Article published on 2023-12-20

Mucoadhesive Drug Delivery System and There Future Prospective: Are a Promising Approach for Effective Treatment?

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Chinese Journal of Applied Physiology, 2023: e20230005

Abstract Mucoadhesive polymers are a new and exciting development in drug delivery systems that have the potential to significantly increase therapeutic efficacy. These polymers stick to mucosal surfaces, increasing the amount of time that medications stay at the site of absorption and improving their bioavailability. These mechanisms include longer contact times with the mucosal surface, better drug solubility, and defence against enzymatic degradation of pharmaceuticals. Mucoadhesive polymers also provide a number of benefits over traditional drug delivery methods, including less frequent dosage, better patient compliance, and fewer adverse effects. Due to their adaptability, Mucoadhesive polymers may be used in the rectal, vaginal, ophthalmic, nasal, and oral routes of drug delivery. Mucoadhesive polymers have advantages now, but they also have potential for the future of medication delivery. Mucoadhesion offers excellent possibilities for the delivery of a range of substances through the nasal, vaginal, buccal, and ocular routes of administration. Furthermore, mucoadhesion facilitates the achievement of an extended local or systemic pharmacological effect. In this study, we covered the mechanisms behind mucoadhesion, possible uses for Mucoadhesive polymers in drug administration, and techniques for assessing Mucoadhesive drug delivery systems. The goal of current research is to create innovative Mucoadhesive polymers that have better biodegradability, biocompatibility, and adhesive qualities. Moreover, it is anticipated that the effectiveness of Mucoadhesive polymers would be increased when combined with other cutting-edge drug delivery technologies, such as micro particles and nanoparticles.

Keywords Mucoadhesive polymer; Promising approach; Drug delivery; Routes of drug administration; Future of drug delivery

1. Introduction

In the ever-evolving field of drug delivery, scientists and researchers are constantly in search of innovative solutions to improve treatment effectiveness. One such solution is the use of Mucoadhesive polymers. These specialized polymers have shown great promise in enhancing the delivery and efficacy of various drugs. Mucoadhesive polymers have unique properties that allow them to adhere to mucosal surfaces, such as

DOI: 10.62958/j.cjap.2023.005
www.cjap.ac.cn

Published by CJAP editorial office and Asian BioMed Innovation Press

the inner lining of the gastrointestinal tract or the respiratory system. This adhesion promotes prolonged drug release, ensuring a more consistent and targeted delivery. Additionally, Mucoadhesive polymers can enhance drug stability and protect it from degradation, further improving treatment outcomes. The applications of Mucoadhesive polymers span across various therapeutic areas, including oral, nasal, buccal, and ocular drug delivery. Whether it's improving the absorption of oral medications or enhancing the effectiveness of nasal sprays, these polymers have the potential to revolutionize drug delivery and patient care. The concept of mucoadhesion has gained significant interest in pharmaceutical technology since the early 1980s. Mucoadhesive drug delivery systems interact with the mucus layer covering the mucosal epithelial surface, increasing the residence time of the dosage form at the site of absorption. These systems offer several advantages over other oral controlled release systems by prolonging the drug's residence time in the gastrointestinal tract (GIT). They facilitate an intimate contact of the dosage form with the underlying absorption surface, thereby improving the drug's therapeutic performance. Mucoadhesive dosage forms have been developed for various routes of administration, including oral, buccal, nasal, rectal, and vaginal, for both systemic and local effects.[1]

2. Theories on Mucoadhesion/ Bioadhesion

2.1 Wetting theory

According to the wetting theory, the intermolecular interactions between the drug delivery system and the mucosal surface cause adhesion to happen. The system wets the mucosal surface causing adhesive forces to form that keep the device in place.

2.2 Electrostatic theory

Positively charged or ionizable groups on the drug delivery system and negatively charged groups on the mucosal membrane interact electrostatically, according to the electrostatic hypothesis. Adhesion is a result of these electrostatic forces.

2.3 Diffusion theory

In accordance with this idea, drug molecules released by the delivery system diffuse into the mucosal tissues, resulting in a gradient in concentration and the system adhering.

2.4 Interlocking

Bioadhesion may also be caused by a mechanical link being formed between the drug delivery system and the mucosal folds. This is known as mechanical interlocking.

2.5 Chemical bonding theory

According to the chemical bonding theory, certain bioadhesive systems may create covalent or ionic connections with the mucosal surface, resulting in a powerful and long-lasting adherence.

2.6 Hydration theory

Hydrogen bonds with the mucosal surface may occur as a result of the hydration of the polymer chains in the drug delivery system, according to the theory of hydration. The hydration of the polymer causes swelling and a larger contact surface, which might lead to adhesion.

2.7 Mucin theory

Mucin-Binding Theory: The mucus layer on mucosal surfaces contains glycoproteins called mucins. Certain ligands in certain bioadhesive systems bind to mucins to produce adherence.

2.8 Van der Waals Forces

Van der Waals forces are weak intermolecular forces that may help a medication delivery device adhere to the mucosal surface.

2.9 Polarity & surface energy

Systems with comparable polarity and surface energies to the mucosal tissues have a tendency to attach better due to advantageous interactions.[2-6]

Table 1: Different Mucoadhesive Polymeric systems and their application.[1]

Route.of.administration	Polymeric.system	Used.drug	Application
Ophthalmic	Liposomes	Pilocarpine.HCL	Increased.miotic.response.and.ocular. bioavailability.of.the.drug
	Nanoparticles	Amikacin,.metipranolol,. indomethacin	For.the.treatment.of.respiratory. diseases/to.treat.glaucoma

Nasal	Liposomes	Acyclovir	Anti.HIV
	Aqueous.solution	Apomorphine	Parkinson's.disease
	Microspheres	Gentamicin	Antibiotic
Buccal	Mucoadhesive. tablets	Miconazole.nitrate,. ketoconazole,. Felodipin,Enalapril.maleate	For.HIV-positive.patients.suffering. from.oropharyngeal.candidiasis
	Tablets.(Nitrogard.R)	Nitroglycerin	To.take.care.of.angina.attack
	Patches	Verapamil.hydrochloride	Preventive.medication.for.migraine.
		Carvedilol	Left.ventricular.dysfunction.following. myocardial.infarction
	Films	Glipizide	Most.potent.of.the.sulfonylurea. antidiabetic.agents
		Clotrimazole	For.oral.Candida.infections
		Glibenclamide	Used.in.the.treatment.of.maturity-onset.diabetes
Vaginal	Suppositories	Acetaminophen	Anti-inflammatory.analgesic
	Solid.dispersion/ Tablet	Benzydamine	Mouth.ulcer
		Clotrimazole	Antifungal.activity,.antifungal. chemotherapy

3. Factors Influence Mucoadhesion

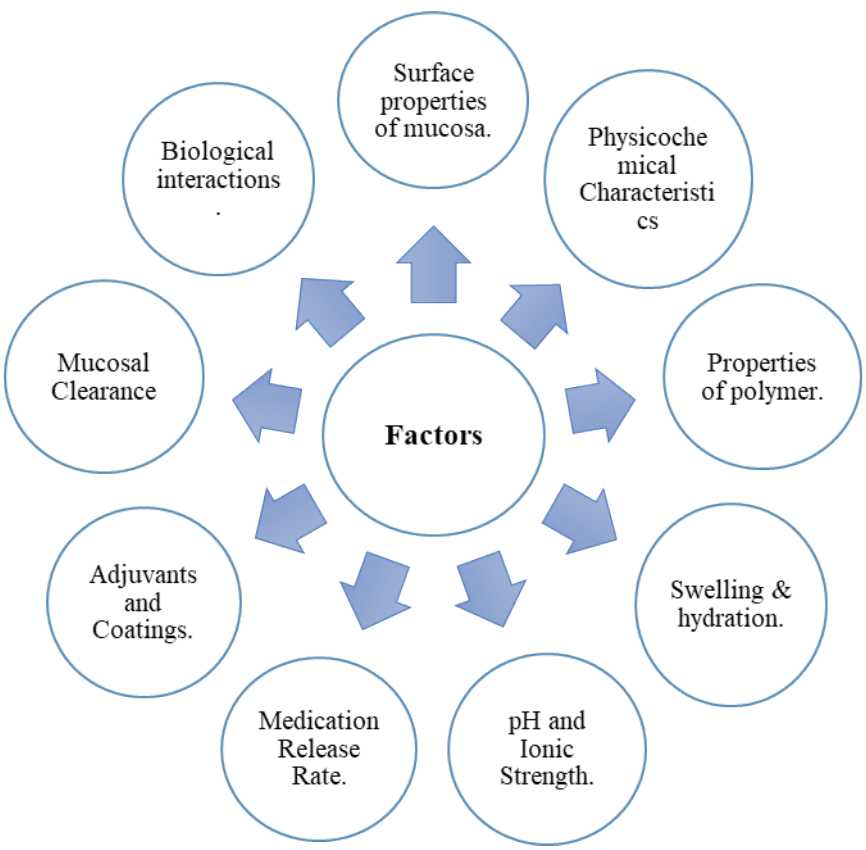

Figure 1: Factors Influence Mucoadhesion

4. Mucoadhesive Polymers

Bioadhesive polymers that stick to the mucin/ epithelial surface are useful and significantly increase oral medication administration by overcoming the comparatively short gastrointestinal (GI) time and improving localization for oral controlled or sustained release drug delivery systems. It is also expected that other mucus-covered medication administration locations would see improvements. Bioadhesive polymers are used in the GI tract, which includes the buccal and rectum, as well as the eye, nose, and vaginal cavity. In order to aid in the active pharmaceutical ingredient's adherence to the oral mucosa, a polymer or mucoadhesion boosting agent is added to the formulation.

