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A REVIEW ARTICLES ON MUCOADHESIVE BUCCAL FILMS: A PROMISING APPROACH FOR ENHANCED DRUG DELIVERY

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Keywords:

Mucoadhesive buccal films, Drug Delivery, Buccal route, Formulation strategies, Enhanced drug delivery

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ABSTRACT: Mucoadhesive buccal films have gained significant attention as a promising drug delivery system for various therapeutic applications. This review article provides a comprehensive overview of the recent advancements in mucoadhesive buccal films, focusing on their formulation strategies, mucoadhesive mechanisms and potential applications. The article discusses the various polymers used in the formulation of mucoadhesive buccal films, including natural, synthetic, and semi-synthetic polymers. The selection of appropriate polymers plays a crucial role in achieving optimal mucoadhesive properties and drug release characteristics. Furthermore, the influence of different formulation factors, such as plasticizers, penetration enhancers, and drug loading techniques, on the performance of buccal films is thoroughly examined. The discussion covers a wide range of topics, beginning with the structure and physiology of the buccal mucosa, which elucidates the particular properties that impact medication absorption. The complete examination of mucoadhesive polymers, nanoparticles, and thin film technologies is included in the comprehensive overview of formulation techniques.

INTRODUCTION: Among the different methods of administering drugs, transmucosal drug delivery provides significant benefits compared to oral administration for achieving systemic effects, and the buccal mucosa is highly suitable for delivering drugs locally and systemically.

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The distinctive physiological characteristics of the buccal mucosa make it an excellent choice for mucoadhesive drug delivery systems. These benefits encompass avoiding the hepatic first-pass effect and circumventing pre-systemic elimination in the gastrointestinal tract [1, 2].

Mucoadhesive buccal films (MBF) are a specific form of pharmaceutical formulation that, upon application to the tongue or oral cavity, utilizes a water-dispersible polymer to rapidly hydrate, adhere, and disintegrate, facilitating efficient systemic drug release [3]. Buccal films represent a recent advancement in buccal drug delivery,

serving as semi-solid dosage forms that are applied to the buccal region and allowed to dissolve. Following administration, they directly enter systemic circulation. These films have quickly gained recognition as a novel administration route, offering improved safety and an enhanced onset of action. Buccal films are an elegant and efficient dosage form, providing superior bioavailability compared to other buccal dosage forms like buccal tablets, lozenges, and wafers. This is achieved by bypassing the hepatic first-pass metabolism. Upon administration, these films dissolve within the patient's buccal mucosa. The oral mucosa serves as the site of drug administration and is further divided into buccal and sublingual mucosa [4].

The primary obstacle to achieving effective buccal drug release is the duration of the dosage forms staying within the oral cavity. It is crucial for the dosage forms to establish continuous contact with the mucous membrane in order to facilitate drug action at the buccal site or ensure absorption through the mucosa. However, the mechanical forces exerted in the oral environment, including saliva flow, chewing, swallowing, and speech, can potentially hinder the adhesion of the dosage forms to the oral mucosa, resulting in diminished or no therapeutic efficacy of the drugs [5, 6]. The buccal epithelium is situated on the inner mucosal surface of the cheeks, alongside the non-keratinized sublingual epithelium. In contrast to other areas within the oral cavity, these regions lack keratinization. The buccal epithelium is characterized by a stratified structure comprising approximately 40–50 cell layers, resulting in an epithelial thickness ranging from 400 to 700 mm (with variability due to invaginations). Additionally, the surface area of the buccal epithelium measures approximately 50 cm [7, 8].

The Structure of the Oral Mucosa:

Structure: The oral mucosa is composed of an outermost layer of stratified squamous epithelium **Fig. 1**. Below this lies a basement membrane, a lamina propria, followed by the submucosa as the innermost layer. The epithelium is similar to stratified squamous epithelia found in the rest of the body in that it has a mitotically active basal cell layer, advancing through a number of differentiating intermediate layers to the superficial layers, where cells are shed from the surface of the epithelium. The epithelium of the buccal mucosa is about 40–50 cell layers thick, while that of the sublingual epithelium contains somewhat fewer. The epithelial cells increase in size and become flatter as they travel from the basal layers to the superficial layers [9, 10, 11].

