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RECENT ADVANCES IN BUCCAL FILM TECHNOLOGY

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ABSTRACT

Buccal film technology has emerged as a promising approach for enhancing drug delivery due to its numerous advantages such as improved patient compliance, rapid onset of action, and avoidance of first-pass metabolism. In recent years, significant advancements have been made in the development of buccal films, aimed at enhancing drug loading capacity, mucoadhesive properties, and controlled release kinetics. This review summarizes recent advancements in buccal film technology aimed at optimizing drug delivery. It encompasses various aspects including formulation strategies, materials used, manufacturing techniques, and therapeutic applications. Additionally, challenges and future prospects in the field are discussed to provide insights for researchers and practitioners. Through this review, we aim to shed light on the potential of buccal film technology to revolutionize drug delivery and improve patient outcomes.

KEYWORDS: Buccal films; transmucosal drug delivery system; solvent casting method; hot melt extrusion technique.

1. INTRODUCTION

The mucoadhesive buccal films, which adhere to biological surfaces coated in mucus, are the primary subject of the current paper. Typically, medications are provided using a variety of dosege forms and ways. Even if taking a medication orally is the preferred method, For the medicine to be absorbed by this route, it is essential that it have delivery, drug solubility, and first pass metabolism sensitivity. The most severe method of administration is the parental route. Only topical or local therapy can make use of topical medicines. Alternative routes are necessary for drugs with high molecular weight, low skin penetration, poor water solubility, and significant first pass metabolism. The mucoadhesive method is increasingly being used to give the majority of medications. Drug delivery methods using mucoadhesive materials through the nasal, rectal, buccal, and sublingual mucosa may be a more thorough and quick non-invasive delivery method.[1]

These days, a special process is used to create buccal films that dissolve on the buccal mucosa of the patient. When compared, for example, to lozenges and tablets, films have also improved patient compliance because of their smaller size and thinner thickness.[2]

Mucoadhesive drug delivery systems are a method of controlled drug release that allow for tight contact between a polymer and a target tissue. They can be used with natural or synthetic polymers. Drug delivery systems that are mucoadhesive make use of the bioadhesion of certain Polymers, which thereafter become sticky when hydrated, allow for the long-term, targeted delivery of drugs to a particular location within the body.[3]

Mucoadhesive buccal films are a unique dosage form that acts quickly, doesn't pass through first-pass metabolism, and—most importantly—has a greater degree of patient acceptance. The purpose of these mucoadhesive buccal films is to deliver medication locally. oral candidiasis and other fungal infections of the mouth cavity. Compared to buccal tablets, mucoadhesive buccal films are viewed as the more comfortable dose form by patients due to their greater flexibility.[4]

The concept of mucoadhesion was created in relation to controlled-release drug delivery systems around the beginning of the 1980s. It is commonly known that mucoadhesion lengthens and deepens the bond between interaction between a mucosal surface and a drug-containing polymer. It is well known that the mucoadhesive qualities prolong the time a medicine remains in the body after being administered. The medicine's bioavailability is increased by both the decreased excretion rate and the direct absorption of the drug. Greater adhesion and longer residence durations may lead to lower API concentrations.[5]

Buccal Mucosa[6]

When it comes to novel pharmaceutical delivery systems, the patient and the physician may both favor the oral route of administration. It's vital to remember that a number of drug classes, most notably peptides and proteins, are not ideal for oral administration due to issues with hepatic first-pass metabolism and GI tract enzymatic breakdown. Therefore, research is being done on alternative drug delivery mechanisms.

Transmucosal routes of drug administration, which include nasal, rectal, vaginal, ocular, and oral mucosa, may have advantages.as an alternative to oral injections when administering systemic medications. This has some potential advantages, such as better enzymatic flora for drug absorption and inhibition of presystemic secretion in the gastrointestinal tract. The oral cavity is widely suitable for the administration of drugs through the sublingual mucosa, which is most effective for the fastest onset of action in angina pectoris. The mucous membrane of the oral cavity covers the inner side of the cheek.

