Mouth dissolving strips– a review

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An open access journal

Supporting Information:

Received: 05 October 2018
Accepted: 28 November 2018
Published: 12 December 2018

Competing Interests:
The authors have declared that no competing interests exist.

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ABSTRACT

In the recent years most useful route of drug delivery system is the oral route in all types of patient. Mouth dissolving strips is the type of drug delivery system which when placed in the oral cavity, disintegrate or dissolve within few seconds without the intake of water. The advantages of mouth dissolving strips are the administration to pediatric and geriatric patient. This technology has been used for local action, rapid release products.These films have a potential to deliver the drug systemically through intragastric, sublingual or buccal route of administration and also has been used for local action. The mouth dissolving strips are available in various shapes, size and thickness.This article is an overview of mouth dissolving strips encompassing materials used in mouth dissolving strips, manufacturing process, applications, business technologies and future business prospects of this technology

Keywords: Strips, Mouth Dissolving Strips, Rapid Release. Dose, Drug delivery

Introduction

Fast-dissolving drug-delivery systems came into existence in the late 1970's as an alternative to tablets, capsules and syrups for pediatric and geriatric patients who has difficulties in swallowing traditional oral solid-dosage forms. These systems consist of the solid dosage forms that disintegrate and dissolve quickly in the oral cavity without the administration of water.[1]

The oral route is one of the most acceptable route for patient compliance. Many pharmaceutical firms have directed their research activity in re-formulating existing drugs into new dosage forms.Research and development in the oral drug delivery segment has led to transition of dosage forms from simple conventional tablets or capsules to modified release tablets or capsules to fast dissolving tablet and in the recent development of mouth dissolving stripss are available for the oral drug delivery system as shown in fig no 1. A number of molecules is introduced into this type of delivery system. They may include cough/cold remedies (anti-tussives, expectorants), sore throat, erectile dysfunction drugs, anti-histaminic, anti-asthmatics, gastrointestinal disorders, nausea, pain and CNS (e.g. anti-parkinson disease). Applications like comprise snoring aid, caffeine strips, sleeping aid , multivitamins etc.

An ideal buccoadhesive system is the one that adhere to the site of attachment for a few hours, releases the drug in a controlled fashion, facilitates the rate and extent of drug absorption, does not cause any irritation or inconvenience to the patient, does not interfere with the normal functions such as talking, drinking etc. and that provides unidirectional drug release toward the mucosa. The mass about the proper way to administer the product like givinginstructions "do not swallow" or "do not chew"[2]

By using technology for transdermal patch it was developed. The delivery system consists of a very thin oral strips, which is simply placed on the patient's tongue or any oral mucosal tissue, instantly wet by saliva the film rapidly hydrates and adheres onto the site of application.[3] conditions has a flow rate of 1–2 ml/min.[5]A strips or film can be defined as a dosage form that employs a water-dissolving polymer (generally a hydrocolloid, which may be a bio adhesive polymer), which allows the dosage form to quickly hydrate, adhere, and dissolve when placed on the tongue or in the oral cavity (i.e., buccal, palatal, gingival, lingual, or sublingual, etc.) to provide rapid local or systemic drug delivery.[6]

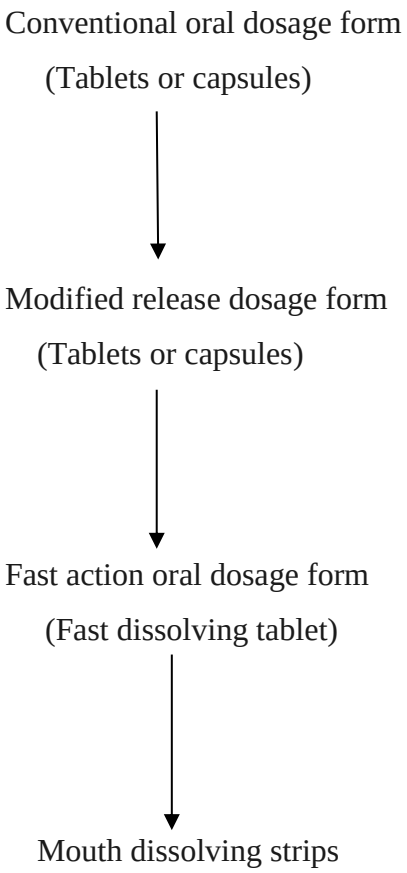


Fig1: Modification in oral dosage form

Developing formulations for children has been a challenging task.Amongst other factors, palatability of formulations of pediatric oralmedications is one of the most significant factors influencing complianceto therapeutic regimens.[7]

Characteristics of Mouth Dissolving Strips (8-11)

- ✓ Do not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds.
- ✓ Compatible with taste masking and other excipients.
- ✓ They posses pleasant mouth feel.
- ✓ Leave minimal or no residue in the mouth after oral administration.

