

Nanoparticles Loaded Mucoadhesive Buccal Patches - Review

Abstract

Drug distribution for both local and systemic conditions is significantly facilitated by buccal methods of administration. When a rapid beginning of action is necessary, they have proven to be a potent substitute for the conventional oral route, the buccal route is regarded as patient-friendly. Although many procedures have been explored, drug permeability and regulated drug release via this route of delivery remain concerns for the effective therapy. They have shown to be an effective alternative to the traditional oral route, especially when fast onset of action is required. The buccal route is considered patient friendly due to its non-invasive nature and ease of administration. Nanotechnology has advanced to the point that clinical uses have been considered. The use of nanoparticles in buccal dosage forms not only provides efficient distribution but also lowers biological system side effects. Many methods for loading and delivering drug-loaded nanoparticles to the buccal mucosa have been proposed, both for topical and systemic administration. The primary objective of this review is to provide an overview of the nanotechnological methods that have been so far developed to enhance the buccal administration of medications.

Key words: Nanoparticles, Buccal Patches, Nanotechnology, Bio/Mucoadhesion, Ethyl Alcohol

1. Introduction

Among the several medication delivery systems available, the oral drug delivery system is probably the most popular among patients.¹The mucoadhesion was initially developed in the 1980s to make it easier to distribute drugs under regulated conditions. This idea of mucoadhesion is a novel method for enhancing the effectiveness of various medication delivery methods.² However, it has some drawbacks, including hepatic first-pass metabolism and enzymatic breakdown in the gastrointestinal system, which limit the oral delivery of certain medication types, primarily peptides and proteins. The mucosal linings of the ocular, nasal, and oral cavity, as well as other transmucosal routes of drug delivery, have specific advantages versus peroral administration for systemic drug delivery. These advantages include the possibility of bypassing the first-pass effect, avoiding pre-systemic clearance in the gastrointestinal tract, and, depending on the prescription, a superior enzymatic flora for drug absorption. Among the several transmucosal routes, buccal mucosa has excellent accessibility, a large span of smooth muscle, and generally immobile mucosa, making it ideal for retentive dosage forms administration. Buccal adhesive drug delivery devices appear to be a feasible choice for ongoing study. To treat systemic and local disorders, the buccal mucosa lines the inner cheek, and buccal dosage forms are placed in the mouth between the upper gums and cheek. The buccal route is one of the possible routes for large, unstable proteins as well as hydrophilic oligonucleotides and polysaccharides, as well as traditional tiny pharmacological molecules. The mouth cavity has

been used to administer both systemic and local drugs. The following are the subcategories of drug distribution through the oral cavity membranes:

- The medicine was injected into the bloodstream via the mucosal membrane lining the mouth's floor.
- By placing a medicine between the cheeks and gums, the buccal drug delivery device transported the drug across mucosal membrane into blood circulation.
- The medicine was given into the mouth cavity via a local drug delivery device.¹

2. Nanoparticles and Nanotechnology

The focus of pharmaceutical research is shifting away from the synthesis of new chemical entities and toward the development of novel drug delivery systems for existing drug molecules in order to maximise their therapeutic and patient protection effects. Nanoparticles are gaining popularity in modern medicinal research due to their potential as a highly efficient medication delivery mechanism.³ Nanotechnology is fast emerging as a topic with applications in numerous fields of science and study for the purpose of creating new chemicals and molecules at the nanoscale level. The term "nano" refers to a billionth of a metre (10⁻⁹) or one billionth of a millimetre. Professor Norio Taniguchi of Japan coined the word "nanotechnology" in 1974 to describe the precision manufacture of nanometer-scale materials. Nanotechnology is a cutting-edge technology that offers a platform for the development and investigation of biological systems, as well as a variety of stimulus models for bio-assembled components. Optical and catalytic properties were demonstrated in nanostructured materials, whether inorganic or organic. These characteristics are mostly determined by the size and shape of the nanoparticles that have been created.³

2.1 The advantage of nanoparticle for buccal delivery

The use of nanoscale-based formulations is now one of the most notable approaches in improving medication permeability via buccal administration. The dosage forms contain nanoparticles by encapsulating or coating their surfaces, resulting in numerous medication delivery benefits. To improve buccal bioavailability, a poorly watersoluble drug can be improved by drug solubility, drug dissolution rates, or controlled drug release. Furthermore, nanoparticles have the ability to protect active pharmacological components, resulting in friendly and biodegradable dosage forms. Because the surface groups on nanoparticles interact with the buccal mucosa via hydrogen bonding, nanoparticles can improve the mucoadhesive behaviour of dosage forms. Aggregation and inhomogeneous distribution of big particles may impair mechanical films and mucoadhesive characteristics; thus, the possibility for aggregation and inhomogeneous distribution of large particles should be considered. However, the natural mucus barrier would be sticky to nanoparticles, or the nanoparticles would be caught in this barrier, resulting in a rapid clearance or an inadequacy of these particles for reaching the target area to exert a medical effect. Therefore, the nanoparticles are likely to be tailored to pass the mucus

barrier, specifically avoiding mucin filaments and steric restriction by the thick fibre mesh for the potential of penetrating the mucosal barrier. These "mucus penetration nanoparticles," which have controlled drug release capabilities at mucosal surfaces, can improve therapeutic efficacy while reducing side effects.⁴

