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# A REVIEW ON BUCCAL PATCH: A MUCOADHESIVE BUCCAL DRUG DELIVERY SYSTEM

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## ABSTRACT

Buccal route is an attractive route of administration for systemic drug delivery and it leads direct access to the systemic circulation through the internal jugular vein bypasses drugs from the hepatic first pass metabolism provides high bioavailability. Drug actions can be improved by developing new oral drug delivery systems such as the mucoadhesive buccal drug delivery system. Mucoadhesion is currently explained by six theories: electronic, adsorption, wettability, diffusion, fracture and mechanical. Various mucoadhesive devices, including tablets, films, patches, disks, strips, ointments and gels, have recently been developed. However, buccal patch offers greater flexibility and comfort than the other devices. Mucoadhesive buccal patches are a type of dosage form that uses controlled release to distribute drugs over a longer period of time. These patches often assist drugs in bypassing the liver's first pass processing and entering the systemic circulation directly. This article provides an information on buccal patches advantages, disadvantages, ideal characteristics and basic components of mucoadhesive buccal patches.

**KEYWORDS:** Buccal patches, Mucoadhesion, Buccal drug delivery, oral mucosa.

## INTRODUCTION

Oral mucosa is one of the most acceptable and convenient route of drug administration. This route offers many advantages when compared to other routes such as preventing enzymatic degradation of the drug molecules in the gastrointestinal tract by passing hepatic first pass metabolism and good patient acceptance when compared to ocular, nasal, rectal and vaginal routes. Since oral mucosa has a larger surface area, it can permeate low molecular weight drugs through mucosal epithelium quickly when compared to ocular and nasal routes.[1] The delivery of medicines by buccal mucosa has attracted great interest because of its convenient availability.[2] Buccal Drug Delivery System (BDDS) has been studied as an advance drug delivery approach instead of using and following traditional drug administration routes.[3]

Drugs can be delivered throughout oral mucosa into three distinct forms:[4]

a) Sublingual delivery of medications: the administration across the layer of the tongue's front surface and the floor of mouth
b) Buccal supply: composed primarily of the lining of the cheeks and the buccal mucosa membrane.
c) Local delivery of drugs: consisted of administration in all places apart from those included in sublingual and buccal.

These sites are bodily different in their drug penetration, delivery rate and ability to sustain a delivery mechanism for a specific time period to release drugs out of the supplies and into the mucous membrane.

## ANATOMY OF ORAL CAVITY[5]

The oral cavity may be divided into two regions, the outer oral vestibule, bounded by the lips and cheeks and the oral cavity itself the border being and formed by the hardened soft palates, the floor of the mouth and tonsils.

The mucosa that lines the oral cavity may be divided into three types, classified according to their function as:-

1. Masticatory mucosa: which includes the mucosa around the teeth and on the hard palate and these regions have keratinized epithelium
2. Lining mucosa: which overs the lips, cheeks, base of the oral cavity, lower part of tongue, buccal mucosa and the soft palate and these regions have non keratinized epithelium.
3. Specialized mucosa: covering the dorsum of the tongue with highly keratinization.

## OVERVIEW OF ORAL MUCOSA[5]

### Structure

The oral mucosa is comprised of squamous stratified (layered) epithelium, basement membrane, the lamina propria and submucosa. It also contains many sensory

receptors including the taste receptors of the tongue. The epithelium of the buccal mucosa is about 40-50 cell layer thick, while that of the sublingual epithelium contain somewhat fewer.