- ✓ They can withstand the rigors of the manufacturing process and post manufacturing handling.[8]
- ✓ Resistant to environmental conditions such as humidity and temperature .
- ✓ They are adaptable and amenable to theexisting processing and packaging machinery.
- ✓ Processing and packaging of strips or films can be done at low costs prices.
- ✓ The strips are thin effective film and available in various size and shapes.
- ✓ The strips have also Unobstructive, Excellent mucoadhesion.
- ✓ Due to presence of larger surface in mouth they have Fast disintegration of formulation and Rapid release of drug.[9]
- ✓ The oral or buccal mucosa being highly vascularized, drugs can be absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism.
- ✓ Enhanced oral bioavailability of molecules that undergo first pass effect.
- ✓ Bypassing the first pass effect leads to reduction in the dose which can lead to reduction in side effects associated with the molecule.[10]

Choice of Drug candidate for Mouth Dissolving Strips (1,8)

- ✓ The drug should have pleasant taste.
- ✓ The drugs to be incorporated have low doseupto 40 mg.
- ✓ The drug have smaller and moderatemolecular weight.[1]
- ✓ The drug should have good stability and solubility in water as well as in saliva.
- ✓ It should be partially unionized at the pH oforal cavity.
- ✓ It should have the ability to permeate oralmucosal tissue.[8]

Advantages of Mouth Dissolving Strips (12-14)

- ✓ Oral dissolving films can be administered withoutwater, anywhere, any time.
- ✓ Due to the presence of larger surface area, filmprovide rapid disintegrating and dissolution in theoral cavity.
- ✓ Oral dissolving films are flexible and portable innature so they provide ease in transportation,during consumer handling and storage.

- ✓ Suitability for geriatric and pediatric patients, whoexperience difficulties in swallowing mentally ill, thedevelopmentally disable and the patients who areun-cooperative, or are on reduced liquid intakeplans or are nauseated.[12]
- ✓ Beneficial in cases such as motion sickness, acutepain, suede episodes of allergic attack or coughing,where an ultra rapid onset of action required.
- ✓ Stability for longer duration of time, since the drugremains in solid dosage form till it is consumed. So,it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms ofbioavailability.[13]
- ✓ As compared liquid formulations, precision in theadministered dose is ensured from each strips of the film.
- ✓ The oral or buccal mucosa being highly vascularizeddrugs can be absorbed directly and can enter thesystemic circulation without undergoing first-passhepatic metabolism. This advantage can beexploited in preparing products with improved oral bioavailability of molecules that undergo first pass effect.

Disadvantages of Mouth Dissolving Strips

- ✓ Oral disintegrating films have limitations in terms of the amount of drug that can be incorporated in each unit dose.
- ✓ Expensive packaging.
- ✓ Dose uniformity is a technical challenge.
- ✓ Water insoluble drug cannot incorporateor taste masking is required.

Biopharmaceutical Consideration of Mouth Dissolving Strips

When designing a new dosage form,before the formulation some biopharmaceutical factors need to be considered.Oral Films disintegrate rapidly so absorption of drug is fast.Factors like age, nature of the oral cavity, and blood flow to oral cavity should be considered. Distribution of drug depends on tissue permeability, perfusion rate; binding of drug to tissue, drug interaction etc. The pharmacodyanamic performance of the dosage form is affected by different factors like age, sex and health of the patient. [15]

Mechanism of Drug Release in Mouth Dissolving Strips

The drug release mechanism in Mouth Dissolving Strips Formulation delivery system include simply stripss placed on a patient's tongue or any mucosal tissue. After placing it the film dissolves within seconds, promoting first pass metabolism as compared to tablet and other immediate release oral solid dosage forms, and may increase the bioavailability of drug.Due to presence of saliva in mouth and presence of hydrophilic polymer and other excipients, the film rapidly hydrates and to release the medication for oromucosal absorption.

Classification of Mouth Dissolving Strips

- ✓ Lyophilized systems
- ✓ Compressed tablet-based systems
- ✓ Oral thin films

Lyophilized systems

The technology around these systems involves taking a suspension or solution of drug with other structural excipients, through the use of a mould or blister pack, forming tablet-shaped units. The units or tablets are then frozen and lyophilized in the pack or mould. The resulting units allows rapid water or saliva penetration and very fast disintegration.

Compressed tablet-based systems

This system is produced using standard tablet technology by direct compression of excipients. Depending on the method of manufacture, the tablet technologies have different levels of hardness and friability. The speed of disintegration for fast-dissolve tablets compared with a standard tablet is achieved by formulating it using water soluble excipients or super-disintegrant or effervescent components

Oral Thin Films

Oral films are a group of flat films which are administered into the oral cavity. Dissolvable oral thin films (OTFs) or oral strips (OS) evolved over the past few years 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. Such systems use a variety of hydrophilic polymers to produce a 50- 200 mm film. This film can reportedly incorporate soluble, insoluble or taste-masked drug substances. The film is manufactured as a large sheet and

then cut into individual dosage units for packaging in a range of pharmaceutically acceptable formats or according to patients needs the oral strips are also called oral wafers.