When the agent comes into contact with saliva, it might have extra qualities like swelling that help to accelerate the breakdown process. Since the polymer/ mucus adhesion may be impacted by these different physical and chemical interactions, as previously described, the polymer should be carefully chosen based on the following ideal characteristics and there classification (Fig 2 & Fig 3).[7-10]

4.1 Ideal Characteristics of Buccal Mucoadhesive Polymer

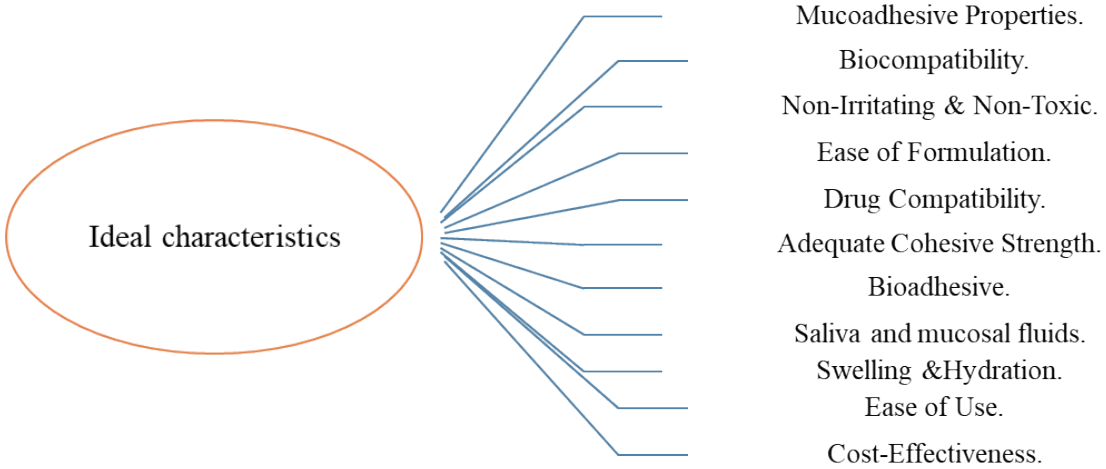

Figure 2: Ideal Characteristics of Mucoadhesive Polymers[1]

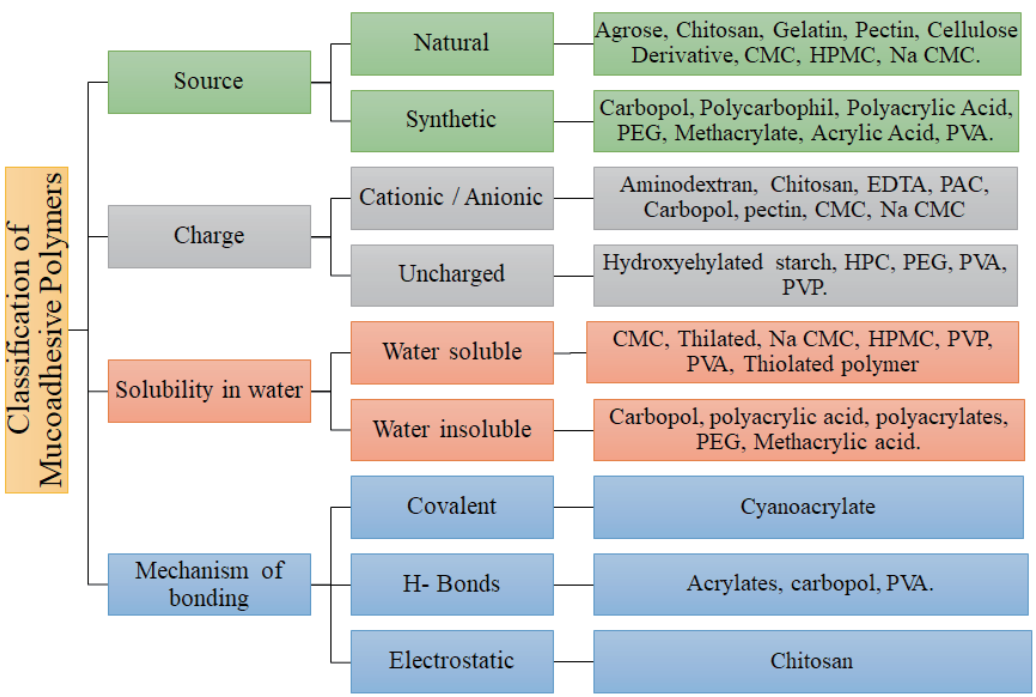

Figure 3: Classification of Mucoadhesive polymer based on different ways i.e. Source, charge, solubility in water, mechanism of bonding.[1],[11]

4.2 Charged polymer

A polymer with both Mucoadhesive and electric charge characteristics is called a charged Mucoadhesive polymer. The capacity of a substance to stick to mucosal surfaces—such as those in the respiratory system, gastrointestinal tract, or other body parts where mucous membranes are present—is known as mucoadhesion. These polymers have the ability to stick to mucosal surfaces for a long time, which is advantageous for biomedical applications such as prolonged medication release or drug administration.[12]

The polymer is said to be "charged" if it contains ionizable groups that have the ability to carry either a positive or negative charge. Typical instances of Mucoadhesive polymers that are charged include: The natural polymer chitosan is made from chitin, which is present in the exoskeleton of crustaceans. It has been well studied for its Mucoadhesive qualities in medication administration systems and is positively charged, Alginate: Derived from brown seaweed, alginate is a negatively charged polymer. Its Mucoadhesive and controlled release capabilities have been examined, and it has the ability to form gels in the presence of divalent cations (such as calcium ions), Poly(acrylic acid): Synthetic polymers that have the ability to carry a negative charge include poly(acrylic acid) and its derivatives. Their potential for Mucoadhesive drug delivery systems has been investigated and Derivatives of polyethylene glycol (PEG): Some PEG derivatives have the ability to functionalize with charged groups, which may make them advantageous for applications involving mucoadhesion.[13]

4.2.1 Anionic polymer

A family of materials known as anionic Mucoadhesive polymers is made to stick to mucosal surfaces by electrostatic interactions, creating a close and long-lasting bond with biological tissues. These polymers can interact with the positively charged mucin glycoproteins found on mucosal epithelial cells because they include negatively charged functional groups, such as carboxylate or sulfate groups. CMC is a well-known instance of an anionic Mucoadhesive polymer used in adhesive applications. Cellulose is the source of CMC, which has had carboxyl groups added to its structure. CMC demonstrates exceptional Mucoadhesive qualities when included into pharmaceutical products such as gels or patches, improving the drug delivery system's retention on mucosal surfaces. Because of their extended residence duration, anionic Mucoadhesive polymers are useful in a variety of pharmaceutical and medical applications due to their enhanced drug absorption, bioavailability, and therapeutic effectiveness.[14]

4.2.2 Cationic Polymer

A family of compounds known as cationic Mucoadhesive polymers is made to stick to mucosal surfaces via advantageous electrostatic interactions. Positively charged functional groups, such amino or ammonium groups, are commonly included in these polymers, which enable robust attachment to the negatively charged mucin glycoproteins on mucosal epithelial cells. One well-known instance of a cationic Mucoadhesive polymer is chitosan. Chitosan, a cationic polymer, is derived from chitin, a naturally occurring polysaccharide present in the exoskeleton of crustaceans, but with the addition of amino groups. Chitosan has exceptional Mucoadhesive qualities when added to biomedical devices or drug delivery systems, creating a strong connection with mucosal surfaces. This sticky contact improves medication absorption and therapeutic efficacy in addition to extending the formulation's residence duration at the target location. Chitosan and other cationic Mucoadhesive polymers are essential for enhancing the efficacy of several pharmaceutical and biological applications, as well as for advancing tissue engineering and controlled drug delivery.[15]

4.2.3 Uncharged Polymer

Non-ionic polymers, sometimes referred to as uncharged polymers, are molecules without any intrinsic electrical charge. Usually, these polymers are made up of units that repeat and are either positively or negatively charged. One often used example of an uncharged polymer is polyethylene glycol (PEG). PEG is a polyether chemical that dissolves well in a variety of organic solvents including water. Being inert and flexible, its lack of charge reduces its interaction with charged surfaces and biomolecules. Because of their hydrophilic character, uncharged polymers like PEG are frequently used in drug delivery systems and other pharmaceutical and biomedical applications. This helps to solubilize hydrophobic medicines and increase their bioavailability. Furthermore, uncharged polymers are useful in the creation of biomaterials and medical devices due to their low immunogenicity and biocompatibility, which promotes progress in a variety of industries, including biotechnology and medicine.[16-17]