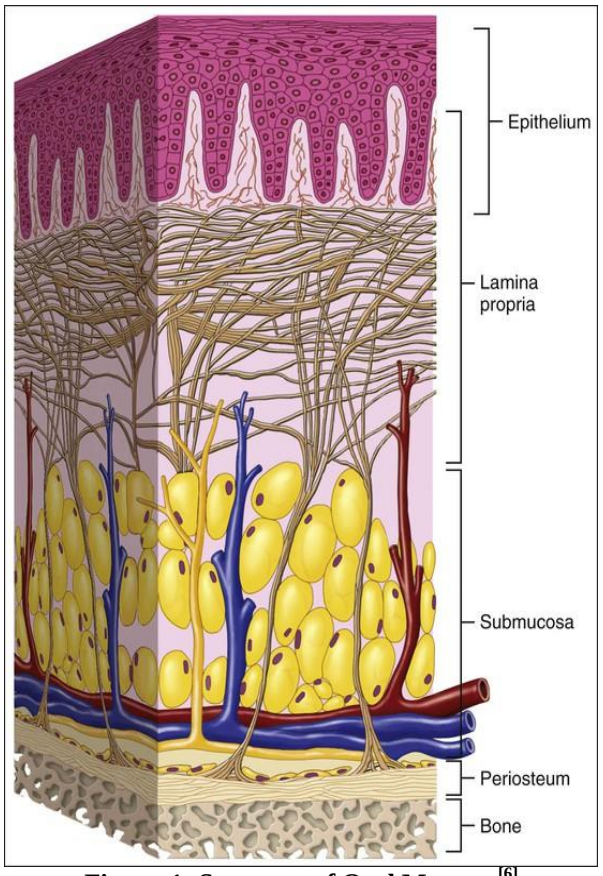


**Fig no. 1: Structure of Oral Mucosa.**[6]

**Permeability**

The oral mucosa is somewhat leaky epithelia intermediate between that of the epidermis and intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin. In general, the permeabilities of the oral mucosae decrease in the order of sublingual greater than buccal and buccal greater than palatal. This rank order is based on the relative thickness and degree of keratinization of these tissues, with the sublingual mucosa being relatively thin and non-keratinized, the buccal thicker and non-keratinized, and the palatal intermediate in thickness but keratinized.

**Composition of Mucus Layer**

Mucus is a translucent and viscid secretion which forms a thin, contentious gel, mean thickness of this layer varies from about 50-450 µm in humans secreted by the globet cells lining the epithelia. It has the following general composition.

-Water-95%
-Glycoprotein and lipids-0.5-300%
-Mineral salts-1%
-Free proteins-0.5-1.0%

**Functions of Mucus Layer**

- Protective: resulting particularly from its hydrophobicity.
- Barrier: The role of the mucus layer as a barrier in tissue absorption of the drugs and influence the bioavailability.
- Adhesion: Mucus has strong adhesion properties.
- Lubrication: It is to keep the mucus from the globlet cell is necessary to compensate for the removal of the mucus layer due to digestion, bacterial degradation and solubilisation of mucin molecules.

## ADVANTAGES OF BUCCAL DRUG DELIVERY[7,8]

- Administration is effortless.
- Drug administration can be possible even in unconscious patients.
- Dosage side effects are few to no.
- Drugs with first pass metabolism are conveniently delivered through this route and have increased bioavailability.
- Various compounds which are easily degraded in the gastric environment like highly acidic or caustic surroundings, can be given via this way.
- Local administration of drug is also suitable for extended time.
- Buccal mucosa provides better permeability than the skin.
- In contrast to rectal and transdermal routes there is greater volume of water as saliva for dissolution of drug in buccal route.
- This route offers better bioavailability of drugs than oral route which shows inferior bioavailability with oral route.

## DISADVANTAGES OF BUCCAL DRUG DELIVERY[9,10,11,12]

- Drug having unpleasant taste or irksome to mucosal cavity cannot be given by this route.
- Buccal routes is not suitable for large doses.
- Surface area is small and absorption area is relatively smaller.
- Continuous saliva secretion results in drug dilution.
- Eating greatly interferes drug administration through this way.
- Drugs having risk of destabilization at Buccal pH cannot be given by this way.

## IDEAL CHARACTERISTICS OF BUCCAL DRUG DELIVERY[13,14]

An ideal buccal drug delivery system should have following characteristics:

- Well moisturized, soluble and biodegradable.
- Polymer and its decaying derivatives should be harmless and free from leaching toxins
- Should have good adhesive properties and mechanical strength.
- Bio-adhesive set should be ductile and have firmness.

- Polymer should be readily accessible and cost-effective.
- Should demonstrate both dry and liquid bio-adhesive properties.
- Molecular weights should be optimal.
- Must indicate acceptable shelf-life.
- Spatial confirmation is necessary.
- Should have good bonding nature.
- Should stick for few hours to the attachment site.
- Should have unidirectional drug release into the mucosa.
- Subject to controlled release of the medication.
- Should effectively enhance absorption rate and duration of medication.
- Should nor irritate patient or trigger any discomfort.
- Should not affect basic processes such as speaking and drinking.

