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Review Article

Fast Dissolving Oral Films: A Review

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ABSTRACT

Buccal drug delivery has lately become an important route of drug administration. But many of the patients (pediatric and geriatric) are unwilling to take solid preparations due to fear of choking. This has made the pharmaceutical industry look for alternative routes of drug delivery like film drug delivery. Fast dissolving oral drug delivery systems have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer, better patient compliance, rapid drug absorption and sudden-onset of drug action with instant bioavailability is possible. So, now-a-days, most of the pharmaceutical companies adopted various technologies to manufacture fast dissolving oral films in large scale despite of several limitations as an alternative to traditional over-the-counter medicine forms such as tablets, capsules etc. This review reflects information regarding formulation ingredients, technologies and evaluation tests employed in the preparation of fast dissolving oral films.

Keywords: Buccal drug delivery, fast dissolving oral films, pediatric patients, geriatric patients.

INTRODUCTION

Among the different routes, the most agreeable route for the patients is oral route. Most of the pharmaceutical companies have directed their research activity in developing viable dosage alternatives from oral route for pediatrics, geriatric, noncompliant or nauseous patients. Research in the oral drug delivery segment has led to evolution of dosage forms from simple conventional tablets/capsules to modified release tablets/capsules to oral disintegrating tablet to wafer to the recent development of fast dissolving oral films[1].

Fast dissolving oral film, a novel drug delivery system for the oral delivery of the drugs is an ultra thin film prepared using hydrophilic polymers that rapidly dissolves on the top or the floor of the tongue or buccal cavity. It is an ultrathin strip (50-150 microns thick) of postage stamp size with an active agent and other excipients developed on the basis of transdermal patch technology. These evolved from the confectionery and oral care markets over past decade in the form of breath strips and became a novel and widely accepted dosage form by consumers for delivering vitamins and personal care products. These fast dissolving oral films have persistent to extend in sales and launched as patient compliant and convenient products effectively addressing issues for pharmaceuticals as well as nutraceuticals that have been traditionally administered as oral solid dosages. The delivery system consists of a very thin oral strip, 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[2]. It then rapidly disintegrates in a matter of seconds and dissolves to release medication for oromucosal absorption. Today, fast dissolving oral films are a well proven and world wide accepted technology for the systemic delivery of active pharmaceutical ingredients (APIs).

ADVANTAGES

Fast dissolving oral films being an advanced evolution of fast dissolving drug delivery systems have some outstanding advantages over conventional dosage forms and orally disintegrating tablets. They are:

- Improved patient compliance.
- As fast dissolving thin oral films are flexible, they are easy to carry, store and handle, which is not the case with orally disintegrating tablets (fragile and brittle).

- Precision in the administered dose is ensured from each of the strips as compared to drops or syrup formulations.
- Water is not needed for administering, so problem encountered in swallowing of tablets or capsules can be evaded.
- Patients suffering from repeated emesis, dysphagia, motion sickness prefer this dosage form as they are unable to swallow large quantity of water.
- Availability of larger surface area leads to fast disintegration and dissolution in the oral cavity.
- As the oral mucosa is being highly vascularized, drugs directly enter the systemic circulation without undergoing first-pass hepatic metabolism. This results in improved oral bioavailability of molecules.
- These films can be manufactured through economically feasible non-sophisticated procedures and uncomplicated equipment.

DISADVANTAGE

High dose cannot be incorporated into the film [3,4].

FORMULATION INGREDIENTS

Drug (1-25%)

Several class of drugs can be formulated as mouth dissolving films including antiasthamatics (Salbutamol sulphate), antiulcer (Omeprazole), expectorants, antitussives, NSAID'S (Valdecoxib, Meloxicam) [5,6,7].

Water Soluble Polymers (40-50%)

To obtain the desired film properties, polymers can be used alone or in combination.