4.2.4 Lectins

A distinct class of proteins known as glycoproteins, lectins are distinguished by their capacity to bind

selectively to carbohydrates. These proteins that bind carbohydrates are widely distributed in nature and may be found in a wide range of species, including microbes and plants. Lectins are essential to many biological processes, mainly because they help in cell attachment and identification. They have particular binding sites that attach to and interact with glycan structures or sugar residues, facilitating important interactions at the molecular and cellular levels.[18]

Lectins are defensive mechanisms found in plants that attach to the surfaces of diseases and pests to neutralize them. Concanavalin A (Con A) from jack beans and Wheat Germ Agglutinin (WGA) from wheat germ are two well-known examples. Lectins support vital physiological processes in animals, including blood coagulation, embryogenesis, and immunological responses. To aid in their adhesion to host cells during infection, certain bacteria and viruses also create lectins.In both pharmaceutical uses and biological research, lectins have attracted a lot of interest. Studies into their possible therapeutic implications, notably in the treatment of cancer, have been prompted by their capacity to attach selectively to particular cell types. Certain lectins attach to cancer cells and stop them from growing, which suggests that they may have anti-cancer properties. Furthermore, lectins are investigated in drug delivery systems, where medications may be targeted to certain tissues or cells by utilizing their specificity.[19]

Even while lectins are important for regular physiological functions, it's important to remember that some lectins can be harmful. Castor bean extract, or ricin, is a notorious example of a very poisonous substance that can be fatal if consumed. It causes disruptions to the production of proteins. For researchers, lectins are useful probes. Their widespread usage as probes to examine and distinguish glycan structures on cell surfaces advances our knowledge of molecular interactions and cell biology. Overall, the relevance of these carbohydrate-binding proteins in many biological situations is highlighted by the different functions played by lectins in nature, their medical uses, and their use as research tools.[20-26]

4.2.5 Acrylates

Because of their propensity to stick to mucosal surfaces, acrylic Mucoadhesive polymers are a family of synthetic polymers that find use in a wide range of pharmacological and biological applications. The cross-linked network of acrylate monomers that makes up these polymers gives them their sticky qualities. Carbopol®, a common polymer used in topical and oral medicinal formulations, is an example of an acrylates Mucoadhesive polymer. Mucoadhesive properties are exhibited by Carbopol®, which forms a gel-like structure when hydrated and encourages extended contact with mucosal tissues. Eudragit® RS, a copolymer comprising methacrylic acid, methyl methacrylate, and ethyl acrylate used in controlled drug delivery systems, is another example. Acrylates polymers are Mucoadhesive, which improves medication absorption and retention at mucosal locations. This provides a flexible platform for targeted drug administration and better therapeutic results. Hear some more Examples of Mucoadhesive polymers made of acrylates.[27,28]

One often used acrylate-based Mucoadhesive polymer is poly(acrylic acid). Because it sticks to mucosal surfaces and forms stable gels, it may be used in a variety of drug delivery methods, such as topical and oral formulations. Hydroxypropyl methylcellulose (HPMC): To improve its Mucoadhesive qualities, HPMC can be treated with acrylate functions even though it is not a pure acrylate polymer. It is widely utilized in oral medication delivery systems and ophthalmic formulations, Poly(ethyl acrylate-co-methyl methacrylate): To provide specific Mucoadhesive qualities, this copolymer blends several acrylate monomers. It has been investigated in the creation of films and Mucoadhesive patches for regulated medication release, Sodium carboxymethyl cellulose (NaCMC) is a cellulose derivative that can have acrylate groups added to it to improve its Mucoadhesive properties. It is frequently used in ophthalmic formulations and oral dosage forms, Mucoadhesive hydrogels are made from the acrylate polymer poly(ethylene glycol) diacrylate, or PEGDA. Its ability to cross-link enables the development of three-dimensional networks with superior Mucoadhesive qualities and Poly(methacrylic acid): Poly(methacrylic acid) is an acrylate derivative that displays Mucoadhesive properties, much like poly(acrylic acid). It is a component of several pharmaceutical formulations, including medication delivery systems for the mouth and the buccal cavity.[29]

4.2.6 Chitosan

Crustacean exoskeletons, such as those of shrimp and crab, contain chitin, which is the natural biopolymer that is converted into chitosan. Its Mucoadhesive qualities are well known, which makes it useful in biomedical and pharmacological applications. Because of its cationic charge, chitosan is Mucoadhesive to negatively charged mucosal surfaces, facilitating interactions with them through electrostatic forces.

When it comes to medication delivery systems, this characteristic is very helpful since it allows for better bioavailability and prolonged release. Chitosan has been used in a number of formulations, including films, gels, and nanoparticles that are Mucoadhesive.[30]

One use for chitosan is in medication delivery systems for the buccal cavity. Buccal films or patches made of chitosan stick to the buccal mucosa, allowing for regulated medication delivery into the circulation. Chitosan's Mucoadhesive qualities let it stay in touch with the mucosal surface for extended periods of time, which improves medication absorption and therapeutic efficacy. Furthermore, chitosan's biodegradability and biocompatibility make it a desirable option for these uses. Nasal medication delivery has also been investigated with chitosan. Chitosan nanoparticle-containing nasal formulations have Mucoadhesive activity, which improves medication retention on nasal mucosa and boosts absorption. This is especially important for medications that aim to deliver to the central nervous system or the systemic circulation. Moreover, Mucoadhesive hydrogels based on chitosan are used in wound healing. These hydrogels' Mucoadhesive properties encourage extended contact with the wound site, allowing for the continuous release of therapeutic medicines and assisting in tissue regeneration. The innate antibacterial properties of chitosan further enhance its efficacy in wound care applications.[31]

4.2.7 Cellulose derivatives

A family of Mucoadhesive polymers known as cellulose derivatives finds extensive usage in pharmaceutical and biomedical applications because of its advantageous attributes, which include biocompatibility, safety, and the capacity to alter their structure to produce desired effects. Notable cellulose derivatives with Mucoadhesive qualities include carboxymethyl cellulose (CMC), hydroxyethyl cellulose (HEC), and hydroxypropyl methylcellulose (HPMC). These polymers have the ability to stick to mucosal surfaces by a number of different processes, including as electrostatic interactions and hydrogen bonds. Applications for hydroxypropyl methylcellulose (HPMC) in Mucoadhesive drug delivery systems are widespread. It creates gels that stick to mucosal tissues, increasing the bioavailability and extending the release of the medication. Because of its adaptability, HPMC may have its viscosity and adhesive strength adjusted to match particular formulation needs. Another cellulose derivative that is employed for its Mucoadhesive qualities is hydroxyethyl cellulose (HEC). It is frequently used in ophthalmic solution formulations because of its capacity to stick to the mucosa of the eyes and provide prolonged medication release. In several pharmaceutical formulations, such as oral, nasal, and topical drug delivery systems, carboxymethyl cellulose (CMC) is commonly used. The Mucoadhesive property of CMC improves formulation retention on mucosal surfaces, which leads to better therapeutic results. The creation of Mucoadhesive films, patches, and gels benefits greatly from the use of these cellulose derivatives. For instance, cellulose derivative-containing Mucoadhesive buccal patches are made to stick to the mouth mucosa and provide regulated medication release for systemic absorption.[32]

4.2.8. Hyaluronic acid

A naturally occurring Mucoadhesive polymer, hyaluronic acid (HA) finds extensive use in pharmacological and biological applications. It is a high-molecular-weight glycosaminoglycan that is present in synovial fluid and connective tissues. Hyaluronic acid's Mucoadhesive qualities are ascribed to its distinct structure and capacity to engage in hydrogen bonding and electrostatic interactions with mucin and cell surfaces. Because it is non-immunogenic, biocompatible, and biodegradable, hyaluronic acid is a popular option for a variety of formulations. Hyaluronic acid finds considerable use in ocular preparations. Hyaluronic acid-containing eye drops are used to increase retention on the ocular surface, which improves ocular medication delivery. Hyaluronic acid's Mucoadhesive qualities help to extend the duration of contact, which raises the bioavailability of medicinal substances for the treatment of diseases like dry eye syndrome. Studies like "Evaluation of the Mucoadhesive properties of hyaluronic acid based eyedrops: rheological behavior and in vivo study on humans" (Benedusi et al., 2012) have investigated the usage of hyaluronic acid in ophthalmic formulations.[33]

Hyaluronic acid has been added to Mucoadhesive hydrogels for wound healing in addition to ocular uses. By creating a moist environment, these hydrogels aid in wound healing and tissue regeneration. Hyaluronic acid's Mucoadhesive quality guarantees extended contact with the wound site, and the healing process is aided by its natural biocompatibility.[34] The usage of hyaluronic acid hydrogels in wound care is explored in the paper "Hyaluronic acid hydrogel for wound healing applications" (Anjum et al., 2017). Hyaluronic acid has also been used to treat bladder disorders by intravesical medication administration. Mucoadhesive qualities improve treatment effectiveness by

facilitating medication retention in the bladder. Hyaluronic acid's potential in such applications is covered in the publication "Intravesical drug delivery systems for the treatment of bladder cancer: a review" (Rist et al., 2018).