## NOVEL BUCCAL DOSAGE FORMS[15]

Tablet, films, patches and powders are few of the novel buccal dosage formulations which are briefly discussed below:

### Buccal mucoadhesive tablets

These are basically dry formulations, which are required to be dampened before allowing to be in proximity with buccal mucosa. For instance, a two layered tablet, having adhesive matrix hydroxypropyl cellulose layer and with an internal centre of cocoa butter including insulin and sodium glycocholate.

### Patches and Films

Two laminations are present in the buccal patches along with aqueous adhesive polymeric solution which is embedded over not permeable backing sheath structure, which gets split into the needed oval structure. Zilactin is a unique muco-adhesive film constituting solution of organic acids, alcohol, and hydroxypropyl cellulose .Film can remain as is when used on buccal mucosa region upto 12 hours.

### Semi-solid formulations

Gels and ointments which are available in bio-adhesive forms do not have much patient compliance as that of solid mucco bio-adhesive dosage forms and mostly all dosage forms are utilized for locally delivering drug. Orabase is a gel based oral formulation which can remain on site for 15-150 mins.

### Powders

As sprinkled on to the rat's BM, powdered form of HPC and beclomethasone show a substantial improvement in residency time compared with oral solution, and 2.5 percent beclomethasone is stored on BM for more than four hours.

## MUCOADHESION OR BIOADHESION[16]

**Introduction**: The term bio-adhesion (also known as mucoadhesion) described by Longer and Robinson as the attachment to the mucus and /or the surface of the synthetic or natural macromolecule. The general concept of polymer adherence to the biological (bio-adhesive) or mucosal (mucoadhesive) surface still exists. A bio-adhesive is defined as a compound that can collaborate with and hold on biological material for an continued span of time.

### Mechanism of Mucoadhesion[17,18]

The adhesion mechanism of some macromolecules to a mucus tissue surface is not yet well understood. To begin proximate contact and thereby maximizing superficial contact, the mucoadhesive must be distributed over the substrate surface, which facilitates the spread of their chains in the mucus. Attraction and repulsion forces exist and the attraction forces must prevail for a mucoadhesive to succeed. The essence of the dosage type and the way it is delivered can encourage each phase. There is also usually a two-step mechanism of mucoadhesion that is:

**1) The contact stage**

Between both the mucus membrane and the mucoadhesive there is an intimate wetting. In certain cases, these two surfaces can be merged physically eg.inside the oral cavity, oculum or vagina and preserved.

**2) The consolidation stage**

The adhesive joints are mixed and tougher with various physicochemical interactions, which contribute to lifelong adherence. Mucoadhesive materials adhere to stable dry surface areas most intensely when they are moisturizing, allowing for an efficient freezing of mucoadhesive molecules, conforming to the surface shape and binding mostly by hydrogen, and a weaker van der Waal bonding method.

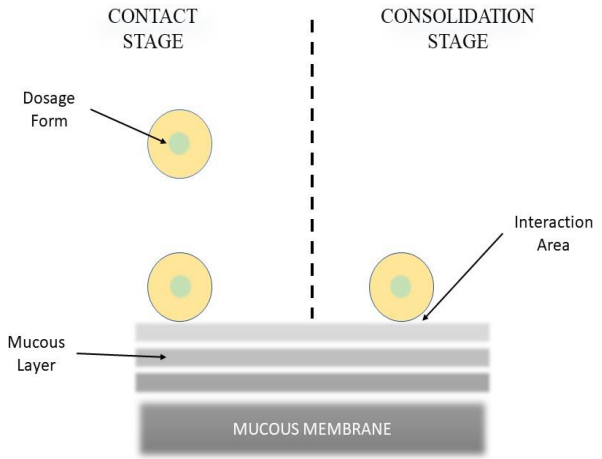


**Figure no: 1 The two-step involved in mucoadhesion process.[17,18]**

## THEORIES OF MUCOAHESION[19]

Several theories are present to elaborate experimental information formed around the bio-adhesive course.

i. **Wetting theory**: This hypothesis is largely appropriate to liquid bio-adhesive systems and

examines adhesive and proximity conduct in references to a liquid or a mush to expand over a biological system.

