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Buccal Drug Delivery System

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ABSTRACT

Buccal drug delivery systems (BDDS) have emerged as a promising alternative to conventional oral drug delivery, offering advantages such as bypassing first-pass metabolism, rapid onset of action, and improved bioavailability for certain therapeutics. This review provides a comprehensive overview of the various approaches and technologies employed in buccal drug delivery, including mucoadhesive systems, patches, films, tablets, and gels. The article explores the anatomical and physiological characteristics of the buccal mucosa that influence drug absorption, alongside formulation strategies to enhance drug retention and permeation. Key polymers and excipients used in the development of buccal systems are discussed, with an emphasis on their role in mucoadhesion and drug release modulation. Additionally, the review outlines current in vitro and in vivo evaluation techniques used to assess the performance, efficacy, and safety of buccal formulations. Recent advances, challenges, and future prospects in the field are also highlighted, aiming to provide valuable insights for researchers and formulators developing novel buccal drug delivery platforms.

INTRODUCTION

Recent advancements in drug delivery technology have provided effective alternatives to traditional oral routes, especially for pediatric, geriatric, bedridden, nauseous, or noncompliant patients. Challenges associated with oral administration, such as significant first-pass metabolism by the liver, drug degradation in the harsh gastrointestinal environment, and the invasiveness of parenteral routes, can be addressed by utilizing the buccal route.

In recent years, buccal drug delivery has emerged as an important method of administration. Buccal films, a cutting-edge technology, have been developed to meet these needs, drawing inspiration from the design principles of transdermal patches. These films are compact, low-dose, and easy to administer, making them more palatable and acceptable compared to alternatives like tablets, lozenges, wafers, gels, or capsules. This delivery system is particularly suitable for drugs that undergo extensive first-pass metabolism, as it enhances bioavailability while reducing the dosing frequency needed to maintain steady plasma levels, thereby minimizing adverse side effects.

The system involves an ultra-thin oral film that can be applied to the tongue or other oral mucosal surfaces. Upon contact with saliva, the film quickly hydrates, adheres to the application site, and begins to disintegrate, releasing the medication for oromucosal absorption. With specific formulation adjustments, the film can also dissolve for subsequent gastrointestinal absorption. Buccal films can be tailored for either systemic or localized therapeutic effects. However, developing high-quality buccal films remains a significant challenge, necessitating thorough evaluation and a deep understanding of their performance characteristics.(1-4)

Special features of mouth dissolving films

• Slim and sophisticated design

• Offered in multiple sizes and shapes

• Discreet and non-intrusive

• Superior mucoadhesive properties

• Quick to disintegrate

• Ensures rapid drug release

Advantages

• Simple and convenient to administer.

• Therapy can be easily discontinued if needed.

• Provides a fast onset of action.

• Eliminates the need for water for swallowing or chewing.

• Delivers the drug directly into systemic circulation, minimizing the hepatic first-pass effect.

• Eliminates the risk of choking.

• Allows for localized and site-specific drug action.

• Compact size enhances patient compliance.

• Increases bioavailability for specific therapeutic agents.

• Effectively masks unpleasant tastes.

• Compact size further improves patient acceptance. [6]

Disadvantages

• Exhibits a delicate, granular characteristic.

• Cannot accommodate larger drug doses in oral film format.

• Requires specialized equipment for packaging.

• Achieving uniformity in the dosage form poses challenges.

• Being hygroscopic, it needs to be stored in a dry environment. [6]

Buccal Mucosa

The oral mucosal drug delivery system is primarily divided into two types: buccal and sublingual. The buccal cavity is commonly used for administering drugs through the mucosal lining, while the sublingual route is often preferred for its rapid onset of action, as demonstrated in the treatment of angina pectoris. The buccal mucosa refers to the lining inside the cheek. Within the oral cavity, drug delivery methods can be further classified into three distinct categories.

1. Sublingual Delivery
2. Buccal Delivery
3. Local Delivery

The oral cavity consists of several structures, including the lips, cheeks, hard palate, soft palate, and the floor of the mouth. It is anatomically divided into two main regions: the outer oral vestibule and the oral cavity proper. The outer oral vestibule is bordered by the lips, cheeks, teeth, and gums (gingiva), while the oral cavity proper extends from the teeth and gums to the fauces, which leads to the pharynx. The hard and soft palates form the roof of the oral cavity, while the tongue originates from the floor. Within the oral cavity, specific areas can be further identified.

