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Pharmaceutical Sciences **Review Article……!!!**

‘‘MUCOADHESIVE BUCCAL PATCHES- A REVIEW”

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ABSTRACT

The buccal cavity, a region of the mouth that has recently been the subject of extensive research, may convey both small and large molecules. By-passing first-pass metabolism, this method allows for the delivery of medicines straight into the systemic circulation. Several *ex-Vivo* mucoadhesion parameters, such as mucoadhesive strength, force of adhesion, and bond strength, as well as weight fluctuation, thickness, folding endurance, drug content, moisture content, and moisture absorption, were assessed. All these manufactured patches adhered to first-order release kinetics and were maintained for 24 hours. The study was planned, and a commercial semipermeable membrane was used in its execution. Using swine buccal mucosa, an *ex-Vivo* drug permeation investigation was also carried out, and factors like flow and lag time were identified. Several *ex-Vivo* mucoadhesion parameters, such as mucoadhesive strength, force of adhesion, and bond strength, as well as weight fluctuation, thickness, folding endurance, drug content, moisture content, and moisture absorption, were assessed. A study on the release of drugs in *in-Vitro* study was planned, and commercial semipermeable membrane was used in its execution.

INTRODUCTION:

The buccal mucosa is regarded as an ideal location for administering medications both for local and systemic absorption. Mucin and polymers interact chemically during the mucoadhesion process. Much emphasis has been paid on the utilization of mucoadhesive polymers in buccal medication delivery.[1] There are now many mucoadhesive dosage forms available, including pills, patches, discs, wafers, ointments, and gels. Buccal patches stand out among them for their higher comfort and flexibility. With their effective carrier capacity, smart materials like stimuli-responsive hydrogels, liposome-based spots, polymeric micelles, etc.[2] play a major part in the creation of these drug delivery systems by extending the drug's residence time at the site of absorption, improving drug bioavailability, reducing the frequency of dosing, and increasing patient compliance. [3]

Targeted drug delivery to specific body regions has grown in importance in the modern world as conventional dosage forms are frequently hampered in their ability to reach the target place with the appropriate dose at the right time. As a result, the creation and assessment of innovative drug delivery systems have recently become increasingly difficult. For better and more efficient therapy throughout the past 20 years, mucoadhesive systems have been regarded as a unique and acceptable drug delivery method. Transmucosal drug delivery methods, such as those through the nasal, rectal, vaginal, ocular, and oral canals, offer greater benefits than peroral drug administration. Several kinds of drug delivery systems increase the medicine's bioavailability and absorption and improve the drug's contact time with the mucosa membrane, as well as the drug's bioavailability. As a result, both patient compliance and the efficacy of the treatment have improved.

This method avoids first-pass metabolism and enzymatic drug degradation while yet providing patients who are unable to swallow or who have difficulty swallowing with effective medication [4.] For the creation of mucoadhesive formulations, polyacrylate, hydroxypropyl methylcellulose, and SCMC were extensively investigated during the 1980s. Since then, acrylate polymers have become more frequently used in the creation of mucoadhesive dosage forms.[5]

Following a thorough investigation, the scientists discovered that a polymer could demonstrate adequate mucoadhesive properties by penetrating the mucus network, forming strong intermolecular hydrogen bonds with the mucosal layer, and wetting the mucosal layer readily. In this unique drug delivery system for diverse medicinal purposes, many types of polymeric systems, comprising smart and non-smart materials, were utilized.