Structure of Oral Mucosa

The oral mucosa consists of an outer layer of stratified squamous epithelial tissue (Figure2).Below this lies a basement membrane, a lamina propria followed by the sub mucosa because the innermost layer. The epithelial tissue is analogous to stratified squamous epithelia found in the rest 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 are shed from the surface of the epithelial tissue.[18]

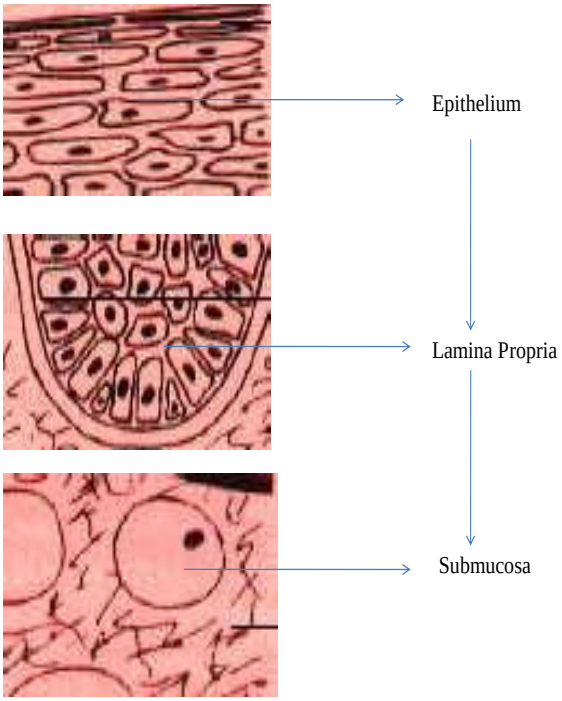


Fig 2: Different layers of oral mucosa

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 tissue layer as an entire. The oral tissue layer thickness varies looking on the site: the buccal mucosa measures at 500-800 μm, whereas the tissue layer thickness of the hard and soft palates, the floor of themouth, the ventral tongue and also the gingivae measure at regarding 100-200 The nonkeratinized epithelia are found to be significantly a lot of permeable to water than keratinized epithelia.

Permeability

The oral mucosa normally is intermediate between that of the epidermis and intestinal tissue layer in terms of permeability. it is calculable that the permeability of the buccal mucosa is 4-4000 times larger than that of the skin.There are appreciable variations in permeableness between different regions of the mouth as a result of the varied structures and functions of the various oral mucosa.

Composition of Oromucosal Region

Oromucosal Cells are created of proteins and carbohydrates. it's adhesive in nature and acts as a lubricator, permitting cells to move relative to one another with less friction.[22] The mucous secretion is additionally believed to play a job in bioadhesion of mucoadhesive drug

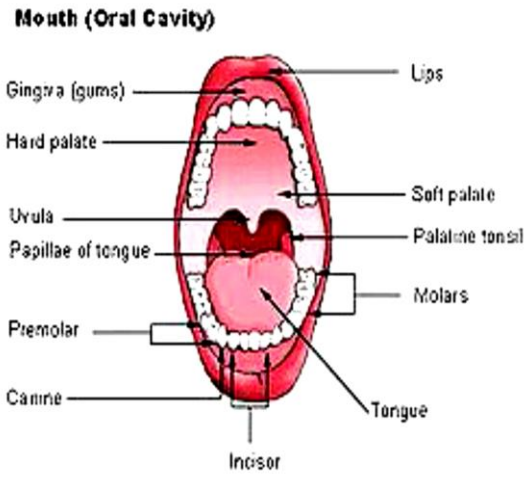


Fig 3 Mouth cavity

delivery systems. In different a part of body mucous secretion is synthesized and secreted by the goblet cells, but within the oral tissue layer, mucous secretion is secreted by the most important and minor secretion glands as a part of secretion. Up to 70th of the whole mucin found in secretion is contributed by the minor secretion glands. Another feature of the mouth is that the presence of saliva (digestive secretion) created by 3 pairs of secretion glands(parotid, submandibular and articulator glands). secretion is usually water with I Chronicles organic and inorganic materials. The organic process enzyme present in secretion is salivary enzyme, that

breaks down starch molecules to shorter chains of glucose molecules. secretion is created from plasma and so contains several of the chemicals that are found in plasma.