4.2.9 Gellan gum (GC)

Because of its special qualities, gellan gum is a flexible Mucoadhesive polymer that has drawn a lot of interest in pharmaceutical and biological applications. Gellan gum is a high molecular weight anionic polysaccharide made of repeating units of glucose, glucuronic acid, and rhamnose that is derived from the bacteria Sphingomonas elodea. It is made by microbial fermentation and sold commercially in multiple grades with varying gelling and rheological characteristics, including high and low acyl. Among Mucoadhesive polymers, gellan gum is unique in that it can produce thermally reversible gels and has good durability in a range of environments. Because of its Mucoadhesive qualities, it is especially advantageous for drug delivery systems that aim to provide targeted therapeutic effects and prolonged release. Gellan gum interacts with mucin glycoproteins found in the mucus layer to produce hydrogen bonds that extend the polymer's contact with mucosal surfaces, which is responsible for its Mucoadhesive properties.[35]

Gellan gum has several noteworthy benefits, including biocompatibility and biodegradability, which qualify it for use in drug delivery systems meant to be administered through mucosal passages. Because of the polymer's temperature-responsiveness, gel-based drug delivery systems, such as in situ gelling systems for controlled release applications, can be created. Additionally, gellan gum's potential in drug delivery formulations for oral, ocular, nasal, and vaginal routes has been investigated. Gellan gum has been studied in a variety of medication delivery scenarios. For example, gellan gum's Mucoadhesive quality helps to extend residence duration and improve absorption in oral medication administration systems when pharmaceuticals are released under control. Gellan gum-based formulations have been investigated for the prolonged release of medications into the eyes in ocular drug administration. To produce targeted and prolonged medication release, gellan gum has also been used to nasal and vaginal drug delivery devices. Sphingomonas elodea bacterium is the producer organism in microbial fermentation, which is the main source of gellan gum. Gellan gum items that are sold commercially can be obtained from reliable vendors in the food and medicine sectors. For use in pharmaceutical applications, gellan gum quality and purity must be guaranteed; several grades of gellan gum are available to satisfy different formulation needs.[36]

4.2.10 Alginates

A common Mucoadhesive polymer in pharmaceutical and biological applications is alginate. Alginate is a brown seaweed derived from Macrocystis pyrifera and Laminaria hyperborea. It is made up of linear chains with guluronic and mannuronic acid units alternated in them. Its distinct Mucoadhesive qualities, biocompatibility, and gelling qualities make it a desirable option for drug delivery systems. Seaweed must first be harvested, then it must be treated alkalinely and the alginate must precipitate from the resultant solution.[37]

The capacity of alginate to form gel-like structures when exposed to divalent cations, such calcium ions, is one of its distinguishing characteristics. This characteristic is very helpful for medication delivery systems since it makes controlled-release formulations possible. The mucus layer's mucin glycoproteins interact with alginate to produce hydrogen bonds, which facilitate adherence to mucosal surfaces and give alginate its Mucoadhesive properties. The enhanced residence duration of medication formulations on mucosal membranes due to this Mucoadhesive characteristic improves absorption and therapeutic efficiency.

Alginate is used in several different medication delivery techniques. Alginate has been utilized in the formulation of Mucoadhesive tablets and beads for controlled medication release in oral drug delivery. These formulations offer increased bioavailability and prolonged drug release by adhering to the mucosal surfaces of the gastrointestinal system. Alginate has also been investigated in the field of wound care. Alginate-based dressings have Mucoadhesive qualities that help them cling to wound surfaces and provide a moist environment that is favorable to healing. Alginate is mostly found in brown seaweeds, which are harvested, cleaned, and treated with an alkaline solution to solubilize the alginate during the extraction process. After that, the alginate solution is precipitated with calcium chloride to produce a gel-like material that may be used for a variety of purposes. Pharmaceutical-grade alginate products may be obtained from reliable vendors, guaranteeing adherence to strict quality and purity requirements.[38-40]

4.2.11 Poloxamers

Within the triblock copolymer class, poloxamers—which include poly(ethylene oxide) (PEO) and

poly(propylene oxide) (PPO) blocks—are well-known for their distinct amphiphilicity. Because of their unique structure, poloxamers have surfactant qualities that make them extremely useful in biomedical and pharmaceutical applications, especially as Mucoadhesive polymers. The capacity of a substance to stick to mucosal surfaces—such as those lining the nose, eyes, gastrointestinal system, and other regions rich in mucous membranes—is referred to as "mucoadhesion". The PEO blocks of poloxamers are mainly responsible for their Mucoadhesive qualities. They form hydrogen bonding and van der Waals forces with mucin molecules to build connections. This property is essential for creating drug delivery systems that can stick to mucosal tissues, prolonging the period that pharmaceutical formulations are in contact with the body and promoting better drug absorption.[41]

A notable illustration of a Mucoadhesive poloxamer is Pluronic F127, sometimes referred to as Poloxamer 407. This specific poloxamer is made up of two hydrophilic PEO blocks on each side of a central hydrophobic PPO block. Poloxamer 407 has been widely used in a variety of drug delivery methods, such as topical applications, oral drug administration, and ocular formulations. For example, Poloxamer 407's Mucoadhesive qualities in ophthalmic formulations are essential for increasing the bioavailability of medications by extending their interaction with the ocular mucosa. Poloxamer 407 has also been used in oral drug delivery to lengthen the duration that drug formulations spend in the gastrointestinal system, which improves drug absorption and therapeutic effectiveness. Additionally, Poloxamer 407's Mucoadhesive properties in topical applications help to maintain medication release, which makes it useful for creating controlled-release formulations.[42]

4.2.12 Pectins

Pectin is a naturally occurring polysaccharide that comes from the cell walls of plants, especially those of apples and citrus fruits. It is a useful polymer in many pharmacological and biological applications because of its well-known Mucoadhesive qualities. The term "mucioadhesion" describes a substance's capacity to stick to mucosal surfaces, as those in the digestive system.[43]

Pectins' distinct structural characteristics play a role in their Mucoadhesive properties. The Mucoadhesive qualities of these polymers, which consist of linear chains of galacturonic acid units, are ascribed to the existence of carboxyl groups that have the ability to create hydrogen bonds with the mucin glycoproteins found in the mucosal layer. Modulating the molecular weight, esterification level, and side chain presence of pectins can change their Mucoadhesive strength. Drug administration systems are one prominent use for pectin as a Mucoadhesive polymer. It is possible to create pectin-based formulations that stick to mucosal surfaces, increasing medication absorption and extending the drug's residence duration at the target location. For the regulated release of medications in the gastrointestinal tract, for instance, pectin-based oral drug delivery systems have been investigated. The creation of Mucoadhesive films, gels, and patches is one use for pectin's Mucoadhesive qualities outside of medicine. These dosage forms provide a prolonged release of medication or other active components because they are designed to stick to mucosal surfaces. For transmucosal medication administration, pectin-based Mucoadhesive patches can be placed to the oral mucosa. Mucoadhesive buccal patches, which are used to administer medications including antiemetics, analgesics, and anti-inflammatory medicines, are an example of a Mucoadhesive formulation based on pectin. Because pectin adheres to mucosal surfaces, it is also used in the creation of Mucoadhesive vaginal gels for medication administration or as a component in formulations for wound healing.[44-46]

4.2.13 Starch

Because of its Mucoadhesive qualities, starch, a polymer of carbohydrates generated from plants, has attracted interest in the biomedical and pharmaceutical industries. Material adherence to mucosal surfaces is known as mucoadhesion, and starch is a good fit for a number of applications due to its unique properties. Two glucose polymers, amylopectin, a branching structure, and amylose, a linear chain, make up the majority of starch. The hydrophilic characteristics of starch and the hydroxyl groups on its glucose units give it its Mucoadhesive qualities. These hydroxyl groups aid in the formation of a strong adhesive connection via hydrogen bonding with mucins on mucosal surfaces.[47]

There are several different kinds of starch, including cross-linked, modified, and native starch. Starch's Mucoadhesive qualities can be improved by modification, and cross-linking increases the material's durability and resistance to enzymatic breakdown. Pharmaceutical formulations for oral medication administration frequently contain starch. Tablets, films, or patches based on starch that are Mucoadhesive can be made to stick to the gastrointestinal tract's mucosal surfaces, allowing for more regulated medication release and absorption. Hydrogels based on starch have also been investigated for use in medication

administration.[48]

For buccal medication administration, starch-based Mucoadhesive patches and tablets are frequently used. The oral mucosa is adhered to by these formulations, which guarantees extended contact with the mucosal surface and improves medication absorption. Mucoadhesive starch pills, for instance, might be utilised to administer painkillers or antifungal medications. Vaginal medication delivery methods use creams and gels that are based on starch to adhere to the mucosa. These formulations stick to the mucosa of the vagina, releasing medication over time to treat infections or other gynaecological diseases. The Mucoadhesive qualities of starch are also utilised in formulas for wound healing. Gels or dressings made of starch can stick to the wound site and form a barrier that protects it while speeding up the healing process. Starch's Mucoadhesive properties help it stay in touch with the wound surface. Because starch is a naturally occurring polysaccharide, it may be used safely and biocompatiblely in a variety of biological applications. Its biodegradability enhances its appeal in these situations even further.[49-50]

