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NOVEL APPROACH OF MUCOADHESIVE POLYMERS: A REVIEW

Surya N., Shalini K., L.V. Vigneshwaran* and M. Senthil Kumar

Sree Abirami College of Pharmacy, Coimbatore-21.

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***Corresponding Author**
L. V. Vigneshwaran
Sree Abirami College of Pharmacy, Coimbatore-21.

ABSTRACT

In order to increase the dosage form's contact and residence times with the mucous membranes, mucoadhesive polymers are employed to improve drug delivery. The process through which polymers adhere to a biological substrate, a synthetic or natural macromolecule, mucus, or an epithelial surface is known as mucoadhesion. Mucoadhesion is a process that occurs when a biological substrate adheres to a mucosal layer. The substrate with a bioadhesive polymer can aid in long-term drug delivery at a particular delivery location. Studies on mucoadhesive polymers offer a clear understanding of mucoadhesion and several variables that can influence a polymer's mucoadhesive characteristics Mucoadhesive buccal patches are made using both natural and synthetic polymers. Because mucosal membranes are highly permeable, the mucoadhesive drug delivery technology allows for fast drug uptake into the systemic circulation without having to undergo first pass metabolism.

INTRODUCTION

In order to apply penicillin to the oral mucosa, gum tragacanth was combined with dental adhesive powder in 1947, leading to the development of bioadhesive drug delivery formulations. Delivery of therapeutic agents via a mucoadhesive drug delivery system has gained a lot of interest in recent years. Some medications are ineffective because of poor bioavailability, GI intolerance, in consistent and unpredictable absorption, or pre-systemic clearance of other possible routes of delivery. The study of mucosal medication delivery has become more intense as a result of recent advancements in drug delivery. Oral, buccal, ocular, nasal, and pulmonary routes are some examples of this route.[1,2] Because it offers the chance to prevent either drug degradation by gastrointestinal contents or hepatic first-pass

inactivation, pharmaceutical features of mucoadhesion have drawn a lot of attention in recent years. The mucoadhesive drug delivery system includes the following:

1. Buccal drug delivery systems
2. Sublingual drug delivery systems
3. Rectal drug delivery systems
4. Vaginal drug delivery systems
5. Ocular drug delivery systems
6. Nasal drug delivery systems

One of the naturally occurring polymers that is frequently employed is chitosan. Glucosamine and N-acetyl glucosamine, which are also components of mammalian tissue, make up chitosan. It is a biodegradable, biocompatible, and non-toxic polymer. This polymer is taken into consideration for its capacity to create films and matrices. Inhibiting enzymes and enhancing permeability are additional uses for chitosan.[3]

MUCOADHESION

The idea of mucosal adhesives, also known as mucoadhesives. The idea of mucoadhesives has made many researchers aware of the potential for these polymers to be exploited to get over physiological obstacles in long-term medication administration.[4] The capacity of a substance to attach to the mucosal layer is referred to as mucoadhesive. Interfacial pressures hold them together for a considerable amount of time. The viscoelastic fluid known as mucus, which is released by goblet cells, makes up the mucosal layer. Visceral organs that are exposed to the outside environment have it lining them.[5]

MUCUS MEMBRANES

Mucous membranes are the wet linings of a number of body cavities, such as the digestive and respiratory systems. They consist of a mucus layer, which normally keeps the surface of the epithelial layer moist, a connective tissue layer, and an epithelium layer.[6] It is possible for epithelia to have one layer, several layers, or stratified epithelial. These later organs either have specialised glands like salivary glands that release mucus onto the epithelial surface, or they are located next to tissues that do. Those in the first category have goblet cells, which produce mucus right onto the epithelial surfaces. There is either a luminal soluble or suspended type of mucus or a gel layer that is adhering to the mucosal surface.[7] Mucin, glycoprotein, lipids, inorganic salts, and water are the main ingredients of all mucus gels. The latter makes up more than 95% of its weight, making it a highly hydrated system.[8] The

