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BUCCAL FILM-BASED NOVEL DRUG DELIVERY SYSTEM: RECENT CONCEPTS AND APPLICATION PERSPECTIVES

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ABSTRACT: To increase patient compliance, safety, and effectiveness, the need for the design and development of a new dosage form has arisen. Novel film technology like buccal film meets all these needs. The buccal film is inserted into the mouth and the medicine is then absorbed *via* the buccal mucosa. Compared to alternative buccal drug delivery systems such as wafers, lozenges, microparticles, gel and tablets, buccal film is a more appealing and acceptable dosage form due to its small size, dose and ease of administration. Because it avoids first-pass digestion, buccal film is a very efficient dose form that significantly boosts bioavailability. It is more practical than other forms of dosing because it sticks well to the buccal mucosa of the mouth. Not ingesting the medicine is necessary; it is non-irritating and cost-efficient; other benefits include its sleek design, ease of use and biodegradability. Therefore, this dose type is preferred by both elderly and young patients. This review focuses on buccoadhesive drug delivery methods, which are reliant on adhering to mucus-coated biological surfaces. There is now a need for further investigation on topics like patient convenience and compliance. This article thoroughly analyzes buccal film, including its uses, drawbacks and advantages, methods of production, assessment criteria and formulation.

INTRODUCTION: This review focuses on buccoadhesive drug delivery methods, which are reliant on adhering to mucus-coated biological surfaces. There is now a need for further investigation on topics like patient convenience and compliance. Another unique approach is the creation of buccal films, which are dissolved directly on the buccal mucosa of patient [1]. This medication administration method is useful for increasing bioavailability while decreasing the frequency of doses to achieve oral plasma peak levels, reducing the potential for unwanted side effects.

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The elderly and young patients may also benefit from its low cost and high efficiency. Films' smaller size and lower thickness than lozenges and tablets have also increased patient compliance [2]. Pharmaceutical companies have begun to see the value of films as dosage forms since they are innovative, patient-friendly, and convenient products. As of late, a lot of attention has been paid to buccal film. While commercially available orally dissolving pills sometimes need special packaging, this dose form does not.

All of these benefits are shared by mucoadhesive buccal films [3]. Furthermore, films may be made to show either a systemic or a local effect since mucoadhesion indicates attachment to the buccal mucosa. Several different types of mucoadhesive buccal films have been developed to release medicine locally when treating oral fungal infections like oral candidiasis.

Mucoadhesion is used when a connection is established with a mucosal surface, whereas bioadhesion refers to sticky interactions with any biological or biologically generated material. High-quality buccal films, essential for ongoing performance assessment and comprehension, provide the most difficulty [4].

Buccal Mucosa: The patient and doctor may both prefer the oral route of administration when it comes to Novel medication delivery systems. It is important to note that several medication types, notably peptides, and proteins, are not well suited for oral delivery because of problems with hepatic first-pass metabolism and enzymatic breakdown inside the GI tract. Therefore, other drug-delivery mucosae are being explored [5].

There are potential benefits to using transmucosal routes of drug delivery (*i.e.* the nasal, rectal, vaginal, ocular, and oral cavity mucosal linings) instead of peroral injection for systemic drug delivery. This has a number of potential benefits, including improved enzymatic flora for medication absorption and avoiding the gastrointestinal tract's presystemic excretion.

The buccal cavity is widely suitable for drug administration *via* mucosa in the sublingual route, which is most effective for quickest start of action, as in the case of Angina pectoris. Mucosa of the buccal cavity covers the inside of the cheek [6].

Inside the oral mucosal cavity, the delivery of drugs is classified into three categories:

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

Structure of Oral Mucosa: The lips, cheeks, hard palate, soft palate and floor of the mouth make up the oral cavity **Fig. 1**. There are really two distinct parts to the mouth. The outer oral vestibule is defined by the gums, lips, teeth and dental arches (gums). The actual mouth, which includes the roof (the hard and soft palate) and the floor (the teeth and gums) and runs from the front of the mouth to the fauces (the opening to the throat). The tongue is positioned at the oral cavity's floor [7].

The oral cavity can be divided into specific areas, including:

- Gingiva
- Hard palate
- Soft palate
- Tonsil
- Tongue

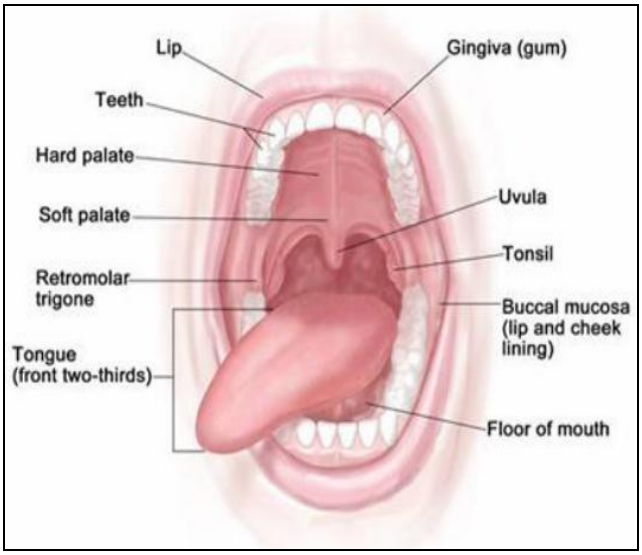

FIG. 1: MUCOSAL REGION OF MOUTH

The major distinction is that oral mucosa and skin are organized differently from the GI tract lining. Skin and the oral cavity contain many layers of cells with varying degrees of differentiation, while the second has a single layer of cells creating the simple epithelium. Due to its chemical resistance and mechanical strength, the masticatory mucosa lines the areas of the mouth that are subjected to the most wear and tear, including the gingival and the hard palate [8]. The keratinized, granular, prickle-cell, and basal layers make up its structure **Fig. 2**. The lips, cheeks, floor of the mouth, and soft palate are covered by non-cornified surface epithelium, while the lining mucosa provides flexibility. There are four distinct layers: the epidermis, dermis, prickle cells, and basal cells. Mucosa with mixed keratinized and non-keratinized layers comprise the third kind of mucosa. The back of the tongue is where the controls are located. Water, lipids, and proteins may all be found in the voids between cells [9].

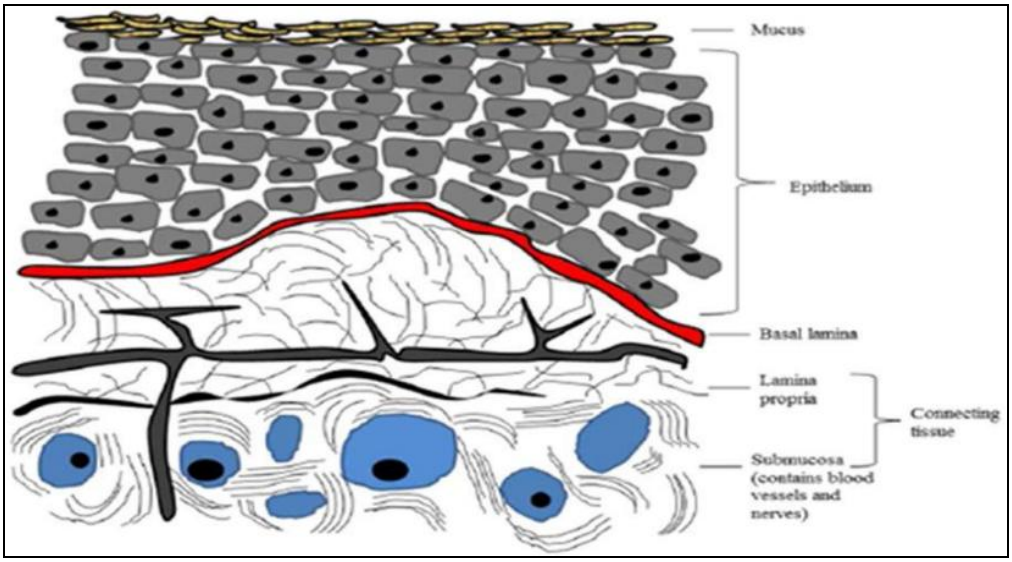

FIG. 2: STRUCTURE OF ORAL MUCOSA

Permeability: The buccal mucosa has been discovered to be 4–4,000 times more permeable than the epidermis. The vast variation in this reported value suggests more research into the fact that the oral mucosa in various parts of the mouth has distinct structures and has different functions. Buccal administration increases oral mucosal permeability as compared to sublingual administration [10]. The sublingual mucosa is thin and nonkeratinized, the buccal mucosa is thicker and nonkeratinized and the palatal mucosa is intermediate in thickness but keratinized. Permeability in the oral mucosa is thought to be due to intercellular material from membrane-coating granules (MCG).

The top two hundred micrometers of skin serve as this barrier [11]. Researchers use tracers with extremely high molecular weights, such as horseradish peroxidase and lanthanum nitrate, to study permeation. When applied to the epithelium's surface, these tracers can only be taken up by the topmost cell layer or two. They may be administered to the submucosal surface and will go up to but not through the epithelium's outermost cell layers. Based on the findings, it is apparent that the surface cell layers pose the most significant barrier to permeation, whereas the more isodiametric cell layers are rather permeable [12].

Saliva: Fig. 3 shows the anatomy and composition of saliva, an exocrine secretion that is roughly 99% water and contains a wide range of electrolytes (sodium, potassium, calcium, chloride, magnesium, bicarbonate, phosphate), as well as proteins, including enzymes, immunoglobulins, and other antimicrobial factors, mucosal glycoproteins, traces of albumin and some polypeptides and oligopeptides vital to oral health [13].