ii. **Diffusion theory**: As per diffusion hypothesis, polymeric series and mixture of mucus to such an extent to form a semi-permanent adhesive bond. Precise extent till which the polymer chain series pierce the mucus relies on diffusion coefficient and contact span. Further, diffusion coefficient, relies on the value of molecular mass between cross links and reduce considerably as the cross-linking density reduces.

iii. **Electronic theory**: In this hypothesis, electronic transfer happens during proximity of an adhesive polymer and mucus glycoprotein connections due to distinctions in their electronic structure, this leads to making of an electronic bilayer at the interface adhesion happens because of attractive forces across the double membrane.

iv. **Adsorption theory**: As per this hypothesis, following the primary association in middle of two surfaces, the components adhere due to surface forces playing role in middle of the atoms in the two surfaces. Two kind of chemical bonds like primary covalent and secondary chemical bonds are implicated in the adsorption method.

## COMPOSITION OF BUCCAL PATCHES

A. Active Ingredients
B. Polymers (adhesive layer): HEC, HPC, polyvinyl pyrrolidine(PVP), polyvinyl alcohol(PVA), Carbopol and other mucoadhesive polymers.
C. Diluents: Lactose DC is selected as diluents for its high aqueous solubility, its flavouring characteristics and its physio-mechanical properties, which make it suitable for direct compression. Other example: microcrystalline starch and starch.
D. Sweetening agents: Sucralose, aspartame, Mannitol etc.
E. Flavouring agents: Menthol, vanillin, clove oil
F. Backing layer: EC etc
G. Penetration enhancer: cyan acrylate
H. Plasticizer: PEG-100;400, propylene glycol

## METHD OF PREPARATION OF BUCCAL PATCHES

Two methods are used to prepare buccal patches

1. **Solvent casting**: In this method, all patch excipients including the drug co-dispersed in an organic solvent and coated onto a sheet of release liner. After solvent evaporation a thin layer of the protective backing material is laminated onto the sheet of coated release liner to form a laminate that is die-cut to form patches of the desired size and geometry.[20,21,22]
2. **Direct milling**: In this, patches are manufactured without the use of solvents. Drug and excipients are mechanically mixed by direct milling or by kneading, usually without the presence of any liquids. After the mixing process, the resultant material is rolled on a release liner until the desired thickness is achieved. The backing material is then laminated as previously described. While there are only minor or even no differences in patch performance between patches fabricated by the two processes, the solvent-free process is preferred because there is no possibility of residual solvents and no associated solvent-related health issues.[23,24]

## EVALUATION OF BUCCAL PATCHES

1. **Surface pH**: Buccal patches are left to swell for 2 hr on the surface of an agar plate. The surface pH is measured by means of a pH paper placed on the surface of the swollen patch.[25]
2. **Thickness measurements**: The thickness of each film is measured at five different locations (centre and four corners) using an electronic digital micrometer.[25]
3. **Swelling study**: Buccal patches are weighed individually (designated as W1), and placed separately in 2% agar gel plates, incubated at 37°C ± 1°C, and examined for any physical changes. At regular 1-hour time intervals until 3 hours, patches are removed from the gel plates and excess surface water is removed carefully using the filter paper. The swollen patches are then reweighed (W2) and the swelling index (SI) is calculated using the following formula.[26,27]

$$SI = \frac{(W2-W1) \times 100}{W1}$$

4. **Water absorption capacity test**: Circular Patches, with a surface area of 2.3 cm2 are allowed to swell on the surface of agar plates prepared in simulated saliva (2.38 g Na2HPO4, 0.19 gKH2PO4, and 8 g NaCl per litter of distilled water adjusted with phosphoric acid to pH 6.7), and kept in an incubator maintained at 37°C ± 0.5°C. At various time intervals (0.25, 0.5, 1, 2, 3 and 4 hours), samples are weighed (wet weight) and then left to dry for 7 days in a desiccator over anhydrous calcium chloride at room temperature then the final constant weights are recorded. Water uptake (%) is calculated using the following equation

$$\text{Water uptake (\%)} = \frac{(Ww-Wf) \times 100}{Ww}$$

Where, Ww is the wet weight and Wf is the final weight. The swelling of each film is measured.[28,29]