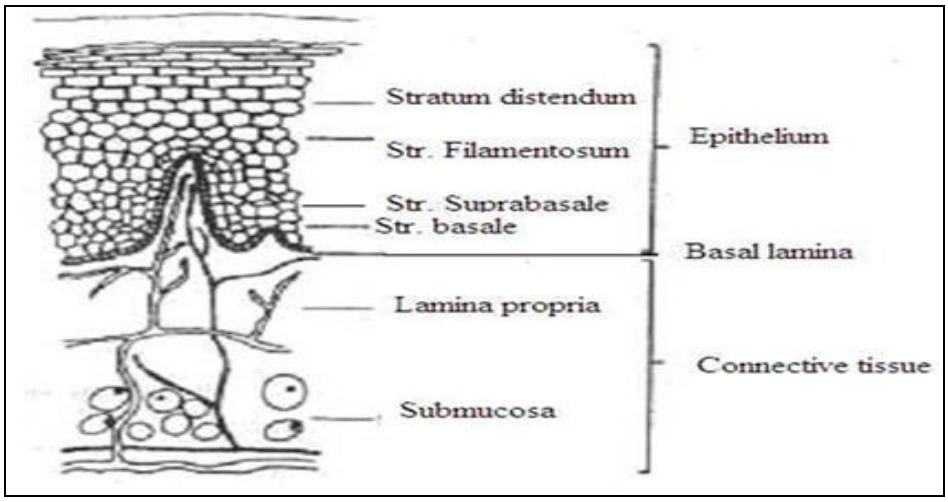

FIG. 1: SCHEMATIC CROSS SECTION THROUGH THE ORAL MUCOSA SHOWING THE EPITHELIUM, BASAL LAMINA, AND CONNECTIVE TISSUE

In a novel drug delivery system, oral route is conceivably the most suggested to the patient and the clinician alike. However, oral administration of drugs has limitations such as hepatic first-pass metabolism and enzymatic degradation within the GI tract that inhibit oral administration of certain classes of drugs, particularly peptides and proteins. As a result, other absorptive mucosae are considered possible sites for drug administration. Trans mucosal routes of drug delivery (i.e., the

mucosal linings of the nasal, rectal, vaginal, ocular, and oral cavities) propose distinct advantages over oral administration for systemic drug delivery. Due to these advantages, possible bypass of the first pass effect, avoidance of presystematic elimination within the GI tract, and, depending on the particular drug, a better enzymatic flora for drug absorption [10]. Sublingual and buccal mucosal sites for vaccine delivery Mucosal vaccine delivery in the mouth can be subdivided into sublingual and buccal delivery. Sublingual delivery occurs *via* the mucosa of the ventral surface of the tongue and the floor of the mouth under the tongue, whereas buccal delivery occurs *via* the buccal mucosa, which is located in the cheeks, the gums, and the upper and lower inner lips. The specific structure and cell composition of the sublingual and buccal regions in the mouth define whether they are more or less suitable for vaccine delivery (as described below). Within the oral cavity, some mucosal regions are lined by a keratinized stratified epithelium (gingival, hard palate, outer lips), whereas other regions are lined by a non-keratinized stratified epithelium. The epithelium is supported by a basement membrane, which separates the two major layers of the oral mucosa: the epithelium and the underlying connective tissue, or lamina propria. The arrangement of the hard palate and gingival, including the pluristratified keratinized mucosal epithelium and the lamina propria that is anchored onto the periosteum of the underlying bone, makes these regions chemically and mechanically resistant to withstand the shearing forces associated with chewing food. The floor of the mouth, the inner surface of the lips and cheeks, and the ventral side of the tongue are covered by a non-keratinized epithelium, rendering these relatively more elastic and pervious than keratinized mucosae and thus potentially more suitable for drug or antigen delivery [12].

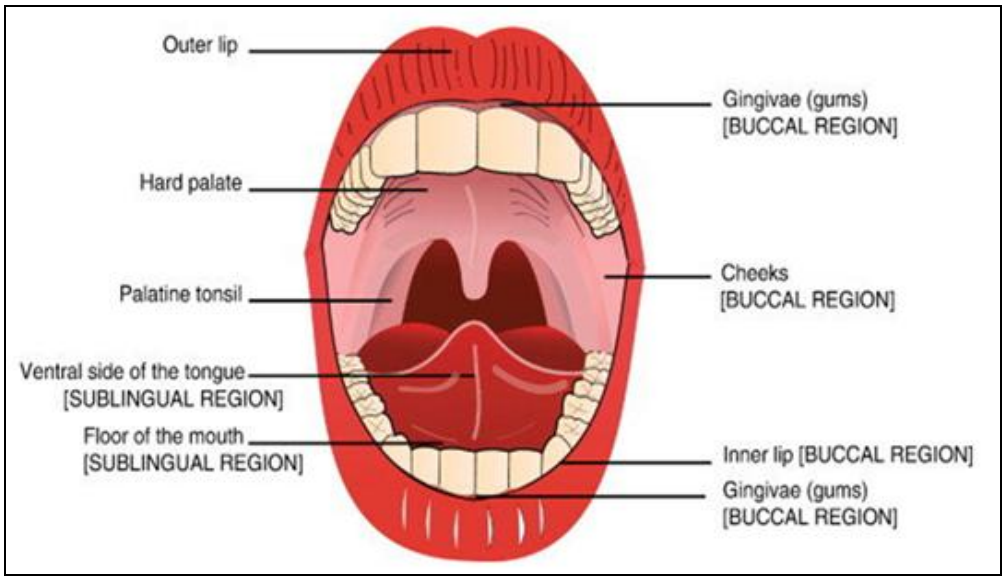

FIG. 2: THE-ANATOMY-OF-THE-ORAL-CAVITY- THE SUBLINGUAL AND-BUCCAL-REGIONS-FOR-VACCINE-DELIVERY, OBTAINED COPYRIGHT PERMISSION UNDER THE CC-BY-NC-ND LICENSE. (https://creativecommons.org/licenses/by-nc-nd/3.0

Advantages of Mucoadhesive Buccal Films [13, 14, 15, 16]:

1. Eliminates the requirement for chewing and swallowing.
2. There is no potential for asphyxiation.
3. The film enhances the overall absorption of drugs in the body as it circumvents the initial liver metabolism.
4. Drugs can be shielded from degradation caused by gastrointestinal enzymes and acidic conditions.
5. There is no risk of choking.
6. Oral films offer a pleasant oral sensation.
7. Oral films are sturdier and more pliable, allowing for easy transportation, handling, and storage.