➢ Gingiva

➢ Hard palate

➢ Soft palate

➢ Tonsil

➢ Tongue [8]

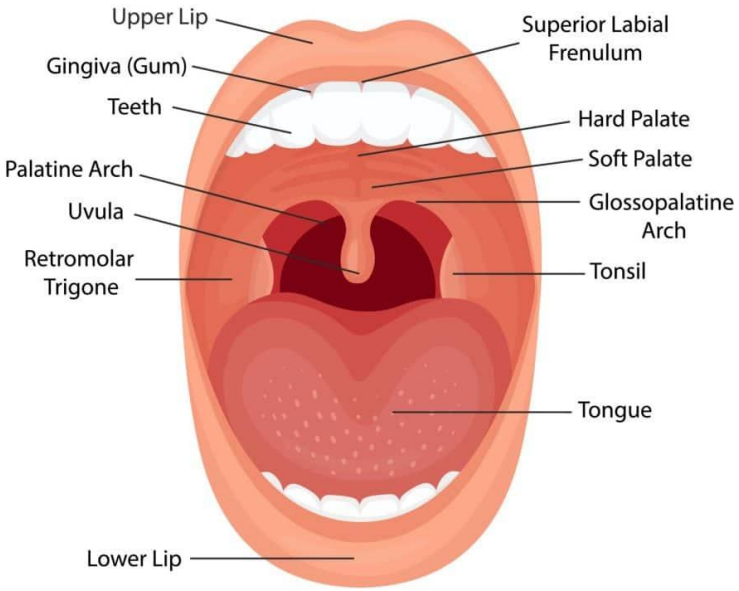

FIG: ANATOMY AND PHYSIOLOGY OF BUCCAL CAVITY

The oral mucosa is made up of several layers, with the outermost layer being the stratified squamous epithelium. Beneath this layer is the basement membrane, followed by the lamina propria, and then the submucosa, which forms the deepest layer. The epithelium resembles other types of stratified squamous epithelial tissue found in the body, featuring a basal cell layer that actively undergoes mitosis. This basal layer differentiates through multiple intermediate stages before forming the superficial layers.

Tongue

The tongue is a voluntary muscular organ located on the floor of the mouth. It is anchored at its base to the hyoid bone and is connected to the floor of the mouth by a fold of mucous membrane called the frenulum. The upper surface of the tongue is covered with stratified squamous epithelium and features numerous small projections known as papillae. These papillae contain the sensory nerve endings responsible for taste, which are commonly referred to as taste buds.(9)

It is classified into three categories

Sublingual delivery: The administration of drugs through the sublingual mucosa, which is the membrane on the ventral surface of the tongue and the floor of the mouth, allows for direct delivery into systemic circulation. The sublingual mucosa is relatively permeable, enabling rapid absorption and good bioavailability for many drugs. This route is convenient, easily accessible, and generally well accepted by patients. Among the various routes of administration, the sublingual route has been the most extensively studied.

Sublingual dosage forms typically come in two designs: rapidly disintegrating tablets or soft gelatin capsules filled with liquid medication. These formulations create a high concentration of the drug in the sublingual area before it is absorbed into the bloodstream through the mucosa.(10)

Buccal Delivery: This refers to the administration of a drug through the buccal mucosa, which is the lining of the cheek, allowing the drug to enter the systemic circulation. The buccal mucosa, however, is significantly less permeable than the sublingual area and generally does not provide the rapid absorption and high bioavailability associated with sublingual administration.

Local Delivery: This method is used for treating conditions within the oral cavity, primarily including ulcers, fungal infections, and periodontal disease. The various oral mucosal sites differ considerably in terms of anatomy, permeability to applied drugs, and their ability to retain a delivery system for a desired duration.(11)

Although the sublingual mucosa offers greater permeability compared to the buccal mucosa, it is not ideal for retentive oral transmucosal delivery systems. The sublingual area lacks a smooth and immobile mucosal surface and is continuously washed by a large amount of saliva, complicating the placement of delivery devices.