Formulation Consideration

In the formulation of mouth dissolving strips excipients play an important role as fallow;

- ✓ Active pharmaceutical ingredient
- ✓ Film forming polymers
- ✓ Plasticizer
- ✓ Stabilizing and thickening agents
- ✓ Saliva stimulating agent
- ✓ Sweetening agent
- ✓ Flavoring agent
- ✓ Coloring agent

Active Pharmaceutical Ingredient

A typical composition of the film contains 1-25% w/w of the drug. Variety of APIs can be delivered through fastdissolving films. Small dose molecules are the best candidates to be incorporated in mouth dissolving strips. Multivitamins upto 10% w/w of dry film weight was incorporated in the films with dissolution time of less than 60 seconds. It is always useful to have micronized API which will improve the texture of the film and also for better dissolution and uniformity in the mouth dissolving strips. Many APIs, which are potential candidates for mouth dissolving strips technology, have bitter taste Complexation technology involves use of cyclodextrins, resins which surround the bitter API and prevents the direct contact with saliva Matrixing of the bitter drug or coating of drug with water insoluble polymer has been used widely for taste masking ofdrugs. The bitter taste of paracetamol was masked with the use of lipidic excipients like hard fat and lecithin.

Film Forming Polymers

A variety of polymers are available for preparation of oral strips. The polymers can be used alone or in combination to obtain the desired stripss properties. The film obtained should be tough enough so that there won't be any damage while handling or during transportation. The robustness of the strips depends on the type of polymer and the amount in the formulation the other hand, fast dissolving strips dosage form should have the property to disintegrate in seconds when placed in\mouth and deliver the drug to the oral cavity instantaneously. Modified starches are also used for preparation of oral strips. Due to low cost of this excipient it is used in combination of pullulan to decrease the overall cost of the product. About 50 to 80%w/w of pullulan can be replaced by starch in the production of oral strips without loss of required properties of Pullulan. Typically 60 to 65%w/w of water soluble polymer is preferred for preparation of oral strips with desired properties. Many times, mixtures of polymers are used to improve hydrophilicity, flexibility, mouth-feel and solubility characteristics of oral strips. Polyvinyl pyrrolidone films are brittle in nature and therefore copovidone is mixed with poly vinylpyrrolidone for preparation of flexible fast disintegrating strips. The bioadhesive polymer used in such formulations imparts the adhesive property to the strips such that it adheres to buccal mucosa to deliver the drug for prolonged period. Bioadhesive polymer should ideally adhere quickly to the buccal mucosa and should have sufficient mechanical strength. Polymers used for oral strips should have good shelf life and they should not aid in causing secondary infections in the oral mucosa or dental regions. It would be ideal to have a polymer that would have local enzyme inhibition action along with penetration enhancing property.

Plasticizer

Plasticizer is a vital ingredient of the oral strips formulation. It helps to improve the flexibility of the strips and reduces the brittleness of the strips. Plasticizer significantly improves the strips properties by reducing the glass transition temperature of the polymer. The selection of plasticizer will depend upon its compatibility with the polymer and also the type of solvent employed in the casting of strips. The flow of polymer will get better with the use of plasticizer and enhances the strength of the polymer. Glycerol, Propylene glycol, low molecular weight polyethylene glycols, phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, Citrate

derivatives such as tributyl, triethyl, acetyl citrate, triacetin and castor oil are some of the commonly used plasticizer excipients.

Stabilizing and Thickening Agents

The stabilizing and thickening agents are employed to improve thev viscosity and consistency of dispersion or solution of the strips spreparation solution or suspension before casting. Natural gums like xanthan gum, locust bean gum, carragenan and cellulosic derivativescan be used in the concentration up to 5%w/w as thickening agents and stabilizing agents Other ingredients such as surfactants and emulsifying agents are also added in small amount to improve the strips properties.

Saliva Stimulating Agent

The purpose of using saliva stimulating agents is to increase the rate of production of saliva that would aid in the faster disintegration of the rapid dissolving strips formulations. Generally acids which are used in the preparation of food can be utilized as salivary stimulants Citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid are the few examples of salivary stimulants, citric acid being the most preferred amongst them. These agents are used alone or incombination between 2 to 6%w/w of weight of the strips. Other oral strips ingredients such as sweeteners also act as salivary stimulants. Food grade sugars as well as synthetic sugars are useful salivary stimulants along with acidulants. Glucose, fructose, xylose, maltose, lactose are few examples of such sweeteners.The stimulation of salivation can be measured by comparing the amount of resting flow and stimulated flow at equal time under same conditions.The stimulant action of sweeteners is dependent on the sweetness value. Fructose has the sweetness value of 1.1 as compared to 0.7 of glucose and 1.0 of sucrose.

Sweetening Agent

Sweeteners have become the important part of the food products as well as pharmaceutical products intended to be disintegrated or dissolved in the oral cavity. The sweet taste in formulation is more important in case of pediatric population.The flavor quality of these artificial sweeteners is different than the natural sweeteners and may not be acceptable to the patients who are accustomed to the natural sugars. The amalgamation of sweeteners may lead to synergism and improvement in the taste of the formulations. Aspartame was used for the preparation of oral strips of valdecoxib. For the oral strips of piroxicam, maltodextrin was

employed as sweetening agent .Generally sweeteners are used in the concentration of 3 to 6 %w/w either alone or in combination Natural sweeteners as well as artificial sweeteners are used to improve the palatability of the mouth dissolving formulations. Suitable sweeteners include:[37]