8. Oral films can be ingested without the need for water, leading to enhanced acceptability.
9. It is convenient to administer to pediatric and geriatric patients, as well as to patients with mental disabilities, physical impairments, or those who may not cooperate.
10. It extends the duration of the dosage form at the absorption site, thereby enhancing bioavailability.

Disadvantages of Mucoadhesive Buccal Films [17, 18, 19]:

1. Saliva is continuously secreted into the oral cavity, diluting drugs at the absorption site and resulting in low drug concentrations on the surface of the absorbing membrane. Naturally, swallowing saliva leads to the removal of a significant portion of dissolved or suspended drugs from the absorption site. Furthermore, there is a risk that the delivery system itself may be swallowed.
2. The properties of the drug can impose restrictions on the use of the oral cavity as a drug delivery site. Factors such as taste, irritant, allergies, and adverse effects such as tooth discoloration or erosion can limit the selection of drugs suitable for buccal administration. Conventional buccal drug delivery systems do not allow patients to eat, drink, or speak during administration in some cases.
3. Buccal films are susceptible to moisture.
4. The incorporated doses should be kept low.
5. Provides a limited surface area for drug absorption into the films.
6. Dissolved drugs should be eliminated through the act of swallowing saliva.

Ideal Characteristics of Mucoadhesive Buccal Films [20, 21, 22, 23, 24]:

1. Should be compatible with drugs.
2. Ensuring a high level of safety and the absence of toxicity.
3. Lack of irritation.
4. Biocompatible pH.
5. Increased flexibility or improved pliability.
6. Immediate adhesion to the buccal mucosa.
7. Extended duration of retention.
8. Ideal rate and extent of drug absorption.
9. Regulated or managed release of the drug.
10. One-way release of the drug into the mucosa.
11. No interference with regular activities such as talking and eating
12. Satisfactory patient adherence without impeding regular activities.
13. Strong mechanical properties.
14. Instant attachment to the buccal mucosa.

