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A Review on Oral Strip

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ABSTRACT

Oral drug delivery is the most widely used and acceptable drug delivery amongst the other delivery. The orally disintegrating tablets are available in the market providing one to two minute of disintegration time. Among fast dissolving drug delivery systems, oral strip (OST) drug delivery system is an alternative to tablets, capsules, and syrups for paediatric and geriatric patients who experience in difficulties of swallowing traditional oral solid dosage forms. This technology has been used for local action, rapid release of products and for direct systemic circulation in the oral cavity to release drug in rapid fashion. And also this delivery protect drug from first pass metabolism and improve the dissolution. The main attention towards OST review article is providing knowledge of materials used in OST, critical manufacturing aspects, applications, commercial technologies.

Keywords: Oral strip, Solvent casting, Semisolid casting, Disintegration time

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INTRODUCTION

Oral delivery of drugs is by far the most preferable route of drug delivery due to the ease of administration, patient compliance and flexibility in formulations. In recent scenario many researchers have developed their mind to new drug delivery system. One such relative dosage form is oral strip drug delivery system. Oral strip is made up of hydrophilic polymers that rapidly dissolve on buccal cavity or on tongue. It is also reported that the permeability of the buccal mucosa is approximately 4–4000 times greater than the skin. Hence the buccal delivery serves as an excellent platform for absorption of molecules. [1]

Advantages of oral strip drug delivery system [1]

1. Availability of larger surface area into the buccal cavity that leads to rapid disintegration and dissolution.
2. Oral strips are flexible, they are not as fragile as most of the oral disintegrating tablets. Hence, transportation becomes easy during consumer handling and storage, too.
3. As compared to drops or syrup formulations, precision in the administered dose is ensured from each of the strips.
4. Ease of swallowing and no need of water have led to better acceptability amongst the dysphagic patients. The difficulty encountered in swallowing tablets or capsules is circumvented. The dosage form can be consumed at any place and anytime as per convenience of the individual.
5. The oral or buccal mucosa is being highly vascularised and having high permeability, drugs can be absorbed directly and can enter the systemic circulation without undergoing first-pass hepatic metabolism. This advantage can be used as in preparing products with improved oral bioavailability of molecules that undergo first pass effect.
6. Since the first pass effect can be avoided, there can be reduction in the dose which can lead to reduction in side effects associated with the API.
7. Patients suffering from dysphagia, repeated emesis, motion sickness, and mental disorders prefer this dosage form as they are unable to swallow large quantity of water.

The disadvantage of OS is that high dose cannot be incorporated into the strip. However, research has proven that the concentration level of active can be improved up to 50% per dose weight. Novartis Consumer Health's Gas-X® thin strip has a loading of 62.5 mg of simethicone per strip.[1]

List of molecules eligible for incorporation in strip delivery dosage forms:[1]

Molecule	Therapeutic category	Dose
Nicotine	Smoking Cessation	1.0–15.0 mg
Nitroglycerin derivatives	Vasodilator	0.3–0.6 mg
Zolmitriptan	Anti migraine	2.5 mg
Loratidine	Antihistaminic	5–10 mg
Desloratidine	Antihistaminic	5.0 mg
Diphenhydramine hydrochloride	Antihistaminic	25.0 mg
Loperamide	Antidiarroheal	2.0 mg
Famotidine	Antacid	10.0 mg
Flurazepam	Anxiolytic, Anticonvulsant	15.0–30.0 mg
Chlorpherinamine maleate	Antihistaminic	4.0 mg
Acrivastine	Antihistaminic	8.0 mg
Oxycodone	Opoid Analgesic	2.5–10.0 mg
Diclyclomine	Muscle Relaxant	25.0 mg
Omeprazole	Proton pump inhibitor	10.0–20.0 mg
Cetrizine	Antihistaminic	5.0–10.0 mg
Ketoprofen	Anti–inflammatory	12.5–25.0 mg
Azatidine maleate	Antihistaminic	1.0 mg
Sumatriptan succinate	Antimigraine	35.0–70.0 mg

EVALUATION PARAMETERES [1]

Thickness

The thickness of strip can be measured by micrometer screw gauge at different strategic locations. 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.

Dryness test/tack tests

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, most of the studies can be adapted intricately to evaluate pharmaceutical OS as well.

Tensile strength

Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by the applied load at rupture divided by the cross-sectional area of the strip as given in the equation below:

$$\text{Tensile strength} = \frac{\text{Load at failure} \times 100}{\text{Strip thickness} \times \text{Strip width}}$$

Percent elongation

When stress is applied, a strip sample stretches and this is referred to as strain. Strain is basically the deformation of strip divided by original dimension of the sample. Generally elongation of strip increases as the plasticizer content increases.

$$\% \text{ elongation} = \frac{\text{Increase in length of strip} \times 100}{\text{Initial length of strip}}$$

Young's modulus

Young's modulus or elastic modulus is the measure of stiffness of strip. It is represented as the ratio of applied stress over strain in the region of elastic deformation as follows:

$$\text{Young's modulus} = \frac{\text{Slope} \times 100}{\text{Strip thickness} \times \text{cross-head speed}}$$

Hard and brittle strips demonstrate a high tensile strength and Young's modulus with small elongation.