Figure 1: Scheme of BDDS components from macromolecules to final products

Figure 1 shows the polysaccharides utilised in BDDS formulations, followed by the numerous shapes in which they can be generated at the micro and nanometric scale, and finally the dosage forms comprise these shapes, all of which are part of the BDDS system.⁵

3. Buccal Dosage forms

3.1 Buccal Patch

Due to their soft, flexible, and adhesive properties, films can deliver unidirectional or multidirectional medication release across the buccal mucosa, improving patient comfort. The phrase 'buccal patch' is sometimes used in scientific literature to refer to the mucoadhesive film. Cellulose derivatives, alginate, pectin, xanthan, carrageenan, hyaluronan, chitosan, and thiolated polysaccharides are among the polysaccharides commonly employed in film/patch compositions.⁵ Due to their greater patient acceptance, buccal patches have drawn a lot of attention in the drug delivery industry. This is mostly because of their simplicity in use, thinness, and flexibility, which cause the patient minimal discomfort.⁵⁰

3.2 Buccal Powders

When sprayed onto the oral mucosa of rats, hydroxypropyl cellulose and beclomethasone in powder form, a considerable increase in residence duration is noted compared to an oral solution, and 2.5 percent of beclomethasone is kept on buccal mucosa for over 4 hours.⁶

3.3 Mouthwashes

The majority of the current research on mouthwashes and oral rinses focuses on their utility in local antibacterial delivery. The mouthwash's substantiality allows for a significant antibacterial effect up to 7 hours after usage.⁷

3.4 Buccal Tablets

Dry dose forms called buccal mucoadhesive tablets must first be softened before being applied to the buccal mucosa. An illustration would be a double-layered tablet with an inner core of cocoa butter containing insulin and a penetration enhancer, and an adhesive matrix layer made of hydroxy propyl, cellulose, and polyacrylic acid on the outside (sodium glycocholate).⁸

3.5 Microspheres, microcapsules, micro particles

Microspheres, microcapsules, or microparticles at the point of adhesion induce less local irritation and give a comforting feeling of having a foreign item inside the oral cavity.⁹

3.6 Gels and ointments

Gels and ointments are examples of semisolid dose forms that have the benefit of being simple to spread over the mouth mucosa. As opposed to tablets, patches, or films, semisolid dosage forms may not provide the most precise drug dosage. The use of mucoadhesive formulations has improved the gels' poor retention at the application site. Some mucoadhesive polymers, like sodium carboxymethylcellulose (carbopol), transition from a liquid to a semisolid state. This alteration increases viscosity, which causes medications to release slowly and under control.¹

3.7 Lozenges

Include antibiotics, corticosteroids, local anaesthetics, antimicrobials, and antifungals that are used topically within the mouth. Because the medication release from lozenges is first high and then rapidly declines, numerous daily doses are necessary.¹¹

3.8 Wafers

Wafers are comparatively new formulations made by freeze drying polymeric gels or solutions. When applied to the buccal mucosa, they quickly hydrate and gel, presenting a sponge-like shape.⁴⁹

4. Mucus

Mucus is a thin, continuous jelly layer of translucent and viscid epithelium surface discharge made up of glycol proteins found in many bodily compartments including the respiratory and gastrointestinal tracts. In humans, a mucus layer with a thickness of 50-450 m serves as a drug sticky interface.¹² Although only around 10% of saliva is produced by sublingual and minor salivary glands, they combined create the majority of mucus and play a crucial role in preserving the mucin layer over the oral mucosa.¹³

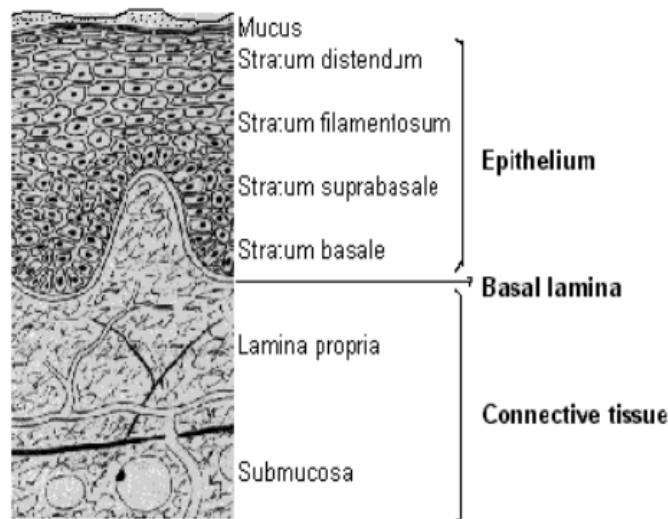


Figure 2: Cross section through Buccal Mucosa

4.1 Role of Mucus

- a. consisting of carbohydrate and proteins
- b. Lubrication
- c. Mucoadhesive drug delivery systems bioadhesion
- d. Cell-cell adhesion¹⁴

4.2 Functions of mucus layer

- a. Because of its hydrophobicity, the mucus layer has a protective character.
- b. The mucosal membrane is lubricated and kept wet by the mucus layer, which is one of its key functions.¹⁵
- c. Cell-cell adhesion¹⁶

5. Adhesion:

Mucus layer with cohesive characteristics permits molecules to adhere to a firm surface.