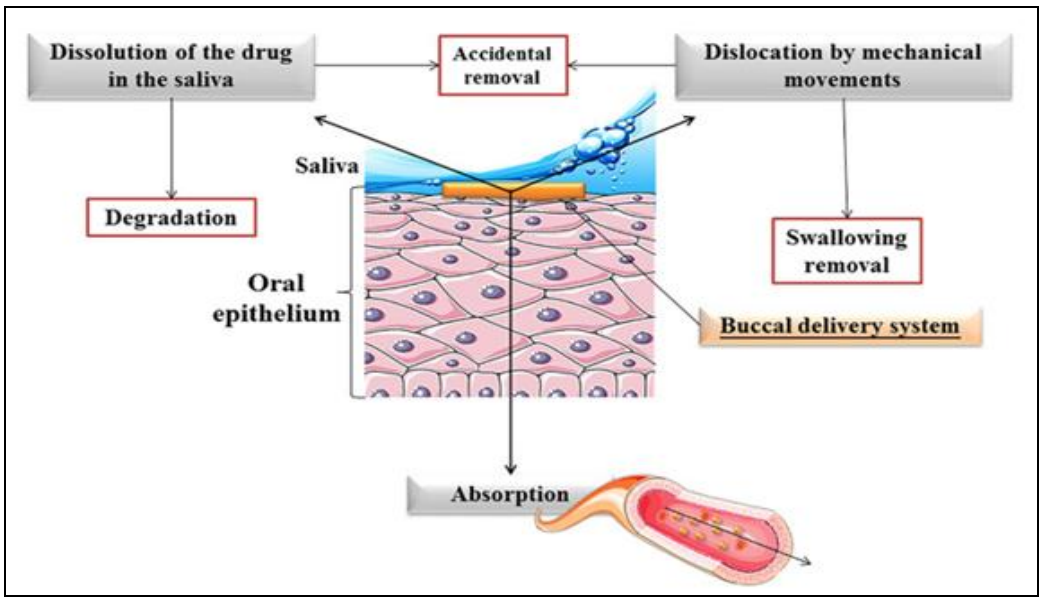

FIG. 3: FACTORS HAMPERING THE BUCCAL UPTAKE OF DRUG

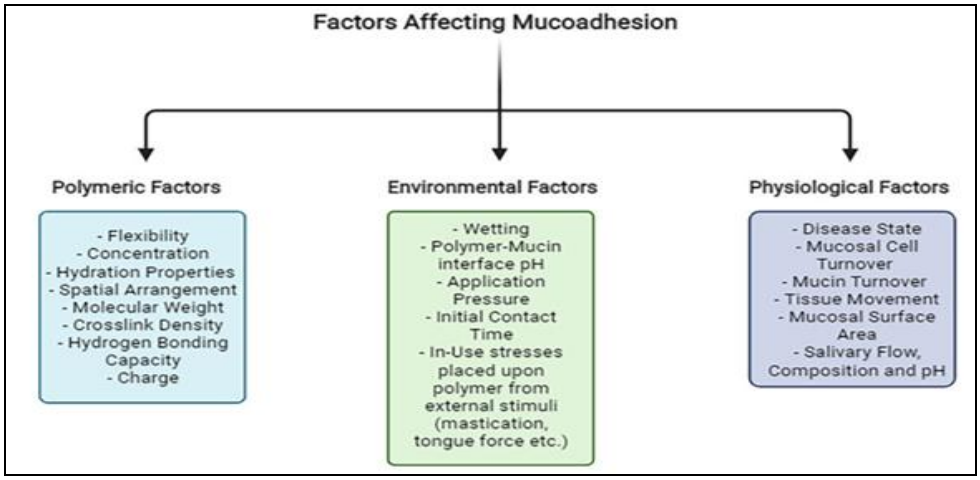

FIG. 4: A DIAGRAM DEMONSTRATING THE POLYMERIC, PHYSIOLOGICAL, AND ENVIRONMENTAL ELEMENTS THAT INFLUENCE MUCOADHESION [25]

Limitation of Mmucoadhesive Buccal Films [26, 27, 28]:

- The surface area of the absorbing membrane is comparatively smaller. If the effective area for absorption is determined by the dimensions of a delivery system, this area then becomes even tinier.
- Saliva is continuously produced in the oral cavity, diluting drugs at the site of absorption and resulting in low drug concentrations at the surface of the absorbing membrane. Involuntary swallowing of saliva leads to a significant portion of the dissolved or suspended drug being eliminated from the site of absorption. Furthermore, there is a risk that the delivery system itself would be swallowed.
- Drug characteristics may restrict the use of the oral cavity as a site for drug delivery. Taste, irritation, allergic reactions, and undesirable properties such as tooth discoloration or erosion may narrow down the list of suitable drugs for this route. Conventional buccal drug delivery systems of a typical nature did not allow the patient to simultaneously eat, drink, or, in some cases, speak.
- Drugs with a bitter flavor cannot be formulated. The drugs that provoke irritation in the oral mucosa, trigger allergic reactions, and lead to tooth discoloration cannot be formulated. A minimal dosage of the drug is necessary. The act of eating and drinking may predominantly impose limitations.

Therapeutic Applications of Mucoadhesive Buccal Films [25, 29]:

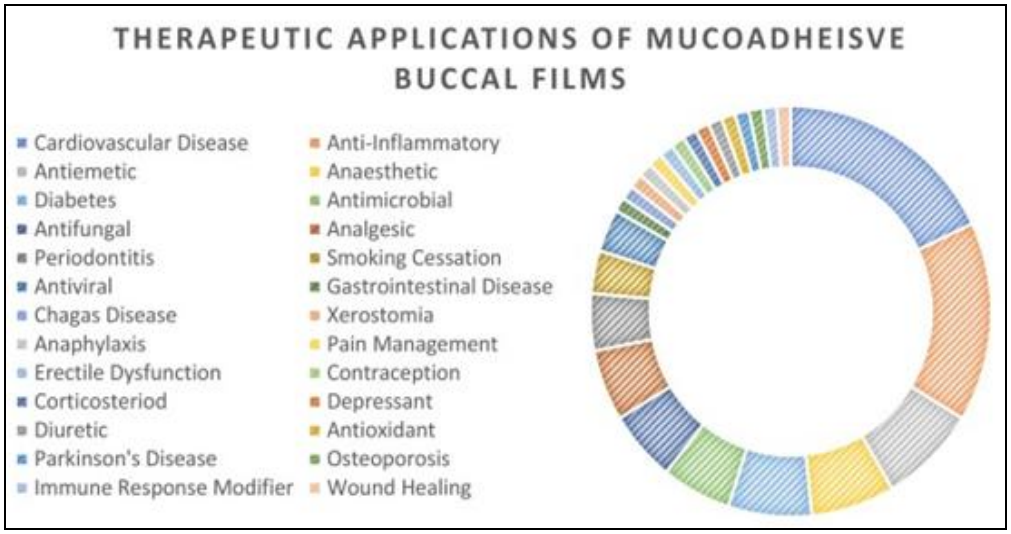

FIG. 5: ILLUSTRATION DEPICTING THE VARIOUS THERAPEUTIC AREAS AND DISEASES WHERE THE EFFICACY OF MUCOADHESIVE BUCCAL FILMS HAS BEEN SHOWCASED

Methods of Preparation of Buccal Films: The following methods are used in the preparation of buccal films:

Semisolid Casting [30]: The semisolid casting method comprises the below-given steps:

1. A water-soluble, film-forming polymer solution is prepared.
2. The resulting solution is then poured into a solution of acid-insoluble polymers (e.g., cellulose acetate phthalate and cellulose acetate butyrate).
3. The required amount of plasticizer is incorporated to obtain a gel mass.
4. In the last step, the gel mass is transformed into films or ribbons by the application of heat-controlled drums.
5. The diameter of the film should be approximately 0.015–0.05 in. The proportion of the acid-insoluble polymer to the film-forming polymer should be 1:4:2.

Solvent Casting: This is one of the most preferred manufacturing methods for quick-dissolving film. The first water-soluble ingredients are mixed in this process to form a viscous solution of water. API and the remaining ingredients are dissolved in a smaller solution quantity and combined with bulk by using the elevated shear processor.