Consequently, the buccal mucosa is the preferred site for retentive oral transmucosal delivery systems and for sustained and controlled-release delivery devices. This preference is largely due to the differences in permeability between the two regions and the buccal mucosa's larger area of smooth and relatively immobile mucosa.

Overview of Buccal Mucosa [3]

A. Structure:

The oral mucosa is anatomically divided into

1) Epithelium

2) Basement membrane and Connective tissues

1) Epithelium: The epithelium consists of approximately 40–50 layers of stratified squamous epithelial cells having thickness 500-800µm. The epithelium of oral mucosa serves as a protective covering for tissues and a barrier to the entry of foreign materials.

2) Basement Membrane and Connective Tissue

The basement membrane (BM) is a continuous layer of extracellular materials and forms a boundary between the basal layer of epithelium and the connective tissues. Connective tissue, along with basement membrane, is not considered to influence the diffusion of most compounds of pharmacological interest although these two regions may limit the movement of some macromolecules and complexes. (12-13)

B. Buccal Mucosa Environment :

The oral cavity is marked by presence of saliva produced by salivary glands and mucus which is secreted by major and minor salivary glands as part of saliva.

Role of Saliva:

• Protective fluid for all tissues of oral cavity.

• Continuous mineralization / demineralization of tooth enamel.

• To hydrate oral mucosal dosage forms. Role of Mucus:

• Made up of proteins and carbohydrates

• Cell-cell adhesion

• Lubrication

• Bioadhesion of mucoadhesive drug delivery systems

Formulation Consideration For Buccal Film:

The development of orodispersible films (ODFs) necessitates careful consideration of several important attributes, such as taste masking, rapid dissolution, visual appeal, and mouthfeel, among others. The excipients used in ODF formulations are categorized according to their specific functions. From a regulatory perspective, all excipients included in the formulation must be recognized as safe and approved for use in oral pharmaceutical dosage forms. The key components of the formulation include.(9)

1. Drug

2. Water soluble film forming polymers

3. Plasticizers

4. Saliva stimulating agent

5. Sweetening agent

6. Flavouring agent

7. Surfactant

8. Colours, Filler

1. Active Pharmaceutical Ingredient:

An active pharmaceutical substance can belong to any class of drugs that can be administered orally or via the buccal mucosa. Examples include antiulcer medications, antiasthmatics, antitussives, antihistamines, antiepileptics, expectorants, and antianginal drugs. For effective formulation, the dosage of the drug should be measured in milligrams, ideally less than 20 mg per day. Typically, about 5% to 30%

w/w of active pharmaceutical ingredients can be incorporated into a buccal film. However, incorporating high doses of certain molecules into the film can be challenging.(5)

2. Film Forming Polymers:

Polymers play a crucial role as the primary ingredient in oral fast-dissolving films. The strength and durability of these films depend on the amount of polymer used in the formulation. These polymers have gained significant attention in both the medical and nutraceutical industries. Generally, approximately 45% by weight of the polymer, calculated based on the total weight of the dry film, is utilized. Hydrophilic polymers are primarily used in buccal films because of their ability to disintegrate quickly when exposed to saliva in the oral cavity. A unique feature of these polymers is their mucoadhesive properties, which allow them to recognize and bind to specific sugar residues on the mucosal surface without disrupting the structure of the ligand. (14

Ideal Properties of Film-Forming Polymers:

• The polymer should be non-toxic and nonirritating.

• It must possess hydrophilic properties.

• It should demonstrate excellent film-forming capability.

• The polymer should have good wetting and spreading characteristics.

• It must be readily accessible and costeffective.

• A sufficient shelf life is essential.

• The polymer should be tasteless and colorless.

• It should not lead to secondary infections in the oral mucosa.

• Adequate peel, shear, and tensile strengths are necessary.

3.Plasticizers

Plasticizers play a crucial role in the formulation of oral films. Their selection depends on two main factors: their compatibility with the chosen polymer and the type of solvent used during the film casting process. These agents enhance the flexibility of the film, give the final product a glossy appearance, and reduce brittleness. Typically, plasticizers are used at concentrations ranging from 1% to 20% by weight based on the dry weight of the polymer. Common examples of plasticizers include glycerol, propylene glycol, low molecular weight polyethylene glycols, citrate derivatives such as triacetin and acetylcitrate, phthalate derivatives like dimethyl, diethyl, and dibutyl phthalates, as well as castor oil.(10)

4. Sweetening Agents

Sweetening agents, both natural and artificial, are used to enhance the flavor of fast-dissolving oral thin films. These agents are especially important in food and pharmaceutical products that are designed to dissolve or disintegrate in the mouth.