Folding endurance

Folding endurance is determined by repeated folding of the strip at the same place till the strip breaks. The number of times the film is folded without breaking is computed as the folding endurance value.

Disintegration time

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. The film as per the dimensions (2 x 2 cm^2) required for dose delivery was placed on a stainless steel wire mesh placed in a petri dish containing 10 ml distilled water. Typical disintegration time for strips is 5–30 s.

Assay/drug content and content uniformity

This is determined by any standard assay method described for the 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%.

Dissolution test

The in vitro dissolution test is carried out in a Ph. Eur. 5.4 ed. paddle dissolution apparatus. 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 strip to float onto the dissolution medium when the paddle apparatus is employed.

Oral strips are dissolving quickly on the tongue in a minute and also prevents first pass metabolism that results into enhancement of dissolution.[1, 2]

Generally many paediatric and geriatric patients are unwilling or facing problems to take solid preparations due to fear of choking. In order to assist these patients, fast-dissolving drug delivery system oral strip have been developed.[3]

Special features of oral strips [3]

• Thin elegant film

• Available in various size and shapes

• Fast disintegration

• Rapid release

Basically the OS can be considered as an ultra-thin strip of postage stamp size with an active agent or active pharmaceutical ingredient and other excipients. Oral strips offer fast, accurate dosing in a safe, efficacious form i.e. convenient and portable, without the need for water or measuring devices.[4]

FORMULATION CONSIDERATIONS [5]

A typical composition contains the following

Drug	1-25%
Water soluble polymer	40-50%
Plasticizers	0-20%
Fillers, colours, flavours etc.	0-40%

1) Drugs

Several classes of drugs can be formulated as mouth dissolving strips including antiulcer (e.g. omeprazole), antiasthamatics (salbutamol sulphate), antitussives, expectorants, antihistaminics, and NSAID'S (e.g. paracetamol, meloxicam, valdecoxib) [6,7,8,9].

2) Plasticizers

Formulation considerations (plasticizer etc.) have been reported as important factors affecting mechanical properties of strips. The mechanical properties such as tensile strength and elongation to the strips have also been improved by the addition of plasticizers. Variation in their concentration may affect these properties. The commonly used plasticizers are glycerol, di-butyl pthallate and polyethylene glycols etc[10].

3) Polymers

The strips have attracted considerable attention in medical and nutraceutical application. The water-soluble polymers achieve rapid disintegration, good mouth feel and mechanical properties to the strips. The disintegration rate of the polymers is decreased by increasing the molecular

weight of polymer strip bases. Some of the water soluble polymers used as strip former are HPMC E3 and E15, Methyl cellulose A3, A6 and A15, Pullulan, carboxy methyl cellulose, Poly vinyl pyrollidone (PVP K90), Pectin, Gelatin, Sodium Alginate, Hydroxy propyl cellulose, Polyvinyl alcohol, Maltodextrins. Polymerized resin is a novel strip forming polymer [8,9,10,11,12,13].

4) Surfactants

Surfactants are used as solubilising or wetting or dispersing agent so that the strip is dissolved within seconds and release active agent immediately. Some of the commonly used are sodium lauryl sulfate, benzalkonium chloride, tweens etc. One of the most important surfactant is poloxamer 407 that is used as Solubilizing, wetting and dispersing agent[14].

5) Flavours

Any flavours can be added, such as intense mints, sour fruit flavours or sweet confectionery flavours[15].

6) Colours

A full range of colors is available, including FD&C colors, EU colours, and natural colours[15].

MANUFACTURING METHODS [16, 17]

One or combination of the following process can be used to manufacture the mouth dissolving strips.

i) Solvent casting

ii)Semisolid casting

iii) Hot melt extrusion

iv)Solid dispersion extrusion

v) Rolling

Solvent casting method

In solvent casting method polymers are dissolved in water and the drug along with other excipients is dissolved in suitable solvent then both the solutions are mixed with stirring and finally casted in to the Petri plate and dried.

Semisolid casting method

In semisolid casting method firstly a solution of water soluble strip forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which was prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the strip is

about 0.015-0.05 inches. The ratio of the acid insoluble polymer to strip forming polymer should be 1:4.

Hot melt extrusion method

In hot melt extrusion method the drug is mixed with carriers in solid form. Then the extruder having heaters to melts the mixture. Finally the melt is shaped into strips by the dies. There are certain benefits of hot melt extrusion.

- Fewer operation units
- Better content uniformity
- An anhydrous process

Solid dispersion extrusion method

In this method immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped into strips by means of dies.

Rolling method

In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water, mixture of water and alcohol. The strip is dried on the rollers and cut in to desired shapes and sizes.

