Orally Dissolving Strips: A New Approach to Oral Drug Delivery System

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Abstract: The oral patch is a new invention with the fastest processing time and improved patient consistency. When placed in the mouth, the mouth patch will become damaged or broken within minutes without absorbing water. It improves API capabilities and enables better planning. This formula is suitable for colds, allergic rhinitis, asthma and central nervous system diseases that need to be treated quickly. Oral test strips provide another level of insight into the molecules that undergo digestion first. This article provides an overview of design, manufacturing, patented technology, measurement and product.

Keywords: oral patch, onset of action, patented technology.

INTRODUCTION

Over the past few years, interest in leading-edge technology has increased in efforts to improve effectiveness, safety, and patient convenience. Since the discovery and development of new drugs is difficult, expensive and time-consuming, the trend has recently shifted towards the design and development of new drugs to complement existing drugs. Among these the most famous drug delivery in the field of paediatrics and geriatrics is oral. Among oral diseases, oral patches are gaining popularity in paediatrics and geriatrics due to the fastest onset of action and better patient compliance. The oral patch is placed on the tongue, breaks within a second by immersion in saliva, and releases the medication from the dosage form. [1-3]

Oral patches, capsules, tablets etc. It is an alternative to oral prescriptions such as The technology behind the development of the oral patch is the transdermal patch. Hydrophilic polymers play an important role in the rapid preparation of oral patches; Release of the drug into the body system through the oral mucosa. Due to the oral mucosal film, the drug is absorbed directly into the systemic circulation and has instant bioavailability and rapid onset of action. [4.5]

Figure 1: Orally Dissolving Strips

Advantages of oral strips: [6]

a) It ensures the fastest start of treatment since the drug enters the body directly.
b) It provides an easy way of management for children and adults facing diseases, bioavailability increased.
c) There is no need for water; thus providing a convenient symbol for traveling patients.
d) Since the surface area is larger, it causes the solution to dissolve quickly.
e) Oral strips are more flexible and easier to use, store and transport.
f) They are available in many sizes and shapes

Disadvantages of oral strips: [6]

a) large doses cannot be packaged on site.
b) Drugs that damage the oral mucosa and whose pH is unstable in the mucosa cannot be used.
c) Mouth tapes must have a special type of packaging as they are fragile and waterproof.

Anatomical And Physiochemical Properties of Oral Mucosal Cavity

The oral mucosa consists of a multilayered squamous epithelial layer. Below this is the basement membrane, lamina propria, and then the submucosa as the inner layer. While the buccal mucosal region provides a smooth and stable surface with vascular perfusion, the sublingual mucosal region does not have a stable mucosal surface. Compared to other mucosal areas, the buccal mucosa is prone to allergy, less susceptible to damage, and has lower enzyme mobility. [8] The use of drugs through the oral cavity

can occur via the transcellular route (intercellular route) or the paracellular route. The oral mucosa is generally between the epidermis and the intestinal mucosa in terms of permeability. The chip dissolves quickly in the mouth and the active ingredient is absorbed by the oral mucosa and enters the bloodstream. [9,10]

TYPES OF ORAL STRIPS

Oral strips are of three types:
1. Flash release strips
2. Mucoadhesive melt away strips
3. Mucoadhesive sustained-release strips

STANDARD COMPOSITION OF ORAL STRIPS[12]

The oral strip is a thin film having an area of 1-20cm2 containing drugs. Not more than 30mg of the drug can be incorporated in a single dose.

The composition of an oral strip includes:
1. Drug
2. Water-soluble polymers
3. Plasticizer
4. Surfactants
5. Sweetening agents
6. Saliva stimulating agents
7. Fillers, colours, and flavour

1. Drug

5-30% w/w of dynamic pharmaceutical fixings are utilized for a standard composition of verbal strips. For the most part, little dose atoms are chosen for verbal strips. Micronization of APIs is exceptionally valuable to progress the disintegration of the strip that will lead to quick retention as well as the instant therapeutic activity of the medicate. Taste concealing specialists will be utilized for veiling the bitter taste of the medicate. Exceedingly lipophilic drugs ought to be favoured for verbal strips. Different categories of drugs are utilized within the verbal strips some of these are antiulcer (e.g. omeprazole) Antiemetic, Antiallergic, antiasthematics (salbutamol sulfate), antitussives, expectorants, antihistaminics, NSAID'S (e.g. paracetamol, meloxicam, valdecoxib). [13,14]

2. Water-soluble polymers

The advancement of the film and the mechanical strength of the film is emphatically related to the determination and concentration of the polymers. These polymers can be used alone or in combination with other polymers to increase the mechanical quality and alter the film property. 45% w/w of the concentration of the polymer is used to create a verbal strip. But it can be expanded up to 60-65% w/w to accomplish the specified characteristics.[15] A polymer that is used for formulation the thin strip should have the following properties.