Oral anatomy

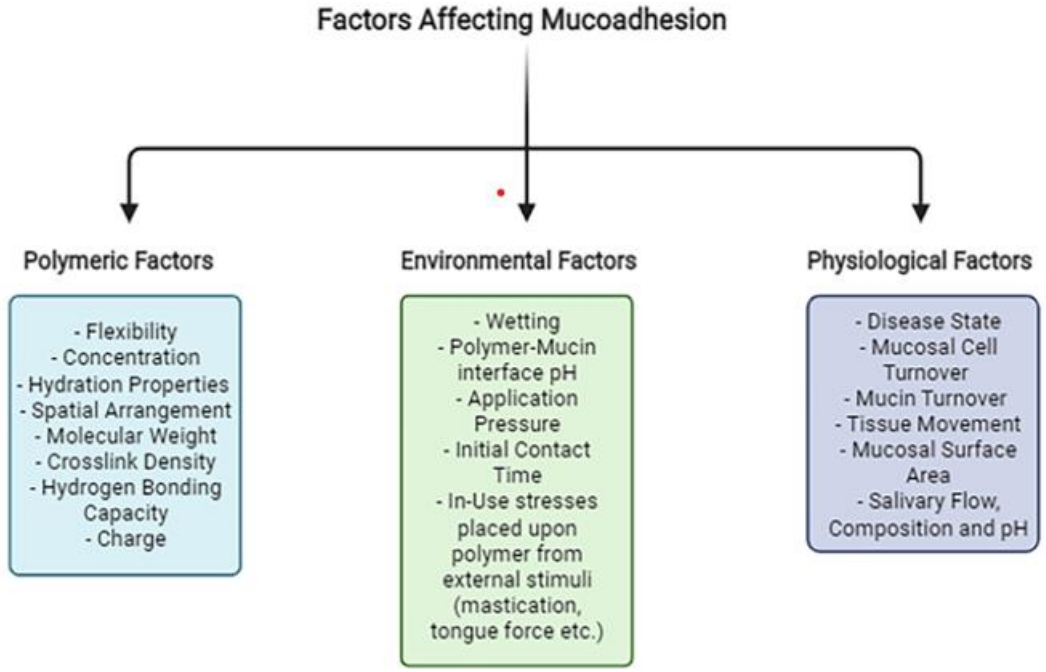
Mucus, a translucent, viscous discharge of epithelial surface that is made up of glycol proteins and found in a variety of bodily cavities from the respiratory and gastrointestinal tract, is a thin, continuous jelly layer that covers the epithelium surface. Human mucus layer thickness ranges from 50 to 450 micrometres, and it acts as an adhesive contact for medications. The lamina propria, submucosa, foundation membrane, and squamous stratification (layered) epithelium make up the oral mucosa.[6]

Depending on the extent of the oral cavity, the oral mucosa with an area of surface of 200 cm^2 as varying thickness and keratinization characteristics. The gingivae and hard mouth are covered with masticatory mucosa, which makes up 25% of the oral mucosa. It is repaired and looks like the skin's epidermis. Contrarily, 60% of the lining mucosa is non-keratinized and covers due to tongue movement and saliva washing during delivery. To administer medications to the body systemically for the treatment of acute illnesses, the sublingual route is typically used. The buccal mucosa, in contrast, offers the best circumstances for long-lasting regulated drug release and is regarded as the preferred route for systemic management of chronic illnesses when the sustained delivery of medicines with systemic effects is necessary. The most significant benefits of oral drug delivery include high blood vessel perfusion, low enzymatic activity and decreased drug inactivation, convenience of administration and superior availability, as well as low dose-dependent adverse effects.[7]

Buccal mucoadhesive patch

The most popular oral drug delivery methods are buccal patches, which are typically made by casting a solution containing a polymer, a medication, and any excipients onto a surface. Hydrophilicity, molecular weight, crosslinking, swelling, spatial conformation, pH, concentration in order of the active polymer, drug concentration, initial force of application, and mucus turnover rate are a few variables that may affect mucoadhesion in buccal patches. These variables have been discussed in some review articles. Mucoadhesive patches are typically 1-3 cm^2 in size and have an oval shape to fit easily into the buccal mucosa's centre, though they can be produced up to 10-15 cm^2 in size.[8]

The surface pH, thickness measurement, swelling study, folding strength, mechanical and thermal examination, morphological characteriszation, *In-Vitro* drug release study, drug permeation evaluation, and *Ex-Vivo* bioadhesion study are some of the most frequently used evaluation tests on buccal mucoadhesive patches.[9]



A suitable mucoadhesive patch needs to possess a number of specific characteristics, including safety and nontoxicity, high flexibility and patient compliance, good mechanical strength, immediate adherence to the mucosa of the mouth, controlled drug release, long drug retention time, optimal drug absorption, and others. Due to the rich blood supply to the oral mucosa in this type of dosage form, drugs are absorbed from the oral cavity through the oral mucosa and transported through a deep lingual or facial a vein into the systemic circulation.