Mucus gives lubrication to the mucosal layer due to moisture in the mucus.¹²

5.1 Mechanism of Mucoadhesion

The two phases of the mucoadhesive polymer's adhesion to the mucin layer of the mucosal tissue are discussed below. The mucoadhesive polymer makes close contact with the mucous membrane during the contact stage, which results in the intimate wetting, spreading, and swelling of the mucoadhesive formulation. The mucosal membrane's ability to retain mucus facilitates these activities. At the consolidation stage, physical entanglement and secondary interactions, like hydrogen bonds, van der Waals forces, and electrical attractions, cause the polymer of the mucoadhesive formulation to penetrate the mucosal surface.¹⁷

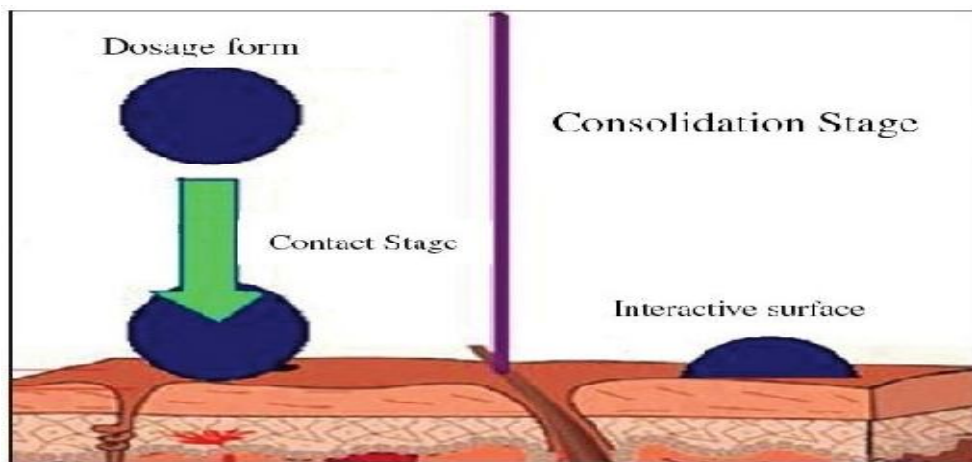


Figure 3: The stages in mucoadhesion

The mucoadhesion mechanism can be divided into two stages:

5.2 Contact stage

The biopolymer and an outer layer must be sufficiently submerged for the bioadhesive to come into close contact (wetting) with the mucus barrier. Alternatively, the bioadhesive may swell.

5.3 Consolidation stage

Various physicochemical interactions take place, such as hydrogen bonding, hydrophobic interactions, and dispersion forces, to consolidate and increase the adhesive junction, resulting in sustained adherence.¹

6. Specifications to carry out the dissolve tests for buccal Patches

When compared to G.I. dissolution, buccal dissolution differs in the following ways.

- lower volume (of saliva)
- a brief period of time (in mouth)
- Transfer of solids
- Makeup of the fluid (saliva composition)
- partial dissolution

The dissolution apparatus must meet the aforementioned Specifications to carry out the dissolve tests for buccal Patches.¹⁸

7. Types

7.1 Matrix

This dosage form is made up of a mixture of the medicine, adhesive, and additive.

7.2 Reservoir type

A reservoir with a cavity for the medicine and additives separate from the adhesive makes up this method. To manage the direction of medication distribution, to lessen patch deformation and disintegration while in the mouth, and to stop drug loss, an impermeable backing is used. The patch can either be built to degrade only slightly when placed in the mouth or it can be made to dissolve almost instantly.¹⁹

8. Definition of bio adhesion

The term "bio adhesion" describes how natural polymer adheres to soft tissues like epithelial cells in bio adhesive drug delivery systems. The adhesion interactions between polymers and mucus or mucosal surfaces are referred to as mucoadhesion.²⁰

8.1 Theories of Mucoadhesion

The phenomena of mucoadhesion is explained by five main ideas.