The vacuum is used to eliminate the entrapped air. The solution formed is then cast as a film, poured into a glass mold, and allowed to the solution is dried in an oven at 45–50 °C and then cut into the desired size [31].

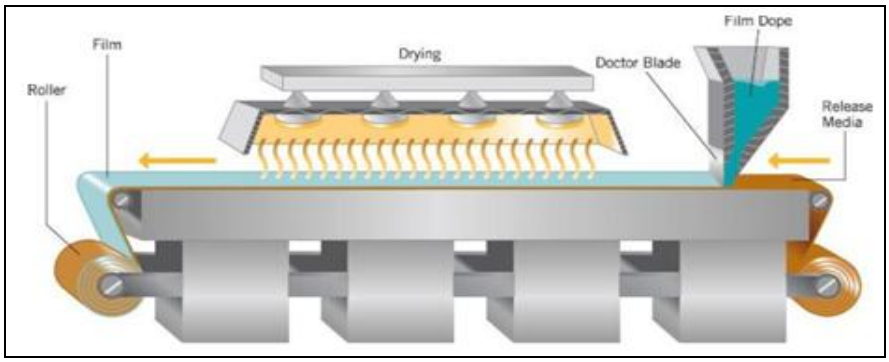

FIG. 6: SOLVENT CASTING METHOD FOR BUCCAL FILM MANUFACTURING (32) COPYRIGHT PERMISSION OBTAINED UNDER CREATIVE COMMONS (CCBY) LICENSE. (http://creativecommons.org/licenses/by/4.0/)

Hot Melt Extrusion Method [33, 34]: In the hot melt extrusion method, a mixture of drugs and other excipients is molten. Then it is forced through an orifice to yield a more homogenous material in different shapes, like granules, tablets, or films. Used for transdermal drug delivery systems.

Step 1: The drug is mixed with carriers in solid form.

Step 2: Extruders with heaters melt the mixture.

Step 3: Finally, the melted mixture is shaped into films by the dies.

Steps Involved in Hot Melt Extrusion Method:

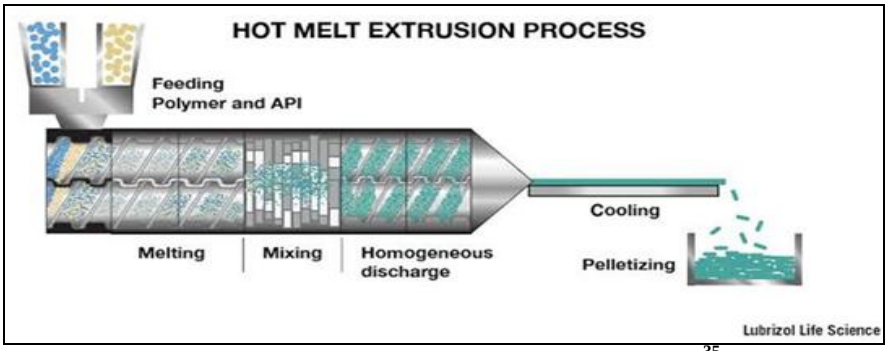

FIG. 7: HOT MELT EXTRUSION PROCESS [35]

Solid Dispersion Method: Dispersing one or more active ingredients in an inert carrier in a solid state. (in the presence of amorphous hydrophilic polymers) is known as solid dispersion. The drug is dissolved in a liquid solvent. Then incorporate this solution into a melt of polyethylene glycol below 70 °C. Obtained solid dispersions are shaped into films by means of dies [36].