5. **Ex-vivo bio adhesion test**: The fresh sheep mouth separated and washed with phosphate buffer (pH 6.8). A piece of gingival mucosa is tied in the open mouth of a glass vial, filled with phosphate buffer (pH 6.8). This glass vial is tightly fitted into a glass beaker filled with phosphate buffer (pH 6.8, 37°C ± 1°C) so it just touched the mucosal surface. The patch is stuck to the lower side of a rubber stopper with cyano acrylate adhesive. Two pans of the balance are balanced with a 5-g weight. The 5- g weight is removed from the left hand side pan,

which loaded the pan attached with the patch over the mucosa. The balance is kept in this position for 5 minutes of contact time. The water is added slowly at 100 drops/min to the right-hand side pan until the patch detached from the mucosal surface. The weight, in grams, required to detach the patch from the mucosal surface provided the measure of mucoadhesive strength.[30,31,32]

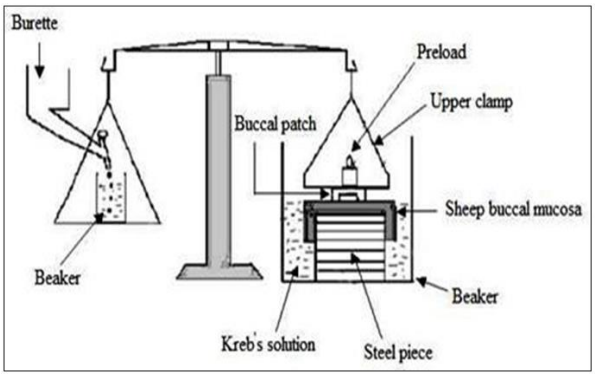


**Figure No 2: Measurement of Mucoadhesive Strength.**

6. **In vitro Drug Release**: The United States Pharmacopeia (USP) XXIII-B rotating paddle method is used to study the drug release from the bilayered and multilayered patches. The dissolution medium consisted of phosphate buffer pH 6.8. The release is performed at 37°C ± 0.5°C, with a rotation speed of 50 rpm. The backing layer of buccal patch is attached to the glass disk with instant adhesive material. The disk is allocated to the bottom of the dissolution vessel. Samples (5 ml) are withdrawn at predetermined time intervals and replaced with fresh medium. The samples filtered through Whatman filter paper and analysed for drug content after appropriate dilution. The in- vitro buccal permeation through the buccal mucosa (sheep and rabbit) is performed using Keshar-Chien/Franz type glass diffusion cell at 37°C±0.2°C. Fresh buccal mucosa is mounted between the donor and receptor compartments. The buccal patch is placed with the core facing the mucosa and the compartments clamped together. The donor compartment is filled with buffer.[333,34]

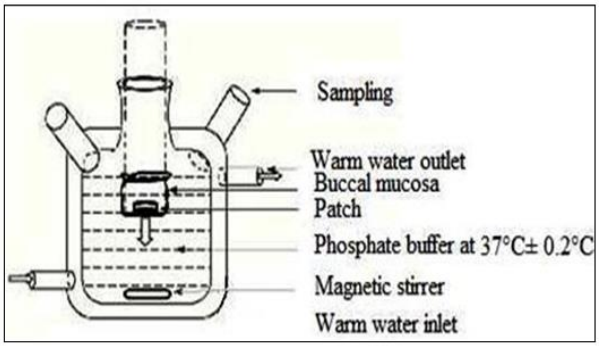


**Figure No 3: schematic diagram of Franz Diffusion Cell for Buccal Patches.**

7. **Permeation study of buccal patch**: The receptor compartment is filled with phosphate buffer pH 6.8, and the hydrodynamics in the receptor compartment is maintained by stirring with a magnetic bead at 50 rpm. Samples are withdrawn at predetermined time intervals and analysed for drug content.[35]
8. **Ex-vivo Mucoadhesion Time**: The ex-vivo mucoadhesion time performed after application of the buccal patch on freshly cut buccal mucosa (sheep and rabbit). The fresh buccal mucosa is tied on the glass slide, and a mucoadhesive patch is wetted with 1 drop of phosphate buffer pH 6.8 and pasted to the buccal mucosa by applying a light force with a fingertip for 30 seconds. The glass slide is then put in the beaker, which is filled with 200 ml of the phosphate buffer pH 6.8, is kept at 37°C ± 1°C. After 2 minutes, a 50-rpm stirring rate is applied to simulate the buccal cavity environment, and patch adhesion is monitored for 12 hours. The time for changes in colour, shape, collapsing of the patch and drug content is noted.[36]
9. **Measurement of mechanical properties**: Mechanical properties of the films (patches) include tensile strength and elongation at break is evaluated using a tensile tester. Film strip with the dimensions of 60 x 10 mm and without any visual defects cut and positioned between two clamps separated by a distance of 3 cm. Clamps designed to secure the patch without crushing it during the test, the lower clamp held stationary and the strips are pulled apart by the upper clamp moving at a rate of 2 mm/sec until the strip break, the force and elongation of the film at the point when the trip break is recorded. The tensile strength and elongation at break values are calculated using the formula 36