8.2 Electronic theory

This notion is based on the fact that both mucus and biological components have opposing electrical charges, allowing for the formation of a double electronic layer at the edge, which aids in the assessment of mucoadhesive strength.¹²

8.3 Wetting theory

The wetting theory emphasises the close contact between the adhesive and the mucus in its primary application to liquid bio adhesive systems. As a result, structural similarity, the degree of cross linking of the sticky polymer, or the application of a surfactant all influence the wetting surface. When an interface is established, the work of adhesion [expressed in terms of surface and interfacial tension (γ) is defined as energy per cm^2 released.²¹

8.4 Diffusion theory

According to this theory, mucoadhesive polymer diffuses into the mucus layer by disrupting the glycoprotein chain network. This diffusion is time dependent and is influenced by both phases' diffusion coefficients and molecular weight.¹²

8.5 Fracture theory

It is measured how much force is required to separate the polymer from the mucus. The mechanical strength of mucoadhesion was measured as the foundation for this theory.²²

8.6 Adsorption theory

The most widely recognised theory of mucoadhesion mechanism involves weak Vander Waals forces and hydrogen bond mediated adhesion. In order to display semi-permanent surface interactions, it requires primary and secondary bonding.¹²

8.7 Mechanical theory

According to mechanical theory, adhesion happens when an adhesive interlocks with a rough surface. More surface area is available for contact on the rough surface.²³

9. Factors affecting Mucoadhesion

9.1 Polymer related factors

Several characteristics of the active polymer are important in mucoadhesion. Concentration, swelling, polymer molecular weight, particular conformation, and polymer chain flexibility both are factors that can influence mucoadhesion.¹

9.2 Initial contact time

The initial time of contact between the muco-adhesive polymer and the mucus layer causes enhanced swelling as well as the interpenetration chain of the muco-adhesive polymer. As a result, the mucoadhesion strength of the polymer chain increases.¹⁶

9.3 Hydrogen bonding capacity

Hydrogen bonding is another essential component in polymer mucoadhesion. Park and Robinson discovered that in order for mucoadhesion to occur, desired polymers must have functional groups able to form hydrogen bonds. They also demonstrated that polymer flexibility is critical for improving hydrogen bonding potential.⁹

9.4 Hydration (swelling)

Hydration is essential for a muco adhesive polymer to expand and form a suitable "macromolecular mesh," as well as to induce mobility in the polymer chains in order to improve the interpenetration process between polymer and mucin.²¹

10. The components of buccoadhesive patches

10.1 Active Pharmaceutical Ingredient (API)

Buccal patches are used to administer a wide range of active medicinal ingredients. Large-scale pharmaceuticals are difficult to incorporate, but the active ingredient in buccal patches has a size limit.²⁴

10.2 Polymers (adhesive layer)

hydroxyethyl cellulose, hydroxypropyl cellulose, polyvinyl pyrrolidone, polyvinyl alcohol, carbopol, and others.⁶

10.3 Diluents

Lactose, microcrystalline starch, and starch are the diluents utilised in buccal patches.²

10.4 Sweetening agents

Sucralose, aspartame, and mannitol are used as sweeteners.²⁴

10.5 Flavouring agents

Menthol, vanillin, clove oil, Peppermint oil, cinnamon oil, spearmint oil, vanilla, cocoa, and chocolate are some of the flavouring compounds utilised in formulations.²⁴

10.6 Penetration enhancer

Cyano acrylate, etc.⁶

10.7 Backing layer

Polyvinyl alcohol, ethyl cellulose, and so on.⁶

11 Methods for preparation of Patches

11.1 Solvent casting method

The solvent-extraction method is mostly used to prepare the buccal film, in which water-soluble components are dissolved to create a clear, viscous solution. A tiny amount of solution is used to dissolve the active medicinal ingredient and other ingredients, which are then combined with

bulk. Then, the mixture is poured into the aqueous solution. Remove any trapped air, and the resulting mixture is cast as patches, dried, and then cut into the required shapes.²³