- Water soluble natural sweetener: xylose, ribose,glucose, sucrose, maltose, stevioside etc.
- Water soluble artificial sweetener: sodium or calcium saccharin salts, cyclamate salts, acesulfame-k etc
- Di-peptide based sweetener: aspartame

Flavoring Agent

Perception for the flavors changes from individual to individual depending upon the ethnicity and liking. It was observed that age plays a significant role in the taste fondness. The geriatric population like mint or orange flavors while younger generation like flavors like fruit punch, raspberry etc. The selection of flavor is also dependant on the type of drug to be incorporated in the formulation. For example,mint flavor is generally added in products used for gastric related ailments like indigestion. The acceptance of the oral disintegrating or dissolving formulation by an individual by and large depends on the initial flavor quality which is observed in first few seconds after the product has been consumed and the after taste of the formulation which lasts for at least about 10 min. Flavoring agents can be selected from synthetic flavor oils, oleoresins, extract derived from various parts of the plants like leaves,fruits and flowers. Flavors can be used alone or in the combination.Peppermint oil, cinnamon oil, spearmint oil, oil of nutmeg are examples of flavor oils while vanilla, cocoa, coffee, chocolate and citrus are fruity flavors. Apple, raspberry, cherry, pineapple are few examples of fruit essence type. The amount of flavor needed to mask the taste depends on the flavor type and its strength. Preferably up to10%w/w flavors are added in the oral strips formulations. Cooling agents like monomethyl succinate can be added to improve the flavor strength and to enhance the mouth-feel effect of the product.

Coloring agent

Pigments such as titanium dioxide or FDC approved coloring agents are incorporated (not exceeding concentration levels of 1%w/w) in oral strips when some of the formulation ingredients or drugs are present in insoluble or suspension form.

Table No. 2. The general formula in mouth dissolving strips include category of excipients with their concentration;

Composition	Concentration
Drug	1-40 %
Water soluble polymer	1-45 %
Plasticizers	0-20 %
Sweetening agent	3- 6 %
Saliva stimulating agent	2 - 6%
Fillers, colors, flavors	0-30 %

Methods of Preparation

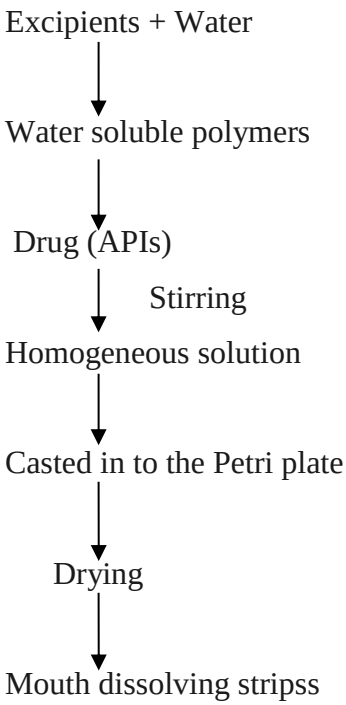
The following process can be used for manufacture the mouth dissolving stripss

- ✓ Solvent Casting Method
- ✓ Semisolid Casting Method
- ✓ Hot Melt Extrusion Method
- ✓ Solid Dispersion Extrusion Method
- ✓ Rolling Method

Solvent Casting Method

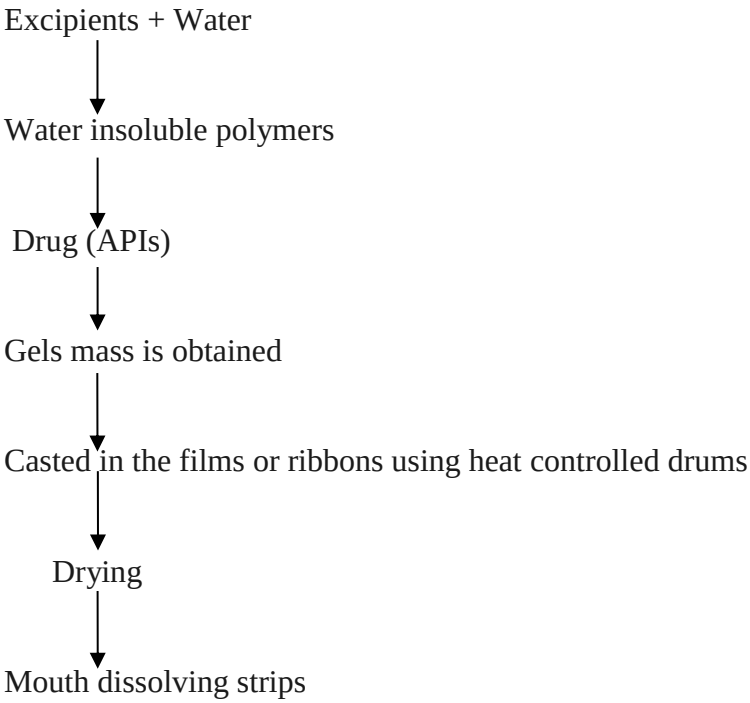
The mouth dissolving strips is preferably formulated using the solvent-casting method, whereby the water-soluble ingredients are dissolved to form a clear viscous solution. The API and other agents are dissolved in smaller amounts of the solution, and combined with the bulk. This mixture is then added to the aqueous viscous solution. 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.[44] Water-soluble hydrocolloids used to prepare mouth dissolving strips