Within the oral membrane, the administration of medicines is classified into three categories

1. Sublingual delivery
2. Buccal delivery
3. Local delivery.

Structure of oral mucosa [7]

The oral mucosa consists of an outer layer of stratified squamous epithelium. Below that is the basement membrane, Lamina propria, followed by the submucosa as the inner layer. The epithelium is similar to the stratified squamous epithelium found in the rest of the body in that it has a mitotically active basal cell layer that progresses through several differentiating intermediate layers to the superficial layers, where cells differentiate in the epithelium. The oral mucosal epithelium is about40–50 cell layers thick, while the sublingual epithelium is slightly less. Epithelial cells enlarge and flatten as they move from the basal to the superficial layers.

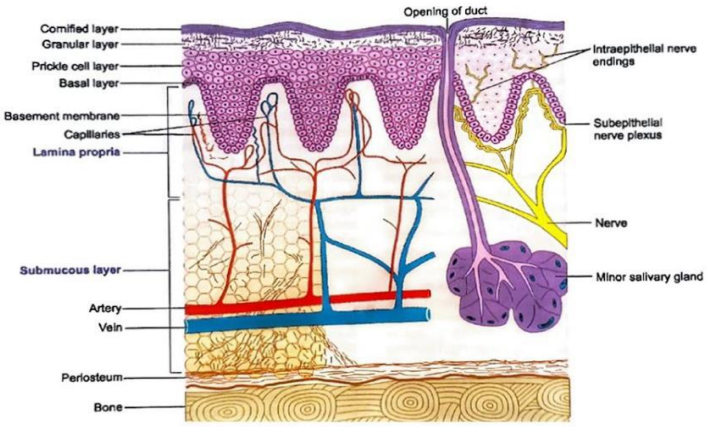

Fig. 1: Structure of oral mucosa.

There is a need to develop a formulation that avoids first-pass metabolism and GI degradation. The oral cavity provides a route of delivery of the therapeutic agent for both topical and systemic administration, so that metabolism and gastrointestinal degradation in the bloodstream can be avoided. In the preparation of patches, the commonly used technique is solvent casting. The oral cavity is easily accessible for self-administration. Stopping the use of the drug is possible, safe, and therefore acceptable to patients. To avoid ingestion of the dosage form or spillage of the dosage, bioadhesive polymers have received considerable attention for oral-controlled delivery. Due to bioadhesion, immobilization of drug-containing particles on the mucosal surface would lead to a longer residence time at the site of absorption or action, localization of the drug delivery system to a specific target site, and increased drug content. Concentration gradient due to direct contact of particles with mucosal surfaces.

Advantages [8]

Dosing the drug through the oral mucosa offers several special advantages

- Compared to other mucosal tissues, the oral mucosa is strong, rich in blood and moderately permeable.
- Avoids the first. -pass effect of the drug and contact with the gastrointestinal fluid.
- Location of the drug API at the site of the disease can also lead to significant cost savings and reduction of dose-specific side effects.
- Greater patient acceptability compared to other non-oral drug delivery systems.
- Tolerance to possible sensitization compared to skin and nasal mucosa.
- Reduced dosage frequency may be due to longer residence time with controlled API emission.
- Oral drug administration avoids harsh environmental variables that can affect
- Ore drug delivery.

- It does not require activation and provides a passive mechanism for drug absorption.
- On the contrary to rectal or cutaneous routes., the presence of saliva provides a relatively significant amount of water for the drug to disintegrate.
- Provides an alternative route for various hormones, narcotic pain relievers, steroids, enzymes, cardiovascular drugs, etc.

