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A Short and Constricted Review on Buccal mucoadhesive patches

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ABSTRACT: Buccal mucoadhesive patches are a novel drug delivery system that adheres to the buccal mucosa, providing controlled drug release for an extended period. They offer several advantages over traditional drug delivery systems, including avoiding first-pass metabolism and improving patient compliance. Recent research has focused on improving their performance, including novel materials, modification of drug release profiles, and permeation enhancements. This review provides an overview of these patches, their composition, mechanism of action, and potential applications in drug delivery

Key words: Mucoadhesive patches, Controlled release, Penetration enhancer.

INTRODUCTION:

Buccal patches are a type of mucoadhesive dosage form that adhere to the inner lining of the cheek or the gums. They offer several advantages over other drug delivery methods, particularly for localized drug delivery. One of the main advantages of buccal patches is that they provide direct entry to the systemic circulation, bypassing the hepatic first-pass metabolism that can reduce the bioavailability of orally administered drugs. This allows for a more rapid onset of action and a higher drug concentration at the site of action. In addition, the systemic effects of the drug can be better controlled with buccal patches, as the drug is released slowly and steadily over time.Another advantage of buccal patches is that they are less likely to be affected by enzymatic degradation than orally administered drugs. The enzymes in the gastrointestinal tract can break down many drugs, reducing their effectiveness. However, buccal patches avoid this problem, as they are placed directly on the oral mucosa, where there is little enzymatic activity.[(1)]

Buccal patches are also suitable for drugs or excipients that may be mildly damaging, such as some antibiotics or antifungal agents. These drugs can cause irritation or damage to the lining of the gastrointestinal tract, but they can be safely administered via buccal patches. Another advantage of buccal patches is that they are painless to administer and can be easily removed if necessary. This makes them a more patient-friendly option than some other drug delivery methods, such as injections or implants.

Buccal patches also offer great flexibility in designing release systems for local or systemic action. They can be designed to release the drug slowly and steadily over time, providing sustained release for systemic effects, or they can be designed to release the drug rapidly for local effects.

Finally, buccal patches are highly versatile and can be used for a wide range of drugs and therapeutic applications. They are particularly useful for localized drug delivery, such as in the treatment of periodontal disease or pain management.

Composition:
The composition of buccal patches typically includes [2]
- Active ingredient
- Mucoadhesive polymers such as hydroxy ethyl cellulose and carbopol
- Diluents like lactose DC or microcrystalline starch
- Sweetening agents such as sucralose or mannitol
- Flavouring agents like menthol or clove oil
- Backing layer made of ethyl cellulose.
- Penetration enhancers like cyanoacrylate and plasticizers such as PEG-100 and propylene glycol.

Types of Buccal Patches:
Matrix: In this typebuccal patches consist of a combination of drug, adhesive, and additives that are mixed. [3]
Reservoir: In this type buccal patches have a separate cavity for the drug and additives, which is isolated from the adhesive. An impermeable backing is applied to control the direction of drug delivery, minimize patch deformation and disintegration while in the mouth, and prevent drug loss. [4]

Mechanism of action:
Adhesion refers to the attachment of two surfaces due to valence interfacial forces or interlocking action. When a synthetic or natural material adheres to a biological surface, it is called bioadhesion, while the adhesion of a material to mucus and/or an epithelial surface is called mucoadhesion. Mucoadhesion occurs in two stages: the contact stage, where wetting, spreading, and swelling of the bioadhesive surface create close contact between a bioadhesive and a membrane, and the consolidation stage, where attractive forces between the two surfaces overcome repulsive forces. Consolidation occurs through either the diffusion theory or the dehydration theory, depending on the properties of the material and mucus. [5]
Advantages of Buccal patches:
- Buccal patches offer several advantages for drug delivery. The oral mucosa has a rich blood supply, allowing for drugs to be absorbed through it and transported directly into the systemic circulation via veins like the deep lingual or facial vein, internal jugular vein, and in nominate vein. [6]
- Bypasses the first-pass effect and avoids contact with digestive fluids that may degrade certain drugs, such as insulin, proteins, peptides, and steroids. Additionally, the rate of drug absorption is not affected by food or gastric emptying rate.
- The buccal membrane has a sufficiently large area to allow for drug delivery systems to be placed on either the left or right side, and administration is painless and comfortable for patients. [8]
- Patients can also control the duration of drug delivery and terminate it in case of emergencies. Overall, buccal drug delivery systems offer better patient compliance compared to other forms of drug administration. [7]