Type of polymer	Example
Natural polymers	Starch polymerized rosin, pullulan, sodium alginate, Pectin, gelatin, and maltodextrins
Synthetic polymers	Polyvinyl alcohol, hydroxypropyl methylcellulose, sodium carboxymethylcellulose, polyvinylpyrrolidone, and hydroxypropyl cellulose

Table 3: Natural and synthetic polymer commonly used in oral strips

Ideal properties of water-soluble polymers:
- Nontoxic
- Nonirritant
- Should not affect the disintegration time of oral strip
- Should have a moderate half-life
- Should have good spreadability
- Should have maximum tensile and mechanical strength
- Easily affordable
- Nowadays both natural and synthetic polymers are used in the formulation of the oral strip. [16]

3. Plasticizers

Plasticizers play an important role in the formulation of oral strips. By the addition of the plasticizers, the mechanical and tensile strength of the film will be improved. The selection of the plasticizer is dependent on the compatibility with the polymer used and type of solvent that employed. Commonly used plasticizers are polyethylene glycol, glycerol, low molecular weight polyethylene glycol, phthalate derivatives and citrate derivatives like tributyl, triethyl, acetyl citrate and castor oil. 0-20% w/w concentration of plasticizer is commonly used that will help to prevent cracking, splitting and peeling of the strip. [17, 18]

4. Surfactant

Surfactants are used to enhance the solubility and wetting property of the film that will provide quick dissolution and release the medicament within a minute, some of the commonly used surfactants are sodium lauryl sulfate, benzalkonium chloride, and a tween, etc. Poloxamer 407 is the most important surfactant used as solubilizing, wetting and dispersing agent. [19]

5. Sweetening agent

Sweeteners have become one of the important ingredients in the pharmaceutical product to mask the bitter taste of the drug. Both natural and artificial sweeteners are used. Natural sweeteners like sucrose, dextrose, fructose, glucose, liquid glucose and isomaltose etc. and artificial sweeteners like monosaccharide's, disaccharides and polysaccharides such as galactose, glucose, mannose, fructose, xylose, ribose, dextrose, maltose, sucrose, sugar, sorbitol, xylitol, mannitol and soluble saccharin salts, saccharin, cyclamate salts, acesulfame-K, Aspartame, Neotame respectively. Now day's popularity of artificial sweeteners in pharmaceutical formulation increasing day by day. Neotame and alitame have more than 2000 to 8000 times sweetening power than sucrose. [20, 21]

6. Saliva stimulating agent

Saliva stimulating agents are helpful for rapid disintegration of the oral strips because they enhance the rate of production of saliva. Citric acid, malic acid, lactic acid, ascorbic acid, and tartaric acid are some of the examples of salivary stimulant. In the oral strip, 2-6% w/w concentration of salivary stimulant is used alone or in combination. Citric acid is one of the preferable stimulants used in the oral strip. [22]

7. Colouring and flavouring agents

FDC approved natural colouring agents are commonly used. The concentration of the colouring agent should within the limit of 1% w/w. Flavouring agents are generally added to the formulation to give the flavour and make the formulation attractive towards paediatric patients. The different flavour can be used such as essential oils or water-soluble extract of menthol, intense mint (peppermint, sweet mint, spearmint,) wintergreen, cinnamon, clove, sour fruit flavour (lemon), fruit essence (apple, raspberry, cherry, pineapple), etc. [23, 24]

METHODS USE FOR FORMULATIONOF ORAL STRIPS

1. Solvent casting method
2. Semi-solid casting method
3. Hot-melt extrusion
4. Solid dispersion extrusion
5. Rolling method

1. Solvent casting method

Dissolve the strip-forming agent, plastic and saliva stimulator in distilled water, and then continuously stir the solution in a magnetic stirrer at 60C for 4 minutes. hour and 1000 rpm. After that, let the solution stand for 1 hour to remove any bubbles that have entered. Meanwhile, in a separate bowl, dissolve additives such as sweeteners, disintegrants, flavourings and medicines in distilled water and stir continuously for 45 minutes. The two solutions were mixed in a separate container and stirred on a magnetic stirrer at room temperature and 1000 rpm for up to 1 hour. Allow the solution to sit for 1 hour to allow the foam to settle. Finally, the solution is poured and dried at 60°C and the strips are cut into the desired sizes. [25, 26,27]

Advantages: [28]

a) Great uniformity of the thickness of the strip.
b) More flexible and better physical properties.
c) Defects are very less in the solvent casting method.

