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REVIEW ON: FORMULATION AND EVALUATION OF SUBLINGUAL FILM

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- **ABSTRACT**

Fast-dissolving orally disintegrating films are formulated to dissolve quickly when they come into contact with wet surfaces or fluids, such as saliva, typically within seconds. Unlike tablets, capsules, or oral liquids, they do not require additional liquids like water, making them a highly convenient dosage form for patients. This formulation also offers significant marketing benefits. Orally disintegrating films are particularly advantageous for pediatric and geriatric patients, as well as those with a fear of choking, due to their ease of administration and popularity. Since the drug is absorbed directly into the bloodstream through the mucosal membrane in the mouth, it bypasses degradation in the gastrointestinal tract and avoids first-pass metabolism. This enhances the drug's availability in plasma, thereby improving its therapeutic efficacy.

- **KEYWORDS:** This formulation also offers significant marketing benefits.

- **INTRODUCTION**

The oral route is the most preferred route of administration for systemic effect. About 60% of all the formulations are solid dosage form. Tablet is the most preferred dosage form due to ease of transportation, manufacturing and more patient compliance.

Generally geriatric, pediatric and bedridden patient experience difficulties in swallowing the conventional oral dosage form. To overcome this problem a novel formulation was developed i.e. oral sublingual films.

There has been increased demand for the novel dosage form to gain more patient compliance. Fast dissolving films recently have acquired great importance in the pharmaceutical industry due to their unique properties and specific advantages like no need of water for disintegration, accurate dosing, rapid onset of action, ease of transportability, ease of Handling, pleasant taste and improved patient compliance

- **Authorised definitions of sublingual films**

Fast-dissolving films have recently gained popularity in the pharmaceutical industry due to their special properties and special benefits such as not requiring water for disintegration, correct consumption, Fast start and ease of use. It is a layer or several layers of suitable material that is easy to dissolve in saliva, can be put in the mouth and dissolve quickly.

A piece of smooth muscle and mucosa is also stable and therefore suitable for control of stored paper. The drug is absorbed into the systemic circulation. The extensive soft tissue and weak mucosa make it suitable for archival management. The drug is absorbed into the systemic circulation through the deep lingual or facial vein, the internal carotid artery, and the brachiocephalic vein bypassing the drug. Since it does not cause first-pass metabolism in the liver, various drug delivery methods have achieved high bioavailability, the oral route will be the most preferred route by patients and doctors. To form a film, put it on the patient's tongue or tissue, and it should be quickly moistened with saliva; It breaks down and dissolves rapidly, releasing the drug for absorption through the oral mucosa. > Environment. The sublingual film is made of hydrophilic polymers that can dissolve rapidly on the tongue or groove and deliver the drug into the body via the sublingual mucosa. Designed for drugs with rapid drug elimination, extensive first-pass metabolismand lower, improved bioavailability.

Advantages and Disadvantages

Advantages

1. Rapid onset of action and increased bioavailability
2. Polymers used should be non-toxic and non-irritating. Increase stability
3. Make it quick. Do not pass metabolism first
4. No water is needed during application
5. Small and easy to store
6. Be friendly to adults and children. Fast digestion and soluble
7. No risk of choking
8. Easy care

Disadvantages

1. Cannot give much medicine.
2. Less can be used for absorption.
3. Eating, drinking and smoking are prohibited.
4. High ionic strength cannot be given.

- **Difference Between Sublingual Film and Sublingual**

Aspects	Sublingual film	Sublingual tablet
1. Physical Appearance	Thin, flexible, paper-like strip	Small, solid, compressed dosage form
2. Administration	Placed under the tongue and adheres to mucosa	Placed under the tongue and dissolves gradually
3. Dissolution Rate	Faster dissolution due to larger surface area	Slower compared to films
4. Drug Release	Rapid and uniform drug release	May have variable release depending on formulation
5. Stability	Generally less stable; requires moisture protection	More stable; easier to store
6. Onset of Action	Faster onset due to rapid drug release	Smaller surface area slows down dissolution
7. Patient Comfort	Comfortable and easy to use; feels lighter May feel bulky or uncomfortable under the	May feel bulky or uncomfortable under the tongue
8. Application	Adheres directly to the sublingual mucos	Sits under the tongue without adherence
9. Manufacturing Process	Requires specialized film-coating and drying techniques	Made using standard tablet compression methods
10. Portability	Ultra-thin and discreet; easy to carr	Compact but bulkier than films
11. Storage Stability	Requires protection from moisture and heat	More stable under typical storage conditions