mucus gel's distinctive gel-like, cohesive, and sticky qualities are the product of the mucin glycoproteins, which are the most significant structure-forming component. This mucus layer can range in thickness from 50 to 450 micrometres in the stomach to less than 1 millimeter in the mouth cavity. Mucus has two main purposes: lubrication and protection.[9] The retention of the dosage format at the site of absorption is a factor that influences the success or failure of the buccal drug delivery method in addition to the minimal surface area available for drug absorption in the buccal cavity. To establish an intimate and sustained contact of the formulation with the oral mucosa and allow for a longer period of absorption, mucoadhesive systems must be used. Some adhesive solutions only allow an impermeable product surface to be exposed to the oral cavity when delivering the drug to the mucosa, preventing drug leakage into the oral cavity. For instance, Lopez and colleagues developed laminated films to offer unidirectional medication delivery and prevent buccal leakage.[10]

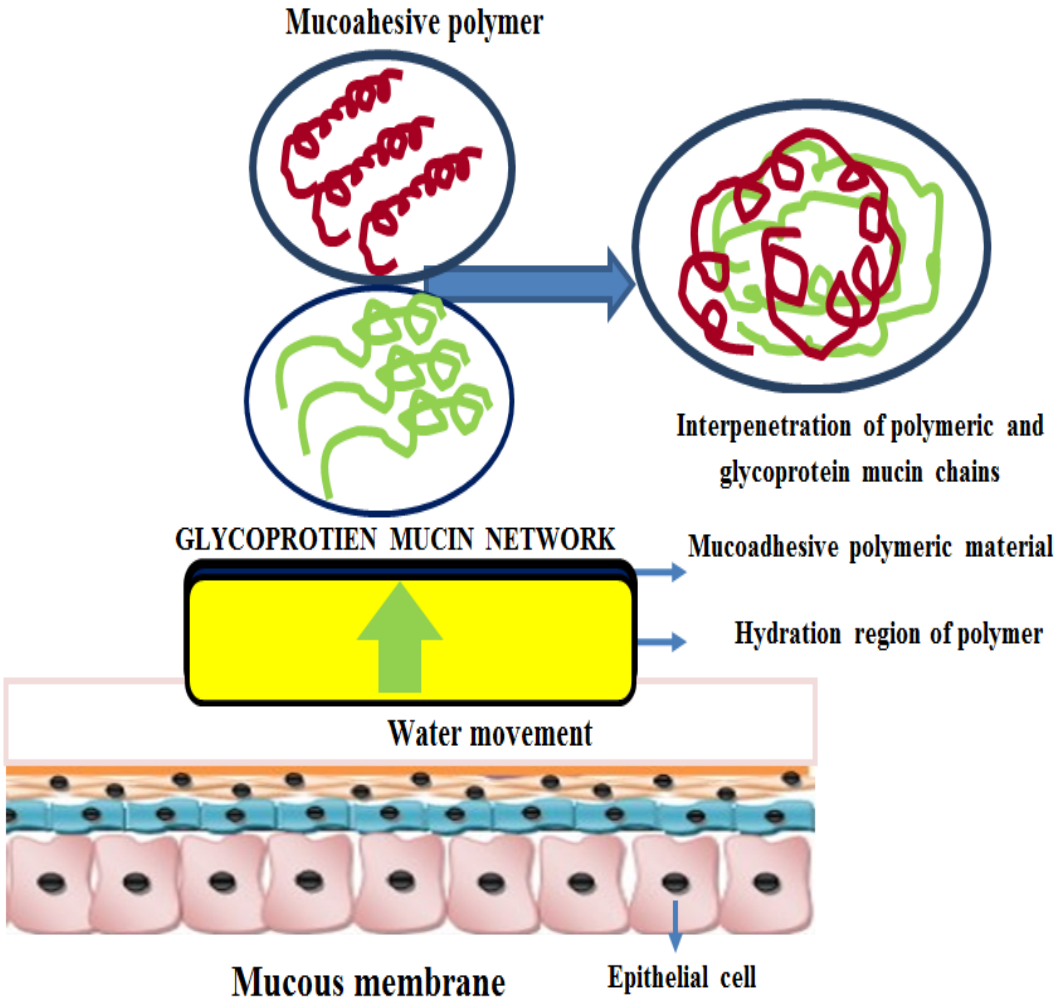

Fig. 1: A two-stage explanation for the occurrence of mucoadhesion.

