of stratified squamous epithelium which is essentially separated from the underlying tissue of lamina propria and submucosa by an undulating basement membrane. It is interesting to note that the permeability of buccal mucosa is approximately 4-4,000 times greater than that of the skin, but less than that of the intestine.Hence, the buccal delivery serves as an excellent platform for absorption of molecules that have poor dermal penetration. The primary barrier to permeability in otiral mucosa is the result of intercellular material derived from the so-called ‘membrane coating granules’ present at the uppermost 200 μm layer. These dosage forms have a shelf life of 2-3 years, depending on the active pharmaceutical ingredient but are extremely sensitive to environmental moisture. An ideal fast dissolving delivery system should have the following properties: High stability, transportability, ease of handling and administration, no special packaging material or processing requirements, no water necessary for application, and a pleasant taste. Therefore, they are very suitable for pediatric and geriatric patients; bedridden patients; or patients suffering from dysphagia, Parkinson's disease, mucositis, or vomiting. This novel drug delivery system can also be beneficial for meeting current needs of the

industry. Rapidly dissolving films (RDF) were initially introduced in the market as breath fresheners and personal care products such as dental care strips and soap strips. However, these dosage forms are introduced in the United States and European pharmaceutical markets for therapeutic benefits. The first of the kind of oral strips (OS) were developed by the major pharmaceutical company Pfizer who named it as Listerine pocket pack and were used for mouth freshening. Chloraseptic relief strips were the first therapeutic oral thin films (OTF) which contained 7 benzocaine and were used for the treatment of sore throat. Formulation of fast dissolving buccal film involves material such as strip-forming polymers, plasticizers, active pharmaceutical ingredient, sweetening agents, saliva stimulating agent, flavoring agents, coloring agents, stabilizing and thickening agents, permeation enhancers, and superdisintegrants. All the excipients used in the formulation of fast dissolving film should be approved for use in oral pharmaceutical dosage forms as per regulatory perspectives.

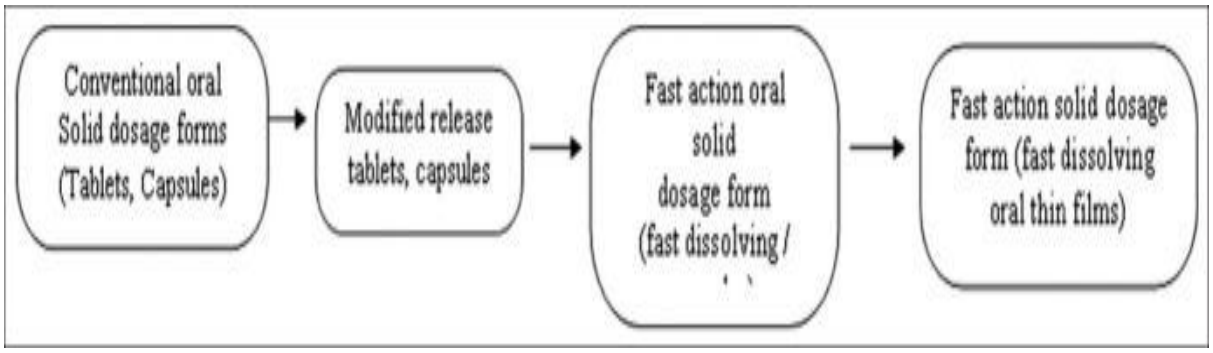

Figure 1: Stages in development of oral solid dosage forms:

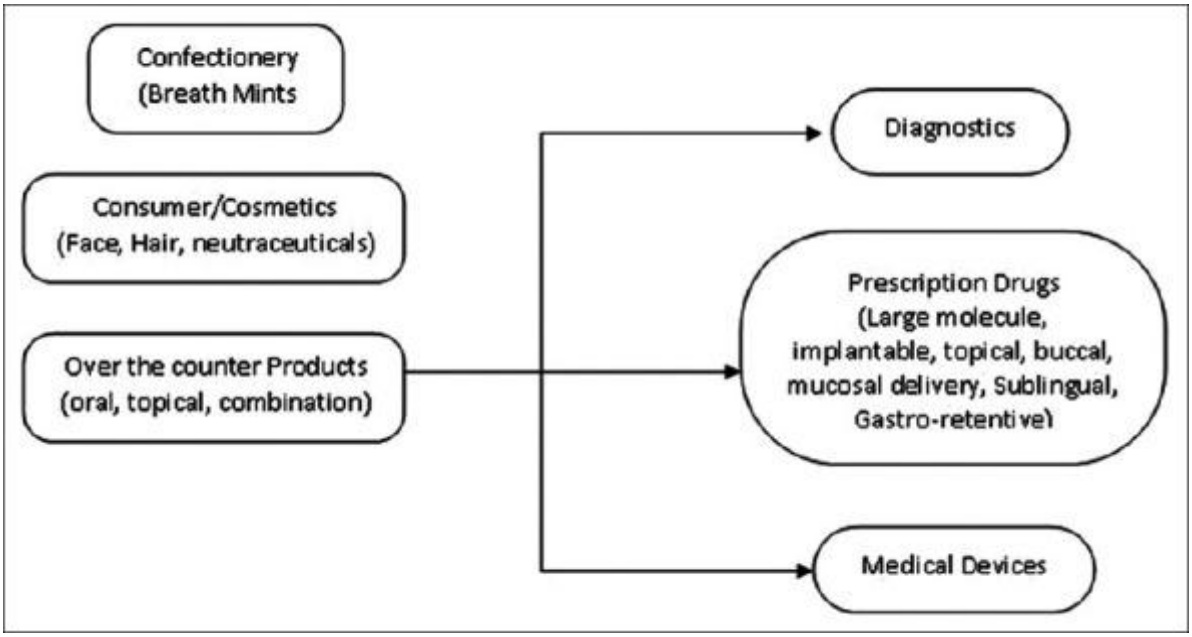

Figure 2: Evolution of Oral soluble filims

Oral soluble filims

Oral films, also called oral wafers in the related literature, are a group of flat films which are administered into the oral cavity. Although oral film systems, the third class, have been in existence for a number of years, they have recently become the new area of interest in fast-dissolve pharmaceutical drug delivery. Dissolvable OTF or OS have evolved over the past few years from confection and oral care markets in the form of breath strips and become a novel and widely accepted form by consumers for delivering vitamins and personal care products. Companies with experience in the formulation of polymer coatings containing active pharmaceutical ingredients (APIs) for transdermal drug delivery capitalized on the opportunity to transition this technology to OTF formats. Today, OTF are a proven and accepted technology for systemic delivery of APIs for over-the-counter (OTC) medications and are in the early- to mid-development stages for prescription drugs.

Table 1 : comparative account of three different fast dissolving technologies.

Properties	Lyophilized system	Compressed tablet based system	Oral thin films
Composition	Solution or suspension of drug with excipients	Active pharmaceutical ingredient with superdisintegrants	Hydrophilic polymers with drug and other excipients
Technology used	Lyophilization	Direct compression	Solvent casting, hot melt extrusion
Characteristics	High porosity which allow rapid water or saliva penetration and disintegration	Different levels of hardness and friability these result in varying disintegration and packaging needs	Large surface area leads to rapid disintegration
Packaging	Blister pack	High density polyethylene bottles	Blister cards with multiunits

SPECIAL FEATURES OF FAST DISSOLVING FILMS

- Film should be thin and elegant.
- Available in various size and shapes.
- Unobstructive.
- It should adhere to the oral cavity easily.
- Should processes fast disintegration without water.
- Rapid release.

ADVANTAGES OF FAST DISSOLVING FILMS

- Convenient dosing.
- No water needed.
- No risk of chocking.

- Taste masking.
- Enhanced stability.
- Improved patient compliance.
- The drug enters the systemic circulation with reduced hepatic first pass effect.
- Site specific and local action.
- Availability of large surface area that leads to rapid disintegration and dissolution within oral cavity.
- Dose accuracy in comparison to syrup.

DISADVANTAGE OF ORAL SOLUBLE FILIMS

- The disadvantage of OS is that high dose cannot be incorporated into the strip. The dose should be between 1-30 mg.
- There remain a number of technical limitations with use of film strips; the thickness while casting the film. Glass Petri plates cannot be used for casting.
- The other technical challenge with these dosage forms is achieving dose uniformity.
- Packaging of films requires special equipments and it is difficult to pack.

