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Formulation development and evaluation of oral dissolving films- a review

Abstract

Oral administration of a variety of pharmaceutical dosage forms, such as tablets, capsules, syrup, suspension, and emulsion, is seen to be one of the more practical ways. Different fast-dissolving preparations, such as mouth dissolving film and MDT, have been produced by fast-dissolving drug delivery methods. The oral thin film is a brand-new dosage form made of hydrophilic polymer that dissolves quickly in the mouth and buccal cavity. Due of its lower production costs, mouth dissolving films are superior to mouth dissolving tablets. Oral films are self-administrable, quickly dissolve, and quickly absorb, making them a versatile dosage form for elderly and pediatrics patients who have trouble swallowing tablets and capsules. The purpose of the current research work is to provide information about various polymers, their concentrations, and applications. This study also focuses on the use of plasticizers, polymers, and sweeteners, as well as the various methods for creating oral films and the various criteria used to evaluate the films.

Keywords: Oral dissolving film, MDT, pediatrics, geriatrics, buccal cavity, dosage forms, cost

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Introduction

Due to its simplicity, non-invasiveness, adaptability, patient acceptance, and convenience of administration, the oral route of drug administration is one of the most popular routes. For pediatrics, geriatric, nauseated, and non-compliant patients, numerous replacements for the oral route of drug delivery have been presented over time employing cutting-edge new technology.[1-4]

Technology has led to the introduction of bio-adhesive mucosal dosage forms, such as patches, gels, and tablets. [4-5]

The usage of polymeric films for administering medication into the buccal cavity has grown significantly in recent years among the many dosage forms. When placed on the tongue, oral disintegrating films (ODFs) quickly hydrate by soaking up saliva after disintegrating or dissolving, releasing the drug from the dose form.[5]

ODFs are a particular class of formulations that are frequently made with hydrophilic polymers, allowing for quick dissolving when in contact with saliva. The two most common types of orally disintegrating medication delivery systems are oral disintegrating tablets and oral disintegrating films.[6-8]

Nevertheless, events involving chewing and swallowing were frequently recorded in spite of these precautions. But ODFs freed the general public from these negative outcomes.[9-10]

Fast dissolving film when placed in the oral cavity quickly gets hydrated, sticks onto the site of application and then disintegrates to release the drug.[15]

The administration of ODFs has numerous advantages and some of them are listed below:[4,11-15]

i. Transport is simple.

ii. Comfortable for geriatrics and pediatrics.

iii. Convenient and accurate dosing.

iv. No water is required for administration.

v. Convenient for dysphasic people who have trouble swallowing pills and tablets.

vi. Bypassing the hepatic first pass effect and enhanced bioavailability, the drug acts quickly and is stable.

Dis advantages

It is not possible to include a high dose in the film.

Formulation of oral dissolving films[16-17]

Drugs: ODFs can contain a variety of drug classes, such as antihistamines, antidiarrheals, antidepressants, vasodilators, anti-asthmatics, and anti-emetics. For taste masking, dimenhydrinate can also be added to ODFs. Salbutamol sulphate, rizatriptan benzoate, verapamil ondansetron, dexamethasone, rofecoxib, cetirizine, pilocarpine, tianeptine sodium, indomethacin, etc. are common examples of medications

Film Formers: Due to their quick disintegration, pleasant tongue feel, and mechanical strength, water-soluble polymers are utilised as film formers. The strip's durability.

Colorants: When certain of the formulation ingredients or medications are present in insoluble or suspension form, pigments like titanium dioxide or FD&C approved colouring additives are incorporated (not exceeding concentration levels of 1%w/w) in oral strips.

Sweeteners: Sweeteners are now a crucial component of both food and medicinal items that are meant to dissolve or disintegrate in the mouth. Artificial and natural sweeteners are both utilised to increase the mouth-feel of mouth-dissolving formulations.

- Hydrophilic Natural Sweetener: glucose, sucrose, maltose, xylose, ribose, glucose, and sativoside.
- Hydrophilic Artificial Sweetener: Acesulfame-K, sodium or calcium saccharin salts.

- Miscellaneous: aspartame, neotame.

Stimulant: Salivary stimulants, which are often acidic in nature and stimulate saliva production in the buccal cavity, aid in the breakdown of ODFs. Citric acid, malic acid, tartaric acid, ascorbic acid, and lactic acid are a few of the regularly utilised saliva-stimulating substances.

Surface active agents: Surfactants are employed as solubilizing, wetting, or dispersion agents to breakdown the film quickly and release the active ingredient. Additionally, surfactants enhance the solubility of poorly soluble medications in rapidly dissolving buccal films. Benzalkonium chloride, benzathonium chloride, tweens and spans, sodium lauryl sulphate, and poloxamer 407 are a few examples.

Flavouring agent: To cover up the unpleasant or bitter taste of an included medicine, flavours are required. The flavor's intensity and nature are influenced by its strength. Any US-FDA authorised flavour, such as sweet, sour, or mint flavour, may be utilised. Research has shown that sucralose, liquorice, and a blend of the flavours mint and sucralose effectively disguise the bitter taste of diclofenac sodium. To differentiate between the effects of various taste-masking agents, electronic tongues are used (TMAs)

Manufacturing Methods

There are several ways to make fast-dissolving films[18-19]

1. The solvent casting process
2. The semisolid casting process
3. Using a hot melt extruder
4. Extruding with solid dispersion
5. Rolling technique

The solvent casting process

This process involves dissolving the medicine along with various excipients in a suitable solvent while also dissolving water-soluble polymers in the solvent. The two solutions are then combined and agitated. The air bubbles in this solution are subsequently settled by degassing it under vacuum. The final step is to cast the bubble-free solution into a Petri dish and let it to dry.