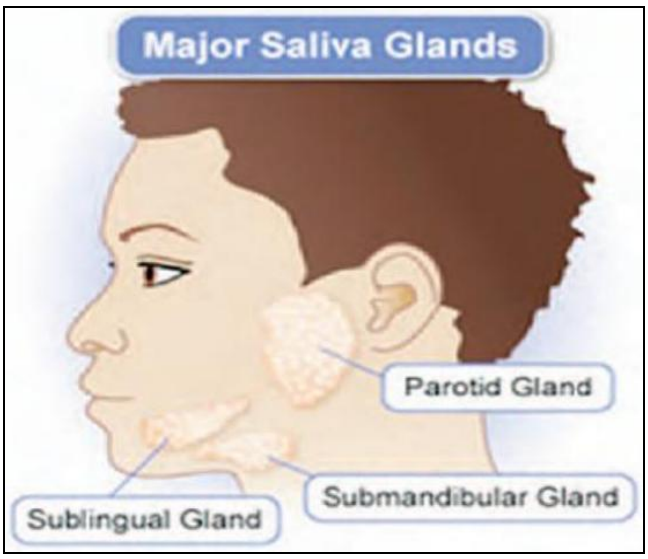

FIG. 3: SALIVARY GLANDS

Functions of Saliva:

- Buffer Capacity.
- Dilution and Cleaning.
- Integrity of Tooth Enamel.
- Protection and Lubrication.
- Digestion.
- Dilution and Cleaning.

- Buffer Capacity.

Mucus: Large mucin glycoproteins are found in mucus with a negative charge. Mucin's protein core is loaded with helix-breaking proline residues and O-glycosylated serine and threonine.

Saliva has a pH between 5.8 and 7.4, consisting of 90 to 95% water, 0.5 to 6% fat, 1.1 to 1.5% minerals, and 0.5 to 1.5% protein [14]. Various mucus membranes and their composition are depicted in **Table 1**.

TABLE 1: VARIOUS MUCUS MEMBRANES AND THEIR COMPOSITION

Mucous Membrane	Surface Area (cm)	Thickness	Layers	Secretion Per Day	Turnover Time
Buccal	30	500-800 µm	Epithelium, basement membrane, and connective tissues	800-1000 mL	5-6 days
Ocular	60	3-10 µm	Epithelium, Bowman's layer, stroma, Descemet's membrane, and endothelium	2-3 µL	15-20 hrs
Nasal	60	150-200 cm	Columnar cells, goblet cells and basal cells	20 mL	10-15 mins
Rectal	300	10-20 cm	Epithelium consists of a single layer of cylindrical cells and goblet cells	3 mL	7 days
Vaginal	6-10	3-10 µm	Lamina propia and stratified squamous epithelium	1-4 mL	7 days

Functions of Mucus:

- Protective in nature due to hydrophobicity.
- Cell-cell adhesion.
- Lubrication.
- Bioadhesion of mucoadhesive drug delivery system.

Mucoadhesion:

Mechanism of Mucoadhesion: Adhesion refers to the condition in which two surfaces are held together by strong interfacial forces, interlocking action, or both upon contact with a pressure-sensitive adhesive substance.

Adherence of a synthetic or natural substance to a biological surface is known as bioadhesion, whereas adhesion to mucus and/or an epithelial surface is known as mucoadhesion [15]. There are two distinct phases of mucoadhesion **Fig. 4**, each of which is affected by the drug's dose form and method of administration.

Stage-I (Contact Stage): The surface of a bioadhesive comes into intimate contact with a membrane after being wetted, distributed, and swollen. Dosage forms are sometimes delivered using a mechanical system in the case of vaginal delivery, aerodynamics in the case of nasal delivery and peristaltic movements in the intestines.

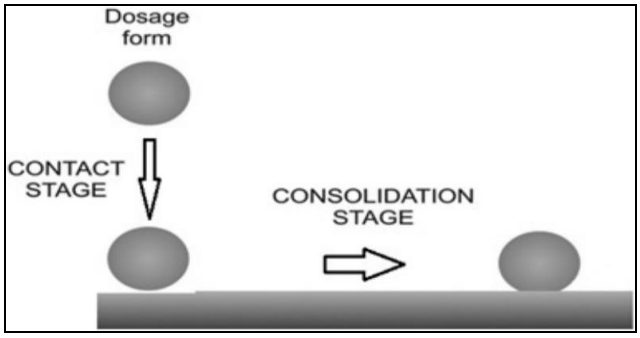

FIG. 4: STEPS OF MUCOADHESION

Stage II (Consolidation Stage): Moisture shatters molecules, setting in motion a chain reaction including electrostatic attractions, hydrogen bonds, hydrophobic forces, and van der Waals forces. Attractive forces must win out over repulsive forces for full bio-adhesion. Two theories explain the consolidation step:

Diffusion Theory: To interact with mucoadhesive molecules, mucus glycoproteins interpenetrate their chains and generate secondary connections. Both chemical and mechanical interactions are at play here.