Method of preparation:
Transdermal patches are a popular drug delivery system that allows drugs to be absorbed through the skin and directly into the bloodstream, bypassing the digestive system. These patches can be prepared using different methods, including solvent casting and direct milling.
Solvent casting:
It involves dispersing the drug and other patch excipients in an organic solvent and coating the mixture onto a sheet of release liner. The solvent is then evaporated, leaving a thin layer of the patch on the release liner. A protective backing material is laminated onto the sheet, and the patches are die-cut to the desired size and shape. Solvent casting is a well-established method that can produce high-quality patches, but it has some drawbacks, such as the possibility of residual solvent and associated health issues. [11]

Direct milling:
It involves mixing the drug and other patch excipients by mechanical milling or kneading, usually without the use of any liquids. The resulting material is then rolled onto a release liner until the desired thickness is achieved. A protective backing material is laminated onto the sheet, and the patches are cut to size. Direct milling is preferred over solvent casting because it eliminates the use of solvents, which can cause health issues and leave residues in the patches.

Solid dispersion extrusion:
Solid dispersion extrusion is a method where immiscible components are combined with a drug and extruded to prepare solid dispersions, which are then shaped into films using dies.

Semisolid casting:
Semisolid casting involves first preparing a solution of a water-soluble film-forming polymer, which is then added to a solution of an acid-insoluble polymer (such as cellulose acetate phthalate or cellulose acetate butyrate) that has been prepared in ammonium or sodium hydroxide. A plasticizer is added to create a gel mass, which is then cast into films or ribbons using heat-controlled drums. The resulting films are typically 0.015-0.05 inches thick, and the ratio of acid-insoluble forming polymer to water-soluble film-forming polymer should be 1:4.

Rolling method:
In the rolling method, a solution or suspension containing the drug is rolled onto a carrier using water or a mixture of water and alcohol as the solvent. The resulting film is then dried on rollers and cut into the desired shapes and sizes.

Hot melt extrusion:
Hot melt extrusion involves first mixing the drug with carriers in solid form, and then using an extruder with heaters to melt the mixture. The resulting melt is then shaped into films using dies. This method has several benefits, including fewer operation units, better content uniformity, and an anhydrous process.

Limitations:[9]
Mucoadhesive drug delivery has some limitations.

- Drugs that are unstable at buccal pH cannot be administered using this route, and drugs with unpleasant taste, nauseating odour, or that cause irritation cannot be given this way.
- This route is suitable only for drugs with a small quantity or dose and those that can be absorbed by passive diffusion. Additionally, drinking and eating may need to be avoided during drug delivery through this route. [10]

Factors affectingMucoadhesion:[12]
Mucoadhesion depends on the properties of the bioadhesive polymer and the surface on which it is present.

Molecular weight:
High molecular weight polymers promote physical entanglement, while low molecular weight polymers favour better mucus layer penetration.

Hydrophilicity:
Hydrophilic functional groups and flexibility aid in mucoadhesion, while high concentrations of polymer can reduce adhesion properties.

Cross-linking density:
Cross-linking density and swelling can affect polymer swelling and water diffusion into the polymer, resulting in lower interpenetration rates.