Common natural sweeteners include sucrose, dextrose, fructose, glucose, liquid glucose, and maltose. Among these, fructose is often preferred because it is sweeter than both sucrose and dextrose and produces a rapid sweetness perception in the mouth. However, natural sweeteners can present challenges for diabetic patients, which has led to an increased popularity of artificial sweeteners in food and pharmaceutical applications.

First-generation artificial sweeteners include saccharin, cyclamate, and aspartame. Second-generation options consist of acesulfame-K, sucralose, alitame, and neotame.(15-18)

Saliva Stimulating Agents

Saliva-stimulating agents are added to increase saliva production, which aids in the rapid disintegration of film formulations. These agents indirectly facilitate the quick breakdown and dissolution of the film. Commonly used substances include food-grade acids such as citric acid, lactic acid, maleic acid, and ascorbic acid.

Cooling Agents

Cooling agents, such as monomethyl succinate, are used to enhance flavor strength and improve the mouthfeel of the film. Other cooling agents, including WS-3, WS-23, and Utracoll II, can be combined with flavoring agents to create a better sensory experience.(19-20)

Coloring Agents

Coloring agents, such as pigments like titanium dioxide and FD&C-approved colorants, may be added to the buccal film formulation. These are typically used at concentrations of up to 1% w/w, especially when insoluble ingredients or suspended drugs are part of the formulation.

Surfactants

Surfactants act as solubilizing or wetting agents, promoting rapid dissolution of the film within seconds and facilitating immediate drug release. They can also enhance the solubility of poorly soluble drugs in buccal formulations. Examples of surfactants include Poloxamer 407, sodium lauryl sulfate, benzalkonium chloride, benzethonium chloride, and various substances like Tweens and Spans.(21)

Stabilizing Agents

Stabilizers and thickeners are crucial for improving the viscosity and consistency of the dispersion or solution before casting the film. Examples include natural gums such as xanthan gum, locust bean gum,

carrageenan, and cellulosic derivatives. These agents are generally used at concentrations of up to 5% w/w.

Methods of preparation of buccal patches [6]

1. Solvent casting

2. Direct milling

3. Solid dispersion extrusion

4. Semisolid casting

5. Rolling method

6. Hot melt extrusion

1. Solvent casting

In this method, all patch excipients including the drug co-dispersed in an organic solvent and coated onto a sheet of release liner. After solvent evaporation a thin layer of protective backing material is laminated onto the sheet of coated release liner to form a laminate that is die-cut to form patches of desired size and geometry. (23)

2. Direct milling

In this, patches are manufactured without the use of solvents. Drug and excipients are mechanically mixed by direct milling or by kneading, usually without the presence of any liquids. After the mixing process, resultant material is rolled on a release liner until desired thickness is achieved. The backing material is then laminated as previously described. While there are only minor or even no differences in patch performance between patches fabricated by two processes, solvent-free process is preferred because there is no possibility of residual solvents and no associated solvent-related health issues. (23-26)

3. Solid dispersion extrusion:

In this method immiscible components are extrude with drug and then solid dispersions are prepared.Finally the solid dispersions are shaped in to films by means of dies. (27)

4. Semisolid casting:

In semisolid casting method first a solution of water soluble film forming polymer is prepared.The resulting solution is added to a solution of acid insoluble polymer (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 films or ribbons using heat controlled drums. Thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble forming polymer should be 1:4. (28-29)

5. Rolling Method:

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

6. Hot melt extrusion:

In hot melt extrusion method, first the drug is mixed with carriers in solid form.Then the extruder having heaters melts the mixture.Finally the melt is shaped in to films by dies.There are certain benefits of hot melt extrusion, Fewer operation units, Better content uniformity, An anhydrous process.(30)

Evaluation of buccal patches

1) Surface pH

To determine the surface pH, a combined glass electrode is used. The patches are kept in contact with 5 ml of distilled water for one hour. The pH is measured by bringing the electrode close to the surface of the formulations and allowing it to equilibrate for one minute.