$$T = \frac{m \times g}{b \times t} \text{ Kg/mm}^2$$

Where, M - is the mass in gm, g - is the acceleration due to gravity 980 cm/sec2, B - is the breadth of the specimen in cm, T - is the thickness of specimen in cm. Tensile strength (kg/mm2 ) is the force at break (kg) per initial cross- sectional area of the specimen (mm2).[37]

10. **Stability study in human saliva**: The stability study of optimized bilayer and multilayered patches is performed in human saliva. The human saliva is collected from humans (age 18-50years). Buccal patches are placed in separate Petri dishes containing 5ml of human saliva and placed in a temperature-controlled oven at 37°C ± 0.2°C for 6 hours. At regular time intervals (0, 1, 2, 3 and 6 hours), the dose formulations with better bioavailability are needed. Improved methods of drug release through transmucosal and transdermal methods would be of great significance, as by such routes, the pain factor associated with parenteral routes of drug administration can be totally eliminated.[37]

## APPLICATION OF MUCOADHESIVE BUCCAL FILM/PATCHES

### Nicotine replacement therapy (NRT)

The habitual nature of smoking is partly due to nicotine in tobacco, which is categorized as a psychoactive substance. In NRT, the nicotine delivery routes are the skin and mucosal membranes, such as buccal and nasal mucosa, because both the neutral and protonated forms of nicotine can readily permeate across the mucosal membranes.[38] Pongjanyakul et al.[39] prepared sodium alginate- magnesium aluminum silicate (SA-MAS) buccal films loaded with nicotine as a potential drug delivery system. The study revealed that the nicotine loaded SA-MAS films provided higher nicotine content and slower rate of nicotine across the mucous membrane than the nicotine loaded SA films. Obaidat et al. conducted a study to determine the feasibility of the formulation as a nicotine replacement product to aid in smoking cessation. The results of the study showed that xanthan mucoadhesive buccal patches are potential candidates for controlled biphasic nicotine delivery. These films helps in fast initial drug release followed by a controlled release over a period of 10 hours.[40]

### Management of oral candidiasis

Systemic antifungals such as fluconazole (100 mg/day for 1 or 2 weeks) are most preferred drugs for management of oral candidiasis. However, this dose of fluconazole could result in notable side effects varying from headache, nausea to liver dysfunction, and hepatic failure. The oral fluconazole may have variety of drug interactions including with oral hypoglycemics, coumarin-type anticoagulants, cyclosporin's, terfenadine, theophylline, phenytoin, rifampin, and astemizole. Thus, the systemic side effects of fluconazole can be reduced by increasing its oral concentration in oral fluids rather than systemic absorption. The reported topical efficacy of fluconazole together with the adverse effects and drug interaction of systemic fluconazole justifies the design of mucobuccal drug delivery system containing a small dose of fluconazole to increase the contact between the drug and the pathogenic yeast for a longer period of time.[41]

### Management of oral pain and inflammation

Inflammatory processes are one of the major reasons for oral cavity diseases such as gingivitis, periodontitis, stomatitis, aphthous ulcerations etc.[24] This problem is managed with topical administration of various NSAIDs like diclofenac, flurbiprofen, ketorolac, ibuprofen etc. The advantage of using mucobuccal patch containing the drug is the reduction of drug dose, drug localization in the target tissue and consequent less systemic side effects.[43] Perioli et al. designed sustained-release mucoadhesive bilayered tablets, using mixtures of mucoadhesive polymers and an inorganic matrix (hydrotalcite), for topical administration of flurbiprofen (20 mg) in the oral cavity. The study results showed better anti-inflammatory response and sustained release of drug in the buccal cavity for 12 hours and thus a reduction in daily drug dosage to 40 mg as compared to dose 70 mg in systemic treatment.[42]