include: hydroxyl propyl methyl cellulose (HPMC), hydroxyl propyl cellulose (HPC), pullulan, sodium alginate, pectin, carboxy methyl cellulose (CMC), polyvinyl alcohol (PVA). The selection of solvent essentially depends on the API to be incorporated into the strips.



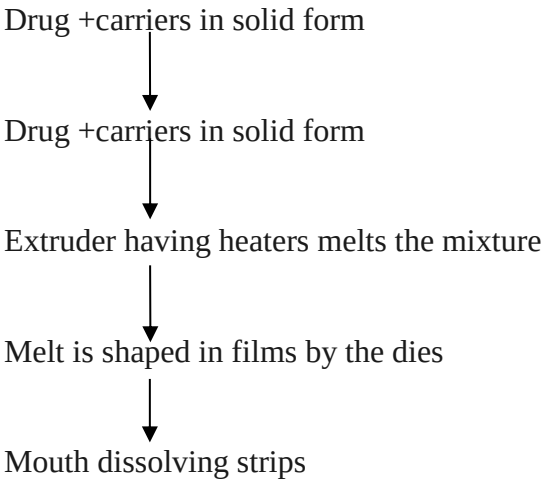
Semisolid Casting Method

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.[45] Acid-insoluble polymers used to prepare films include: cellulose acetate phthalate, cellulose acetatebutyrate. Acid insoluble polymer and film forming polymer should be used in the ratio of 1:4.



Hot Melt Extrusion Method

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 80^0C (zone 1), 115^0C(zone 2), 100^0C (zone 3) and 65^0C (zone 4). The extrudate(T = 65^0C) then pressed into a cylindrical calendar in orderto obtain a film.[46] There are certain benefits of hot melt extrusion such as- Fewer operation units,Better content uniformity,An anhydrous process.



Solid Dispersion Extrusion Method

The term "solid dispersions" refers to the dispersion of one or more active ingredients in an inert carrier in a solid state in the presence of amorphous hydrophilic polymers and also using methods such as melt extrusion .This involves a drug which is first dissolved in a suitable liquid solvent and then this solution is incorporated into the melt of suitable polymer, obtainable below 70^0C without removing the liquid solvent.[46] The selected solvent or dissolved drug may not be miscible with the melt of the polymer. In simply this method include immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films with the help of dies.

Drug + suitable liquid solvent.

↓

Solution is incorporated into melt

↓

Shaped into the films by means of dies

↓

Mouth dissolving strips

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 therollers and cut in to desired shapes and sizes.

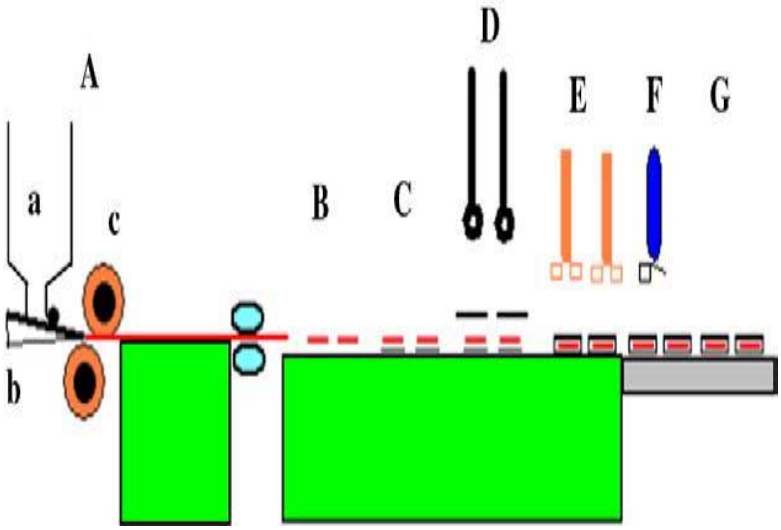


Fig 4: Schematic representation of mouth dissolving strips manufacturing unit

A – Formation ofmedicated film takes place. The rollers can be adjusted to get the desired film thickness. After formation of film, it is dried.

a– Reservoir for the film forming materials ,b – Deaerator and film applicator, c – Rollers.

B – The driedmedicated film is slit and cut into little strips of desired size.

C – Strips are placed into lower packaging web.

D– Laser printer prints on upperpackagingweb.

E – Sealing head seals the strips into single dose sachets.

F – Introduction oftear-notch/slit/cut off to sachet.

G – Quality control conveyer to final packaging.