IDEAL CHARACTERISTICS OF A SUITABLE DRUG CANDIDATE For Oral soluble FILIMS

- The drug should have pleasant taste.
- The drug to be incorporated should have low dose up to 40 mg.
- The drug should have smaller and moderate molecular weight.
- The drug should have good stability and solubility in water as well as saliva.
- It should be partially unionized at the pH of oral cavity.
- It should have ability to permeate the oral mucosal tissue.

CLASSIFICATION OF OTF

There are three subtypes of oral fast dissolving films:

- Flash release.
- Mucoadhesive melt-away wafer.
- Mucoadhesive sustained release wafers.

Table 2 lists three types of oral fast dissolving films along with their properties.

Properties	Flash release	Mucoadhesive melt-away wafers	Mucodhesive sustained released wafers
Area (cm^2)	2-8	2-7	2-4
Thickness (μm)	20-70	50-500	50-250
Structure	Single layer	Single or multilayer	Multilayer system
Excipients	Soluble hydrophilic polymers	Soluble hydrophilic polymers	Low/nonsoluble polymers
Drug phase	Solid solution	Solid solution or suspended drug particle	Suspension and/or solid solution
Application	Tongue (upper palate)	Gingival or buccal region	Gingival, (other region in the oral cavity)
Dissolution	60 s	In few minutes forming gel	Maximum 8-10 h
Site of action	Systemic or local	Systemic or local	Systemic or local

FILM FORMING POLYMERS

A variety of polymers are available for preparation of fast dissolving oral films.The use of film forming polymers in oral films has attracted considerable attention in medical and nutraceutical applications. The selection of film forming polymers, is one of the most important and critical parameter for the successful development of film formulation. The polymers can be used alone or in combination to provide desired film properties. The polymers used in oral film formulation should be.

- Nontoxic and nonirritant.
- Devoid of leachable impurities.
- Should not retard disintegration time of film.
- Tasteless.
- Should have good wetting and spread ability property.
- Should have sufficient peel, shear, and tensile strength.
- Readily available.
- Inexpensive.
- Sufficient shelf life.
- Should not aid in causing secondary infections in oral mucosa.

Presently, both natural and synthetic polymers are used for the preparation of orally dissolving films.

Table 3: Represent various natural and synthetic polymers used for preparation of fast dissolving films.

Polymer	Examples
Natural polymer	Pullulan, starch, gelatin, pectin, sodium alginate, maltodextrins, polymerized rosin
Synthetic polymer	Hydroxypropyl methylcellulose, sodium carboxymethylcellulose, polyethylene oxide, hydroxypropyl cellulose, polyvinylpyrrolidone, polyvinyl alcohol, ethyl cellulose

APPROACHES USED FOR THE FORMULATION OF FAST DISSOLVING FILMS

Conventional approaches

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

Solvent casting method

In this method, firstly the water soluble polymers are dissolved in water at 1,000 rpm and can be heated up to 60°C. All the other excipients like colors, flavoring agent, sweetening agent, etc., are dissolved separately. Then both the solutions obtained are mixed thoroughly stirring at 1,000 rpm. The obtained solution is incorporated with the API dissolved in suitable solvent. The entrapped air is removed by vacuum. The resulting solution is cast as a film and allowed to dry, which is then cut into pieces of the desired size.

Hot-melt extrusion

In hot melt extrusion method, the initial mass is formed with the help of carriers. To form initial mass, the drug is mixed with carriers and a solid mass is obtained and dried. Then dried granular material is introduced into the extruder. The extruder is divided into four zones having following degrees of temperature: 800 (zone 1), 1150 (zone 2), 1000 (zone 3), and 650°C (zone 4). The speed of extruder screw speed should be set at 15 rpm in order to process the granules inside the barrel of extruder for approximately 3-4 min so that mass should be properly melted. The extrudate (T = 650°C) obtained is then pressed into a cylindrical calendar in order to obtain a film. There are certain benefits of hot melt extrusion:

Fewer operation units, minimum product wastage, possibility to scale up, an anhydrous process, absence of organic solvents, include shorter temperature and shorter residence time of the drug carrier mix, and better content uniformity.

