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REVIEW ARTICLE

FAST-DISSOLVING ORAL FILMS A BOON TO PHARMACEUTICAL INDUSTRY: A REVIEW

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ABSTRACT:

Oral route is the most preferred route for the delivery of the drugs till date as it bears various advantages over the other route of drug administration, but oral drug delivery systems still need some advancements to be made because of their some drawbacks related to particular class of patients which includes geriatric, pediatric and dysphasic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms. Orally fast-dissolving film is new drug delivery system for the oral delivery of the drugs. It was developed on the basis of technology of the transdermal patch. 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. It then rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption. Present review focus on about fast dissolving oral film their advantages, disadvantages, method of preparation and detailed review.

Keywords: Oral route, fast-dissolving oral film, Fast disintegration, Pediatric Patients, Geriatric Patients.

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INTRODUCTION:

Oral route is the most preferred route for the delivery of the drugs till date as it bears various advantages over the other route of drug administration, but oral drug delivery systems still need some advancements to be made because of their some drawbacks related to particular class of patients which includes geriatric, pediatric and dysphasic patients associated with many medical conditions as they have difficulty in swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take solid preparations due to fear of choking. Even with fast dissolving tablets there is a fear of choking due to its tablet type appearance. One study showed that 26% of 1576 patients experienced difficulty in swallowing tablets. The most common complaint was tablet size, followed by surface form and taste. The problem of swallowing tablets was more evident in geriatric and pediatric patients, as well as travelling patients who may not have ready access to water.[1-4]

Orally fast-dissolving film is new drug delivery system for the oral delivery of the drugs. It was developed on the basis of technology of the transdermal patch. 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. It then rapidly disintegrates and dissolves to release the medication for oromucosal and intragastric absorption. Technology Catalysts forecasts the market for drug products in oral thin film formulations was valued of $500 million in 2007 and could reach $2 billion in 2012. Based on upward global growth trends of the past decade, the fast dissolving dosage market could produce revenues of $13 billion by 2015.[5]

Oral dissolving films can be administered without water, anywhere, any time.[6]

- Due to the presence of larger surface area, films provide rapid disintegrating and dissolution in the oral cavity.
- Oral dissolving films are flexible and portable in nature so they provide ease in transportation, during consumer handling and storage.
- Suitability for geriatric and pediatric patients, who experience difficulties in swallowing mentally ill, the developmentally disable and the patients who are un-cooperative, or are on reduced liquid intake plans or are nauseated.
- Beneficial in cases such as motion sickness, acute pain, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required. Stability for longer duration of time, since the drug remains 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 of bioavailability.

- As compared liquid formulations, precision in the administered dose is ensured from each strip of the film.
- 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. This advantage can be exploited in preparing products with improved oral bioavailability of molecules that undergo first pass effect.[7]
- The sublingual and buccal delivery of a drug via thin film has the potential to improve the onset of action, lower the dosing, and enhance the efficacy and safety profile of the medicament.
- Provide new business opportunity like product differentiation, product promotion, patent extension.

Disadvantages of fast dissolving oral films

- High doses cannot be incorporated.
- Dose uniformity is a technical challenge.
- Drugs which are unstable at buccal pH cannot be administered.
- Drugs which irritate the mucosa cannot be administered by this route.
- Taste masking- Most drugs have bitter taste, and need taste masking.
- Special packaging- OFDFs are fragile and must be protected from water so it needs special packaging.

FORMULATION INGREDIENTS

Drug

This technology has the potential for delivery of variety of APIs. However, there are some limitations like the size of dose, taste of drug. Drugs having high dose are difficult to incorporate in films and bitter tasting drugs require taste masking. Several classes of drugs can be formulated as fast dissolving films including antiulcer, anti-asthmatic, antitussives, expectorants, antihistaminic, NSAID'S etc.[8]

Film Forming Polymers

Water-soluble polymers are used as film formers as they provide rapid disintegration, good mouth feel and mechanical strength to the films. The robustness of the strip depends on the

type of polymer and its amount in the formulations. Water-soluble polymers film adheres to the tongue or oral mucosa and rapidly disintegrates and dissolve to release medication for absorption into the systemic circulation. Various polymers are available for preparation of films of which pullulan, hydroxyl propyl methyl cellulose(HPMC),hydroxyl ethyl cellulose(HEC) gelatin and polyvinyl alcohol (PVA) are most commonly used.[9]

Plasticizers

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(PEG), 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.[11]

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.[12]

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.[13]

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), flavor 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.