Disadvantages [9]

- Enzymatic degradation of the digestive tract.
- Delay between the time of administration and asorption.
- Requirements for a rapid onset.
- Limited absorption area -total area membranes the oral cavity used for drug absorption is 170 cm2, of which ~ 50 cm2 represents non- keratinized tissues, including the oral membrane.
- Continuous secretion of saliva (0.5-2 l/day) leads to further dilution of the drug.
- The risk of suffocation due to accidental ingestion of the distribution system is a concern.
- Ingestion of saliva can also result in loss of dissolved or suspended drug and ultimately inadvertent disposal of the dosage form.

MUCOADHESION [10]

Mechanism of mucoadhesion: Adhesion refers to the state in which two surfaces are held together by strong interfaces, adhesion, or both when in contact with a pressure-sensitive adhesive. Adhesion of a synthetic or natural substance to a biological surface is called bioadhesion, while adhesion to a mucosal and/or epithelial surface is called mucoadhesion 15. Mucosal adhesion has two distinct phases, each of which is affected by the dosage form and the method of drug administration.

Phase I (contact phase): The surface of the bioadhesive is in close contact with the film after it has been moistened, spread and expanded. Dosage forms are sometimes administered by a mechanical system through the vagina, aerodynamics for nasal administration, and peristaltic movements in the intestine.

Phase II (solidification phase): Moisture breaks down the molecules and starts a chain reaction, including electrostatic electricity. attractive forces, hydrogen bonds, hydrophobic forces and van der Waals forces. For full bioadhesion to occur, attractive forces must overcome repulsive forces. Two theories explain the solidification phase.

Diffusion theory: Mucoglycoproteins penetrate their chains and form secondary bonds to interact with mucoadhesive molecules. Both chemical and mechanical interactions are involved.

Dehydration theory: When mucus comes into contact with a substance, the substance loses water until the osmotic pressure of the mucus and substance are the same, and a gel forms. According to this view, no preparation, solid or liquid, is effective.

THEORIES OF MUCOADHESION [10]

Five different theories explain the phenomenon of slime adhesion.

Electronic theory: This theory is based on the fact that both the slime layer and the biological materials have opposite electric charges, which are able to form an electric double layer at the edge. and thus, helps determine mucoadhesive strength.

Wetting theory: liquid or less viscous molecules penetrate the mucosal surface and bind and prevent surface tension at the interface. This property is related to the contact angle, wetting ability and diffusion ability of the molecule. Contact angle (θ) and interfacial tension (γ) can be determined using the following equation

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

Where γLG is the surface tension of liquid gas, γSdL is the surface area. is the tension of the solid and γSG is the surface tension of the gaseous solid.

Diffusion theory: This theory suggests that the mucoadhesive polymer spreads into the mucosal layer by disrupting the glycoprotein chain network. This diffusion is time-dependent and depends on the diffusion coefficient and molecular weight of both phases.

Adsorption theory: Weak Vander Waals forces and hydrogen bond-mediated adhesion associated with the adsorption theory are the most accepted theories of mucoadhesion mechanisms. It includes primary and secondary bonding to indicate semi-permanent surface interactions.

Theory of Fracture: This is another accepted theory that explains the forces required to separate two surfaces after attachment. This force is called tensile strength or ultimate strength and can be determined by the following equation:

$$Sm= Fm/Ao$$

Where Sm: tensile strength, Fm: maximum force of detachment Ao: surface area

OR

$$Sf= (gcE) / c ½$$

where Sf: ultimate strength, gc: fracture energy (Wr + Wi = new work done to produce fracture surfaces + irreversible work of adhesion), E: Young's Modulus and c: critical crack length. theory is equally important to describe the mucoadhesion process. It is possible that the mucin first becomes wet and then the polymer diffuses

into the mucin layer, where disintegration of the layers affects adhesion, electronic transfer or a simple adsorption phenomenon, ultimately leading to mucosal adhesion.

THREE-DIMENSIONAL (3D) PRINTING[11]

Obstacles related to formulation that arise during the manufacture of buccal films may be resolved via 3D printing. Due to their low drug loading capacity, buccal dosage forms are currently usually reserved for strong medications. By layering formulation layers on top of one another, 3D printing could address the problem of restricted mucosal surface area for drug absorption and incorporate more active material per unit area of a mucoadhesive film, for example. Through the compartmentalization of buccal film layers, this layered technique may also offer a potential solution to problems involving incompatible substances.