4.2.14 Poly Ethylene Glycol (PEG)

Polyethylene glycol, or PEG, is a multipurpose polymer that finds use in the food, cosmetics, and pharmaceutical sectors, among other disciplines. PEG is a Mucoadhesive polymer with special qualities that enable it to stick to mucosal surfaces, including the mucous membranes or the gastrointestinal system. Here are some samples and in-depth remarks on PEG as a Mucoadhesive polymer: PEG's capacity to establish hydrogen bonds with mucin, a glycoprotein found in mucus secretions, gives it its Mucoadhesive qualities. By strengthening PEG's residence duration on mucosal surfaces, these linkages enable longer contact times and better medication absorption. PEG can be utilised in the creation of medication delivery systems with controlled release. PEG's Mucoadhesive properties aid in the drug's continuous release at the intended spot.[51]

Examples of Mucoadhesive formulations based on PEG: 1. PEGylated Nanoparticles: PEG is frequently utilised to alter a particle's surface in order to enhance its Mucoadhesive qualities. This is useful in medication delivery systems when mucosal surfaces require nanoparticle adhesion. 2. PEGylated Hydrogels: PEG-containing hydrogels have the ability to stick to mucosal surfaces and deliver medication over time. Numerous medical applications, including medication administration and wound healing, make use of these hydrogels. 3. PEGylated Buccal Films: PEG-based Mucoadhesive buccal films are intended for buccal administration of medication. The buccal mucosa is adhered to by these films, enabling regulated medication release.[52]

To further improve Mucoadhesive characteristics, new PEG compounds and combinations with other polymers are being investigated in ongoing research. New developments in nanotechnology are enabling the creation of increasingly complex PEG-based medication delivery devices.[51]

4.2.15 Sulfated polysaccharide

A family of polymers called sulfated polysaccharides is well-known for its Mucoadhesive qualities. The term "mucicoadhesion" describes a substance's capacity to stick to biological tissues' mucus layer, which includes mucosal surfaces such as those found in the respiratory system, gastrointestinal tract, and other mucosal membranes. Owing to their special qualities, sulfated polysaccharides have been thoroughly researched for their possible uses in medication administration, wound healing, and as biomaterials. Typically, sulfated polysaccharides come from natural sources such animal tissues, bacteria, fungus, and seaweeds.[53]

They are made up of lengthy chains of monosaccharides, or sugar molecules, to which sulphate groups are joined. Mucoadhesion results from electrostatic interactions between the negatively charged mucin molecules in mucus and the sulphate groups on the polysaccharide chains. Mucoadhesion improves medication absorption and bioavailability by lengthening the residence duration of drug delivery systems on mucosal surfaces. Sulfated polysaccharides that possess Mucoadhesive properties include Dextran Sulphate, Carrageenan, Heparin, and chondroitin sulphate. Mucoadhesive polymers are utilised in pharmaceutical and research applications. They improve tissue adhesion and aid in the healing of wounds when used as wound dressings. The application of sulfated polysaccharides in the creation of biomaterials, such as implants and scaffolds for tissue engineering, is being researched. In order to prevent viral infections, topical preparations containing certain sulfated polysaccharides—which have antiviral properties—are now being investigated.[54-55]

4.2.16 Carrageenan

Red seaweed yields a linear sulfated polymer called carrageenan. It is a common thickening, gelling, and stabilising ingredient in the food business. It is a useful substance for biomedical and pharmaceutical applications due to its Mucoadhesive qualities.

Through hydrogen bonds, electrostatic interactions, and van der Waals forces with mucin found on mucosal surfaces, carrageenan exhibits mucoadhesion. Three primary forms of carrageenan are distinguished by their chemical structure and gel-forming abilities: kappa, iota, and lambda. Iota-carrageenan is one of them that is well-known for having Mucoadhesive properties. Carrageenan is utilised in drug delivery systems to improve medication bioavailability and extend drug release, particularly in oral and nasal applications.[56] Wound dressings with carrageenan form a Mucoadhesive barrier that keeps the dressing in place and promotes wound healing. Mucoadhesive carrageenan gels offer extended contact with oral surfaces and are utilised in mouthwash and toothpaste solutions. creation of a Mucoadhesive gel for oral medication distribution that combines glycerin, water, and iota-carrageenan. The gel sticks to the oral mucosa, releasing the active medication component gradually also nasal spray to extend the medication's retention period on the nasal mucosa and increase drug absorption.[52]

4.2.17 Gelatine

Because of its special qualities, gelatin is a Mucoadhesive polymer that is frequently used in pharmaceutical and biological applications. The protein collagen, which is present in animal connective tissues, is the source of gelatin, which has outstanding biocompatibility and biodegradability. Its capacity to stick to mucosal surfaces—such as those in the gastrointestinal system or mucous membranes—is referred to as its Mucoadhesive nature. Because of this property, gelatin is a great option for drug delivery systems that aim to increase the sustained release and bioavailability of pharmaceuticals.[57] The creation of Mucoadhesive drug delivery systems for oral administration is one noteworthy use of gelatin. Gelatin-based formulations have the potential to boost absorption and therapeutic effectiveness in this situation by prolonging the duration of medication residence on mucosal surfaces. To improve gelatin's Mucoadhesive qualities even more, it is frequently mixed with other polymers or bioadhesive substances. For example, the synergistic Mucoadhesive properties of formulations including gelatin and chitosan, a polysaccharide produced from crab shells, have been investigated. Drugs can be released from gelatin-based Mucoadhesive systems in a regulated manner, minimising changes in drug levels and lowering the possibility of unwanted effects. Because of its adaptability, gelatin has been used to create a variety of dosage forms, such as films, gels, and microspheres, each of which meets a unique need for drug administration. Personalised medicine and drug delivery are two areas where gelatin's potential as a biomaterial is demonstrated by its application in Mucoadhesive formulations.[58]

5. Various Mucoadhesive drug delivery Route

A flexible method that improves medication absorption and extends the residency duration at mucosal surfaces is Mucoadhesive drug administration. Mucoadhesive formulations, such buccal patches or tablets, stick to the buccal mucosa in the mouth cavity, providing a practical and non-invasive method of delivering systemic drugs. Gels and sprays that are nasal Mucoadhesive take use of the nasal mucosa's high vascularization to offer a quick and efficient way for drugs to be absorbed. The use of ocular Mucoadhesive systems, such as eye drops or inserts, enhances the retention of ocular drugs and prolongs the therapeutic benefits. Targeting the vaginal mucosa, vaginal Mucoadhesive formulations—such as gels or rings—offer controlled release and improved bioavailability for local or systemic medication administration. These diverse Mucoadhesive drug delivery methods demonstrate how this tactic may be tailored to distinct anatomical locations for better therapeutic results. The oral mucosa is comparatively more porous and has a large blood supply (Fig. 4).[1]

5.1 Oral drug delivery

Oral medication delivery is convenient, easy to give, and patient compliance is high, it is a commonly used approach for giving pharmaceutical substances. The capacity of a drug delivery system to cling to the mucosal surfaces of the gastrointestinal tract, improving drug retention and absorption, is known as mucoadhesion, and it is a key concept in oral drug administration. A layer of mucus covers the mucosal surfaces, acting as a barrier of defense. Mucoadhesive drug delivery devices take use of this interaction to allow for extended contact between the formulation and the mucosal layer.[59] The use of buccal adhesive patches is one prominent instance of Mucoadhesive oral medication administration. These patches transfer the medication straight into the circulation by adhering to the buccal mucosa, the inside lining of the cheek. Treatment of chronic illnesses, including hypertension or pain management, is one area of notable use, where the maintenance of therapeutic levels requires prolonged and regulated drug delivery.[60]

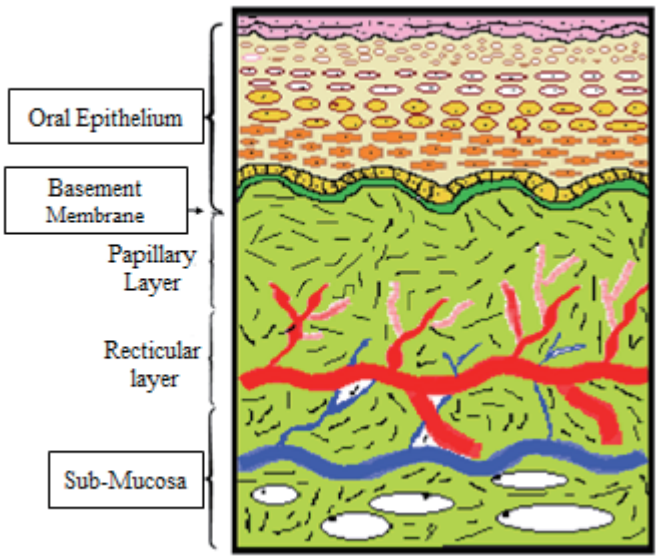

Figure 4: Oral Mucosa Membrane physiology[1]