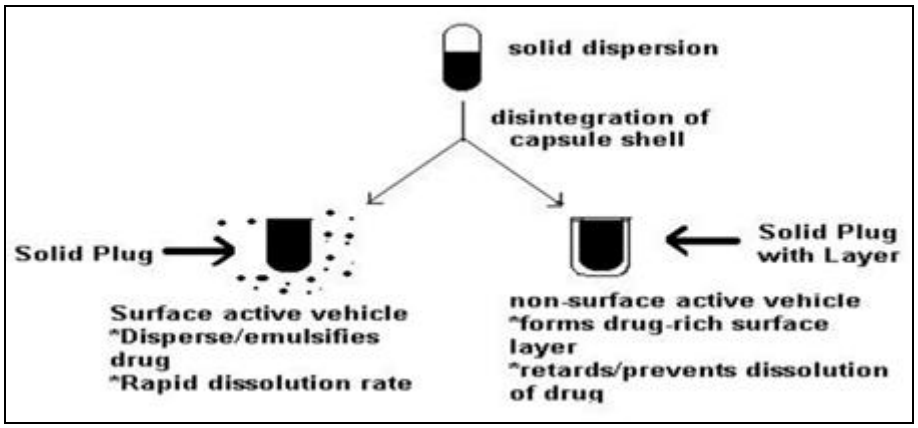

FIG. 8: SOLID DISPERSION TECHNIQUES

Formulation Aspects of Mucoadhesive Buccal Films Active Pharmaceutical Ingredients: In the case of both mucosal and transmucosal administration, traditional dosage forms are unable to ensure therapeutic drug levels on the mucosa and in the bloodstream. This is due to the physiological clearance mechanisms of the oral cavity (saliva's cleansing effect and mechanical stress), which displace the formulation from the mucosa, resulting in insufficient exposure time and unpredictable drug distribution at the target site. To achieve the desired therapeutic effect, it is thus necessary to extend and enhance the interaction between the active substance and the mucosa. To meet the therapeutic requirements, buccal administration formulations should include the following functional components: mucoadhesive agents to maintain a close and prolonged contact of the formulation with the absorption site; permeation enhancers to improve drug penetration across the mucosa (transmucosal delivery) or into deeper layers of the epithelium (mucosal delivery); and enzyme inhibitors to potentially shield the drug from degradation by mucosal enzymes [37]. The active pharmaceutical ingredient can belong to any category of pharmacologically active substances suitable for oral or buccal mucosal administration. Examples include medications for ulcers, asthma, cough suppression, allergies, epilepsy, expectoration, and angina treatment. To achieve optimal formulation, the drug dosage should be in milligrams (less than 20 mg per day). Typically, buccal films can accommodate active pharmaceutical ingredients ranging from 5% w/w to 30% w/w. It becomes challenging to incorporate high dosages of molecules into the film [38].

Drug: A variety of therapeutic substances can be administered *via* buccal film; however, there are still several limitations and constraints, particularly when it comes to drugs with high dosages and molecular weights. Formulating such drugs as buccal films can be challenging. Typically, the buccal film formulation consists of 5–30% (w/w) of the drug. Hydrophilic drugs are either in a dissolved state or as a solid solution, while hydrophobic drugs are evenly dispersed within the buccal film [13]. The drug's release can be altered, and the desired release pattern can be achieved by incorporating therapeutic agents in milled, micronized, or nanoparticle forms. The use of micronized particles of the drug improves the consistency, dissolution profile, and uniformity of the drug content in the buccal film. Buccal film delivery is particularly effective in treating conditions such as coughs, allergies, motion sickness, pain disorders, and certain local oral diseases [39].

Polymer: Selecting the appropriate mucoadhesive polymer is of utmost importance when developing a mucoadhesive drug delivery system, as it significantly contributes to the proper formulation of buccal films. These polymers should exhibit rapid adhesion, stability, inertness, non-irritating properties (causing no irritation), non-toxicity

(without any harmful effects), affordability, and compatibility with medications [40].

The following types of mucoadhesive polymers are currently accessible [41, 42]:

TABLE 1: TYPES OF MUCOADHESIVE POLYMERS

Type	Example
Natural	Tragacanth, Sodium alginate, Guar gum, Xanthan gum, Soluble starch, Gelatin, Lectins (naturally occurring proteins), Antigen K99-fimbriae, an attachment protein derived from E. coli
Synthetics	Polyacrylic acid (PAA), Polyvinyl alcohol (PVA), Hydroxypropyl methyl cellulose (HPMC), Hydroxyethyl cellulose (HEC), Hydroxypropyl cellulose (HPC) and Sodium alginate, glyceryl monooleate (GMO), chitosan or deacetylated Ellan gum

Plasticizer: Plasticizers enhance the flexibility, a mechanical property of the film, such as tensile strength and elongation, of oral films while reducing their brittleness. They are crucial excipients in oral films. Plasticizers significantly enhance the properties of the strip by lowering the glass transition temperature of the polymer. It is important to choose a plasticizer that is compatible with the polymers, drugs, and other excipients used in the oral film. Plasticizers can enhance flow and increase the strength of the polymer.

Inappropriate plasticizers can lead to film splitting, cracking, and peeling. The concentration of plasticizers used in the preparation of oral films ranges from 0 to 20% (w/w) of the dry polymer weight. Various plasticizers employed in the formulation of oral films include polyethylene glycol, glycerol, propylene glycol, dimethyl phthalate, dibutyl phthalate, diethyl phthalate, tributyl phosphate, triethyl citrate, acetyl citrate, castor oil, and triacetin [43].

Sweetening Agents: Sweeteners play a crucial role in pharmaceutical formulations designed for either mouth disintegration or dissolution. The conventional sources of sweeteners encompass sucrose, dextrose, fructose, glucose, liquid glucose, and isomaltose. Fructose, with its quick recognition of sweetness in the mouth compared to sucrose and dextrose, serves as a versatile sweetener employed in various industries.

Moreover, fructose surpasses sorbitol, mannitol, and other polyhydric alcohols in terms of sweetness. Polyhydric alcohols offer reduced carcinogenic risks and lack the undesirable bitter aftertaste, which is an important parameter in oral preparation. Herbal sweeteners, such as Rebiana, derived from the South American plant Stevia rebaudiana, can also be utilized, boasting sweetness levels 200–300 times higher than sucrose [44].

Coloring Agent: The compliance of patients with oral disintegrating films hinges on the incorporation of flavoring agents, which, in turn, depends on the drug category present in the formulation. For instance, peppermint oil and cinnamon oil can be employed [45].

Surfactant: Surfactants serve as agents for wetting, solubilizing, or dispersing, ensuring that the film dissolves within seconds and immediately releases the active agent.

Commonly employed surfactants include poloxamer 407, benzethonium chloride, sodium lauryl sulfate, tweens, and benzalkonium chloride. Among these, poloxamer 407 stands out as the most frequently used surfactant [46].