Dehydration Theory: When mucus comes into touch with a substance, the substance loses water until the mucus's osmotic pressure and the substance are equal, creating a gel. According to this view, no formulation, solid or liquid, is effective [16].

Theories of Mucoadhesion: There are five different theories which explain the phenomenon of mucoadhesion:

Electronic Theory: Since the mucus layer and biological components have opposite electrical charges, they are able to generate a double electronic layer at the edge, which may be used to measure mucoadhesive strength [17].

Wetting Theory: Molecules with low surface tension can penetrate the mucosal surface and anchor there **Fig. 5A**. This attribute is associated with the molecule's contact angle, wetting, and spreading abilities [18]. Contact angle (θ) and interfacial tension (γ) can be determined from following equation:

$$\gamma SG = \gamma SL + \gamma LG\cos S = \gamma SG - (\gamma SL - \gamma LG)$$

Where, γLG is liquid–gas surface tension, γSL is solid–liquid surface tension and γSG is solid–gas surface tension.

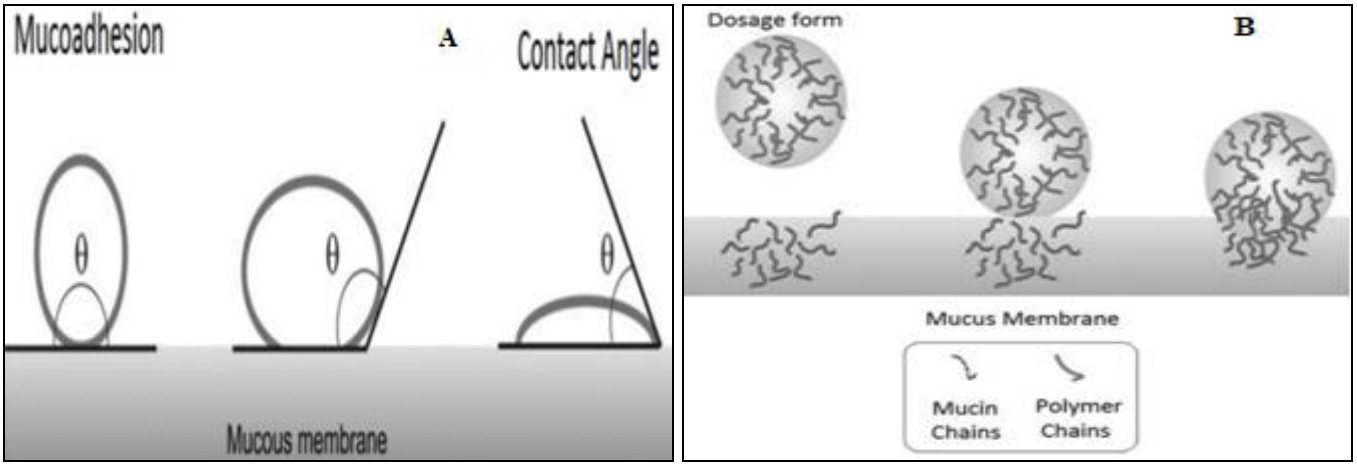

FIG. 5: THEORIES OF MUCOADHESION (A) WETTING THEORY (B) DIFFUSION THEORY

Diffusion Theory: In this model, the mucoadhesive polymer diffuses into the mucus layer through a disruption in the glycoprotein chain network **Fig. 5B**. time and the molecular weights of both phases are crucial factors in this diffusion [19].

Adsorption Theory: Currently, the most widely recognized idea of the mechanism of mucoadhesion involves weak Vander Waals forces and hydrogen bond mediated adhesion. These surface contacts are only partially permanent but include primary and secondary bonding [20].

Fracture Theory: This explanation accounts for the forces needed to separate the two surfaces after adhesion and is the second most popular. The following equation may be used to calculate the tensile stress, also known as the fracture strength, of a material [21]:

$$Sm = Fm / Ao$$

Where Sm: Tensile stress, Fm: maximum force of detachment and Ao: surface area

Or

$$Sf = (gcE / c)\ ½$$

Where Sf: fracture strength, gc: fracture energy (Wr + Wi = work done to produce new fracture surfaces + irreversible work of adhesion), E: Young's modulus of elasticity and c: critical crack length.

A wide variety of theories may describe the mucoadhesion process. Perfect mucoadhesion may result from a sequence of events beginning with the wetting of the mucin and ending with the diffusion of the polymer into the mucin layer, causing a fracture in the layers and setting in motion the adhesion, electronic transfer or simple adsorption phenomenon.

Buccal Drug Delivery System: Since there are several places in the mouth where drugs might be administered, a buccal-controlled drug delivery system was designed. Acid hydrolysis and the first step of metabolism are skipped. Drug delivery through buccal film is affected by the constant production of saliva. The oral mucosa's mucin layer presents a chance to create a mucoadhesive system,

which keeps substances in place at the absorption site for longer. Because of the drug's proximity to the absorption membrane, more of it is absorbed. The medicine is unaffected by the buccal cavity's acidic environment with the correct dosage form design and composition. Controlling and manipulating the local environment of the buccal mucosa allows for drug permeation [22].