The formulation frequently contains polymers such as hydroxypropyl methylcellulose, polyacrylic acid, or chitosan to produce the Mucoadhesive qualities. These polymers engage with the mucus layer's mucin molecules to establish bonds that keep the drug delivery mechanism attached. By reducing first-pass metabolism and lengthening the drug's residence duration at the absorption site, this Mucoadhesive technique may increase the drug's total bioavailability. In (Table-2) some pharmaceutical dosage form which is available in market are shown.[1]

5.1.1 Buccal Tablet

Specifically made for localized drug release, buccal tablets are intended to be inserted into the buccal cavity—the space between the cheek and the gums—for oral medication administration. A crucial feature of buccal tablets is mucoadhesion, which guarantees extended contact with the buccal mucosa and promotes improved drug absorption. Typically, the tablets include Mucoadhesive polymers that stick to the mucin layer in the buccal cavity, including hydroxypropyl methylcellulose, chitosan, or carbomer. Suboxone®, a well-known brand of buccal tablets used to treat opiate dependency, contains buprenorphine and naloxone. Because of the tablet's Mucoadhesive qualities, the active components may be released gradually, maintaining therapeutic levels and reducing variations in drug concentration.[61]

Onsolis®, a buccal soluble film that contains fentanyl to treat breakthrough cancer pain, is another illustration. Because the film sticks to the buccal mucosa, it acts quickly and prevents the liver's first-pass metabolism, which is common with oral drug administration. Buccal tablets' Mucoadhesive properties have a number of benefits, including as increased patient compliance, less adverse effects, and better absorption. Because of these characteristics, buccal tablets are a desirable choice for medications that need exact control over the kinetics of release and systemic absorption. The creation and application of buccal tablets exemplify the creative ways in which mucoadhesion may be leveraged to enhance therapeutic results and optimize medication delivery.[62]

5.1.2 Buccal Patch

A buccal patch is a type of drug delivery device that attaches to the inner lining of the cheek, known as the buccal mucosa, and releases medicine into the circulation. One important characteristic of buccal patches is their mucoadhesion, or their capacity to stick to mucosal surfaces and release the medication in a regulated way. The avoidance of first-pass metabolism in the liver and the more prolonged and regulated release that results from this mode of drug administration increase therapeutic effectiveness, among other benefits. The Fentanyl buccal patch is one type of buccal patch available on the market. Strong opioid analgesic fentanyl is used to treat extreme pain, especially in cancer patients.[63] The regulated release of fentanyl into the bloodstream is made possible by the buccal patch's attachment to the buccal mucosa. For patients who need ongoing pain control, this mode of administration offers a reliable and long-lasting analgesic effect. Other medications, such nicotine replacement treatment patches for quitting smoking and hormone replacement therapy patches,

Table 2: Marketed formulations available in market[1]

Route. of.administration	Polymeric.system	Used.drug	Application
Ophthalmic	Liposomes	Pilocarpine.HCL	Increased.miotic.response.and.ocular. bioavailability.of.the.drug
	Nanoparticles	Amikacin,.metipranolol,. indomethacin	For.the.treatment.of.respiratory. diseases/to.treat.glaucoma
Nasal	Liposomes	Acyclovir	Anti.HIV
	Aqueous.solution	Apomorphine	Parkinson's.disease
	Microspheres	Gentamicin	Antibiotic
Buccal	Mucoadhesive.tablets	Miconazole.nitrate,.ketoconazole,. Felodipin,Enalapril.maleate	For.HIV-positive.patients.suffering. from.oropharyngeal.candidiasis
	Tablets.(Nitrogard.R)	Nitroglycerin	To.take.care.of.angina.attack
	Patches	Verapamil.hydrochloride	Preventive.medication.for.migraine.
		Carvedilol	Left.ventricular.dysfunction.following. myocardial.infarction
	Films	Glipizide	Most.potent.of.the.sulfonylurea. antidiabetic.agents
		Clotrimazole	For.oral.Candida.infections
		Glibenclamide	Used.in.the.treatment.of.maturity-onset.diabetes
Vaginal	Suppositories	Acetaminophen	Anti-inflammatory.analgesic
	Solid.dispersion/Tablet	Benzydamine	Mouth.ulcer
		Clotrimazole	Antifungal.activity,.antifungal. chemotherapy

are also delivered by Mucoadhesive buccal patches. By providing a simple and non-invasive method of medication administration, reducing adverse effects, and guaranteeing a more consistent pharmacokinetic profile, these patches improve patient compliance. In general, buccal patches are a novel method of drug administration that maximize therapeutic results by utilizing the special qualities of mucoadhesion.[64]

5.1.3 Buccal Film

With the help of the extensive network of blood arteries found in the oral cavity, buccal films—thin, flexible dosage forms—are intended to stick to the buccal mucosa, the inside lining of the cheek, and transfer medications into the bloodstream. Buccal films' Mucoadhesive qualities are essential for maintaining extended contact with the mucosal surface, which facilitates regulated medication release and improved bioavailability. The capacity of a substance to stick to mucosal surfaces and withstand being removed by saliva or other bodily fluids is known as mucoadhesion. Polymers having Mucoadhesive qualities, such as polyvinyl alcohol (PVA), sodium carboxymethylcellulose (NaCMC), and hydroxypropyl methylcellulose (HPMC), make up buccal films. By forming bonds with the buccal mucosa's mucin glycoproteins, these polymers can provide a prolonged drug delivery platform.[65]

Ondansetron is one medication that is frequently administered via buccal films; it is used to stop nausea and vomiting that come after chemotherapy or surgery. The buccal films of ondansetron exhibit effective mucoadhesion, guaranteeing an extended interaction with the buccal mucosa and a continuous release of the medication into the circulation. Another illustration is the opioid analgesic buprenorphine, which is used

to treat pain. Because of their Mucoadhesive qualities, buccal films containing buprenorphine offer a different method of administration that improves patient compliance and allows for regulated drug release.[66]

5.1.4 Buccal gels and ointments

Pharmaceutical compositions called buccal gels and ointments are intended to be administered through the mouth cavity's buccal mucosa. One important characteristic of these formulations is mucoadhesion, which is the gel or ointment's capacity to stick to the mucosal surface and increase medication absorption and residence duration. The buccal route is a desirable choice for systemic drug distribution since it avoids first-pass metabolism and has a mucosa that is reasonably porous. Buccal gels are semisolid dosage forms with the appropriate viscosity and bioadhesive qualities made of hydrophilic or hydrophobic polymers. In contrast, ointments are usually hydrophobic and might include lipophilic ingredients to improve medication penetration. These formulations include bioadhesive polymers, including carbomers, chitosan, sodium alginate, and hydroxypropyl methylcellulose, to obtain their Mucoadhesive qualities.[67] "Zyban" (bupropion hydrochloride), a medication used to help people stop smoking, is an illustration of a buccal gel. The dopamine and norepinephrine reuptake inhibitor bupropion is packaged as a bioadhesive gel to improve absorption and extend its duration of residence in the buccal cavity. "Orabase" (amlexanox), an ointment used to treat aphthous ulcers, is another example. The anti-inflammatory drug amlexanox is mixed with an adhesive ointment base to maintain long-term contact with the mouth mucosa and promote localized therapeutic effects. Because buccal gels and ointments are Mucoadhesive, they provide regulated drug release and enhanced bioavailability, which makes them useful for medications with limited therapeutic indices or those needing continuous release. These formulations are especially helpful for pediatric and geriatric populations since they eliminate the requirement for swallowing, which further enhances patient convenience. Buccal drug delivery systems are expected to find further development and application in a variety of therapeutic areas as pharmaceutical research advances.[68]

5.2 Ophthalmic drug delivery

Mucoadhesive polymers have become a viable method for ocular drug delivery systems, greatly enhancing the efficacy of therapy. These polymers, which include carbomer, hyaluronic acid, and chitosan, stick to the surface of the eyes, extending the amount of time that medications are in touch with the cornea and conjunctiva. For instance, by extending the duration of time that antiglaucoma medications like dorzolamide and timolol remain on the ocular surface, Mucoadhesive polymers may improve the bioavailability of these medications when used to treat glaucoma. The ability of Mucoadhesive polymers to produce a thin, flexible film across the ocular surface is one of its major advantages.[3] By prolonging the drug's residence period, this movie lowers the frequency of administration while enhancing patient compliance. For example, Mucoadhesive polymers such as hydroxypropyl methylcellulose (HPMC) may decrease the frequency of artificial tear administration and increase the durability of the tear film when treating dry eye syndrome. Mucoadhesive polymers also provide the possibility of continuous drug release, guaranteeing a therapeutic concentration that is consistently present at the target region. For instance, Mucoadhesive polymers may extend the release of medicines like moxifloxacin in the treatment of bacterial conjunctivitis, guaranteeing longer exposure to the pathogen and enhancing treatment results.[69]

5.3 Vaginal drug delivery

Mucoadhesive polymers have become a viable method for vaginal drug delivery systems, providing a number of benefits that increase treatment efficacy. These polymers, which include chitosan, polycarbophil, and hydroxypropyl methylcellulose, may stick to the mucosa of the vagina, increasing the amount of time that medications are in touch with the vaginal epithelium and improving absorption. For example, Mucoadhesive polymers may enhance the retention and bioavailability of antifungal or antibacterial medications such as metronidazole, clotrimazole, or miconazole for treating vaginal infections like candidiasis or bacterial vaginosis. In addition to increasing therapeutic effectiveness, this increased retention lowers medication administration frequency and boosts patient compliance.[70] The ability of Mucoadhesive polymers to establish a durable and bioadhesive layer on the vaginal mucosa is one of their greatest benefits. Drugs have a longer residence time after seeing this movie, which enables continuous release over time. Mucoadhesive polymers, for instance, may maintain the release of oestrogen during hormone replacement treatment, ensuring a steady therapeutic dosage and enhancing patient compliance. Mucoadhesive polymers also provide the possibility of targeted medicine administration to certain vaginal locations, including the cervix or vaginal fornix.