DISTINCT MUCOADHESIVE POLYMERS CAN BE CLASSIFIED UNDER THE FOLLOWING CATEGORIES

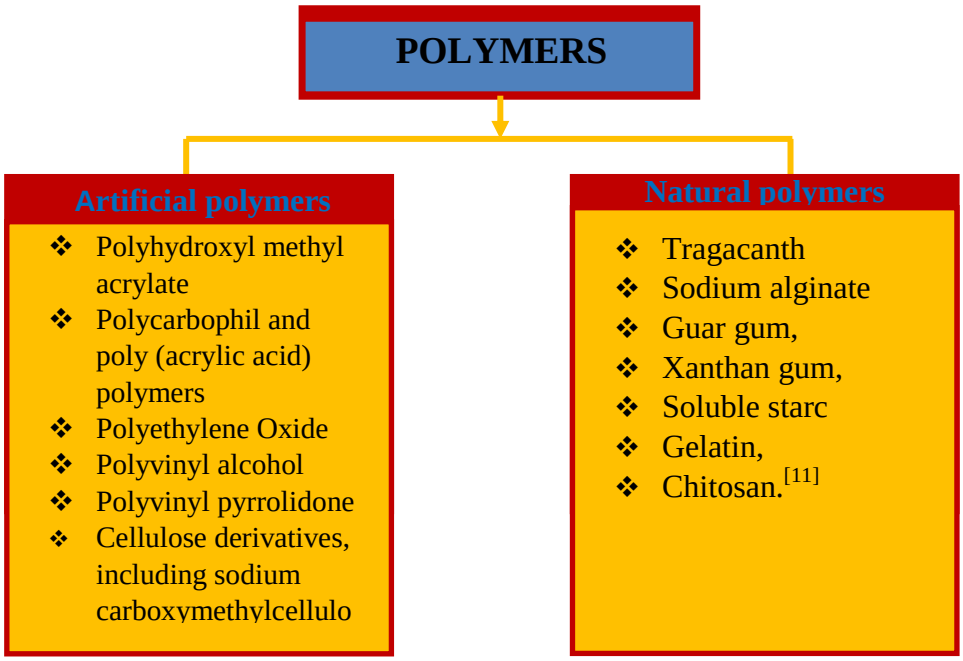

Fig 2: TYPES OF POLYMERS

ORAL MUCOSAL SITES

There are three types for medication administration within the oral mucosal cavity.

a). Sublingual delivery

The administration of medication to the body's circulatory system through the sublingual mucosa, a membrane covering the ventral surface of the tongue and the mouth's floor.

b). Buccal delivery

The process of delivering medication to the bloodstream through the buccal mucosa, which lines the cheek.

c). Local delivery

For the treatment of oral cavity conditions, primarily periodontal disease, fungal infections, and ulcers. These oral mucosal locations are quite different from one another in terms of their anatomical make-up, permeability to drugs, and capacity to hold a delivery system in place for the necessary amount of time.[12,13]