Novel Buccal Dosage Forms: Innovative buccal dosage forms include tablets with an adhesive coating, patches, films, semisolids (ointments and gels) and powders.

Buccal Mucoadhesive Tablets: The buccal mucoadhesive pill is a dry dose form that becomes wet upon contact with the buccal mucosa. Insulin and a penetration enhancer may be sandwiched between layers of cocoa butter in a double-layered tablet with an adhesive matrix layer made of HPC and polyacrylic acid (sodium glycocholate).

Patches and Films: An aqueous solution of the sticky polymer is cast onto an impermeable backing sheet, and the laminate is then cut into an oval form to create a buccal patch.

Semisolid Preparations (Ointments and Gels): Most solid bioadhesive dosage forms are only utilized for localized medication treatment inside the oral cavity, and bioadhesive gels or ointments do not have the same patient acceptance.

Powders: When powdered HPC and become-this one are sprayed into the oral mucosa of rats, the residence period is significantly prolonged in comparison to an oral solution and 2.5% of beclomethasone is kept on buccal mucosa for more than 4 hours [23].

Buccal Film: Fig. 6 depicts buccal film, a non-dissolving thin matrix modified release dosage form made up of one or more polymer films or layers that have been prefilled with the medication and/or additional excipients. Drugs may be released either into the oral mucosa (unidirectional release) or the oral cavity (bidirectional release) from the film, depending on whether or not it has a mucoadhesive polymer layer that adheres to the oral mucosa, gingiva, or teeth (bidirectional release). After a certain amount of time, the patch is taken out of the mouth and thrown away [24].

FIG. 6: BUCCAL FILM

Advantages of Buccal Film:

- There is no danger of choking.
- Avoid the trouble of chewing and swallowing.
- Fast working time with little negative effects.
- Dosing is more precise than with liquids.
- Cover up the flavor if desired.
- Positive stability and a pleasant experience for the mouth.
- Needs less excipients.
- Portability, shelf life, and user friendliness all score well.
- Less Money Spent
- Patients of all ages, from infants to the elderly, as well as those with special needs or who are uncooperative, will have no trouble receiving their medication.
- Increases bioavailability by increasing the amount of time the dose form spends at the site of absorption.
- In the stomach's acidic environment, the drug may be preserved.
- Because of its high surface area, buccal film dissolves quickly in the mouth [25].

Disadvantages of Buccal Film:

- Saliva is constantly being released in the mouth, diluting medication concentrations at the absorption site. The medicine dissolved or suspended in the saliva is eliminated from the absorption site to the greatest extent when the

patient instinctively swallows their saliva. There is also the possibility that the delivery mechanism itself might be ingested.

- The nature of the medicine itself may impose limits on the mouth as a drug delivery site. Drug candidates for the buccal route may be limited by taste, irritancy, allergy, and undesirable characteristics (e.g., tooth discolouration or erosion). Patient inability to eat, drink, or engage in conversation during traditional buccal medication delivery methods [26].

Characteristics of an Ideal Buccoadhesive System:

- Features: Good mechanical strength, Patient compliance Non-hazardous
- Adherence to the buccal mucosa is instantaneous; medication release is regulated; and drug absorption is maximized [27].

Formulation Aspects for Buccal Film:

Active Pharmaceutical Ingredient: The active pharmaceutical ingredient might come from any class of pharmaceutically active compounds that are suitable for buccal mucosal administration for medications for ulcers, asthma, coughs, allergies, seizures, angina, expectorants, *etc*. Dosage of the medicine should be in milligrams (less than 20 mg per day) for optimal effectiveness. Buccal film may often integrate active medicinal components at concentrations between 5% w/w and 30% w/v. Molecular doses that are too high to be safely incorporated into film [28].

Ideal Characteristics of the Drug to be Selected:

- Good stability in water and saliva
- Capable of penetrating oral mucosal tissue
- Dose less than 20 mg
- No Bitter Taste
- Low Molecular Weight

Mucoadhesive agents: Depending on the dose type, there may be a variety of circumstances that call for buccal mucoadhesion. Polymer hydration and swelling qualities are likely most important in dry or partly hydrated compositions. An increase in mucouscohesive properties that promote mucoadhesion may result from polymer hydration and, subsequently, mucus dehydration. Polymer chains should become more flexible and the mucin chains should be more easily penetrated as the gel expands. When mucin is added to completely hydrated dosage forms, the spreading coefficient and the capacity to create physical or chemical connections with mucin both increase. Therefore, polymers with varying properties must be taken into account depending on the formulation. Polyacrylic acid (PAA), polyvinyl alcohol (PVA), sodium carboxymethyl cellulose (NaCMC), hydroxypropyl methylcellulose (HPMC), hydroxyethyl cellulose (HEC), hydroxypropyl cellulose (HPC) and sodium alginate are the most often employed polymers in buccal dry or partly hydrated dosage forms. That these chemicals may detect and bind certain mucosal sugar residues without changing the structure of the identified ligand is what makes the mucoadhesion process so unique [29].