Flavoring Agents: The required quantity of flavoring agents to mask the taste depends on the type and strength of the flavor. Commonly utilized flavors encompass fruity flavors (vanilla, cocoa, coffee, chocolate, citrus), flavor oils (peppermint oil, cinnamon oil, nutmeg oil), as well as flavors derived from oleo resins, synthetic flavor oils, and extracts from various plant parts, such as fruits and flowers.

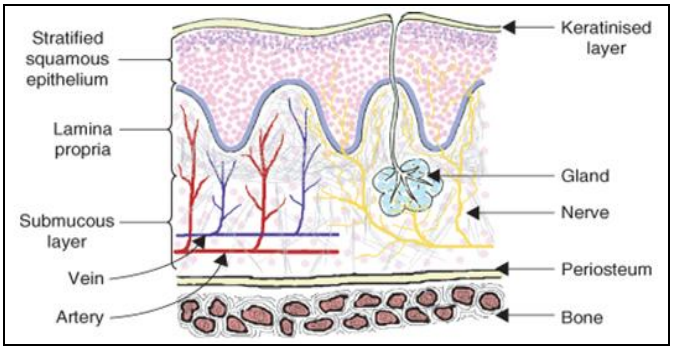

FIG. 9: A SIMPLIFIED VISUAL REPRESENTATION OF THE LAYERS PRESENTS IN THE ORAL MUCOSA, ILLUSTRATING THE OUTERMOST LAYER OF CELLS (EPITHELIUM

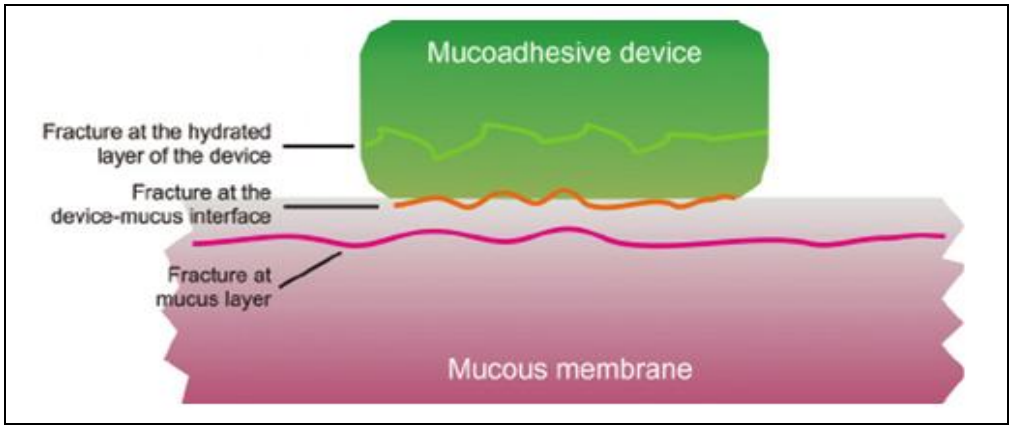

FIG. 10: FRACTURE OCCURRING FOR MUCOADHESION

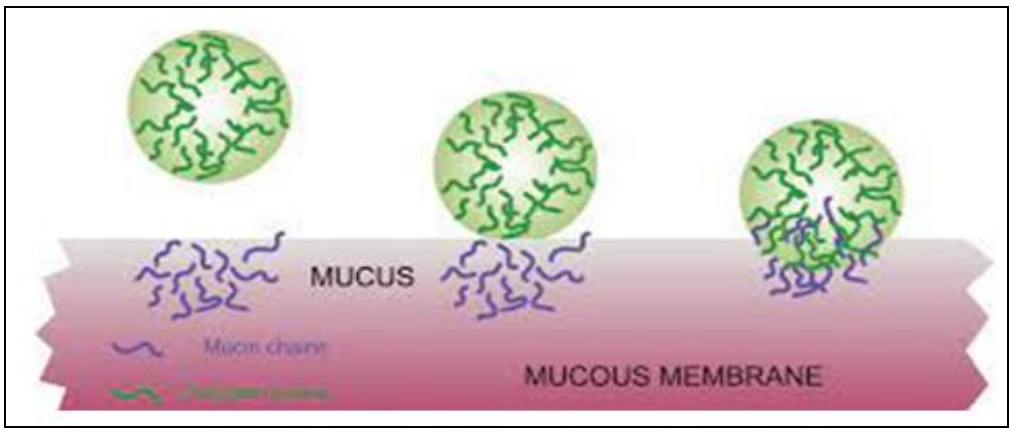

FIG. 11: INTERPRETATION OF BIO ADHESIVE AND MUCUS POLYMER CHAIN

Evaluation of Mucoadhesive Oral Films:

Thickness: It can be measured using a micrometer screw gauge at various locations. It is vital to assess the uniformity in film thickness, as it directly impacts the accuracy of the dosage in the strip.

Folding Endurance [47]: The flexibility of the thin film is important when considering its breakage-free administration. The flexibility of the polymeric thin films can be measured by assessing their folding endurance. Folding endurance is determined by repetitively folding the film at a 180° angle in the same spot until it breaks. A film that exhibits a folding endurance value of 300 or more is considered to have excellent flexibility [47].