12. Patient Compliance	Higher, as it is easier to handle and more comfortable Moderate, may feel bulky under	Moderate, may feel bulky under the tongue
13. Cost of Production	Higher due to advanced technology and materials	Lower due to simpler production methods
14. Usage in Specific Groups	Ideal for children and elderly who have difficulty swallowing	May not always be preferred by such groups
15. Examples of Us	Fast-acting drugs like antiemetics, painkillers	Emergency drugs like nitroglycerin tablets

- **Formulation**

All excipients utilized in the formulation and development of orally disintegrating films are regarded as safe (GRAS-listed) and are approved for use in oral pharmaceutical dosage forms from a regulatory perspective. These oral thin films typically have a surface area ranging from 1 to 20 cm^2, depending on the drug dose and loading capacity.

1. Drug

The active pharmaceutical ingredient (API) in films is usually present at a concentration of 1–30% w/w. Micronized APIs improve the film's texture, ensuring rapid dissolution and uniformity in fast-dissolving films, making them essential for an optimal formulation.

Characteristics for Oral Strip Formulations.

For developing oral strip formulations, the drug should exhibit the following characteristics:

1. Low dosage requirement.
2. Extensive first-pass metabolism.
3. A non-bitter taste profile.
4. Rapid onset of action.
5. High solubility and permeability (classified as BCS Class I). Example: Captopril, Metoprolol.

2. Polymer

Polymers are a critical component in film formulation.

Hydrophilic polymers are employed to ensure the film dissolves quickly in the oral cavity, facilitating drug delivery to the bloodstream via dissolution upon contact with saliva on the mucosal membrane.

Water-soluble polymers are used as film modifiers, offering quick disintegration, a pleasant mouthfeel, and desirable mechanical properties. Polymers can be used individually or in combination to enhance film attributes such as hydrophilicity, elasticity, taste, and solubility. The disintegration rate of the polymer is controlled by adjusting the molecular weight of the polymeric film bases.

The polymers used in oral films should possess the following ideal characteristics:

1. Non-toxic and non-irritating.
2. Tasteless, non-bitter, free from leachable contaminants, affordable, and easily available.
3. Should not interfere with the film's disintegration process.
4. Must exhibit good hydration and spreadability.
5. Should provide sufficient peel, shear, and tensile strength.
6. Must have a long shelf life.
7. Should not cause any significant oral infections.

3. Plasticizers

Plasticizers are essential excipients in oral films, enhancing their flexibility and mechanical properties, such as tensile strength and elongation, while reducing brittleness. By lowering the polymer's glass transition temperature, they significantly improve the film's characteristics. It is important to select plasticizers that are compatible with the drug, polymer, and other excipients. Inappropriate plasticizers can lead to tearing or delamination of the film. They are typically used in concentrations of 0–20% by the dry polymer weight. Common plasticizers include glycerin, propylene glycol, polyethylene glycol, dimethyl, dibutyl, diethyl phthalate, tributyl, triethyl, acetyl citrate, triacetin, and castor oil.

4. Sweetening Agents

Sweeteners are incorporated to mask the bitterness of drugs and enhance palatability. They are used alone or in combination, typically at concentrations of 3–6% by weight. Both natural and artificial sweeteners are utilized. Natural sweeteners include xylose, ribose, glucose, sucrose, maltose, stevioside, dextrose, fructose, liquid glucose, and isomaltose, with fructose being particularly popular due to its higher sweetness compared to sorbitol and mannitol. Artificial sweeteners such as saccharin sodium or calcium salts, cyclamate, acesulfame K, and sucralose are also used, with acesulfame K and sucralose being 200 and 600 times sweeter, respectively.