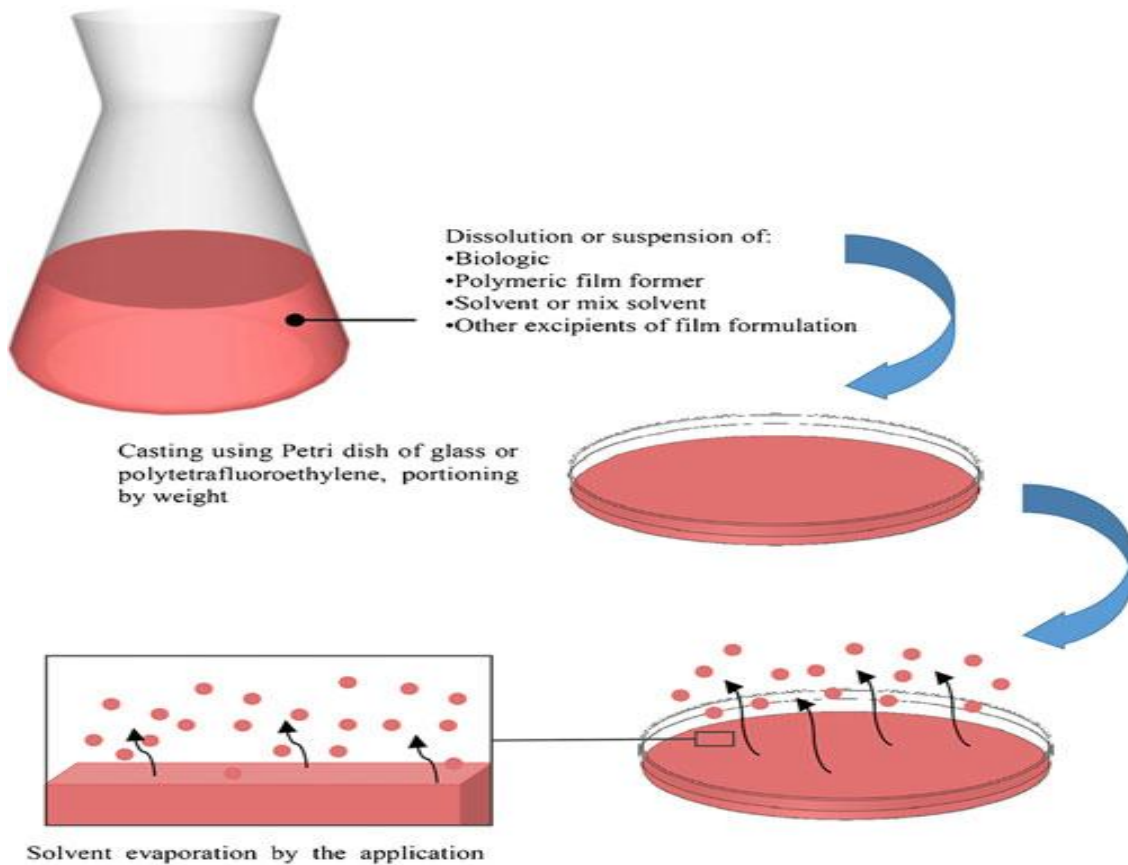


Figure 4: Schematic diagram of the solvent casting film manufacturing process

11.2 Direct milling

Patches are created without the use of solvents in this method. For motorised mixing of medicine and excipients without the presence of any liquid solution, direct milling or kneading procedures are used. Rolling the resulting material achieves the desired thickness. After that, the backing material is laminated. Because there is no risk of leftover solvents or health risks caused by solvents, the solvent-free option was chosen.²⁴

11.3 Semisolid Casting method

The initial step in semisolid casting is to make a water-soluble film-forming polymer solution. The solution is then mixed with a sodium hydroxide solution of an acid-insoluble polymer (cellulose acetate phthalate). The needed amount of plasticizer is then added, resulting in a gel mass. The gel mass is then shaped into films or ribbons using heat-controlled drums. The

thickness of the film ranges from 0.015 and 0.05 inches. Use a 1:4 acid-insoluble polymer ratio.²⁶

11.4 Hot melt extrusion

The hot melt extrusion method involves melting a mixture of medicinal components and forcing it granules, and oral through an aperture to produce various shapes. Controlled release matrix tablets, pellets, disintegrating films dosage forms have all been made by hot melt extrusion. Immiscible components are extruded with the medication, and then solid dispersions are created. Finally, dies are used to mould the solid dispersions into films.²⁴