In 3D printing, fused deposition modeling, or FDM, is one of the most widely utilized techniques. The printed object in FDM is created by layering thermoplastic filaments that are either molten or softened. extruded through a nozzle in conjunction with computer-aided design (CAD) to create a pre-defined geometry. The material is heated to just over its melting point inside the printer head, whereupon it is deposited and quickly solidifies to form a three-dimensional object. Mucoadhesive buccal films containing lidocaine, diclofenac sodium, and another buccal film containing lidocaine has been produced using FDM in conjunction with inkjet printing.

Semi-solid materials are deposited layer by layer using a syringe-based tool head in semi-solid extrusion (SSE) 3D printing. These materials are created by combining polymeric ingredients. With suitable solvent (s) to create a substance that has the right viscosity for printing. The features of the starting materials (heated thermoplastic filament versus semi-solid), the printing temperatures (room temperature versus 180 degrees Celsius for polylactic acid filament), and the mechanical characteristics of the printed object (solid but "wet" versus rapidly solid, hard, and dry) are the main distinctions with the FDM process Because SSE-printed products are still "wet," post-printing drying is necessary for further processing and solidification. The semi-solid nature of the beginning ingredients may result in unintentional shrinkage, deformation, or collapse of the printed product during the drying phase. due to inadequate hardness. By adding an in-process drying phase to an SSE 3D printer, Gajdziok et al. showed that the device was feasible by using it to produce multi-layered orodispersible films of benzydamine hydrochloride.

BUCCAL FILM FORMULATION ASPECTS

i. Active pharmaceutical ingredient (API)[12]

The active ingredients of the oral films must have the following properties: A single dose of the usual medication must be small. Drugs with a biological half-life of 2 to 8 hours are good candidates for controlled drug dosing. Larger differences in the maximum amount of the drug or higher values occur with oral administration.

ii. Plasticizer [12]

The plasticizer is an important factor influencing the mechanical properties of films. Mechanical properties of films**,** such as tensile strength and elongation**.** Changing the concentration of plasticizers affects these properties. The plasticizer reduces the fragility of the membrane and increases its flexibility.

iii. Mucoadhesive polymers[13]

Polymers with different properties must be considered, depending on the type of formulation. Depending on the dosage form, different situations are possible in cases of oral mucoadhesion.

iv. Sweetening agents [13]

Sweeteners have become important excipients in the oral integrated drug delivery system. The sweet taste of the preparation is more noticeable in children. Natural sweeteners, and artificial sweeteners are used to improve the taste of oral preparations.

***v. Saliva stimulating ag*ent[14]**

The purpose of using substances that stimulate the production of saliva is to increase the rate of saliva secretion, which would contribute to the faster integration of rapidly dissolving film preparations. In general, acids are used in food preparation can be used as salivary stimulants.

vi. Flavoring agent[15]

Flavoring Agents an orodispersible system may contain another substance known as a flavoring agent. The taste and acceptability of an orodispersible dosage form, such as an oral film, depend on the initial taste quality, which must be observed within seconds of administration.

Coloring agents

Coloring agents are used to improve the appearance of the oral film.

Table 1: List of Buccal film Formulation aspect.

Sr .No.	*Excipients*	*Concentration*	*Example*
1.	API	5-30%	Clinidipine, Lisnopril, Duloxetine hydrochloride etc
2.	Mucoadhesive polymer	40-50%	HPMC, HPC, Sodium alginate, Carbopol, NaCMC etc.
3.	Plasticizer	1-20%	Glycerol, propylene glycol, polyethylene glycol etc.
4.	Sweetning agent	3-6%	Sucrose, fructose, glucose, maltose etc.