Plasticizers: It plays a vital role in oral films. It won't be employed if the plasticizer is incompatible with the polymer or the solvent used to cast the film. The film's pliability is increased while its brittleness is decreased. They are typically added at a concentration of 1-20% w/w of dry polymer weight. Glycerol, propylene glycol, low molecular weight polyethylene glycols, citrate derivatives like triacetin and acetylcitrate, phthalate derivatives like dimethyl, diethyl and dibutyl, castor oil, *etc*. are all examples [30].

Sweetening agents: Food and medicines that need to be dissolved or disintegrated in the mouth rely on sweetening ingredients. Standard sweeteners include sucrose, dextrose, fructose, glucose, liquid, and maltose. Fructose, in contrast to sucrose and dextrose, is quickly absorbed by the tongue and recognized for its sweetness. However, diabetic individuals face serious problems while using natural sweeteners. This is why artificial sweeteners are increasingly used in both food and medicine. The first generation of artificial sweeteners includes saccharin, cyclamate and aspartame; the second generation includes acesulfame-K, sucralose, alitame and neotame [31].

Saliva Stimulating Agents: Including this ingredient in the formulation is crucial since it speeds up saliva production, facilitating the quick

breakdown and absorption of the film in the buccal cavity. It is well known that cooking acids may be used to stimulate saliva production. There are a few salivary stimulants, the most popular of which is citric acid, while malic acid, lactic acid, ascorbic acid and tartaric acid all work. Between 2% and 6% w/w of the film's weight may be made up of these agents [32].

Cooling Agent: With monomethyl succinate as a cooling agent, the intensity of the film's flavors and the viewer's overall sensory experience are enhanced. Flavoring may be employed with various cooling agents, including WS3, WS23 and Utracoll II [33].

Flavoring Agent: It was found that the flavoring ingredient was a crucial factor in the enjoyment of the taste. Flavoring agents may range from synthetic flavor oils and oleo resins to extracts sourced from leaves, fruits, and flowers. The quantity of flavoring ingredients required to cover up a given taste completely varies with the potency of that flavoring agent [34].

Coloring Agent: When some formulation components or medications are insoluble or in a suspension state, pigments like titanium dioxide or FD&C-approved colorants are used (not exceeding concentration levels of 1%w/w) in buccal film formulation [35].

Surfactants: As a wetting or solubilizing agent, surfactants play an important role in many industries. In a few seconds, the surfactant dissolves the film, and the medicine is released. Using a surfactant may increase the buccal solubility of medicines with low solubility. Sodium lauryl sulfate, Polaxamer 407, benzalkonium chloride, benzethonium chloride, Tweens, Spans, *etc*. are all such chemicals [36].

Stabilizing and Thickening agents: Precast film preparations benefit greatly from the addition of stabilizing and thickening agents, which increase the dispersion's or solution's viscosity and consistency. Stabilizing and thickening agents include natural gums like xanthan gum, locust bean gum, carrageenan, and cellulose derivatives, to name a few. They may be utilized in concentrations up to 5% weight-per-weight [37].

Manufacturing Methods of Buccal Film: Buccal film formulation is mainly prepared by following three methods:

Solvent Casting Method: Fig. 7 depicts the solvent casting process, in which the necessary amount of polymer is dissolved in distilled water. There is a trace amount of the active medicinal component in this liquid. The plasticizer is added to the solution, and the mixture is well mixed. Subsequently, place the petridish with the solution cast on it into a 40-degree Celsius hot air oven to dry. After drying for 24 hours in a desiccator, remove it from the petri dish by slicing it in half. Henceforth, shape and size may be adjusted as needed [38].

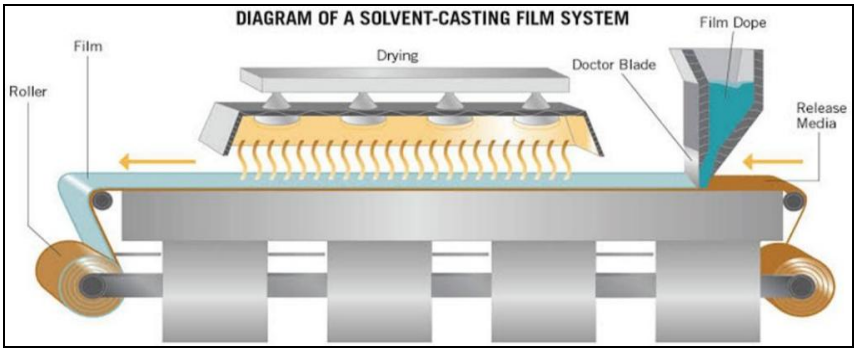

FIG. 7: SOLVENT CASTING PROCESS

Steps Involved in Solvent Casting Method:

- First: Making the Casting Solution
- Second, the solution is deaerated.
- Third, pour the right amount of solution into the mold.
- Fourth, the casting solution is dried.