These medications avoid the first pass effect because they enter the systemic circulation directly. Furthermore, neither food nor gastric emptying rate affects the rate of drug absorption.[10]

Oral films are a useful dosage form for the localized treatment of oral disorders and the delivery of systemic medications due to their perfect properties. In addition, compared to alternative dosage forms like gels and sprays, mucoadhesive patches offer a more precise dosing of drug delivery.

Mucoadhesive patch with sustained drug release

A permeable backing layer and a mucoadhesive patch are regarded to be insoluble system that releases the medicine in a regulated manner. In actuality, it permits a prolonged period of gradual medication release. As mucoadhesive biopolymers in these systems, derivatives of chitosan are frequently employed.[11]

These types of drug delivery systems have been the subject of extensive research due to their benefits over traditional dosage forms. In a sustained drug-release mucoadhesive patch, the frequency of dosing is reduced. Moreover, in the case of chronic illnesses where patients require the plasma concentrations of a drug to be within its therapeutic range to avoid breakthrough

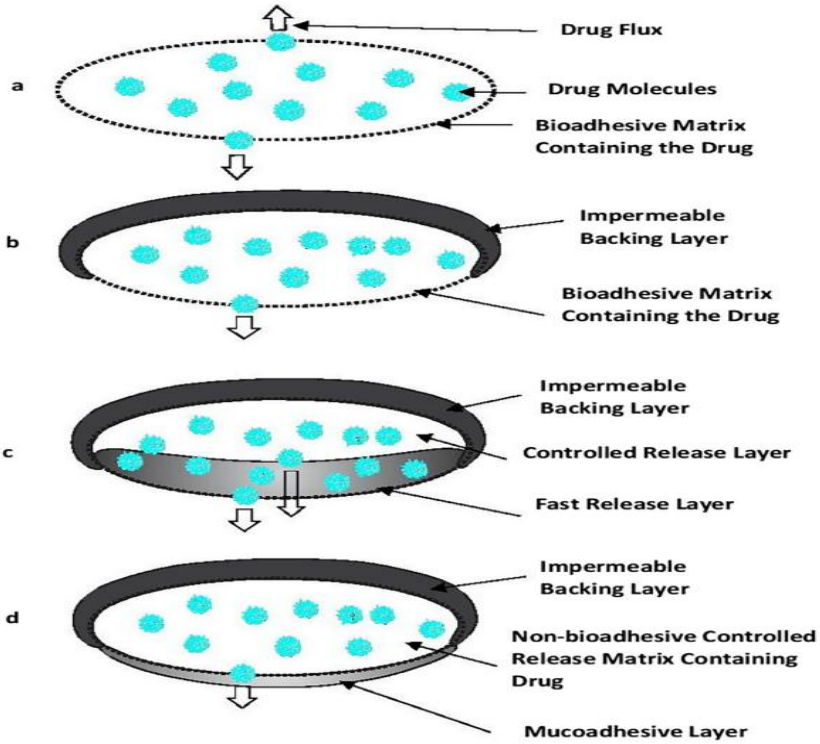
symptoms, these patches are highly demanded. The reduction of side effects, improvement in patient compliance, better control of therapeutic drug concentration and cost-effective manufacturing are the most important advantages of mucoadhesive patch with sustained drug release.[12]