5.	Saliva stimulating agent	2-6%	Citric acid, lactic acid, malic acid, tartaric acid, ascorbic acid etc.
6.	Flavouring agents	q. s	Peppermint oil, cinnamon oil, vanilla, coca etc.
7.	Coloring agent	q. s	FD&C approved

METHODS TO MANUFACTURE BUCCAL FILMS

i. Solvent casting method
ii. Hot melt extrusion method
iii. Direct milling method.

i. *Solvent casting method*[16]

In the solvent casting process, the necessary amount is added, and the polymer is dissolved in distilled water. A tiny amount of an active medicinal component was added to this mixture. After adding plasticizer to the mixture, thoroughly stir it. After that, the solution is cast into a petri dish and placed in a hot air oven at 40°C to dry. Once it has dried, take it off the petri plate with a knife and let it sit in a desiccator for a full day. From now on, cut to the appropriate size and form.

Procedures for the Solvent Casting Method

Get the casting solution ready.

↓

Let the solution deaerate.

↓

Pour the right amount of solution into the mold.

↓

Drying the casting solution is step four.

↓

Cut the last dose form to ensure the correct amount of medication is contained.

ii. *Hot melt extrusion method*[17]

hot-melt extrusion process contains drugs and excipients that can be melted. The material is then pressed through a hole to obtain a more homogeneous thread in various forms, such as granules, tablets, or films. It is used for the transdermal delivery of drugs.

Steps of the hot melt extrusion process

In solid form, drugs and carriers are added together in this process.

↓

The mixture is allowed to liquefy during heating and is obtained in liquid form.

↓

The Molds finally form the molten mixture into films.

Advantages

• Fewer work units.
• Better content consistency
• A process that does not contain water

Disadvantages

• Heat treatment can cause harm or defects which can cause instability.
• The specific flow properties of polymers are not necessary because they play an important role in the formation of the oral membrane.
• Only a few polymers are available.

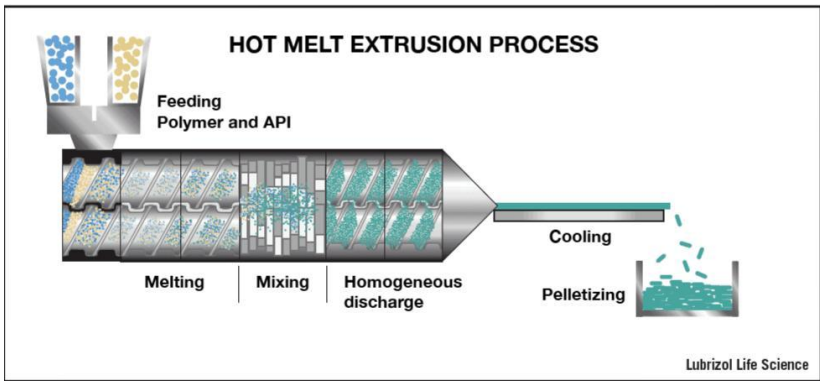

Fig 2: Hot melt extrusion technique.

iii. *Direct milling method*[18]

Here, the films are made without solvents. The drug and excipients are mechanically mixed by direct milling or grinding, usually without liquids. After the mixing process, the resulting material is rolled on a removable coating until the desired thickness is reached. The background material is then laminated as previously described. While there is little or no difference in the yield of fibers produced by the two processes, the solvent process isfavored due to the absence of solvents and the health problems associated with solvents.

API and excipients are blended by direct milling

↓

Blended mixture is rolled with the help of roller

↓

Followed material is laminated

Finally, film is collected.