When treating diseases like cervical dysplasia or localised infections, this tailored administration may be very important. The future of vaginal medication administration seems to be bright for Mucoadhesive polymers, thanks to continuous developments in formulation methods and polymer chemistry. They provide efficient treatments for a range of vaginal ailments, such as infections, atrophy, contraception, and maybe even illnesses transmitted by sex. In the field of vaginal healthcare, Mucoadhesive polymers have the potential to greatly improve patient outcomes and quality of life by enhancing medication retention, bioavailability, and targeted administration.[71]

5.4 Nasal drug delivery

Nasal medication administration has attracted a lot of interest because of its many benefits, which include non-invasiveness, quick absorption of the drug, and avoidance of first-pass metabolism. Mucoadhesive polymers have become a viable method for nasal medication delivery systems, greatly increasing the efficacy of therapy. These polymers, which include xanthan gum, carbomer, and chitosan, stick to the nasal mucosa to increase the amount of time that medications are in touch with the nasal epithelium and to enhance drug absorption. Mucoadhesive polymers, for example, may enhance the bioavailability and retention of antihistamine medications such as azelastine or corticosteroids such as fluticasone in the treatment of allergic rhinitis, resulting in improved therapeutic effects.[72] The ability of Mucoadhesive polymers to create a persistent, bioadhesive film on the nasal mucosa is one of its key benefits. This improves the residence duration of medications and enables continuous release over a prolonged length of time. Mucoadhesive polymers, for instance, may maintain the release of decongestants like oxymetazoline in the treatment of nasal congestion brought on by the common cold, resulting in longer-lasting alleviation and increased patient compliance.Mucoadhesive polymers have enormous potential for the future of nasal medication administration due to continuous developments in formulation methods and polymer chemistry. By providing efficient treatments for a range of nasal ailments, such as allergies, infections, and congestion, they enhance patient outcomes and quality of life.[73]

6. Mucoadhesion evaluation methods

In drug delivery systems, Mucoadhesive polymers are essential because they prolong the residence period and increase the bioavailability of medicines at mucosal surfaces. To make sure these polymers are successful in drug delivery, it is crucial to assess their Mucoadhesive qualities. Mucoadhesive qualities are often assessed using the following techniques:[74]

6.1 Tensile Strength Measurement

One often used technique for assessing the Mucoadhesive qualities of polymers is the tensile strength test. This technique measures the greatest force needed to separate a Mucoadhesive polymer from a mucosal surface. For example, a tensile strength tester was used in a research by Abdelbary and Tadros (2011) to assess the Mucoadhesive qualities of several chitosan-based formulations. The tensile strength of the formulations was considerably raised by the addition of Mucoadhesive polymers, as shown by the findings, suggesting better Mucoadhesive characteristics. Similarly, a tensile strength test was used in another work by Bonengel et al. (2017) to assess the Mucoadhesive qualities of different hydrogel formulations. The findings indicated that hydrogels with Mucoadhesive polymers had greater values of tensile strength than hydrogels without such polymers, underscoring the significance of Mucoadhesive polymers in augmenting the Mucoadhesive characteristics of hydrogel compositions. In general, the tensile strength test is frequently utilised in the development of Mucoadhesive drug delivery systems and yields important information regarding the adhesive qualities of Mucoadhesive polymers.[75]

6.2 Shear Strength Measurement

By calculating the force necessary to separate a Mucoadhesive formulation from a mucosal surface under shear stress, the shear strength test is a commonly used technique to assess the Mucoadhesive qualities of polymers. The following formula may be used to get the shear strength (τ):

$$\tau = A/F$$

Where:

τ = Shear strength (N/m^2)

F = Force required for detachment (N) A = Area of contact (m^2)

For instance, a shear strength test was used in a research by Smart et al. (2014) to assess the Mucoadhesive qualities of various gel formulations. Using the previously indicated formula, the shear strength was determined. The findings demonstrated that the formulations including chitosan had much greater shear strength values than the formulations

without chitosan, suggesting superior Mucoadhesive characteristics. Similar to this, Zhang et al. (2019) used a shear strength test to assess the Mucoadhesive qualities of nanoparticles loaded with a medication. The findings showed that the shear strength values of coated nanoparticles were greater than those of uncoated nanoparticles, underscoring the significance of Mucoadhesive polymers in augmenting the Mucoadhesive characteristics of nanoparticles. All things considered, the shear strength test is often used in the creation of Mucoadhesive drug delivery systems and offers useful information regarding the adhesive qualities of Mucoadhesive polymers.[76-78]

6.3 Ex-Vivo Techniques

A vital technique for assessing the Mucoadhesive qualities of polymers using removed human or animal mucosal tissues is the ex vivo Mucoadhesive test. Measuring the force necessary to separate a Mucoadhesive formulation from the mucosal surface is one such technique. For instance, porcine buccal mucosa was used in a research by Yoncheva et al. (2012) to assess the Mucoadhesive qualities of polymeric nanoparticles. With the use of a texture analyzer, the force necessary to separate the nanoparticles from the mucosal surface was determined, yielding important details on their Mucoadhesive characteristics. Similar to this, Lee et al. (2018) used excised rabbit nasal mucosa to assess the Mucoadhesive qualities of thermosensitive hydrogels. Using a similar method, the force needed to separate the hydrogel formulations from the mucosal surface was assessed, proving the hydrogels' efficacy as Mucoadhesive drug delivery vehicles. All things considered, the ex vivo Mucoadhesive test is a crucial technique in the development of Mucoadhesive drug delivery systems and offers insightful information on the adhesive qualities of Mucoadhesive polymers.[79]

6.4 In-Vivo investigations

An essential technique for assessing a polymer's Mucoadhesive qualities in living animals or humans is the in vivo Mucoadhesive test. In this test, Mucoadhesive formulations are administered, and the drug concentration at the administration site is tracked over time. For instance, the Mucoadhesive qualities of nasal formulations comprising various Mucoadhesive polymers were assessed in rabbits in a research conducted by Illum et al. (2001). The formulations were applied intranasally, and microdialysis was used to track the drug's concentration in the nasal mucosa over time. The findings demonstrated that formulations with Mucoadhesive polymers had better Mucoadhesive qualities as seen by increased medication concentrations in the nasal mucosa in comparison to formulations without such polymers. Comparably, human participants were used in another investigation by Lupo et al. (2016) to assess the Mucoadhesive qualities of vaginal formulations including several Mucoadhesive polymers. The medication content in the vaginal fluid was monitored over time after the formulations were given intravaginally. The results showed that, in comparison to formulations without Mucoadhesive polymers, those with Mucoadhesive polymers had enhanced bioavailability and sustained drug release. All things considered, the in vivo Mucoadhesive test offers insightful knowledge on the adhesive qualities of Mucoadhesive polymers and their suitability for use in drug delivery applications.[80]

6.5 Peel strength test

By calculating the power needed to remove a Mucoadhesive formulation from a mucosal surface, the peel strength test is a popular technique for assessing the Mucoadhesive qualities of polymers. For instance, a peel strength test was used in a research by El-Hammadi et al. (2015) to assess the Mucoadhesive qualities of buccal films containing various Mucoadhesive polymers. Using a texture analyzer, the force needed to remove the films from the porcine buccal mucosa was assessed. The findings demonstrated that films with chitosan had better Mucoadhesive qualities as they displayed greater peel strength values when compared to films without chitosan. A peel strength test was also used in another work by Khutoryanskiy et al. (2009) to assess the Mucoadhesive qualities of nanoparticles coated with Mucoadhesive polymers. A similar method was used to quantify the force needed to remove the nanoparticles from the pig intestinal mucosa. The results showed that, in comparison to uncoated nanoparticles, coated nanoparticles with Mucoadhesive polymers had greater peel strength values. This underscores the significance of Mucoadhesive polymers in augmenting the Mucoadhesive characteristics of nanoparticles. In general, the peel strength test is widely utilised in the development of Mucoadhesive drug delivery systems and yields important information regarding the adhesive characteristics of Mucoadhesive polymers.[81-84], [1]