2) Weight Uniformity and thickness

Three samples, each measuring 1.5 cm x 1.9 cm, are randomly selected from each patch and weighed individually. The data is then analyzed to determine the mean weight and standard deviation. The thickness of the samples from each patch is measured three times, and the average values are reported.(31)

3) Content Uniformity

Drug content uniformity is evaluated by dissolving each patch in 10 ml of solvent and filtering it through Whatman filter paper (0.45 µm). The resulting filtrate is evaporated, and the drug residue is then dissolved in 100 ml of phosphate buffer at pH 6.8. A 5 ml portion of this solution is further diluted with phosphate buffer (pH 6.8) to a total volume of 20 ml. This diluted solution is again filtered through 0.45 µm Whatman filter paper, and its absorbance is measured using a UV spectrophotometer, using phosphate buffer at pH 6.8 as the blank. All experiments are conducted in triplicate, and average values are reported.(32-34)

4) Folding Endurance

The folding endurance of patches is assessed by repeatedly folding a single patch at the same location until it breaks or up to 300 times without breaking. The experiments are conducted in triplicate, and the average values are reported.

5) Percentage moisture loss

This test is conducted to assess the integrity of films under dry conditions. Three films, each with a diameter of 1 cm, are cut out and accurately weighed. These films are then placed in desiccators that

contain fused anhydrous calcium chloride. After 72 hours, the films are removed and weighed again. The average percentage of moisture loss from the three films is then calculated.

6) Water absorption capacity test

Circular patches with a surface area of 2.3 cm^2 are placed on the surface of agar plates prepared in simulated saliva, which consists of 2.38 g of Na_2HPO_4, 0.19 g of KH_2PO_4, and 8 g of NaCl per liter of distilled water, adjusted to a pH of 6.7 using phosphoric acid. These plates are maintained in an incubator at a temperature of 37°C ± 0.5°C.

At various time intervals (0.25, 0.5, 1, 2, 3, and 4 hours), the samples are weighed to obtain the wet weight. After weighing, the patches are left to dry for 7 days in a desiccator over anhydrous calcium chloride at room temperature until a constant weight is achieved. The percentage of water uptake is calculated using the following equation:

Water uptake (%) = (Ww - Wf) / Wf × 100

where Ww is the wet weight and Wf is the final weight.(36-37)

7) Characterization of Drug Release

Two methods are used to characterize drug release from patches. The first method is simple dissolution, which employs a modified paddle apparatus. This method uses special flasks containing 100 ml of dissolution medium. The second method involves a diffusion cell for determining drug release and is considered an improvement over dissolution. In this method, only one face of the patch is in contact with the medium through a hydrated hydrogel, which more closely mimics the moist surface of the buccal cavity.(38)

(a). In Vitro Methods

Beaker method

The dosage form in this method is made to adhere at the bottom of beaker containing the medium and stirred uniformly using overhead stirrer. Volume of medium used in the literature for study varies from 50-500 ml and the stirrer speed from 60-300 rpm.

Dissolution apparatus

The United States Pharmacopeia (USP) XXIII-B rotating paddle method is used to study the drug release from the bilayered and multilayered patches. The dissolution medium consisted of phosphate buffer pH 6.8. The release is performed at 37°C ± 0.5°C, with a rotation speed of 50 rpm. The backing layer of buccal patch is attached to the glass disk with instant adhesive material. The disk is allocated to the bottom of the dissolution vessel. Samples (5 ml) are withdrawn at predetermined time intervals and replaced with fresh medium. The samples filtered through whatman filter paper and analyzed for drug content after appropriate dilution.(39)

Other methods

Other methods involve plexiglass sample blocks placed in flasks, agar gel method, Valia-Chien cell, USP 2 dissolution apparatus, etc. Although a number of methods have been reported, the ideal method would be one where sink condition is maintained and dissolution time in vitro simulates dissolution time in-vivo.