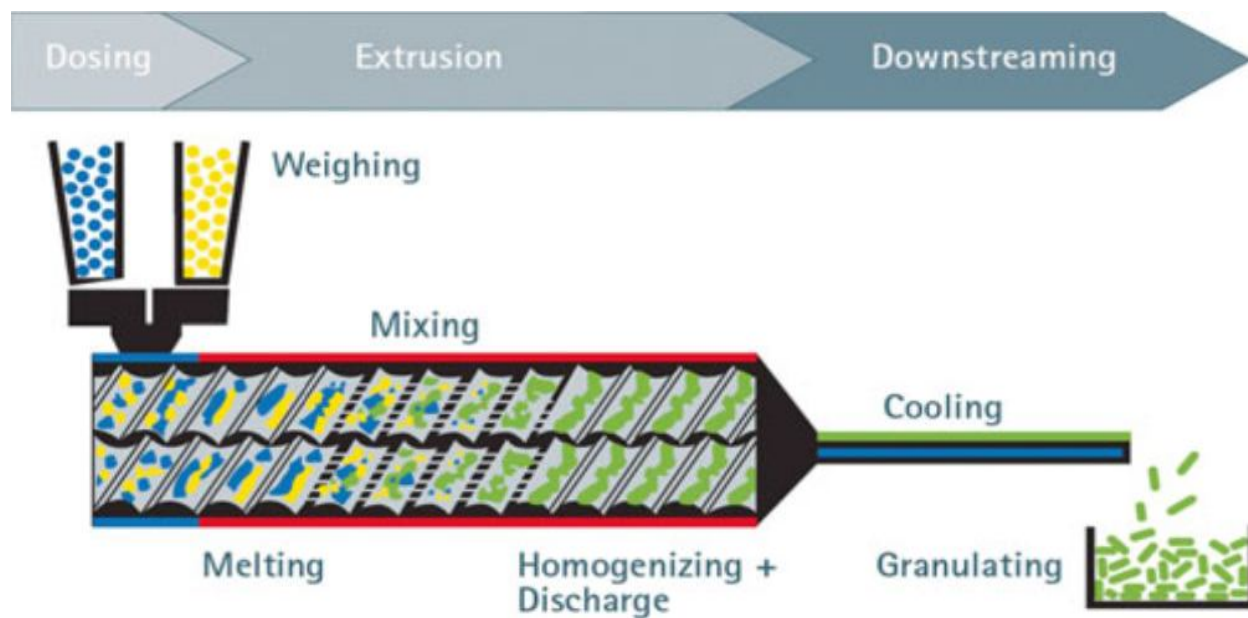


Figure 5: The manufacture of films via hot melt extrusion is depicted in this diagram

11.5 Solid dispersion extrusion method

This immiscible component is extruded with the medication, and solid dispersions are subsequently formed. The solid dispersions are then formed into films using dies.²⁷

11.6 Rolling method

A drug-containing solution or suspension is rolled on a carrier in this approach. Water and a combination of water and alcohol make up the majority of the solvent. The film is cut into suitable shapes and sizes after being dried on rollers.²⁴

12 Evaluation Parameters of Buccal Patches

12.1 Surface pH

Buccal patches were put to the surface of previously prepared agar media plates for 1 hour, and pH was evaluated by using pH paper on the swelled patch's surface.²⁴

12.2 Thickness measurements

The measurement is done with a screw gauge with a minimum count of 0.01 thickness. The thickness was measured five times and the average value calculated.²⁴

12.3 Swelling study

The buccal patch is weighed and placed in a 1.5 percent agar gel plate, which is then incubated at 37°C. The patch is taken from the petri dish and any further surface water is thoroughly desiccated using the filter paper every one hour time intermissions up to three hours. The swelling index is calculated after reweighing the swollen patch.²⁴

12.4 Folding endurance

The patch's folding endurance was measured by folding it in the same spot until it broke. The value of folding endurance was determined by the number of times the patch could be folded at the same location without breaking.²⁷

12.5 Thermal analysis study

A differential scanning calorimeter is used to do the thermal analysis (DSC).²⁶

12.6 Permeation study of buccal patch

The receptor compartment is filled with phosphate buffer pH 6.8, and the hydrodynamics are maintained in the receptor compartment by swirling at 50 rpm using a magnetic bead. At regular times, samples are taken and tested for drug content.²⁶

12.7 Percentage moisture loss

Film integrity is checked with this. After being trimmed, the film is weighted. Following storage in a desiccator with fuse anhydrous calcium chloride. It is taken out and weighed after 72 hours. The formula below can be used to calculate average % moisture loss.²⁸

$$\text{Percentage Moisture Loss} = (\text{Initial weight} - \text{final weight}) / \text{Initial weight} \times 100$$

12.8 Drug Content uniformity

Buccal film is separately dissolved in 100 ml of pH 6.8 buffer, and the combination is then appropriately diluted. At 242 nm, the amount of medication in the film is determined by spectrophotometric absorbance measurement. An estimate of drug content on average is made.²⁸

12.9 Buccal patches morphological characterization

The morphological characteristics of patches are studied using a scanning electron microscope.²⁴

12.10 In-vitro release

The in vitro release investigation is performed at 100rpm with a USP dissolving equipment type 2 in 400ml drug soluble media. To prevent patches from floating over the disintegration media, a 2 cm² patch is taken and attached to a glass side. The cumulative percent release is estimated after measuring the sample's absorption with a UV-visible spectrometer.²⁹

12.11 Stability study

Patches are placed in an aluminium foil-lined beaker and housed in a humidity chamber for one month at 40°C and 75% relative humidity. At the conclusion of each week, the appearance and medication content of the stored patches are examined.³⁰ Researchers are currently searching for new drug transport mechanisms outside of conventional polymer networks. Currently, the most successful oral dosage forms on the market are solid dosage forms, liquids, and gels. The distribution of tiny proteins and peptides and vaccine formulations represent the future of buccal adhesive medication delivery.³¹

13 Packaging of buccal film

In the pharmaceutical industry, it is critical that the package chosen appropriately protects the product's integrity. To protect the dosage form during manufacturing and storage, expensive packaging, precise processing, and particular attention are required. For films, which are medicinal items, single packaging is required; the most typical packaging shape is an aluminium bag. The Rapid card is a customised and patented packaging mechanism developed by APR-Labtec specifically for the Rapid films. Each side of the fast card stores three rapid films and is the same size as a credit card. Every dose can be taken separately.³²

The chosen material must possess the following properties.