Surface pH: To determine the surface pH, a combination of glass electrodes is utilized. The patches are placed in contact with 5 ml of distilled water for 1 hour. The pH can be determined by bringing the electrode near the surface of the formulations and allowing it to equilibrate for 1 minute [48, 49].

Organoleptic Properties: The desired sensory characteristics, such as color, flavor, and taste, can be evaluated through visual inspection of the film composition. E-tongue software is helpful in assessing the flavor intensity and determining the amount of flavor added, or if further adjustment is required. Uniformity in color and aroma, as well as an acceptable taste, enhance patient acceptance [50].

Swelling Study: The oral patches are individually weighed (designated as W_1) and placed in separate 2% agar gel plates, which are then incubated at 37°C ± 1°C. The patches are periodically removed from the gel plates, and excess surface water is carefully eliminated using filter paper. The swollen patches are then reweighed (W_2) and the swelling index (SI) is calculated using the following formula [14]:

$$SI = (W_2-W_1) / W_1 \times 100$$

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

Tensile strength = Load at Failure × 100 / Strip thickness × Strip Width

Drug Content Uniformity: Drug content uniformity is determined by dissolving each patch in 10 ml of solvent and filtering it using Whitman filter paper (0.45 μm). The filtrate is evaporated, and the remaining drug residue is dissolved in 100 ml of phosphate buffer (pH 6.8). A 5 ml solution is diluted with phosphate buffer (pH 6.8) up to 20 ml, filtered through a 0.45-μm Whitman filter paper, and the absorbance is measured using a UV spectrophotometer against pH 6.8 phosphate buffer used as a blank. The experiments are conducted in triplicate, and the average values are reported [37, 38].

Moisture Content Moisture Uptake: The prepared films are individually weighed and placed in a desiccator containing calcium chloride at room temperature for 24 hours. The films are then reweighed at specified intervals until they reach a constant weight. The percentage moisture content is calculated using the following formula [51]:

% Moisture Content = Initial weight – Final weight / Final weight × 100

Moisture Uptake: Weighed films are placed in desiccators at room temperature for 24 hours. They are then exposed to 84% relative humidity by using a saturated solution of potassium chloride in the desiccator until a constant weight is achieved. The percentage moisture uptake is calculated as follows [51]:

% Moisture Uptake = Final weight – Initial weight / Initial weight × 100

***In-vitro* Dissolution Studies:** Dissolution studies are conducted for all the formulations using the USP dissolution apparatus at 37 ± 0.5ºC, with a constant rotation speed of 50 rpm and employing 900 mL of dissolution medium. A sample of the drug film is used in each test. An aliquot of the sample is periodically withdrawn at suitable time intervals, and the volume is replenished with fresh dissolution medium. The sample is then analyzed spectrophotometrically at specified nanometers [52, 53].

Permeation Study of Buccal Patch: The permeation study of the buccal patch is conducted by filling the receptor compartment with phosphate buffer pH 6.8, and the hydrodynamics in the receptor compartment are maintained by stirring with a magnetic bead at 50 rpm. Samples are withdrawn at predetermined time intervals and analyzed for drug content [54].

TABLE 2: LIST OF PERMEATION ENHANCER [55]

Sl. no.	Permeation enhancer	Sl. no.	Permeation enhancer
1	Aprotinin	11	Polyoxyethylene
2	Azone	12	Polysorbate 80
3	Benzalkonium chloride	13	Phosphatidylcholine
4	Cetylpyridinium chloride	14	Sodium EDTA
5	Cetyltrimethyl ammonium	15	Chitosan
6	Bromide	16	Sodium glycocholate
7	Cyclodextrin	17	Sodium glycodeoxycholate
8	Dextran sulfate	18	Sodium lauryl sulfate
9	Glycol	19	Sodium salicylate
10	Lauric acid	20	Sodium taurocholate

TABLE 3: CATEGORIES OF MUCOADHESIVE POLYMERS USED IN BUCCAL PATCHES [56]

S. no.	Natural Polymer	Synthetic Polymer
1	Tragacanth	Cellulose derivatives (MC, EC, HEC etc.)
2	Sodium alginate	Poly (Acrylic acid) polymers (Carbomers, Polycarbophil).
3	Guar gum	Poly hydroxyl ethyl methyl acrylate
4	Xanthan gum	Polyethylene oxide
5	Soluble starch	Polyvinylpyrrolidone
6	Gelatin	Polyvinyl alcohol
7	Chitosan	---

CONCLUSION: Moreover, mucoadhesive buccal films offer controlled drug release, allowing for precise dosing and maintaining therapeutic drug levels over an extended period of time. This can be especially beneficial for drugs with a narrow therapeutic window or those requiring sustained release profiles. Additionally, the films can be easily formulated with various drugs, including

both hydrophilic and lipophilic compounds, making them versatile for a wide range of therapeutic applications. Furthermore, the buccal route of administration provides direct access to the rich vasculature of the oral mucosa, enabling rapid and efficient drug absorption. This can result in a faster onset of action and improved bioavailability compared to other routes. The buccal films also offer the advantage of avoiding the hepatic first-pass effect, which is particularly beneficial for drugs susceptible to extensive metabolism.

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