Surfactants

Surfactants are used as solubilising or wetting or dispersing agent .By the use of surfactant the film gets dissolved within seconds and release active agent immediately. Solubility of poorly soluble drugs in fast dissolving oral films can be improved by using surfactant. Some of the examples are polaxamer 407, sodiumlauryl sulphate, benzalkonium chloride,benzthonium chloride, tweens and spans etc.

MANUFACTURING METHODS

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

a. Semisolid casting

In this method at first a solution of water soluble 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.[14]

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.[15]

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.[14]

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.[15]

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.[16]

EVALUATION OF FILM

1. Weight of Films

Mouths dissolving oral films were weighed on analytical balance and average weight can be determined for each film. It is desirable that films should have nearly constant weight. It is useful to ensure that a film contains the proper amount of excipients and API.

2. Thickness of Films

By using micrometer screw gauge the thickness of the film was measured at five different places; an average of three values was calculated. This is essential to ascertain uniformity in the thickness of the film this is directly related to the accuracy of dose in the film.

3. Tensile strength

Tensile strength is a maximum stress applied to a point at which the strip specimen breaks. It is calculated by applied load at rupture divided by the cross sectional area of the strip as given in the following equation.[17]

Tensile strength = Load at failure × 100/film thickness × film width

4. Percent Elongation

When stress is applied to a film sample it stretches and this is referred 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.[17]

% Elongation = Increase in length× 100/ Initial length of film

5. Drug 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%.[18]

6. Surface pH

The film to be tested was placed in a Petri dish and was moistened with 0.5 ml of distilled water and kept for 30 s. The pH was noted after bringing the electrode of the pH meter in contact with the surface of the formulation and allowing equilibration for 1 min. The average of three determinations for each formulation was done.[19.20]

7. *In vitro* disintegration test

Disintegration time is the time when an oral film starts breaking when brought in contact with water or saliva. For a fast dissolving film, the time of disintegration should be in range of 5-30 s. United State Pharmacopoeia (USP) disintegration apparatus can be used to study disintegration time. In another method, the disintegration time can be visually determined by

dipping the film in 25 ml water in a beaker. The beaker should be shaken gently and the time was noted when the film starts to breaks or disintegrates.[21]

8. *In vitro* dissolution studies

Dissolution is defined as the amount of drug substance that goes into the solution per unit time under standardized conditions of liquid/solid interface, temperature, and solvent concentration. The standard basket or paddle apparatus described in any of the pharmacopoeia can be used for dissolution testing. The selection of dissolution medium will essentially depend as per the sink conditions and highest dose of API. The temperature of dissolution medium should be maintained at 37 ± 0.5°C and rpm at 50. When the paddle apparatus is employed, it has a disadvantage that oral films have a tendency to float over the dissolution medium used stainless steel wire mesh with sieve opening of approximately 700µm used to dip salbutamol fast dissolving film inside the dissolution medium.[22,23]

Conclusion

A recently Fast dissolving oral film have gained popularity as novel dosage form and is most acceptable due to its excellent flexibility and accurate dosing form which bypasses the hepatic system and show more therapeutic response. Fast dissolving oral films are having great potential of delivering the medicinal agent systemically as well locally and have several advantages over many dosage forms even over the fast disintegrating tablets. Due to their immense importance during the emergency cases such as allergic reactions, coughing and asthmatic attacks. Due to high patient compliance, fast dissolving oral films have evolved as consumer friendly dosage forms. This technology is a good tool for product life cycle management for increasing the patent life of existing products.

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