Evaluation Parameter

The Quality control test for Mouth Dissolving Strips is as fallows

- ✓ Organoleptic test
- ✓ Thickness
- ✓ Dryness/tack test
- ✓ Tear resistance
- ✓ Tensile strength

- ✓ Percent elongation
- ✓ Young's modulus
- ✓ Folding endurance
- ✓ Swelling test
- ✓ Surface pH test
- ✓ Disintegration test
- ✓ Assay
- ✓ *In-vitro* Dissolution test

Organoleptic test

In Organoleptic test some general tests are carried out such as size, shape, taste of the product should possess the desired features of sweetness and flavor which is acceptable to a large mass of population. For evaluation of psychophysical evaluation of the product, special controlled human taste panels are used. In-vitro methods of utilizing taste sensors, specially designed apparatus and drug release by modified pharmacopoeia methods are being used for this purpose. These in-vitro taste assessment apparatus and methodologies are well suited for high through put taste screening of oral pharmaceutical formulations.

Color is a vital means of identification for many pharmaceutical products and is also usually important for consumer acceptance. The color of the product must be uniform within a dosage form, Odor is also be important for consumer acceptance of oral dosage forms and can provide an indication of the quality of oral strips.

Thickness

The thickness of film can be measured by digital micrometer screw gauge or digital venire at different planned locations. This is essential to ascertain uniformity in the thickness of the film as this is directly related to the accuracy of dose distribution in the film. The thickness of film should be in range of the 5-200 micrometer. The thickness of the film can be adjusted depending upon the surface area and thickness of different areas in mouth.

Dryness/Tack test

Dryness is the property is to measure the water or used solvent content in the formulation. Tack is the tenacity with which the film adheres to an accessory (a piece of paper) that has been pressed into contact with the film.About eight stages of film drying process have been identified

and they are set-to-touch, dust-free, tack-free (surface dry), Dry-to-touch,dry-hard, dry-through (dry-to-handle), dry-to-recoat and dry print free.Although these tests are primarily used for paint films.

Tear resistance

Tear resistance of plastic film or sheeting is a complex function of its ultimate resistance to rupture. Basically very low rate of loading 51 mm (2 in)/min is employed and is designed to measure the force to initiate tearing. The maximum stress or force (that is generally found near the onset of tearing) required to tear the specimen is recorded as the tear resistance value in Newton.

Tensile strength

Tensile strength is the maximum stress (applied at one point) required for a oral strips to breaks. It is calculated by the applied load at crack divided by the cross- sectional area of the strips as given in the equation below.

$$\text{Tensile strength} = \frac{\text{Load at failure} \times 100}{\text{Strips thickness} \times \text{Stripsswidth}}$$

Percent Elongation

When stress is applied, a film sample stretches and this is referred to as strain. Strain is basically the deformation of film divided by original dimension of the sample. Generally elongation of film increases as the plasticizer content increases. The following formula helpful in determination of Percent elongation.

$$\text{Percent elongation} = \frac{\text{Increase in length of strips} \times 100}{\text{Initial length of strips}}$$

Young's modulus

Young's modulus or elastic modulus is the measure of stiffness of strips. It is represented as the ratio of applied stress over strain in the region of elastic deformation as following formula.

$$\text{Young's modulus} = \frac{\text{Slope X } 100}{\text{Strips thickness} \times \text{cross –headspeed}}$$

Folding endurance

Folding endurance is determined by repeated folding of the film till the film breaks. The number of times the film is folded without breaking is computed as the folding endurance value. [51]

Swelling test

Film swelling studies are conducted using a simulated saliva solution. Each film sample is weighed and placed in a preweighed stainless steel wire mesh. The mesh containing film sample is submerged into a 15 ml medium in a plastic container. An increase in the weight of the film was determined after 20 min weight of strips was observed.The degree of swelling was calculated using formula.

$\alpha = wt - wo/wo$

Where, wt =weight of film at time

wo=weight of film at time zero

Surface pH test

Surface pH of the films was determined by placing the film on the surface of 1.5% w/v agar gel followed byplacing pH paper (pH range 1-11) on films. The change in the color of pH paper was observed and reported.

Disintegration test

The disintegration time limit of 30 s or less for orally disintegrating tablets described in CDER guidance can be applied to fast dissolving oral strips. Although, no official guidance is available for oral strips, this may be used as a qualitative guideline for quality control test or at development stage. Pharmacopoeia disintegrating test apparatus may be used for this study. Typical disintegration time for strips is 5–30 sec.

Assay or Content Uniformity

The test for the content uniformity is carried out taking a sample film of size 1×1 cm^2 which is placed in a beaker containing 10 ml of a suitable medium. The contents were stirred in a cyclo-mixer to dissolve the film which was transferred to a volumetric flask (10 ml).The absorbance of the solution was measured against the corresponding blank solution at particular wavelength using a standard assay method described for the particular API

mentioned in any of the standard pharmacopoeia. Content uniformity is determined by estimating the API content in individual film. Limit of content uniformity is 85–115%.