5. Flavoring Agents

Flavoring agents improve patient acceptance by enhancing the taste of oral films. They are added at concentrations of up to 10% w/w, chosen based on the drug type and patient preferences. For example, pediatric patients often prefer chocolate or fruit flavors, while geriatric patients may favor orange or mint flavors. Flavoring agents are typically derived from plants, fruits, or flowers, such as vanilla, orange, and peppermint.

6. Coloring Agent

Coloring agents are essential for providing color to the formulation and are selected based on the flavor of the product. FD&C-approved coloring agents are commonly incorporated into oral films to enhance their aesthetic appeal. These agents play a significant role in improving the overall appearance of the formulation and are typically used in concentrations up to 1% w/w, with titanium dioxide being a common example.

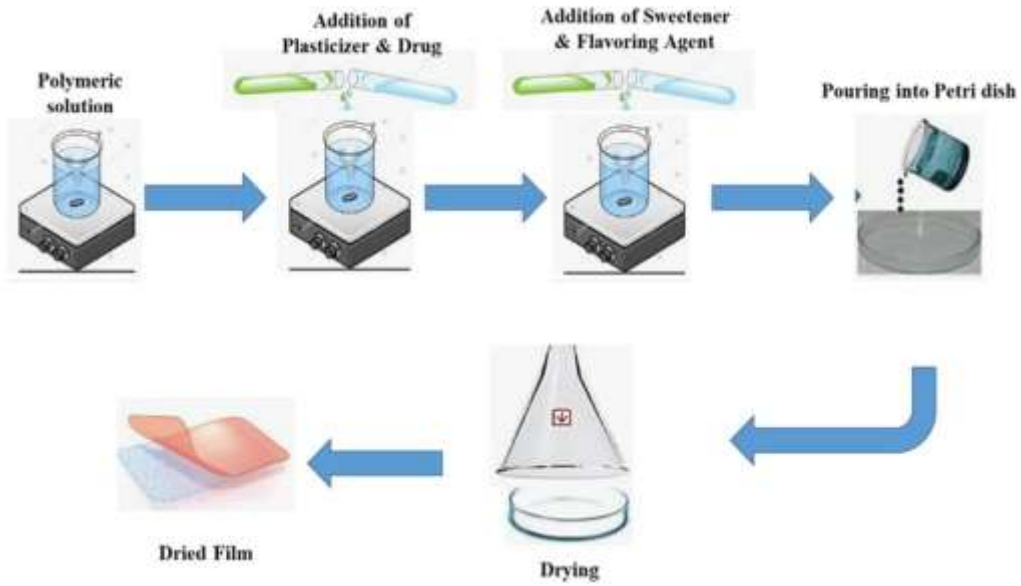
7. Saliva-Stimulating Agents

Saliva-stimulating agents enhance salivary flow, aiding in the rapid breakdown and dissolution of oral films in the mouth. These agents are often food-grade acids that can be used individually or in combinations at concentrations ranging from 2% to 6% by weight of the oral strip.

Examples include citric, malic, lactic, ascorbic, and tartaric acids, with citric acid being the most preferred. Salivary stimulation can be evaluated by comparing the resting saliva volume with the stimulated saliva volume under identical conditions.

Method of preparation - Solvent casting method

It is the most commonly used method for the preparation of ODF. It uses water-soluble additives, polymers and chemicals dissolved in deionized water; High shear force generated by the processor to obtain a homogeneous mixturein a volatile solvent such as water or ethanol.



Evaluation test

1. Thickness

The thickness of the film is measured with a micrometer screw gauge or a calibrated digital vernier caliper. The thickness should be assessed at five different locations (four corners and one in the middle) and the film thickness balance should be determined because it is directly related to the accuracy of the dose in the film distribution.