EVALUATIONS OF BUCCAL FILMS

i. Weight variation[19]

Film weight variation: Bulk films were weighed on an analytical balance and the average weight of each film can be determined. It is desirable that the weight of the films be almost constant. It is useful to ensure that the film contains.

ii. Thickness[20]

Thickness: The thickness of the oral membrane is assessed with a calibrated micrometer screw gauge. The film thickness is measured at five different locations, and the average is calculated. This is done to ensure non-uniformity in film thickness because it directly correlates to film dosage accuracy and ensures the reproducibility of the method used in the formulation.

iii. Surface pH [21]

The membranes are allowed to swell by keeping them in contact with 1 ml of distilled water for 2 hours at room temperature, and the pH is recorded by bringing the electrode into contact with the membrane surface. It balances for 1 minute.

iv. Folding endurance[22]

The folding endurance of the film was determined by repeatedly folding a small strip of film (2x2cm) in the same place until it broke. How many times can the film be folded? a given place without breaking based on the value of the folding endurance.

v. Drug content uniformity[23]

The uniformity of the drug content of the films was tested by a UV spectrophotometric method. 2×2 cm films were cut from the cast films in three different locations. Each film was placed in a 100-ml volumetric flask and dissolved in simulated saliva at pH 6.8, and 5 ml was taken and diluted to 10 ml with water. The absorbance of the solution was measured with a UV/visible spectrophotometer (Shimadzu) at λmax in nm. The percentage of drug concentration was determined.

vi. Tensile strength[24]

The property of a film that requires a load that causes deformation and possible membrane failure is called tensile strength. Two equally spaced brackets are arranged so that film strips are placed between them. If a load is applied at the moment of failure and the cross-sectional area of the broken film is known, the tensile strength can be calculated using the following equation

Tensile strength (N/mm2) = breaking strength (N) / sample cross-sectional area (mm2).

vii. Percentage moisture loss[24]

Three films are placed in a desiccator with anhydrous calcium chloride, and the films are taken out after 3 days and then weighed. The percentage moisture loss was calculated by the formula

Percentage Moisture Loss = [(Initial weight - Final weight) / Initial weight] × 100

viii. Swelling index[24]

The weight and diameter of the original membrane samples are measured, then the samples are allowed to swell on the surface of an agar plate kept in an incubator at 37 ±0.2 °C. The mass of the membranes (n = 3) is determined after different time intervals (1–5 h).

Percentage expansion S is calculated using the following equation

Percentage expansion [% S] = [Xt -Xo /Xo] ×100,

Where Xt = weight of expanded film after time t, x
Xo = expanded mass of film at zero instant.

ix. In vitro dissolution study[24]

USP type II apparatus (basket type apparatus) was used for dissolution studies with pH 6.8. buffer (50 ml) as a dissolution medium at 37°C and speed at 50 rpm. 1ml of sample solution was withdrawn and equilibrated with a fresh dissolution medium. Whatman Filter paper of 0.45 µm was used to filter the buccal films, and API was analyzed. spectrophotometrically at λmax.

x. In vitro disintegration time[25]

This can be visually analyzed in a petri dish with 2 ml of distilled water, swirling every 10 seconds. The time required for the membrane to degrade or rupture is recorded as the in vitro degradation time.

xi. In vitro drug release[25]

In vitro dissolution studies were conducted on a USP XXIV Type II apparatus under consumer conditions. The dissolution medium was500 ml of simulated saliva pH 6.75 at 37±0.50c, and the mixing rate depends on the dosage form at fixed intervals. Samples are taken at a fixed intervals and replaced with an appropriate volume of fresh dissolution medium. The amount of drug released in the dissolution medium was determined by UV spectroscopy.

RECENT ADVANCES IN BUCCAL DRUG DELIVERY SYSTEM[26]

Vaccination against major infectious diseases has been shown to be effective in preventing disease and has significantly increased life expectancy in many parts of the world, especially among children. Several variables can affect the effectiveness of vaccination to ensure optimal mucosal protection.

The pathway and antigen-processing capacity of antigen-presenting immune cells, such as macrophages and dendritic cells, are the most important determinants of mucosal vaccine efficacy. Most vaccinations are currently administered parenterally or by other invasive methods.