Semi-solid casting

This method is mostly preferred when film ingredient involves acid insoluble polymer. In this firstly, the water soluble polymers are dissolved in water. The obtained solution is added to the acid insoluble polymer solution which is separately formed. Both the solutions are mixed properly. After mixing the two solutions, appropriate amount of plasticizer is added to the obtained final solution so that gel's mass can be obtained. At last, the gel mass is casted onto the films or ribbons using heat controlled drums. The thickness of the film should be about 0.015-0.05". The ratio of the acid insoluble polymer to film forming polymer should be 1:4. Examples of acid insoluble polymers are cellulose acetate phthalate and cellulose acetate butyrate.

Solid dispersion extrusion

Method involves the solid dispersion of drug incorporated in melted polymer solution so that drug can be loaded. The drug is dissolved in suitable liquid solvent and obtained solution is added to the melt of suitable polymer, obtainable below 70°C without removing the liquid solvent to obtain the solid dispersion. Finally the obtained solid dispersions are shaped into films by means of dyes.

Rolling method

In rolling method, both the drug solution and film forming polymer solution are mixed thoroughly and the resultant solution or suspension is subjected to the roller. The solution or suspension should have specific rheological consideration. The film is dried on rollers and cut into desired shapes and sizes.

Patented approaches

XGel

XGel™ film provides unique product benefits for healthcare and pharmaceutical products: It is nonanimal derived, approved on religious grounds, and is suitable for vegetarians; the film is genetically modified organism (GMO) free and continuous production processing provides an economic and competitive manufacturing platform. XGel™ film can be taste masked, colored, layered, and capable of being enteric properties whilst also having the ability to

incorporate active pharmaceutical ingredients. The XGel™ film systems can be made to encapsulate any oral dosage form and can be soluble in either cold or hot water. XGel™ film is comprised of a range of different water soluble polymers, specifically optimized for the intended use.

Soluleaves

This technology is used to produce a range of oral delivery films that can incorporate active ingredients, colors, and flavors. Soluleaves™ films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients, and flavors. This quality makes edible films an excellent delivery method for a large range of products requiring fast release in the mouth. For pharmaceutical uses, this method of administration is especially useful for pediatric or elderly patients who may have difficulty swallowing traditional tablets or capsules. The delivery system can be used for the cough/cold, gastrointestinal, and pain therapeutic areas as well as delivering nutritional products. Soluleaves™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 min.

Wafertab

Wafertab™ is a drug delivery system that incorporates pharmaceutical actives into an ingestible filmstrip. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The Wafertab™ filmstrip can be flavored for additionally improved taste masking. The active ingredient is precisely dosed and integrated into the body of a premanufactured XGel™ film, thus preventing exposure to unnecessary heat and moisture and potentially enhancing product stability. The Wafertab™ system lends itself to many possibilities for innovative product design, enabling multiple films with different actives to be bonded together. Wafertab™ can be prepared in a variety of shapes and sizes and is an ideal method for delivery of medicines, which require fast release or for use by patients who have difficulty in swallowing.

Foamburst

It is a special variant of the Soluleaves™ technology where an inert gas is passed into the film during production. This results in a film with a honeycombed structure, which dissolves rapidly giving a novel mouth sensation. Foamburst™ has attracted interest from food and confectionary manufacturers as a means of carrying and releasing flavors.

Micap

Micap plc signed an option agreement in 2004 to combine its expertise in microencapsulation technology with the Bio Progress water soluble films. The developments will be aimed at providing new delivery mechanisms for the $1.4 billion global market for smoking cessation products (SCPs).

APPLICATIONS OF OTF IN DRUG DELIVERY SYSTEMS

- Oral mucosal delivery via sublingual, buccal, and mucosal routes by use of oral thin film could become preferential delivery method for therapies requiring rapid drug absorption, including those used to manage pain, allergies, sleep, and central nervous system disorders.
- Topical applications: The use of dissolvable films may be feasible in delivery of active agents such as analgesic or antimicrobial agents in the wound care and other applications.
- Gastrorententive delivery system: Dissolvable films are being considered in the dosage form for which water soluble and poorly soluble molecules of various molecular weight are contained in film formate. Dissolution of film could be triggered by pH or enzyme secretion of gastrointestinal tract (GIT) and could potentially be used for treatment of gastrointestinal disorder.
- Diagnostic devices: Dissolvable films may be loaded with sensitive reagent 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.

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