In-vitro Dissolution test

Dissolution testing can be performed using the standard USP paddle over disc and basket or paddle apparatus described in any of the pharmacopoeia. The volume of the dissolution medium will essentially be selected as per the sink conditions and highest dose of the API. Many times the dissolution test can be difficult due to tendency of the film to float onto the dissolution medium when the paddle apparatus is employed. Another method to determine the drug release from the oral strips via conductivity.

Applications

The following some application of mouth dissolving strips in drug delivery

- ✓ In mouth dissolving strips formulation drugdelivery via Buccal, sublingual, and mucosal route.
  - ✓ Mouth dissolving strips could become a better delivery method for therapies in which rapid absorption is desired.
  - ✓ Mouth dissolving strips used to manage pain, allergies, sleep difficulties, and central nervous system disorders.[52]
  - ✓ Mouth dissolving strips used in Topical applications for delivery of active agents such as analgesics or antimicrobial ingredients for wound care and other applications.
  - ✓ Dissolution of the strips could be triggered by the pH or enzyme secretions of the gastrointestinal tract, and could potentially be used to treat gastrointestinal disorders.
  - ✓ Dissolvable strips are being considered in dosage forms for which water-soluble and poorly soluble molecules of various molecular weights are contained in a strips format.
  - ✓ Stripssmay be loaded with sensitive reagents to allow controlled release when exposed to a biological fluid.

Marketed Products

The following some mouth dissolving strips for oral Dosage Form Products are available in market;-

Table No.3. Mouth Dissolving strips Marketed Products

Product	Manufacturer	Active Pharmaceutical Agent	Dose
Triaminic	Novartis	Dextromethorphan HBr	7.5 mg
Theraflu	Novartis	Diphenhydramine HCl	12.5 mg
Sudafed	Pfizer	Phenylephrine HCl	10 mg
Benadryl	Pfizer	Diphenhydramine HCl	12.5 mg
Setofilm	BioAlliancePharma	Ondansetron	4 mg
Zuplenz(R)	Strativa Pharmaceuticals	Ondansetron	5 mg
Chloraseptic	Prestige	Benzocaine/menthol	3mg/3 mg
Suppress®.	InnoZen®, Inc	Menthol	2.5 mg

Conclusion

Mouth dissolving strips is relatively easy to fabricate; thus reducing the overall cost of the therapy. The application of Mouth dissolving strips has not only been limited to buccal fast dissolving system, but also expands its horizon to other applications like gastroprotective, topical, implantable, sublingual delivery options. Mouth dissolving strips discovered excellent uniformity and stability of incorporated drug and rapidly disintegrated in water. All the population groups, particularly geriatric, pediatric patients and patients with swallowing difficulties can take it

References

1. Bhushan S.Y., Sambhaji S.P., Anant R.P. and Mahadik K.R., New drug delivery system for elderly, Indian Drugs, 2003, 37, 7, 312-318.
2. Rizk S., Barthelemy C., and Duru C., Investigation on a new modified USP Xanthan with tablets disintegration properties, Drug Develop Ind Pharm, 1997, 23, 19-26.
3. Indian Pharmacopoeia, Fourth edition, Vol - II, Controller of publication, Govt. of India, New Delhi, 1996, 736.
4. Meyya Nathan S.N., Mathew Philip, and Suresh B., Spectrophotometric Determination of Baclofen in its Dosage forms, Indian Drugs, 1998, 35, 183-187.

5. Knistch A, Hagen E, Munz HD. Production of porous tablets. US patent 4134843, 1979. 14)
6. Roser BJ, Blair J. Rapidly soluble oral dosage forms, methods of making the same and composition thereof. US patent 5762961, 1998.
7. Ahmed IS, Fatahalla FA. Pilot study of relative bioavailability of two oral formulations of ketoprofen in healthy subjects, a fast dissolving lyophilized tablet as compared to immediate release tablet. Drug Dev Ind Pharm 2007; 33:505-11.
8. Ahmed IS, Nafadi MM, Fatahalla FA. Formulation of fast dissolving ketoprofen tablet using freeze-drying in blister technique. Drug Dev Ind Pharm 2006; 32:437-42.
9. Corveleyn S, Remon JP. Formulation and production of rapidly disintegrating tablets by lyophilization using hydrochlorothiazide as a model drug. Int J Pharm 1997, 152:215-25.
10. Remon JP, Corveleyn, S. Freeze-dried rapidly disintegrating tablets. US patent 6010719, 2000
11. Marshall K, Lachman N, Liberman HA. The theory and practice of industrial pharmacy. 3rd Ed. Mumbai, Varghese Publishing House; 1987, p. 66-69.
12. Yunxia B, Yorinobu Y, Kazumi D, Akinobu O. Preparation and evaluation of oral tablet rapidly dissolving in oral cavity. Chem Pharm Bull 1996; 44(11):2121-27.