A systemic immune response can be triggered by invasive vaccine injection, although mucosal immune defense may not be significantly enhanced. In contrast, effective mucosal vaccinations not only improve local immune protection but also showed a systemic response similar to parental vaccination.

Therefore, it is necessary to investigate the creation of mucosal vaccination methods that can stimulate both mucosal and systemic immunity. In mucosal vaccine research, several nanocarrier systems are now used, such as multiple emulsions, liposomes, polymeric nanoparticles, dendrimers, immunostimulatory complex (ISCOM), and others. In addition to the systemic immune reaction, the important first line of defense of the body - immunization - can be induced in various mucosal barriers by the mucosal diffusion and vaccination of antigens containing nanocarriers.

The recent developments in buccal drug delivery systems are as follow[27,28]

Buccal delivery by means of iontophoresis

To enable therapeutic drug distribution via the oral mucosal route, many chemical absorption enhancers and enzyme inhibitors have been utilised, and these enhancers have been extensively studied.

Recently, physical approaches such as sonophoresis and electric fields have also been employed. An electric field can act as an extra driving force on drug ions (iontophoresis), push water (or physiological fluids) to flow with the dissolved medication or metabolites (electroporation), or temporarily change tissue architecture to make them more permeable (electroporation). Such techniques may have advantages in that they allow for greater quantities of pharmacologically active chemical to be transported across the buccal mucosa.

Buccal mucosa and photodynamic therapy

In this approach, photodynamic therapy (PDT) and photodynamic antimicrobial chemotherapy (PACT) involve the use of a photoactive dye (photosensitizer) that is activated by exposure to light of a specific wavelength in the presence of oxygen to kill target cells.

PDT is used clinically and is approved as minimally invasive and minimally toxic. for the treatment of many diseases of the oral mucosa, including neoplastic and neoplastic diseases. PACT has been shown to eradicate a wide variety of pathogens from the oral cavity, do not respond well to traditional antibiotics and antifungals. In the future, this approach may play an important role in persistent infections. The correct composition for distribution of the photosensitizer in the oral cavity has an important effect on the success of the treatment. Molecular size, pH, and lipophilicity of photosensitizers all affect the site of action of their transport.

CHALLENGES IN BUCCAL DRUG DELIVERY DEVELOPMENT[26,32]

- The oral environment causes serious problems in the administration of systemic drugs. The drug must be making this therapy considered an alternative therapy for infections that released from the formulation and delivered to the site of administration (e.g., buccal or sublingual) before it passes through mucosal layers and enters the systemic circulation. Certain physiological characteristics of the oral cavity, such as pH, fluid volume, enzyme activity, and permeability of the oral mucosa play an important role in the process. Mucosal surface structure and mobility are also performance criteria.for drug delivery systems designed for prolonged release in the oral cavity (e.g., mucoadhesive systems).

- The main physiological environment of the oral cavity in terms of pH, liquid volume, and composition is formed by saliva secretion. Saliva is secreted by three primary salivary glands (salivary gland, mandibular, and sublingual) and minor salivary glands, or oral glands, located on or below the mucous membrane. The parotid and mandibular glands secrete a watery secretion, while the sublingual glands secrete viscous saliva with minimal enzyme activity. Saliva has various functions, such as lubricating the oral cavity, promoting swallowing, and preventing tooth mineralization. It also promotes the digestion of carbohydrates and modulates the normal microflora, regulating oral pH and enzyme activity.

- The amount of saliva secretion per day varies from 0.5 to 2.0 liters. However, the volume of saliva continuously present in the mouth is approximately 1.1 ml, resulting in a relatively modest amount of liquid available for drug release via delivery devices. compared to GIT. This obstacle can be overcome if the oral cavity provides a relatively stable and hospitable physiological environment for drug delivery, maintained by continuous saliva production. Saliva is a mobile fluid with little mucus, minimal enzymatic activity, and almost no proteases compared to GIT secretions. Saliva is a poor buffer, with a pH of 5.5-7.0. Due to the higher percentage of salt and bicarbonate, it may increase a bit depending on the high flow rate. Minimal enzymatic activity in saliva can overcome this barrier.