Disadvantages: [28]

a) The solubility of the polymer is important in a volatile solvent or water.
b) Viscosity and the minimum solid content of the solution are essential.

2. Semi-solid casting method[29]

1. A solution of water-soluble film-forming polymer is prepared first.
2. The resulting solution is then added to acidinsoluble polymer (cellulose acetate phthalate, cellulose acetate butyrate) solution which can be prepared with ammonium or sodium hydroxide.
3. For obtaining the gel mass exact amount of plasticizer is added.
4. Finally, the obtaining gel is then cast into a strip using a heat controlling drum.
5. The ratio between the acid-insoluble polymer and film-forming polymer should be 1:4.

3. Hot-melt extrusion method

Hot-melt extrusion method is commonly used for the preparation of various dosages form in the pharmaceutical industry like sustained-release tablet, granules, transdermal and transmucosal drug delivery systems. [28] In this method, the drug and polymer are firstly blended in a mixer for 10minutes and plasticizer is added slowly and in the presence of the anti-sticking agent, the mixer is granulated. The prepared granules are dried overnight at room temperature and pass the dried granules in 250µm sieve and standardize. The standardize granules are then poured into the extruder. The speed of the extruder is set to 15 rpm in order to process the granules inside the drum approximately less than 3mintues at 65 °C and then pressed into a cylindrical calendar in order to obtain a strip with a thickness about 200µm. for further testing, the strip is cut into the required size and shape and stored at 25 °C .[30, 31]

Advantages: [28]

a) No water or solvent used.
b) Less processing steps.
c) For poorly soluble drugs it possesses good dispersion mechanism.
d) Uniform dispersion of the fine particles is more because of intense mixing and agitation.

Disadvantages: [28]

a) The process is thermal so there will be a problem with drug/polymer stability.
b) Flow properties of the polymer are important for processing.
c) Availability of polymer is low.

4. Solid dispersion extrusion

The drug is dissolved in an appropriate liquid solvent. The obtained solution is then added to the pre-melted suitable polymer to form the solid dispersion. Finally obtained solid dispersion is shaped into the strips by using dyes of different size and shapes. [32]

5. Rolling method

In the rolling method, the solution containing drug is prepared in a solvent of water or mixture of water and alcohol. Then the prepared solution or suspension is rolled on a carrier. The strip is dried on the roller. After drying the strip is cut to the desired shape and size.

Patented Approaches for Manufacturing of The Oral Strips[34-38]

1. XGel
2. Soluleaves
3. Wafertab
4. Foambrust
5. Micap

1. X gel

This technology is produced by Bio progress to produce a newer technology to product manufacturing. X gel film provides unique product benefits for healthcare and pharmaceutical products: it is non-animal- derived, the film is continuous production processing provides an economic and competitive manufacturing platform.

2. Soluleaves

This technique is used to formulate the quick dissolving films by adding with active ingredient, flavour, and colour to fill the pleasant and easy acceptable form.

3. Foam

burst This method gives an effect like the melt in the mouth like sensation because at time of preparation of film gas is blown on the film due to this films gives honeycomb-like structure and this void is empty or filled with other material to acquire the specific test or odour.

4. Wafertab

In this system drug load in film after casting. 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.

5. Micap

Micap plc signed an option agreement in 2004 to combine its expertise in microencapsulation technology with the Bio Progress water-soluble films. The aim of this company to make the smoke sensation product.

CONCLUSION

From the above, it can be concluded that oral strips have has proven to be an innovative drug delivery system for all patient population groups with a problem swallowing. Oral strips have proven valuable whenever a rapid onset of action is necessary as in asthma attack, heart failure and epilepsy. Oral Strips are used as a good life cycle extension tool existing product by obtaining a patent on it product as rapidly dissolving oral films. So this technology is growing at a fast pace challenging for most of them pharmaceutical companies to develop oral films for the general public a number of active pharmaceutical substances. Lots of research work is ongoing and will be started in the near future the future on fast-dissolving oral strips. However, for the future in terms of growth, the fast-dissolving oral strips sector it is well located. It seems that the value of the total the market for oral thin films will grow considerably.

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