- Fifth, when the medicine has been formed into a dosage form, it must be cut to the appropriate size.

Hot Melt Extrusion Method: Drug and excipient mixtures are melted in the hot melt extrusion technique **Fig. 8**.

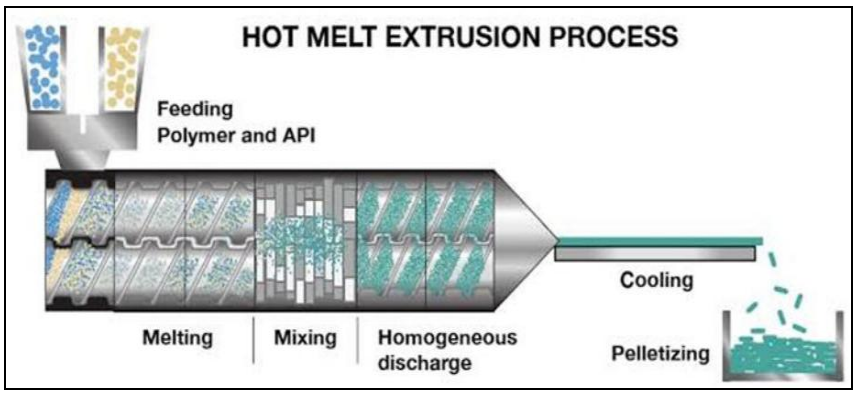

FIG. 8: HOT MELT EXTRUSION PROCESS

Steps Involved in Hot Melt Extrusion Method:

- As a first step, the drug is combined with solid carriers.
- In step two, the ingredients are melted in an extruder equipped with heaters.
- Third step, the dies are used to give the molten material the form of films.

Advantages:

- The anhydrous process allows for fewer operating units and improved content consistency.

Disadvantages:

- The thermal process compromises the stability.
- The processing of polymers relies heavily on their flow characteristics.
- There is a scarcity of available polymers.

Direct Milling Method: This technique doesn't need the use of any solvents. This process involves kneading or direct milling to combine the medicine and excipients without fluids. Once the desired thickness has been achieved, the material is rolled on a release liner. The lack of residual solvent and the absence of any health risks linked to solvents make this approach the standard of care [40].

The material is then compressed via an aperture to create uniform grains, tablets, or films. Drugs may be delivered transdermally using this system [39].

Evaluation Parameters of Buccal Film:

Weight of the Film: An accurate weighing balance is used to measure the weight of the buccal film. The individual weight of each film is computed. The standard film weight is determined and examined.

Thickness: Accurate measurement of buccal film thickness requires a calibrated micrometer screw gauge. The average thickness is determined by taking measurements at five distinct locations throughout the film. This is done to support the repeatability of the formulation procedure and guarantee consistency in the film thickness, which is directly associated with the accuracy of the dosage in the film [41].

Tensile Strength: Films have tensile strength if they can withstand loads before they stretch or break. Film strips of a certain width and length are sandwiched between two clamps. The tensile strength of a film may be determined by using the following equation and using the load at rupture and the cross-sectional area of the shattered film as inputs.

$$\text{Tensile strength } (N/mm^2) = \text{breaking force } (N) / \text{cross sectional area of sample } (mm^2)$$

Surface pH: After soaking the films in 1 ml of distilled water for 2 hours at room temperature, the pH is measured by placing the electrode in contact

with the film's surface and recording the reading after letting the solution equilibrate for 1 minute.

Folding Endurance: To test the film's folding durability, it will be folded over and over again in the same spot until it snaps. The value of the film's folding endurance is determined by counting the number of times it can be folded in the same spot before snapping.

Percentage Moisture Loss: The film industry relies on this to ensure flawless productions. It's common practice to clip off film sections and then weigh them. After that, store it in a desiccator with some fuse anhydrous calcium chloride. The object is taken away and weighed after 72 hours. The following calculation may be used to determine the typical percentage of moisture loss.

Percentage Moisture Loss = (Intial weight film weight) × 100 / Initial weight

Drug Content Uniformity: The buccal film is dissolved in 100 ml of pH 6.8 buffer, and the resulting liquid is diluted to the appropriate concentration. Absorbance spectrophotometry at 242 nm is used to determine the film's medication concentration. The typical amount of medication is determined.

***In-vitro* Disintegration Time:** Visual inspection of a petri dish containing 2 ml of distilled water stirred at 10-second intervals provides the result. The in vitro disintegration time is the moment at which the film first begins to break down.