2. Tensile Strength

The maximum stress at the point of rupture of a strip is called tensile strength. It is calculated from the equation - strip carrying the breaking load at break x strip width tensile strength.

3. Folding Endurance

Folding Strength is measured by manually folding the film in the same position until it breaks. The number of times a film can be folded without breaking is called the folding strength value.

4. Weight variation

Cut out four square centimeter (2 X 2 centimeter) photographs of three different sections of the film crew. Weigh each film and calculate the weight change.

5. Dryness/ Tack test

Test Dryness is a tool that measures the amount of solvent or water present in the film; tackiness is the adhesiveness of the film to adhere to the paper pressed into contact with the strip. The film drying process has been approved in eight stages: dry to the touch, dust-free, non-sticky, dry to the touch, hard dry, and no need for re-coating and dry pressing.

5. Percent Elongation

When under tension, the film structure is stretched, which is called strain. Strain is the simple deformation of the film divided by the sample size.

Generally speaking, the elongation of the film increases with the increase of the plasticizer content. Percentage

Elongation L*100/LO L=increase in film length Lo=original length of film

6. Transparency

Measurement of oral dragon Film transparency can be measured by: simple UV spectrophotometer. Cut the sample film into rectangles and place them inside the spectrophotometer cell. Now measure the transmittance of the film at 600 nm. Concentration.

7. Swelling test

1) Film swelling studies is conducted using simulated saliva solution.
2) Each film sample is weighed and placed in a preweighed stainless steel wire mesh.
3) The mesh containing film sample is submerged into 15ml medium in a plastic container.
4) Increase in the weight of the film was determined at preset time interval until a constant weight was observed. The degree of swelling was calculated by W=Wt-Wo/Wo Where, Wi-is weight of film at time t, Wo is weight of film at time zero.

8. Surface ph test

The surface pH of oral soluble film may have adverse effects on the oral mucosa, so the surface pH of the film should be measured. female gender. For this, a pH electrode combination can be used with the help of water, the membrane dissolved in the mouth is slightly wetted and the pH measurement can be made by bringing the electrode to the location of the oral membrane. This was done on at least six films of each production and the average can be calculated as 50.

Another method for determining surface pH is to place a film on a 1.5% w/v agar gel.

A pH test strip is then placed on the film and the pH paper changes color. pH test paper on film. Surface pH of the film.

9. Content uniformity

This is determined by the test procedure described for the specific API in the Standard Pharmacopoeia. Show the amount of drug in each strip. The percentage difference is 85-

115%. Losartan content uniformity test The drug content of each prescription was determined by the ultraviolet spectrophotometric method. For this purpose, 2 x 2 cm2 films were cut and dissolved in 100 ml of pH 6.8 phosphate buffer. Filter the solution and record the absorbance at 206 nm. The drug content is calculated from the drug calibration curve. All readings were obtained in triplicate.

10. Disintegration test

Disintegration time limit is less than 90 seconds. Although there are no verbal test instructions. Pharmacopoeia Disintegration test apparatus can be used for this study. Oral disintegration time is 5-30 seconds. > Long density fiberboard is rapidly degraded with the concentration of plasticizer, which is because the hydrophilic plasticizer absorbs water quickly, then swells and forms hydrogen bonds immediately.

CONCLUSION

This drug delivery system is innovative for all patient groups with swallowing difficulties, such as pediatric and geriatric patients. It offers several advantages over other dosage forms, including improved drug bioavailability and a faster onset of action. Since drug absorption occurs in the oral cavity, drugs that are degraded by gastric acid or inactivated by first-pass metabolism can also be incorporated into orally disintegrating films. This dosage form allows for rapid termination of therapy in cases of incorrect drug delivery, overdose, incompatibility, or allergic reactions. Due to its quick onset and action, it is particularly suitable for emergency situations. In conclusion, fast-dissolving orally disintegrating films, with their excellent patient compliance and numerous benefits, have significant potential for the future.

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