13.1 They must safeguard the preparation against the elements.

13.2 They must be approved by the FDA.

13.3 They must pass all required tamper-resistance tests.

13.4 They should not react to the product.

13.5 They must not transmit any flavours or scents to the product.

13.1 Foil, paper or plastic pouches

The flexible pouch is a packaging design capable of offering not just a package that is temperature resistant, but also a product that is environmentally friendly due to good material selection. A flexible pouch is normally made by vertical or horizontal forming, filling, or sealing machinery during the product filling operation. Single pouches or aluminium pouches can be used.³²

13.2 Single pouch and Aluminum pouch

A peelable pouch for "rapid dissolve" soluble films with high barrier qualities is a soluble film drug delivery pouch. For product display, the pouch is transparent. The usage of a two-structure combination allows one side to be clear and the other to be laminated with a cost-effective foil. Gas and moisture transmission are virtually non-existent through the foil lamination. The package has a flexible thin film alternative for nutraceutical and pharmaceutical products, as well as the lid stock, which seals the blister. Heat softens a sheet of thermoplastic resin, which is then vacuum-drawn into a shaped mould to create the blister package. After cooling, the sheet is removed from the mould and sent to the packing machine's filling station. The product is placed into the semi-rigid blister that was previously made, and the heat sealable backing material is used to close it. Aluminum foil is commonly used for the lid stock. Plastic is commonly used to make the cavity, which can be engineered to protect the dosage form from moisture.³²

13.3 Barrier Films

Because many pharmacological preparations are particularly sensitive to moisture, strong barrier coatings are required. Polychlorotrifluoroethylene (PCTFE) film and Polypropylene are two materials that can be utilised to provide moisture protection. Under no circumstances can polypropylene stress crack. It works well as a gas and vapour barrier. The lack of clarity is a disadvantage. The single dose pouch protects both the substance and the dosage. The most frequent type of bag is aluminium.³²

14 Stability Studies in Human Saliva

Buccal patches are tested for stability in natural human saliva. Human saliva is gathered from people (age 18-50 years). Buccal patches are placed in separate Petri plates with 5 ml of human saliva and baked for 6 hours at 37°C 0.2°C in a temperature-controlled oven. The patches are checked at regular intervals (0, 1, 2, 3, and 6 hours) for changes in colour, shape, and drug content.²⁹

14.1 Functions of Saliva

- a. Buffer Capacity
- b. Dilution and Cleaning
- c. Lubrication Digestion and

d. Integrity of Tooth Enamel Protection³³

15 Merits

- a. The oral mucosa has a plentiful supply of blood. Drugs enter the systemic circulation through the deep lingual or face vein, internal jugular vein, and brachiocephalic vein after being absorbed through the mouth mucosa.
- b. Patients can control the period of administration or terminate delivery in case of emergencies. The buccal drug delivery systems easily administered into the buccal cavity. The novel buccal dosage forms exhibit better patient compliance.
- c. Buccal patches are well known for their easy accessibility to the tissues that line the mouth cavity, which makes administration comfortable and painless.³⁴

16 Patents and commercial products approved for oral transmucosal administration

In order to improve transmucosal administration, numerous dosage forms, including tablets, lozenges, gels, patches, films, and microspheres, have been created. The majority of items that are commercially advertised are pills and lozenges. Few businesses were successful in creating patches and films for quick drug release and clinical results.³⁵

17 Advantages of buccal drug delivery

- Because of the large surface area, the drug disintegrates and dissolves quickly in the oral cavity, promoting systemic absorption of the active pharmaceutical ingredient.
- There is no danger of choking.³⁶
- Quick operation formed.
- High blood flow rates and a good blood supply lead to rapid absorption.
- Improved interaction with the client.³⁷
- Precise administration of the dosage
- Increased safety and stability³⁸
- If there are any negative reactions, it is simple to remove from the administration site.³²
- Gels and ointments for the buccal mucosa are semi-solid dosage forms that have the benefit of being simple to apply to the mucosa.³⁹

18 Disadvantages of buccal drug delivery

The buccal membrane is less permeable than the sublingual membrane.

- There is a limited amount of surface area available for absorption.
- This route cannot be used to administer medications that irritate the mucosa, have a bitter or unpleasant taste, or emit an obnoxious odor.
- This route is unsuitable for drugs that are unstable in the pH of the buccal environment.
- The continuous secretion of saliva (0.5-2 l/day) results in dilution of the drug.
- Large-dosage medications are difficult to administer.³⁰

19 Limitations in buccal patches

- The absorptive membrane has a smaller surface area. If the dimensions of a delivery system dictate the effective area for absorption, this area becomes even smaller.⁴⁰
- Only drugs with lower dose requirements are permitted to be administered.⁴¹
- Drugs may be swallowed with saliva, negating the benefits of the buccal route.
- Eating and drinking may be restricted.⁴¹
- Only the medication that required a tiny dose can be delivered.
- The ability to eat and drink may be limited.
- Drugs that become unstable at the pH of the buccal cavity cannot be given.⁴²