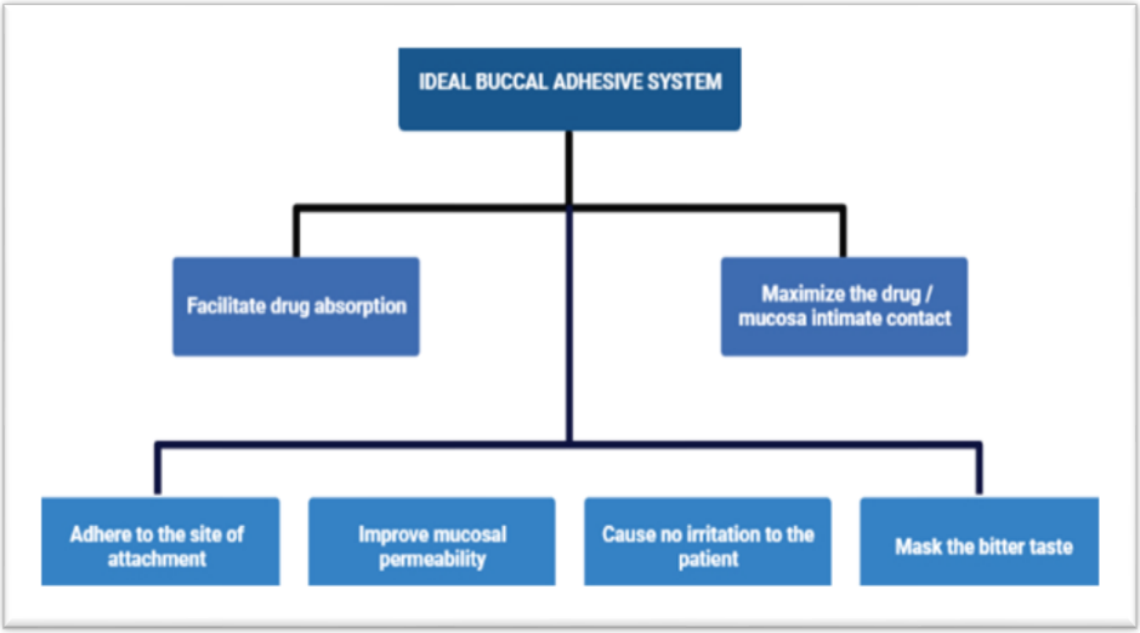

Fig 3: Graph outlining the essential characteristics of the appropriate buccoadhesive dosage form.

MUCOADHESIVE PROPERTIES EVALUATION

A variety of in vivo and in vitro techniques are used to gauge how well a polymer matrix adheres to mucous membranes. Tensile strength testing, shear strength testing, and chip-based systems are some of the frequently utilised in vitro/ex vivo approaches, whilst various imaging techniques are employed to assess delivery systems in vivo. The numerous techniques used to research the mucoadhesive characteristics are described in this section. By dipping filter paper in an 8%8 mucin dispersion, in vitro tensile strength is measured. The mucin-coated filter paper is then exposed to the hydrated polymeric samples for a predetermined amount of time, and the maximal force necessary to separate the filter paper and polymer surfaces is then measure.[8] The mucin-coated filter paper in ex vivo experiments is replaced by excised mucosal tissues, such as buccal mucosa, intestinal mucosa, and vaginal mucosa, in a manner similar to that described above.[14,15] The wash-off test can also be used to assess a delivery system's mucoadhesiveness. Using double-sided cyanoacrylate tape, mucosal tissue is affixed to a glass slide for the test. The delivery system is then placed on the tissue's surface before being vertically attached to the USP pill disintegrator device, which is equipped with a reservoir holding 1 l of physiological solution that is kept at a constant 37°C. The mechanism for delivering tissues moves up and down as a result of the equipment's operation. The study's cutoff point for the delivery system's total detachment was mucus layer determined.[16]

POLYMERS IN THE DELIVERY OF MUCOSAL DRUGS: Mucoadhesive delivery techniques are being investigated for the localization of active drugs to a specific area or site. In order to extend the active agent's residence period at the intended area, polymers have been crucial in the design of such systems. Natural or artificial polymers may be used in mucosal delivery systems. We will briefly go over a few of the most popular kinds of mucoadhesive polymers in this section.

a). hydrophilic polymers

These types of polymers can dissolve in water. matrixes created using these When placed in an aqueous medium, polymers swell and the matrix dissolves as a result. When compared to neutral polymers, the mucoadhesive characteristics of the polyelectrolytes are stronger.[17,18] Due to their capacity to demonstrate strong hydrogen bonding with the mucin present in the mucosal layer, anionic polyelectrolytes, such as poly(acrylic acid) and carboxymethyl cellulose, have been widely used to construct mucoadhesive delivery systems. Due to its outstanding biocompatibility and biodegradable qualities, chitosan serves as a superb example of a cationic polyelectrolyte that has been widely employed for producing mucoadhesive polymer.[19]

b). Hydrogels

A three-dimensionally cross-linked polymer chain with a porous structure known as a hydrogel is able to store water. The presence of hydrophilic functional groups like hydroxyl, amino, and carboxyl groups is primarily responsible for the hydrogels' ability to hold water. In general, there is a correlation between a reduction in mucoadhesion and an increase in cross-linking density. The thermal cross-linking of poly(acrylic acid) with methyl cellulose was described by Thielmann et al. According to their findings, there was a decrease in swelling and solubility parameters with an increase in cross-linking density, which reduced mucoadhesion.[20] The cross-linking density increased along with the mucoadhesive characteristic in hydrogels made by the condensation reaction of poly and sucrose.