Charge:
Anionic polymers have stronger mucoadhesive properties, and some cationic polymers like chitosan show higher bioadhesive properties in neutral or alkaline mediums. [13]

Evaluation of buccal patches:[14]

1. **Surface pH measurement**: To measure the surface pH, buccal patches are placed on an agar plate and allowed to swell for two hours. A pH paper is then placed on the surface of the swollen patch to measure the pH.
2. **Thickness measurement**: The thickness of each buccal film is measured at five different locations (the centre and four corners) using an electronic digital micrometre.
3. **Swelling study**: To study the swelling of buccal patches, each patch is weighed individually (designated as W1) and placed in a 2% agar gel plate. The gel plates are then incubated at 37°C ± 1°C, and the patches are examined for any physical changes at regular one-hour intervals for up to three hours. After each time interval, the patches are removed from the gel plates and excess surface water is carefully removed using filter paper. The swollen patches are then reweighed (W2), and the swelling index (SI) is calculated using the following formula:SI = (W2 - W1) / W1. [15]
4. **Folding endurance:** The folding endurance of buccal patches is determined by repeatedly folding one patch at the same place until it breaks or is folded up to 200 times without breaking.
5. **Thermal analysis study:** To perform thermal analysis, a differential scanning calorimeter (DSC) is used.
6. **Morphological characterization**: The morphology of the buccal patches is studied using a scanning electron microscope (SEM).
7. **Water absorption capacity test:** Circular patches with a surface area of 2.3 cm^2 are placed on agar plates prepared in simulated saliva and kept in an incubator at 37°C± 0.5°C. At various time intervals (0.25, 0.5, 1, 2, 3, and 4 hrs), the patches are weighed (wet weight) and then dried for seven days in a desiccator over anhydrous calcium chloride at room temperature. The final constant weights are then recorded, and the water uptake (%) is calculated using the following equation: Water uptake (%) = (Ww – Wi)/Wf x 100,
   Where Ww is the wet weight,
   Wi is the initial weight, and
   Wf is the final weight. The swelling of each film is also measured.
8. **Permeationstudyof buccal patches:** It is conducted by filling the receptor compartment with phosphate buffer pH 6.8. The hydrodynamics in the receptor compartment are maintained by stirring with a magnetic bead at 50 rpm. Samples are collected at predetermined time intervals and analyzed for drug content.
9. **Measurement of mechanical properties:** To measure the mechanical properties of the films or patches, tensile strength and elongation at break are assessed using a tensile tester. A film strip with dimensions of 60 x 10 mm and without any visible defects is cut and placed between two clamps separated by a distance of 3 cm. The lower clamp is held stationary, and the upper clamp moves at a rate of 2 mm/sec to pull the strip apart until it breaks. The force and elongation of the film at the point of breakage are recorded. Tensile strength and elongation at break values are calculated using the following formula: T = m x g/ b x t Kg/mm^2, where M is the mass in grams, g is the acceleration due to gravity (980 cm/sec^2), B is the breadth of the specimen in cm, and T is the thickness of the specimen in cm.
10. ***In Vitro* drug release:**The drug release from bilayered and multi-layered patches is studied using the USP XXIII-B rotating paddle method. The dissolution medium used is phosphate buffer pH 6.8, and the release is carried out at 37°C ± 0.5°C with a rotation speed of 50 rpm. The glass disk is attached to the bottom of the dissolution vessel, and the backing layer of the buccal patch is fixed to the disk using instant adhesive material. Samples of 5 ml are taken out at predetermined time intervals, and fresh medium is added to maintain the volume. The drug content of the samples is analyzed after appropriate dilution. For *in vitro* buccal permeation through the buccal mucosa of sheep and rabbit, Keshary-Chien/Franz type glass diffusion cell is used at 37°C± 0.2°C. The donor compartment is filled with buffer, and 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 are clamped together.

CONCLUSION:

The buccal mucosa is a highly attractive site for controlled drug delivery due to its rich blood and lymphatic supply, which allows for systemic delivery of drugs while bypassing the first pass metabolism in the liver and pre-systemic elimination in the gastrointestinal tract. Additionally, the buccal mucosa is ideal for retention of a drug delivery device, making it an appealing option for patients. Further research in the field of buccal drug delivery is needed to optimize the use of this route of administration and to develop new drug delivery technologies that can enhance drug absorption and retention. With the ongoing advancements in drug delivery systems, buccal drug delivery is likely to remain an important area of research and development for the delivery of a wide range of drugs.

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