Generally water-soluble polymers are used as film formers as they achieve rapid disintegration, good mouthfeel and mechanical properties to the films. The strength of the film depends on the type of polymer and the amount in the formulation. By increasing the molecular weight of polymer film bases, disintegration rate of the polymer decreases. Polymers frequently used as film formers are water soluble grades of cellulose ethers, polyvinyl alcohol, polysaccharides, polyvinylpyrrolidone K-90, polyethylene glycols, pullulan, gelatin, carboxmethylcellulose cekol 30, hydroxy propyl methyl cellulose E-3 and K-3, methyl cellulose A-3, A-6 and A-15, pectin, sodium alginate, hydroxypropylcellulose, maltodextrins and eudragit RD10 [8,9,10].

Plasticizers (0-20%)

Plasticizer enhances mechanical properties such as tensile strength and elongation to the film by reducing the glass transition temperature of the polymer. It also reduces brittleness of the strip as a result improves its flexibility. Choice of plasticizer depends upon type of solvent used and its compatibility with the polymer. Some of the commonly employed plasticizers are phthalate derivatives like dimethyl, diethyl and dibutyl phthalate, low molecular weight polyethylene glycols, castor oil, citrate derivatives like tributyl, triethyl, acetyl citrate, triacetin and glycerol. Improper use of plasticizer may lead to blooming, film cracking, splitting and peeling of the strip[8,11,12,13].

Surfactants

Surfactants are used as wetting or solublising or dispersing agent so that the film is getting dissolved within seconds and release active agent immediately. Commonly employed are polaxamer 407, bezathonium chloride, sodium lauryl sulfate, tweens, benzalkonium chloride, etc. Out of these most predominantly used surfactant is polaxamer 407 [14].

Sweetening agents

Some of the commonly employed sweeteners are dextrose, sucrose, fructose, glucose, isomaltose, polyhydric alcohols (sorbitol, mannitol), etc. Artificial sweeteners like saccharin, cyclamate, aspartame (first generation) and acesulfame-K, sucralose, alitame, neotame (second generation) can also be used [15].

Saliva stimulating agents

Saliva stimulating agents are used to increase the rate of production of saliva that would help in the faster disintegration of the rapid dissoving strip formulations. Examples of salivary stimulants are citric acid, malic acid, lactic acid, ascorbic acid and tartaric acid. Among these the most preferred one is citric acid [16].

Flavouring agents

The quantity of flavouring agent required to mask the taste depends on the flavour type and its strength. Commonly employed are fruity flavours (vanilla, cocoa, coffee, chocolate, citrus), flavour oils (peppermint oil, cinnamon oil, oil of nutmeg). Flavours can also be chosen from oleo resins, synthetic flavour oils and extract derived from various parts of the plants like fruits, flowers etc.

Colouring agents
Generally incorporated colouring agents are FD&C colours, natural colours, pigments such as titanium dioxide etc [17].

MANUFACTURING METHODS
To manufacture fast dissolving oral films, following methods are generally employed:

a. Semisolid casting.
b. Rolling.
c. Solvent casting.
d. Solid dispersion extrusion.
e. Hot melt extrusion.

a. Semisolid casting
In this method at first a solution of watersoluble film forming polymer is prepared. Then the resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate) which was prepared in ammonium or sodium hydroxide. The ratio of the acid insoluble polymer to film forming polymer should be 1:4. A gel mass is obtained on addition of suitable amount of plasticizer. By the means of heat controlled drums, finally the gel mass is casted in to the films or ribbons [18].

b. Rolling
Solvents mainly used in this method are water and mixture of water and alcohol. By the means of high shear processor, active agent and other ingredients are dissolved in small portion of aqueous solvent. Water soluble hydrocolloids are dissolved in water to form homogenous viscous solution. Then the resultant solution or suspension containing drug is rolled on a carrier. Finally the obtained film is cut in to desired shapes and sizes [19].

c. Solvent casting
In this method water soluble polymers are dissolved in water and the drug along with other ingredients is dissolved in suitable solvent. Then both the solutions are mixed,stirred, finally casted in to the petri plate and dried [18].

d. Solid dispersion extrusion
Firstly solid dispersion is prepared by extruding immiscible components with drug and then shaped in to films by the means of dies [19].

e. Hot melt extrusion
In hot melt extrusion method at first drug is mixed with carriers in solid form. Then the mixture is molten by the means of extruder having heaters. Lastly the melt is shaped in to films by the dies [20].