(b). In Vivo Methods

The most desirable in vivo approach is to perform experiments in human volunteers or patients. However, it is very difficult to begin with this approach, because of difficulties of cost, time, toxicity of drug and ethical considerations. Therefore, animal models are being usually used for this purpose. The most important and difficult aspect of experimental design is the choice of animal species. Animal models such as dog, cat, rabbit, rat and sheep have been used to determine the oral mucosal absorption characteristics of drugs. Very few, and certainly no extensive in vivo (animal) in vivo (human) correlation have been reported, which would allow investigator, to compare oral mucosal absorption characteristics of a particular animal with those of its human counterpart. However, the methods used in in vivo studies are absorption cells and perfusion cells. (40)

Disc methods

These methods have the advantage of allowing the study of drug absorption across a defined area of oral mucosal tissue. A polytef disc, approximately 3.5 cm in diameter and 1 cm in height, is used for this purpose. The disc features a central depression that is 4 mm deep. A moisture-soaked filter paper disc is placed in this depression, and a known amount of the drug is spread onto it. Once the drug has dissolved, the device is positioned on a specific area of the oral mucosa and held in place for 5 minutes. After removal, a non-impregnated disc is used to gently wipe the oral mucosa, and the two discs are then combined and analyzed.

Disc methods enable researchers to investigate drug loss from a fixed area of the oral cavity membrane. However, there are significant limitations to this technique, including the potential for the disc to adhere to the membrane, leakage of the drug from the disc, and interference from saliva.(41)

Perfusion cells for animal studies

Veillard et al. developed a perfusion cell made from a medical-grade silicon polymer. This cell has a volume of 0.075 cm^3 and an exposed area of 0.25 cm^2. Barshun et al. constructed a pliable cell using a hydrophilic vinyl polysiloxane polymer, which has an internal volume of 1 mL and allows for the perfusion of a buccal membrane area of 1.8 cm^2. This design also features a sealing lip to prevent leaks. Ranthbone reported on a buccal perfusion cell design constructed from inflexible materials such as nylon or Teflon. The buccal perfusion cells mentioned above provide fixed, known interfacial areas through which transfer can occur into a defined oral cavity membrane.(42)

Human Techniques

Animal models play an important role in the development of an oral mucosal drug delivery system, but these models are appropriate to use only for screening of a series of compounds, investigating the mechanisms and usefulness of permeation enhancers or evaluating a set of formulations, if one is certain that the route of penetration,structure and composition of permeation barrier for both drug and excipients are an exact mimic of its human counterpart.

8. Ex-Vivo Buccal Permeation Study

The in vitro buccal permeation study through goat buccal mucosa is performed using a Keshary-Chien type glass diffusion cell at 37°C ± 0.2. Goat buccal mucosa is obtained from a local slaughterhouse and used within 2 hours of slaughter. Freshly obtained goat buccal mucosa is mounted between donor and receptor compartments. The patch is placed on the mucosa, and compartments are clamped together. The donor compartment is filled with 2 ml of phosphate buffer (pH 6.8). The receptor compartment (10-mL capacity) is filled with isotonic phosphate buffer (pH 7.4), and hydrodynamics in the receptor compartment are maintained by stirring with a magnetic bead at 50 rpm. At predetermined time intervals, a 1-ml sample is withdrawn and analyzed for drug content.

9. Ex-Vivo Mucoadhesive Strength

Fresh goat buccal mucosa is obtained from a local slaughterhouse and used within 2 hours of slaughter. The mucosal membrane is separated by removing the underlying fat and loose tissues. The membrane is washed with distilled water and then with phosphate buffer (pH 6.8) at 37 °C ±1. The patch's bioadhesive strength is measured on a modified physical balance. Fresh goat buccal mucosa is cut into pieces and washed with phosphate buffer (pH 6.8). A piece of buccal mucosa is tied in the open mouth of a glass vial; filled with phosphate buffer (pH 6.8). This glass vial is tightly fitted in the center of a glass beaker filled with phosphate buffer (pH 6.8, 37°C ± 1) so that it just touches the mucosal surface. The patch is stuck to lower side of a rubber stopper with cyanoacrylate adhesive. Two pans of balance are balanced with a 5 g weight on the right-hand side pan. The 5 g weight is then removed from the left-hand side pan, which lowers the pan along with patch over the mucosa. The balance is kept in this position for 5 minutes of contact time. The water is added slowly at 100 drops/min to the right-hand side pan until the patch detaches from the mucosal surface. The weight, in grams, require to detach the patch from mucosal surface provides the measure of mucoadhesive strength. The experiments are performed in triplicate, and results are reported.