20 Applications of buccoadhesive patches

Drugs with poor bioavailability and quick enzymatic degradation after oral administration have the advantages of high accessibility and low enzymatic activity. Hydrophilic polymers like SCMC, HPC, and polycarbophil were utilised in these systems to transport peptides, proteins, and polysaccharides for the treatment of periodontal disorders.⁴⁴ Numerous problems have been observed, including the need for special packaging for product stability and safety, large doses, trouble with dose uniformity, the hygroscopic nature of the medication, and high doses.⁴⁵

21 Future Perspectives and Directions

The difficulties posed by medications that are subject to high first-pass metabolism in the liver and pre-systemic clearance in the gastrointestinal tract have prompted pharmaceutical researchers to develop and market alternate drug delivery systems. Buccal delivery, which can be used for both systemic and local activities, has offered drug delivery studies new dimensions. Many commercial products have resulted from the concentrated and resolute efforts of scientists all across the world, including Zilactin, Pilobuc, and the BEMA system, among others.⁴⁶ The buccal mucosa has a number of advantages when it comes to regulated drug administration over long periods of time. Both vascular and lymphatic drainage are well-supplied in the mucosa. Novel medication delivery techniques, including as nanoparticles and microspheres, are also being investigated for their potential in buccoadhesion. However, the necessity for safe and effective buccal permeation/absorption enhancers is a critical component for a promising future in the domain of systemic buccal drug administration, while a product's acceptable organoleptic profile remains a caveat for both locally and systemically effective systems.⁴⁷ Many of the aspects and developments discussed in this article are promising for therapeutic formulations in the future. The use of mucoadhesive polymers in drug delivery for targeted delivery of specific drugs to easily accessible mucosal surfaces such as buccal, nasal, ocular, and vaginal mucosae appears to have the brightest future. Finally, by revolutionising mucosal research and investigations, the pharmaceutical horizon will be expanded and novel possibilities will emerge.⁴⁵ Currently, scientists are working to develop buccal adhesive systems using various approaches to improve the bioavailability of orally less/inefficient drugs by manipulating formulation strategies such as the inclusion of pH modifiers, enzyme inhibitors, permeation enhancers, and so on. A novel buccal adhesive delivery system that directs drug delivery to the buccal mucosa while protecting the local environment is also gaining interest. Solid dosage

forms, liquids, and gels applied to the oral cavity are currently commercially successful.⁴⁶ It might not be too far-fetched to imagine more and more nasal goods using mucoadhesive polymers in the future, according to the authors, who predict that both academic and industrial efforts will be made to investigate this new area of mucoadhesive drug delivery, such as nasal medication administration.⁴⁸

22 Marketed available products

Table 1: Marketed available products

S.NO	Name of the drug	Brand name	Generic name	uses
1	Acyclovir	Zovirax	Acyclovir	Used to treat fever, blisters.
2	Glimepiride	Amaryl	Glimepiride	Used to treat type 2 diabetes mellitus.
3	Salbutamol	Combivent	Salbutamol	Used to treat Asthma, Bronchitis.
4	Miconazole	Oravig	Miconazole buccal tablets	Used to treat fungal infections affecting with vagina.
5	Metronidazole	Metrocream	Metronidazole	used to treat bacterial infections, as well as prevent postoperative infections.
6	Propranolol	Innopran	Propranolol	used to treat hypertension, angina, atrial fibrillation, myocardial infarction, migraine.

7	Omeprazole	Prilosec	Omeprazole	used to treat Gerd associated conditions such as heartburn and gastric acid hyper secretion, and to promote healing of tissue.
8	Pantoprazole	Protonix	Pantoprazole	used to treat erosive esophagitis, gastric acid hypersecretion, and to promote healing of tissue damage caused by gastric acid.
9	Theophylline	Uniphyll	Theophylline	used to manage the symptoms of asthma, and lung conditions caused by reversible airflow obstruction.
10	Carbamazepine	Carbatrol	Carbamazepine	used to treat various types of seizures and pain resulting from trigeminal neuralgia.

Conclusion

Systemic medication distribution is greatly facilitated by buccal methods of administration. In particular when a rapid beginning of action is required, they have proven to be a successful alternative to the conventional oral route. Additionally, they are helpful for individuals who struggle to swallow as well as for medications that are highly cleared by the liver or degraded in the gastrointestinal tract. Additionally, buccal adhesive dose forms have been utilised to treat

local conditions at the mucosal surface (such as mouth ulcers) in order to lower the overall dosage requirement and reduce any potential negative effects from systemic drug administration. Researchers are currently searching for new drug transport mechanisms outside of conventional polymer networks. With an emphasis on mucoadhesive films, several effective methods for administering drug-containing nanoparticles via buccal delivery have been suggested. Surprisingly, multilayer films comprising nanostructure materials have been proposed as a means of facilitating the distribution of nanoparticles, with benefits including strong adherence and the avoidance of nanoparticle diffusion in saliva.

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