EVALUATION TESTS
Morphology study
The morphology of the films is studied using Scanning Electron Microscopy (SEM), at a definite magnification[5].

Organoleptic evaluation
For this purpose invitro methods of utilizing taste sensors and specially designed apparatus are being used. These *invitro* taste assessment apparatus are apted for high-throughput taste screening of oral pharmaceutical formulations[21].

Thickness
It can be measured by micrometer screw gauge at different locations. It is crucial to determine uniformity in the thickness of the film as this is directly related to the accuracy of dose in the strip.

Mechanical properties
Three mechanical properties namely tensile strength, tear resistance, elastic modulus and percentage elongation are calculated.

1. Tensile strength
Tensile strength is the maximum stress applied to a point at which the strip specimen breaks. It is calculated by formula

$$\text{Tensile strength} = \frac{\text{Load at Failure X 100}}{\text{Strip thickness X Strip Width}}$$

2. Tear resistance
Principally 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) necessary to tear the specimen is noted as the tear resistance value in newtons (or pounds-force).

3. Elastic modulus
It is calculated by formula

$$\text{Elastic modulus} = \frac{\text{force at corresponding strain}}{\text{Cross sectional area (mm}^2\text{)}} \times \frac{1}{\text{Corresponding strain}}$$

4. Percentage elongation

It is calculated by formula

$$\% \text{ Elongation} = \frac{\text{Increase in length of strip}}{\text{Intial length of strip}} \times 100$$

5. Folding endurance

It is determined by folding the films of uniform cross sectional area and thickness at the same place repeatedly until it breaks.

Swelling property

Each film sample is weighed and placed in a preweighed stainless steel wire mesh. Then the mesh containing film sample is submerged into 15ml medium (simulated saliva solution) in a plastic container. Increase in the weight of the film was determined at preset time interval until a constant weight was observed.

$$\text{Degree of swelling} = \frac{W_t - W_0}{W_0}$$

Where, W_t is weight of film at time t, and W_0 is weight of film at time zero[22].

Disintegration time

It is determined visually in a glass dish of 25ml distilled water with swirling every
10 sec. The disintegration time is the time when the film starts to break or disintegrates. Normally disintegration time for fast dissolving oral films is 5–30 s [23].

Dissolution test

Dissolution testing can be performed in simulated saliva solution or pH 6.4 phosphate buffer using the standard basket or paddle apparatus described in any of the pharmacopoeia at 37±0.5°C. Samples are withdrawn at regular time intervals and analyzed by UV-Visible spectrophotometer [5,24].

CONCLUSION

The growing success and popularity of fast dissolving oral film recently in global market is evidence to the need for effective taste masked, "without water" pharmaceutical formulations. Fast dissolving oral films being a natural evolution of fast dissolving drug delivery systems have prominent advantages over conventional dosage forms and orally disintegrating tablets. Due to their immense importance during the emergency cases such as allergic reactions and high patient compliance, fast dissolving oral films have evolved as consumer friendly dosage forms. So many of the pharmaceutical companies are launching this technology as these films can be manufactured through non-sophisticated, uncomplicated equipment and procedures. Due to these, fast dissolving films have economically feasible developmental futuristic opportunities.

Some of the examples of marketed Fast Dissolving Oral Films

Product	Manufactured by	Indication
Caffeine films	Dow chemical company	CNS stimulant.
Dextromethorphan fast dissolving films	Hughes medical corporation	Anti-tussive agent.
Ondansetron Rapidfilms®	Labtec Pharma	Postoperative nausea and vomiting.
Methylcobalamin fast Dissolving films	Hughes medical corporation	Peripheral neuropathy, Diabetic neuropathy.
Chloraseptic® Relief strips™	Innozen Inc	Minor irritation, pain and sore throat.
Folic acid fast Dissolving films	Huges Medical Corporation	Anaemia.
Triaminic Thin Strips®	Novartis Pharmaceuticals	Nasal decongestant.
Diphenhydramine Hydrochloride films	MonoSolRX	Antihistaminic.

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