Different designs of buccal patches

In general, various designs are considered for the preparation of buccal patches based on the desired properties of mucoadhesive drug delivery films with different designs and drug delivery features

i. **Matrix systems (Bi-directional**): In these systems, the drug and other additives are uniformly disseminated or dissolved in a polymer matrix, and the penetration through the polymeric network affects the drug's release characteristics. Drugs are released through bidirectional patches into the mouth and mucosa. The most significant drawbacks of a bi-directional architecture are hence incomplete absorption and reduced medication bioavailability.[13]

ii. **Reservoir systems (unidirectional)**: In these systems, the drug and other additives are uniformly disseminated or dissolved in a polymer matrix, and the penetration through the polymeric network affects the drug's release characteristics. Drugs are released through bidirectional patches into the mouth and mucosa. The most significant drawbacks of a bi-directional architecture are hence incomplete absorption and reduced medication bioavailability. without the use of needles, can be administered as a mucosal vaccination. In a different design, a membrane-based system made up of two layers with fast and controlled release characteristics and an impermeable layer is present. This design is appropriate for oozing control and pain relief during the initial course of treatment. In the third type, a controlled release system is made using a mucoadhesive polymer matrix, a non-adherent polymer carrying medication, and the presence of a non-penetrating protective barrier. For all of the aforementioned designs, the drug is released to the mucous membrane and absorption site without any drug loss or saliva penetrating the mucoadhesive layer that contains the drug.[14]



Various designs of buccal mucoadhesive patches

Manufacturing of mucoadhesive buccal patches

There are several ways to make mucoadhesive buccal patches, including solvent casting and direct printing,hot-melt extrusion, solid dispersion the extrusion process semisolid casting, and milling.

Despite being a popular preparation technique due to its ease of use and low cost, it has disadvantages of its own. Buccal films have recently been created using electrospinning, electrospraying, and 3D printing techniques, all of which show promise. These techniques are more effective and do not have issues with solvent casting.[15]

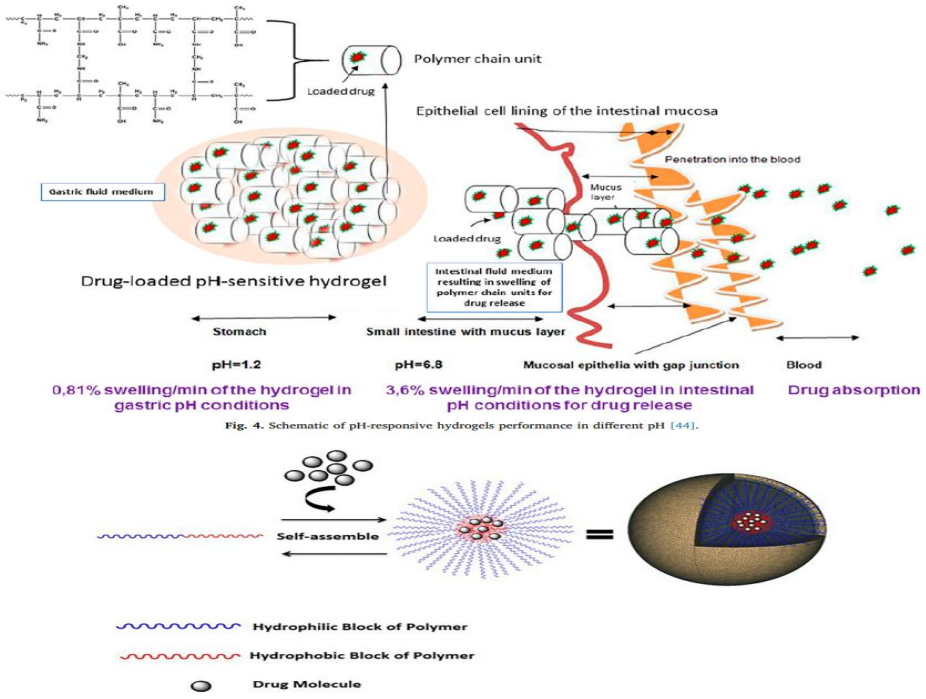


Fig. 4. Schematic of pH-responsive hydrogels performance in different pH [44].