10. Measurement of mechanical properties

Mechanical properties of films (patches) include tensile strength and elongation at break is evaluated using a tensile tester. Film strip with dimensions of 60 x 10 mm and without any visual defects are cut and positioned between two clamps separated by a distance of 3 cm. Clamps are designed to secure the patch without crushing it during test, the lower clamp held stationary and strips are pulled apart by upper clamp moving at a rate of 2 mm/sec until the strip breaks. The force and elongation of film at the point when the

strip break is recorded. The tensile strength and elongation at break values are calculated using the formula. Where, M - is the mass in gm, g - is the acceleration due to gravity 980 cm/sec 2 B - is the breadth of the specimen in cm T - is the thickness of specimen in cm. Tensile strength (kg/mm2) is the force at break (kg) per initial cross- sectional area of the specimen (mm2).

11. Stability study in human saliva

A stability study of bilayered and multilayered patches was conducted using human saliva. Saliva samples were collected from individuals aged 18 to 50 years. Buccal patches were placed in separate petri dishes containing 5 ml of human saliva and maintained in a temperature-controlled oven at 37°C ± 0.2°C for a duration of 6 hours. The films were examined at regular time intervals (0, 1, 2, 3, and 6 hours) for any changes in color, shape, collapse, and overall physical stability.

12. Ex Vivo Residence Time

The ex vivo mucoadhesion time was studied (n = 3) after applying patches to freshly cut goat buccal mucosa. The mucosa was fixed on the inner side of a beaker, approximately 2.5 cm from the bottom, using cyanoacrylate glue. One side of each patch was wetted with one drop of phosphate buffer (pH 6.8) and then adhered to the goat buccal mucosa by applying light pressure with a fingertip for 30 seconds. The beaker was filled with 200 ml of phosphate buffer (pH 6.8) and maintained at 37°C ± 1. After 2 minutes, a stirring rate of 50 rpm was applied to simulate the conditions of the buccal cavity, and patch adhesion was monitored for 12 hours. The time required for the patch to detach from the goat buccal mucosa was recorded as the mucoadhesion time.

13. Swelling study

Buccal patches are weighed individually (designated as W1), and placed separately in 2% agar gel plates, incubated at 37°C ± 1°C, and examined for any physical changes. At regular 1-hour time intervals until 3 hours, patches are removed from gel plates and excess surface water is removed carefully using filter paper. The swollen patches are then reweighed (W2) and swelling index (SI) is calculated using the following formula.

$$S1 = (W2-W1) / W1 \times 100$$

14. Water vapor transmission rate:

For this study, vials of equal diameter are used as transmission cells. These cells are washed thoroughly and dried in an oven. About 1 g of calcium chloride is taken in the cell and polymeric films measuring one cm2 area are fixed over the brim with the help of an adhesive. The cells are weighed accurately and initial weight is recorded, and kept in a closed desiccators containing saturated solution of potassium chloride. The humidity inside desiccators is found to be in between 80-90% RH. The cells are taken out and weighed after 18, 36, 54, and 72 hrs. Water vapour transmission rate is calculated by using the following formula. Water Vapour Transmission Rate = WL/S Where, W is water vapour transmitted in mg, L is thickness of the film in mm, S is exposed surface area in cm 2.(40-44)

CONCLUSION

The review concluded that buccal films are among the most acceptable and palatable dosage forms available. This formulation presents a promising avenue for further research, especially for the systematic delivery of drugs that are ineffective when taken orally. By bypassing first-pass metabolism, buccal films enhance the bioavailability of active pharmaceutical ingredients. Their unique characteristics make them superior to other innovative buccal drug delivery systems.Buccal films are particularly beneficial for geriatric and pediatric patients, as well as individuals who have difficulty swallowing. This innovative dosage form offers a cost-effective, non-irritating solution for drug delivery within the oral cavity. Additionally, it provides a non-invasive alternative for administering potent peptides and protein-based drugs. With strong mucoadhesive properties, buccal films enable a rapid onset of action, improving the safety, efficacy, and stability of active ingredients.The development of oral thin film technology also supports brand extension and serves as a tool for product lifecycle management by extending the patent life of existing drugs. This novel technology optimizes therapeutic efficacy and has been extensively studied for its potential applications. Overall, buccal films offer significant advantages over traditional dosage forms, and there remains substantial scope for future research in this area.

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