7. Mechanism of mucoadhesion

Mucoadhesive polymers work by forming chemical or

physical bonds with the mucosal surfaces they come into contact with. These bonds allow the polymers to adhere to the mucosa for an extended period, providing a controlled release of the drug over time. The adhesion of Mucoadhesive polymers is primarily attributed to their ability to interact with the mucus layer, which is rich in negatively charged glycoproteins. One mechanism by which Mucoadhesive polymers adhere to mucosal surfaces is through hydrogen bonding. Many Mucoadhesive polymers contain functional groups, such as hydroxyl or carboxyl groups, that can form hydrogen bonds with the glycoproteins in the mucus layer. This interaction creates a strong bond between the polymer and the mucosa, ensuring prolonged drug release.[2],[85] Another mechanism is the electrostatic interaction between the positively charged Mucoadhesive polymers and the negatively charged mucosal surfaces. Polymers such as chitosan, which is derived from chitin, a natural polysaccharide found in the exoskeletons of crustaceans, are known for their Mucoadhesive properties due to their positive charge. This electrostatic interaction allows the polymer to adhere to the negatively charged mucus layer, providing sustained drug delivery. In addition to their adhesive properties, Mucoadhesive polymers can also improve drug stability by protecting it from degradation. The mucus layer acts as a barrier that can prevent the drug from being degraded by enzymes or acidic conditions in the gastrointestinal tract or respiratory system. By adhering to the mucosa, Mucoadhesive polymers create a protective layer that shields the drug from degradation, ensuring its efficacy.[86]

8. Current challenges in drug delivery and how Mucoadhesive polymers address them

Drug delivery faces several challenges that can impact treatment effectiveness. One of the major challenges is the rapid clearance of drugs from the site of administration. For example, in oral drug delivery, drugs are often cleared rapidly from the gastrointestinal tract, resulting in poor bioavailability. Mucoadhesive polymers address this challenge by adhering to the mucosal surfaces, preventing rapid clearance and allowing for prolonged drug release.[87] This sustained release ensures better absorption and utilization of the drug, overcoming the limitations of rapid clearance. Another challenge is the degradation of drugs by enzymes or acidic conditions in the gastrointestinal tract or respiratory system. This degradation can reduce the efficacy of the drug and limit its therapeutic potential. Mucoadhesive polymers provide a protective barrier that shields the drug from degradation, ensuring its stability and efficacy. By creating a barrier between the drug and the harsh conditions of the mucosal environment, these polymers enhance drug stability and improve treatment outcomes. Furthermore, the lack of targeted delivery can limit the effectiveness of drugs, especially those with a narrow therapeutic window or drugs that are associated with systemic toxicity. Mucoadhesive polymers offer the advantage of localized drug delivery by targeting specific mucosal surfaces. By delivering the drug directly to the site of action, these polymers minimize systemic exposure and potential side effects, improving the safety and efficacy of the treatment.[88]

9. Recent advancements in Mucoadhesive polymer research

Recent research in the field of Mucoadhesive polymers has focused on developing new formulations and improving drug delivery systems. One area of advancement is the synthesis of novel Mucoadhesive polymers with improved adhesive properties and biocompatibility. Researchers are exploring the use of various polymers, such as polyethylene glycol (PEG) derivatives, polyvinyl alcohol (PVA), and polyacrylic acid (PAA), to develop Mucoadhesive systems with enhanced drug delivery capabilities. Another area of research is the development of Mucoadhesive nanoparticles. These nanoparticles, made from biodegradable polymers, have shown promise in improving drug delivery to mucosal surfaces. By encapsulating drugs within these nanoparticles, researchers can achieve controlled release and targeted delivery to specific mucosal sites. The small size of the nanoparticles allows for easy penetration through the mucus layer and enhances drug absorption. Researchers are exploring the use of Mucoadhesive polymers in combination with other drug delivery technologies, such as nanotechnology and microneedles. By combining different approaches, researchers aim to enhance drug delivery efficiency and overcome the limitations of individual systems. For example, the use of Mucoadhesive polymers in conjunction with microneedles can facilitate the delivery of drugs across the skin barrier, opening up new possibilities for transdermal drug delivery.[89]

10. Case studies showcasing the effectiveness of Mucoadhesive polymers

in drug delivery

Several case studies have demonstrated the effectiveness of Mucoadhesive polymers in improving drug delivery and treatment outcomes. These case studies highlight the impact of Mucoadhesive polymer-based delivery systems across different therapeutic areas. One such case study focused on the use of Mucoadhesive polymers in oral drug delivery. Researchers developed a Mucoadhesive tablet containing a drug for the treatment of peptic ulcers. The Mucoadhesive tablet enhanced drug bioavailability and sustained drug release, resulting in improved ulcer healing rates compared to conventional tablets. The targeted delivery of the drug to the ulcer site minimized systemic exposure and reduced the risk of side effects.[90] In another case study, Mucoadhesive polymers were used in nasal drug delivery to improve the effectiveness of an antiallergic drug. Researchers developed a Mucoadhesive nasal spray containing the drug and conducted clinical trials in patients with allergic rhinitis. The Mucoadhesive nasal spray showed superior efficacy compared to conventional nasal sprays, with reduced symptoms and improved patient satisfaction. The targeted delivery of the drug to the nasal mucosa enhanced drug absorption and therapeutic effect.[91] Furthermore, a case study in ocular drug delivery demonstrated the effectiveness of Mucoadhesive polymers in improving the bioavailability of an ophthalmic drug. Researchers developed Mucoadhesive eye drops containing the drug and conducted a study in patients with glaucoma. The Mucoadhesive eye drops showed improved drug penetration and prolonged drug release, leading to better intraocular pressure control and reduced need for additional medications.[92]

11. Future trends and potential developments in Mucoadhesive polymer-based drug delivery

The future of Mucoadhesive polymer-based drug delivery holds exciting possibilities for improving treatment effectiveness. Several trends and potential developments are expected to shape the field in the coming years. One trend is the development of smart Mucoadhesive polymers that can respond to specific stimuli or conditions. Researchers are exploring the use of stimuli-responsive polymers, such as temperature-sensitive or pH-sensitive polymers, to create Mucoadhesive systems that can release drugs in response to changes in the physiological environment. These smart polymers have the potential to enhance drug delivery precision and further improve treatment outcomes.[93] Another trend is the integration of Mucoadhesive polymer-based delivery systems with personalized medicine approaches. With advancements in genomics and personalized medicine, researchers aim to develop Mucoadhesive systems that can be tailored to individual patient needs. By considering factors such as genetic variations, disease characteristics, and patient preferences, personalized Mucoadhesive drug delivery systems can optimize treatment outcomes and improve patient satisfaction. Furthermore, the future of Mucoadhesive polymer-based drug delivery may include the development of novel administration routes and devices. Researchers are exploring innovative routes of administration, such as vaginal, rectal, or pulmonary delivery, to expand the applications of Mucoadhesive polymers. The development of novel devices, such as implants or patches, can offer new opportunities for controlled and localized drug delivery. Additionally, regulatory considerations and safety assessments will play a crucial role in the future of Mucoadhesive polymer-based drug delivery. As these systems become more advanced and widespread, regulatory agencies will need to establish guidelines and standards for their development, manufacturing, and use. Safety assessments will be essential to ensure the biocompatibility and long-term safety of Mucoadhesive polymer-based delivery systems.[94-98]

12. Conclusion

With the potential to significantly increase treatment efficacy, mucoadhesive polymers have shown to be a viable method in drug delivery systems. These polymers extend the duration of medication residence at the site of absorption and improve drug bioavailability by attaching themselves to mucosal surfaces. More time spent in touch with mucosal tissues not only increases drug absorption but also shields medications from enzymatic breakdown, improving the effectiveness of treatment. Mucoadhesive polymers provide a number of benefits over traditional drug administration methods, such as less systemic adverse effects, better patient compliance, and fewer dose frequency. Their adaptability makes them appropriate for a variety of therapeutic applications by enabling use in several drug delivery channels, including oral, nasal, ophthalmic, vaginal, and rectal routes. In anticipation of the future, current investigations are concentrated on creating new Mucoadhesive polymers that possess improved adhesive characteristics, biodegradability,

and biocompatibility. Mucoadhesive polymers have the potential to target certain tissues or cells and improve drug delivery effectiveness when combined with other cutting-edge drug delivery technologies like micro particles and nanoparticles. In summary, Mucoadhesive polymers provide better therapeutic efficacy, patient compliance, and low side effects, making them a flexible and useful strategy in drug delivery systems. With further study and advancement, Mucoadhesive polymers have the potential to significantly influence medicine delivery in the future and improve patient outcomes. Mucoadhesive polymers have the potential to revolutionize drug delivery systems and enhance patient care. With ongoing research, advancements in formulation technologies, and the integration of personalized medicine approaches, the future of Mucoadhesive polymer-based drug delivery holds great promise for improving treatment outcomes and transforming patient experiences.

Author contribution

All authors contributed to the idea and design of the review, with drafting of the article, and revision of the article.

Conflicts of interest

The authors declare that there is no conflict of interest.

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