The Semisolid casting process

The water-soluble film-forming polymer solution is made using this procedure. The resultant solution is mixed with an acid-insoluble polymer solution (Examples: cellulose acetate butyrate, cellulose acetate phthalate). The right quantity of plasticizer is then added to create a gel mass. Using heat-controlled drums, this gel mass is subsequently cast into the films or ribbons. The films should be between 0.015 and 0.05 inches thick. The ratio of film-forming polymer to acid-insoluble polymer should be 1:4.

Using a hot melt extruder

Using heat, a polymer is formed into a film using this method. A mixture of dry pharmaceutical materials, including API, is added to the hopper, transported, mixed, and heated before being extruded out in molten form by the extruder. The resulting molten mass is utilised to cast the film. The casting and drying process is a crucial phase. This method offers various benefits, including continuous operation, absence of organic solvents, and shorter residence durations for the drug carrier mix at lower temperatures.

Solid dispersion

When one or more active chemicals are dispersed in an inert carrier in a solid form while amorphous hydrophilic polymers are present, this is referred to as solid dispersion. In this process, medications are dissolved in suitable solvents before being added to the polyethylene glycol melt at a temperature below 70 °C. Finally, using dies, solid dispersions are moulded into the films.

Rolling Technique

In the rolling procedure, a drug-containing solution or suspension is rolled on a carrier. Water and an alcohol-water mixture make up the majority of the solvent. The film is cut into the desired shapes and sizes after it has dried on the rollers. Using a high shear processor, additional materials, including the active substance, are dissolved in a tiny amount of aqueous solvent. Hydrocolloids that are water soluble are dissolved in water to create a homogeneous viscous solution.

Quality Control Tests:[20-21]

Scanning Electron Microscopy (SEM) is used to investigate the morphology of the films at a specific magnification.

Organoleptic evaluation

In-vitro techniques involving taste sensors and equipment with unique construction are being used for this aim. These in vitro taste evaluation tools are suitable for high-throughput oral pharmaceutical formulation taste testing.

Thickness

At several sites, it can be measured with a micrometre screw gauge. The precision of the dose in the strip is closely tied to the uniformity of the film's thickness, so this must be determined.

Mechanical properties

Calculations are made for three mechanical properties: tensile strength, tear resistance, elastic modulus, and percentage elongation.

Tensile strength: The highest tension at which a strip specimen breaks is its tensile strength. It is determined using a formula.

$$Tensile\ Strength = FMax\ /\ A$$

Tear resistance: Primarily, a rate of loading of 51 mm (2 in.)/min, which is relatively low, is used to assess the force needed to start tearing. The tear resistance, measured in newtons, is the highest stress or force required to rip the specimen (which is typically present close to the beginning of tearing) (or value pounds-force).

Elastic modulus: It is calculated by formula

$$Elastic\ Modulus = \frac{F}{A} * 1 / Cs$$

Where F= Force at Corresponding strain, A= cross sectional area, Cs= Corresponding Strain

% Elongation: It is calculated by formula

$$\%\ Elongation = Increase\ in\ length\ /\ Initial\ Length\ of\ Strip * 100$$

Folding endurance: It is calculated by repeatedly folding films with the same cross-sectional area and thickness at the same location until it breaks.

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Swelling property

Each film sample is weighed and put into a stainless steel wire mesh that has already been pre-weighed. The film sample on the mesh is then dipped into a 15 ml vial of medium (simulated saliva solution). The film's weight increased over the course of the current time interval until a steady weight was noticed.

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

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

Disintegration time

In a glass dish filled with 25 ml of distilled water, it is determined visually with 10 seconds of spinning. The film begins to shatter or disintegrate at the disintegration moment. Fast-dissolving oral films typically dissolve in 5 to 30 seconds.[22-24]

Dissolution Test

With the usual basket or paddle apparatus described in any of the pharmacopoeia, dissolution tests can be carried out in simulated saliva solution or pH 6.4 phosphate buffer at a temperature of 37±0.5°C. Samples are taken out and examined using a UV-Visible spectrophotometer at regular intervals.[25-26]

Table 1 Comparison between oral films and oral tablets

Oral films	Oral tablets
Oral films have greater dissolution due to large surface area.	Oral tablets have lesser dissolution area as compared to oral films.
They have better longevity than oral tablets.	They have less longevity than oral films.
They have more patient compliance than oral tablets. [4,5]	They have less patient compliance as compared to oral film.
There is no risk of choking.	There is a risk of choking.

Conclusion

The current review demonstrates that one of the unique techniques in the world of pharmaceutical sciences is the use of oral fast dissolving films. In comparison to conventional dose forms, they have higher acceptance and patient compliance, no risk of choking, and superior safety and efficacy. The main motivation for developing ODFs was to address the issue of pediatrics, geriatric, and psychiatric patients with dysphagia finding it challenging to swallow traditional oral dose forms. ODFs are currently readily accessible, which reflects their significance for conditions including hypertension, acidity, allergies, pain, etc. The administration of such a dosage form without the need of water satisfies the desire of the target population for convenience in medication administration while also avoiding hepatic metabolism, thereby improving therapeutic response.

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None

Conflicts of interest

None

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