Solvent Casting

A mucoadhesive polymer, medication, and other excipients dissolve in an appropriate solvent while being stirred by a magnet in the solvent-based casting process to create a homogenous solution. It is then dried after being cast into a petri dish. Numerous studies have been conducted on mucoadhesive films made using the solvent-casting technique. For instance, a double-layer mucous adhesive patch was created using the solvent casting approach in a work. Located inside the mucoadhesive layer.

To regulate blood pressure, take atenolol. Both Carbopol and Sodium Alginate were presented as a mucous adhesive layer with a protective backing membrane made of ethyl cellulose. This design allows for saliva infiltration into the Patch and drug disintegration rates were modest, and drug release was done under strict monitoring.

Solvent casting is often a quick and easy process.

It does, however, have the following Limitations:

• The polymer needs to be dispersed in a volatile solvent. In addition, some solvents may still be present in the finished film.

• Solvent cast films have a limited capacity for drug loading.

• The synthetic film lacks the necessary homogeneity.[16]

Electrospinning

Currently, electrospinning is viewed as a promising technique for creating oral patches. In reality, electrospinning is a straightforward, affordable, and adaptable technique that yields continuous nanofibers with distinctive qualities such as high porosity and a high surface-to-volume ratio. These properties offer increased loading capacity, improved

encapsulation, rapid dissolution, high biodegradability, and various drug delivery. These outstanding qualities have increased the efficiency of electrospun nanofibers in medication delivery systems.[17]

Electrospraying

The electrospray technique has received a lot of attention in recent years because of its straightforward experimental setup, many applicability, and low cost. The creation of micro and nanoparticles for use in medication delivery systems can be done using an altered version of the electrospinning method called electro spraying. These electrospray-produced polymeric micro and nanoparticles can be employed as oral, injectable, inhalable, topical, and local drug delivery systems.

Additionally, electro spraying can get around the problems with traditional particle-producing techniques for creating the drug-contained layer in the patch. The most popular methods for creating polymeric micro and nanoparticles include solvent evaporation, single and double emulsions, spray drying, porous glass membrane emulsification, and coacervation.[18]

3D Printing

Electrospinning is typically only used to create arbitrary 2D structures. Additionally, the porosity and pore size of fibrous electrospun films are not sufficiently controlled. Additionally, the desired dosage form geometry must be cut or shaped into electrospun drug-polymer films. The most recent technology, such 3D printing, can be used to create mucoadhesive oral films. The needs of individual patients can be satisfied to a great extent with this technique. Additionally, this approach is highly flexible and economical. Greater control over fibre formation and deposition is offered by the novel 3D printing technique known as electrohydrodynamic (EHD) jet printing. Additionally, dosage forms can be customised and personalised and drug loading can be increased.[19]

Conclusion

The buccal mucosa is typically a favorable site for delivering acting medications for the treatment among the numerous transmucosal routes. Electrospinning and electrospraying simultaneously from two different nozzles. Chronic diseases are becoming more prevalent because of their accessibility, according to A. Rohani Shirvan et al. in European Polymer Journal 119 (2019) 541–550. Therefore, compared to non-oral drug delivery systems, oral local drug delivery offers a more focused release, increased drug bioavailability at the site of absorption, and decreased side effects. Some recently proposed systems, like oral patches, have drawn more and more attention in the

pharmaceutical industry among oral mucoadhesive dosage forms. Mucoadhesive buccal patches come in a variety of shapes, including matrix or reservoir (mono/multi-layered) designs, and are innovative and promising drug delivery devices. Buccal mucoadhesive patches can be created using a variety of polymeric methods. Stimulus-responsive polymers are regarded as one of the most crucial among them. In other words, a promising approach to increase the bioavailability of oral delivery has been found in the potential direction of combining two or more features, such as pH sensitivity and mucoadhesion. The creation of an oral film involves a number of innovative procedures, each with their own benefits and traits, such as electrospinning, electrospraying, and 3D printing. Buccal patches are one type of oral drug delivery that is predictable given its special features.

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