***In-vitro* Dissolution Study:** USP class II equipment is used for in vitro dissolution research (Basket type apparatus). At 37 degrees Celsius and 50 revolutions per minute, pH 6.8 buffer is utilized as a dissolving media. Samples of 1 ml were taken at regular intervals and swapped out for new dissolving media of the same volume. The maximum absorbance value of the buccal film is measured spectrophotometrically, and the concentration of the active medicinal component is determined [42].

Dissolution Kinetics Study: The optimal mathematical model for the formulas is chosen. The dissolution data calculates the R and k values for various mathematical models. The model with the greatest R-value is the one that is most likely to represent the data in question accurately. The n value for the best-fit model is recorded, then used to establish whether the formulation exhibits fickian or non-fickian diffusion.

Zero-order Kinetic:

$$Qt = Q_0 + k_0t$$

Where, Qt is amount of drug release at time t K_0 is zero order release rate constant. Q_0 is amount of drug present initially at t = 0

First-order Kinetic:

$$\ln (100 - Q) = \ln Q_0 - k1t$$

Where, Q = amount of drug release at time t Q_0 = amount of drug present initially K1 = first order release rate constant

Higuchi Equation:

$$Q = kH\ t_{1/2}$$

Where, Q = amount of drug release at time t KH = Higuchi dissolution constant

Swelling Index: A digital balance is used to establish the film's starting weight (W0). The petri plates with the films on them are placed in an incubator set to 37 degrees Celsius so that the films may grow. For a period of 5 minutes, the inflated film's weight (Wt) is measured at regular intervals [43]. How much swelling (% S) there is may be expressed as a percentage using the following formula:

$$\% S = (Wt - W_0) \times 100 / W_0$$

Where Wt is the weight of swollen patch after time t, W_0 is the initial weight of patch at t=0.

***Ex-vivo* Diffusion Study:** Goat buccal mucosa membrane serves as the barrier in a Phosphate buffer (pH 6.8) *in-vitro* release research. The Franz diffusion cell measures how much drug is released from the film. Between the donor and receptors compartments lies a buccal mucosa membrane. The mucosal membrane is where the film will be applied. The diffusion cell is submerged in simulated saliva at 37 degrees Celsius. In order to keep the hydrodynamics stable, 50 mL of phosphate buffer (pH 6.8) is added to the receptor compartment while being stirred with a magnetic

bead at 50 rpm. Maintaining the sink condition requires the removal of 1 mL of the sample and adding 1 mL of new medium. In order to determine the characteristics of the samples, an ultraviolet spectrophotometer is used at a predetermined wavelength.

Stability Study: A drug's stability refers to how well it maintains its physical, chemical, microbiological, medicinal and toxicological properties when stored in a certain container and closure system. All formulations were tested for stability at a range of temperatures as the International Council for Harmonization (ICH) recommended. The storage conditions used in the stability research ranged from 30°C/75% RH for 24 to 36 months to standard room temperatures and humidity for 6 months (40°C/75% RH). DSC, FTIR, folding endurance, disintegration time, drug content, and in vitro drug release are measured after the film has been packaged in a packaging material such as aluminum foil [44].

FDA-Approved Buccal Films: Use of buccoadhesive buccal films is an option. Substances of sufficient strength to meet the requirements for administration through the buccal film are applied [45]. At present, USFDA has approved 4 buccal films **Table 2**.

TABLE 2: LIST OF FDA-APPROVED BUCCAL FILMS

Drug	Year of Approval	Company	Applications
Ondansetron	2010	APR Applied Pharma Research and Labtec Ltd.	Prevention of nausea and vomiting before and after of Cancer Chemotherapy .and radiotherapy
Suboxone	2010	Reckitt Benckiser Pharmaceutical Inc.	Psychological support and patient counseling
Zelapar	2005	Valent Pharmaceuticals International Inc.	Parkinson's Disease
Zuplenz	2010	PharmFilm Technology	Prevention of nausea and vomiting before and after of Cancer Chemotherapy

CONCLUSION: Based on the data presented here, it is clear that buccal film is the most user-friendly and delicious dose form currently available. Bypassing first-pass metabolism and increasing bioavailability of the active molecule are two of the system's distinguishing qualities that set it apart from other innovative buccal drug delivery systems.

The many benefits of buccal film make it a novel dosage form for patients of all ages who have trouble swallowing, including the elderly, children, and those with other medical conditions. Since buccal films are inexpensive and cause no irritation to the mouth, they provide a fresh method for replacing traditional dosing forms. Continued research on buccal film holds great promise for the systematic administration of ineffective pharmaceuticals when taken orally. Effective peptide and protein drugs may be delivered without requiring surgical incisions, making this a viable alternative delivery method. Due to the effective buccoadhesive nature of buccal films, their therapeutic effects may be felt very immediately after administration. To improve the safety, effectiveness, and stability of the active pharmaceutical component, a buccal film is used as a buccoadhesive drug delivery device. The improved therapeutic effects that may be achieved using buccal film make it an innovative technological advancement.

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