### Management of postoperative periodontal pain

NSAID are most commonly prescribed drugs for postoperative periodontal pain. However, they have numerous side effects. As a result, nutraceuticals such as curcumin are widely used for its well-known safety and medicinal values. A split-mouth study was conducted to evaluate the efficacy of a curcumin mucoadhesive film for pain control after periodontal surgery among 15 patients with 30 sites. The study concluded that curcumin mucoadhesive film showed promising results in reducing postoperative pain and swelling over a period of 1 week, hence showing its analgesic effect after periodontal surgeries.[44]

### Management of herpes

Acyclovir, an antiviral drug is widely used in the management of oral herpetic lesions. Since the permeability of acyclovir is low in oral mucosa, the efficiency of acyclovir is greatly reduced. In a study by Nair et al, acyclovir was incorporated into the polymeric materials and formulated as nanoparticles. The prepared nanoparticles were then loaded into various films (F5-F7) prepared with varying quantities of hydroxyethyl cellulose and Eudragit RL 100. The prepared films were evaluated for physico-mechanical characters (mucoadhesion, swelling), in vitro acyclovir release and ex vivo diffusion. The results of the study showed adequate mucoadhesive strength and excellent physico-mechanical properties. This study concludes that the drug loaded nanoparticles impregnated buccal film could be an alternative approach to enhance the oral bioavailability of acyclovir, and need to be proved in vivo.[45]

### Management of aphthous stomatitis

Recurrent aphthous stomatitis (RAS) is one of the most common ulcerative diseases of the oral mucosa which is recurrent, painful and slow to heal. Treatment is primarily for pain relief, reduce healing time and the rate of recurrence. A study was conducted to prove the effectiveness of topical buccal bilayer mucoadhesive films containing sodium alginate and gellan gum loaded with low dose of 1 mg prednisolone sodium phosphate in reducing the treatment period and decrease side effects of systemic treatment. The bilayer films were thin, flexible with good water uptake, mucoadhesive and mechanical properties. The results of the study suggested that buccal application of the developed bilayer mucoadhesive films loaded with only 1mg of prednisolone provided mucoadhesive and convenient application and was able to promote RAS healing with shorter treatment duration.[46]

### Targeted therapy for oral cancer

Targeted therapy is the most desired treatment for oral cancer, aiming for specific site delivery and thereby lowering the side effects and levels of systemic toxicity.

The delivery of therapeutics through nanodelivery systems consisting of polymers or lipids have demonstrated increased solubility, stability and bioavailability, accumulating even inside tumor cells. A study was conducted for the development of a mucoadhesive patch of methotrexate (MTX) for targeted delivery in oral cancer. The developed liposomes and liposomes cast in the film formulation were evaluated for cytotoxicity in Haemopoietic stem cells (HSC-3) using an MTT assay, and a significant decrease in the half maximal inhibitory concentration of MTX was identified with the MTX-entrapped liposomal film, M-LP-F7. The results of the mitochondria-dependent intrinsic pathway demonstrated that there was significant mitochondrial membrane potential disruption with M-LP-F7 compared with the plain drug. M-LP-F7 increased the rate of apoptosis in HSC-3 cells by almost 3-fold. Elevated levels of reactive oxygen species provided evidence that M-LP-F7 exerts a pro-oxidant effect in HSC-3 cells.[47]

## CONCLUSION

A mucoadhesive drug delivery system offers numerous advantages in terms of economy, accessibility, administration, withdrawal and patient compliance. Mucoadhesive dosage forms provide prolonged contact time at the site of attachment, cost effective with high patient compliance. Buccal mucosa is well supplied with both vascular and lymphatic drainage and avoid extensive first pass drug metabolism, allows controlled drug delivery for extended periods of time. With the right dosage form design and formulation, the permeability and the local environment of the mucosa can be controlled and manipulated in order to accommodate drug permeation. However, the need for safe and effective buccal permeation is a crucial component for a prospective future in the area of buccal drug delivery. Additionally, these novel mucoadhesive formulations require much more research work to understand how to deliver drug clinically for the treatment of both systemic and topical diseases.

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