Application of Buccal film[32,33]

Controlled and sustained release

Sustained-release Buccal films are used in hospital preparations, and different polymers excipients such as chitosan derivatives because they help with wound dressings and reduce toxicity, and have strong water resistance and adhesive characteristics.

Nicotine replacement therapy
Tobacco contains nicotine, a psychoactive substance that adds to smoking's addictive qualities. Due to its ease of entry via the mucosal barrier, the mucosal method of delivery is the most effective in this therapy.

Antifungal infections
When treating oral candidiasis, the systemic antifungal fluconazole is frequently chosen for mucosal delivery. It is possible to reduce its systemic negative effects by increasing its oral concentration. For a longer duration, the medication and pathogenic yeast have increased contact. using fluconazole in small dosages via mucoadhesive buccal films, which ultimately increased its effectiveness.

Targeted therapy of oral cancer
Targeted therapy is the most generally prescribed treatment for oral cancer. It aims to deliver the medication to the affected site with the least amount of toxicity and side effects. Gaining access to polymer films as nanodelivery methods and increasing their solubility have been shown to Bioavailability and stability increased even within tumor cells.

Asthma
Sodium cromoglycate is intended to be administered through buccal patches in order to treat asthma. The medication needs to be designed with a controlled release mechanism due to its short half-life. Both a reduction in the blood's maximum plasma concentration and an increase in the time needed to reach it were the outcomes of using this medication in buccal patches. It provided controlled medication release as well.

***FDA-Approved Buccal Films*[34,35,36]**
The use of buccoadhesive buccal films is an option. Substances of sufficient strength to meet the requirements for administration through the buccal film are applied. At present, the USFDA has approved four buccal films.

Table 2: List of FDA approved Buccal films.

Drug	Year of approval	Company	Application
Ondansetron	2010	Applied Pharma Research and Labtec Ltd.	Prevention of nausea and vomiting before and after 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

***Future prospects*[37]**
When it comes to cost, accessibility, administration, withdrawal, and patient compliance, a buccal adhesive solution offers many advantages. Researchers are actively looking at traditional polymers for novel drug delivery strategies. Given the state of the world today, scientists are investigating several methods for creating buccal adhesive dose forms in order to boost the oral bioavailability of drugs. The second generation of mucoadhesive polymers has shown a great deal of promise. A brand-new technique for delivering buccal adhesives has surfaced that guides drug delivery toward the buccal mucosa while accounting for the oral cavity's surrounding environment. Patients accept solid dosages nowadays. Commercially available solids, liquids, and gels are delivered orally. The dispersion of vaccine formulations and peptides will shape the future of buccal adhesive medication delivery. When creating buccal formulations for combined medicine delivery, bilayer buccal tablets, films, and patches are the best options. The current attraction of microparticulate or nanoparticulate bioadhesive systems is their ability to protect therapeutic entities and improve absorption through the longer contact times provided by the bioadhesive component.

CONCLUSION
According to the current review, buccal film is the most precise and widely accepted dose form because it improves bioavailability, increases patient compliance, and delivers drugs faster while avoiding the first-pass effect. Due to their advantages over conventional dosage forms and their low cost of production, buccal films will eventually supplant both rapid-dissolving tablets and traditional dosage forms. Buccal films, on the other hand, are a more practical formulation because of their characterization, drug loading, and ease of manufacturing. A non-invasive drug delivery method called buccal film can be utilized to overcome medications that are susceptible to first-pass metabolism. In the future, this will be a more reliable option to maximize the therapeutic efficacy of various APIs. Oral mucoadhesive dosage forms may continue to be a fascinating area of study for improving drug absorption. especially for the upcoming generation of medications. Drug delivery methods based on polymers that are administered buccal route are outlined in this review. Utilizing these technologies is driving more research and development into buccal delivery systems and biomaterials.

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