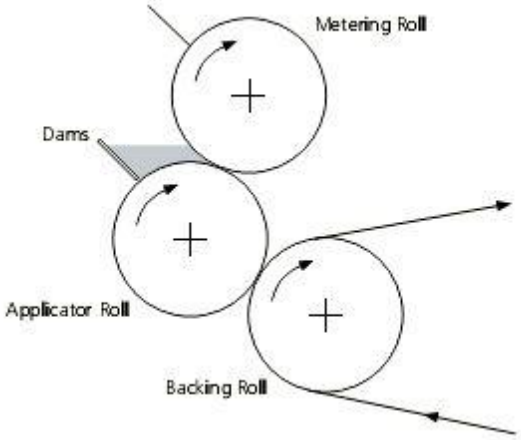

Figure1. Three roll coating unit.

TECHNOLOGIES[18, 19, 20, 21]

SOLULEAVES™[18]

It is an edible film strip based on non-animal derived materials. SoluLeaves™ technology is used to produce a range of oral delivery films that can incorporate active ingredients, colours and flavours. SOLULEAVES™ films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients and flavours. 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 paediatric or elderly patients who may have difficulty swallowing traditional tablets or capsules. The delivery system can be used for the cough/cold, gastrointestinal areas. SOLULEAVES™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 minutes. Similarly, the films can be used as a means of adding flavours to beverages either as a product or as a processing aid in manufacture.

Features of Soluleaves™:

- A vegetable based polymer film that carries low levels of active ingredients and flavouring
- Fast dissolution in the mouth
- Enhanced taste masking
- Enhanced convenience, portability and discreet format
- Gelatin free (suitable for vegetarians, vegans and those with religious dietary restrictions)
- Sugar free variant suitable for diabetics
- Aqueous based and solvent free
- Application in a range of vitamins, flavourings, and pharmaceutical actives
- Suitable for paediatric and geriatric patients
- The SoluLeaves™ system is patented

WAFERTAB™[18] is a drug delivery system that incorporates pharmaceutical actives into an ingestible film strip. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The WAFERTAB™ film strip can be flavoured for additionally improved taste masking. The active ingredient is precisely dosed and integrated into the body of a pre-manufactured XGEL™ film, thus preventing exposure to unnecessary heat and moisture and potentially enhancing product stability. 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 swallowing.

Features of Wafer Tab™:

- Very stable format, fast dissolving oral film
- Enhanced taste masking
- Enhanced convenience, portability and discreet format
- GMO and gelatin free (suitable for vegetarians, vegans and those with religious dietary restrictions)

- Sugar free variant suitable for diabetics
- Aqueous based and solvent free
- Applications in unstable pharmaceutical forms, particularly salt forms.
- The WaferTab™ system is uniquely patented

XGEL™[19, 20] films is at the heart of Meldex International's intellectual property, used in all its film systems and its ingestible dosage delivery technologies. The film is continuous production processing provides an economic and competitive manufacturing platform. XGEL™ film can be taste masked, coloured, 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 optimised for the intended use. All of the XGEL ingredients are well known and generally regarded as safe (GRAS).

FOAMBURST™[21] 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 flavours.

MARKETED FILMS[22, 23, 24,25,26,27]

S.No	Product	Manufactured By
1.	Dextromethorphan HBr (cough suppressant),Diphenhydramine Citrate (cough and cold),Breath Strips	MonoSolRx
2.	Doneprezil rapid dissolving films, Ondansatron rapid dissolving films	Labtec Pharma
3.	Life-saving rotavirus vaccine to infants	Johns Hopkins undergraduate Biomedical engineering students.
4.	Methylcobalamin fast dissolving films, Diphemhydramine HCl fast dissolving films, Dextromethorphan fast dissolving films, Folic Acid 1mg fast dissolving films, Caffeine fast dissolving films	Hughes medical corporation
5.	Altoid cinnamon strips, Boots vitamin c strips, Cool shock peppermint strips, Benzocaine films, Caffeine films	Dow chemical company
6.	Listerine Pocket Paks Breath Freshening Strips	Pfizer's Warner-Lambert consumer healthcare division
7.	Energy strips - Caffeine 20mg, Acetyl Salicylic Acid (ASA), Ondansetron HCl, Dexamethasone, Nitroglycerine, Risperidone Vitamin B12, melatonin, folic acid	ODF Technologies Inc.

CONCLUSION

The present review concludes that oral strip is widely acceptable and accurate oral dosage form which bypasses the hepatic system and show more therapeutic response. Oral strips have several

advantages over conventional dosage forms and fast dissolving tablets. It seems to be an ideal dosage form for use in young children, especially in geriatric and pediatric patients. Oral strips are new emerging novel drug delivery system, so they have great importance during the emergency cases whenever immediate onset of action is required. This delivery system has great business potential for future aspect in pharmaceuticals, nutraceuticals as well as cosmeceuticals.

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