c). Thiolated Polymers

Free thiol groups in the polymeric skeleton aid in the formation of disulfide bonds with the cysteine-rich sub-domains in mucin, which can significantly enhance the polymers' mucoadhesive properties as well as the uptake of the bioactive agents by paracellular membranes.[21,22] Chitosan-iminothiolane, polycysteine, polyhomocysteine, chitosan-

thioglycolic acid, chitosan-thioethylamidine, alginate-cysteine, polycystin, and sodium carboxymethylcellulose-cysteine are a few examples of different thiolated polymers.[23]

d). Polymers derived fromLectin

In addition to numerous bacteria, lectins are proteins that have the capacity to reversibly interact with particular sugar/carbohydrate residues.[24] They are found in both the animal and plant kingdoms. Numerous lectins have been proven to be immunogenic and poisonous, and when exposed repeatedly to vulnerable people, they can cause systemic anaphylaxis. It is being investigated to provide targeted delivery systems because lectins have a unique custom-adhesive property for sugar or carbohydrate residues. Numerous targeted delivery strategies have been investigated using lectins derived from legumes. The different lectins from Ulex europaeus I, soybean, peanut, and Lens culinarians have all demonstrated specific binding to the mucosa.[25] Due to its capacity to attach to the intestinal and alveolar epithelium and its least immunogenic reactions among the known lectins, wheat germ agglutinin has become increasingly popular for use in the development of oral and aerosol delivery methods.[26]

A THEORY OF MUCOADHESION

Mucoadhesion is a complicated process, and several hypotheses have been put up to explain how it works. Among these theories is.

1. Wetting theory
2. Diffusion theory
3. Fracture theory
4. The electronic theory
5. The adsorption theory.[27]

DIFFICULTIES IN THE DEVELOPMENT OF BIOADHESIVE DRUGS DELIVERY SYSTEMS

Novel approaches to the formulation of oral mucoadhesive drug delivery systems,

The development of bioadhesive buccal patches,

The delivery of calcitonin through the vaginal canal using hyaluronic acid formulations,

The use of ocular bioadhesive drug delivery systems, and

The use of bioadhesive preparations as topical dosage forms.[28]

BIODIFFUSIVE POLYMER

Characterizing and choosing appropriate bioadhesive polymers for the formulation is the first step in creating mucoadhesive dosage forms. In mucoadhesive medication delivery systems, bioadhesive polymers are crucial. Polymers are also utilized in matrix devices, which regulate the timing of medication delivery by enclosing the drug in a polymer matrix.[29] Bioadhesive polymers are among the most diverse materials and are widely employed in the treatment and care of patients. Through the use of the core layer or rate-controlling layer, the medicine is released into the mucous membrane. The oral drug delivery mechanism is significantly improved by bioadhesive polymers that stick to the mucin or epithelial surface.[30]

CONCLUSION

Mucoadhesive buccal patches have recently become more significant in the delivery of medications. In the formulation of buccal patches, natural polymers are being used more and more. This study aims to provide an overview of the work completed so far and to illustrate the future direction of the development of buccal mucoadhesive patches made of natural polymer. Compared to regulated medication delivery over prolonged periods of time, the buccal mucosa has a number of benefits. First-pass metabolism in the liver and pre-systemic elimination in the digestive tract are prevented by the mucosa's adequate vascular and lymphatic drainage. The dosage form has uses in a variety of fields, such as the development of new mucoadhesives, device design, permeability improvement, and mucoadhesion processes. However, the study on mucoadhesives is still in its early stages, and more advancements must be achieved for the concept to successfully be applied in practice for regulated medication administration.

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