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Review Paper

Mucoadhesive Drug Delivery System: A Review

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Abstract

Drug actions can be improved by new drug delivery system, such as mucoadhesive system. This system remains in close contact with the absorption tissue, the mucous membrane, releasing the drug at the action site leading to improvement in both local and systemic effects. There are many routes of mucoadhesive drug delivery system, oral route is the most ancient as well as preferred by patient being convenient to take. However peroral route has shortcomings such as hepatic first pass metabolism and enzymatic degradation in GIT which is a hindrance to the absorption of most proteins and peptides groups of drugs. The mucosa of the oral cavity presents a formidable barrier to drug penetration, and one method of optimizing drug delivery is by the use of adhesive dosage forms and the mucosa has a rich blood supply and it is relatively permeable. The buccal mucosa is very suitable for a bioadhesion system because of a smooth and relatively immobile surface and accessibility. Mucoadhesion can be achieved by using mucoadhesive polymers. There are different types of mucoadhesive polymers are available. Laminated devices have been developed to achieve sustained drug release.

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INTRODUCTION

MUCOADHESIVE DRUG DELIVERY SYSTEM

Mucoadhesive drug delivery systems are delivery systems which utilize the property of bioadhesion of certain polymers which become adhesive on hydration and hence can be used for targeting a drug to a particular region of the body for extended periods of time.

Bioadhesion is an interfacial phenomenon in which two materials, at least one of which is biological, are held together by means of interfacial forces. The

attachment could be between an artificial material and biological substrate, such as adhesion between a polymer and a biological membrane. In the case of polymer attached to the mucin layer of a mucosal tissue, the term "mucoadhesion" is used. [1]

Mucoadhesive drug delivery systems can be delivered by various routes:-

- Buccal delivery system
- Oral delivery system
- Vaginal delivery system
- Rectal delivery system
- Nasal delivery system
- Ocular delivery system

MUCOADHESIVE ORAL DRUG DELIVERY SYSTEMS

Oral route is the most preferred route for the delivery of any drug. Drug delivery via the membranes of the oral cavity can be subdivided as:-

- Sublingual delivery: This is systemic delivery of drugs through the mucosal membranes lining the floor of the mouth.
- Buccal delivery: This is drug administration through the mucosal membranes lining the cheeks (buccal mucosa).
- Local delivery: This is drug delivery into the oral cavity.

Within the oral mucosal cavity, the buccal region offers an attractive route of administration for controlled systemic drug delivery. Buccal delivery is the administration of drugs through the mucosal membrane lining the cheeks. Although the sublingual mucosa is known to be more permeable than the buccal mucosa, the latter is the preferred route for systemic transmucosal drug delivery. This is because the buccal mucosa has an expanse of smooth muscle and relatively immobile mucosa, which makes it a more desirable region for retentive systems. Thus, the buccal mucosa is more appropriate for sustained direction of drug delivery. [2]

ADVANTAGES OF ORAL MUCOADHESIVE DRUG DELIVERY SYSTEMS:

- Prolongs the residence time of the dosage form at the site of absorption, hence increases the bioavailability.
- Excellent accessibility, rapid onset of action.
- Rapid absorption because of enormous blood supply and good blood flow rates.
- Drug is protected from degradation in the acidic environment in the git.
- Improved patient compliance. [3]

DISADVANTAGES OF MUCOADHESIVE DRUG DELIVERY SYSTEMS:

- Occurrence of local ulcerous effects due to prolonged contact of the drug possessing ulcerogenic property.
- One of the major limitations in the development of oral mucosal delivery is the lack of a good model for *in vitro* screening to identify drugs suitable for such administration.
- Patient acceptability in terms to taste and irritancy.
- Eating and Drinking is prohibited. [3]

COMPONENTS / STRUCTURAL FEATURES OF ORAL CAVITY

Oral cavity is that area of mouth delineated by the lips, cheeks, hard palate, soft palate and floor of mouth. The oral cavity consists of two regions.

- Outer oral vestibule, which is bounded by cheeks, lips, teeth and gingival (gums).
- Oral cavity proper, which extends from teeth and gums back to the fauces (passage which lead to pharynx) with the roof comprising the hard and soft palate. The tongue projects from the floor of the cavity.

ANATOMY AND NATURE OF ORAL CAVITY:

The oral cavity may be divided into two regions, the outer oral vestibule, bounded by the lips and cheeks

and the oral cavity itself the borders being, and formed by the hardened soft palates, the floor of the mouth and tonsils.

Physical Description of Oral Cavity:

The mucosa that lines the oral cavity may be divided into three types, classified according to their function as:-

1. Masticatory mucosa: Which includes the mucosa around the teeth and on the hard palate and these regions have keratinized epithelium.
2. Lining mucosa**:** Which covers the lips, cheeks, base of the oral cavity, lower part of tongue, buccal mucosa and the soft palate and these regions have non keratinized epithelium.
3. Specialized mucosa: Covering the dorsum of the tongue with highly keratinization. [1]

OVERVIEW OF THE ORAL MUCOSA

Structure

The oral mucosa is comprised of squamous stratified (layered) epithelium, basement membrane, the lamina propria and submucosa. It also contains many sensory receptors including the taste receptors of the tongue. The epithelium of the buccal mucosa is about 40-50 cell layers thick, while that of the sublingual epithelium contains somewhat fewer.

Permeability

The oral mucosa in general is somewhat leaky epithelia intermediate between that of the epidermis and intestinal mucosa. It is estimated that the permeability of the buccal mucosa is 4-4000 times greater than that of the skin**.** In general, the permeabilities of the oral mucosae decrease in the order of sublingual greater than buccal and buccal greater than palatal. This rank order is based on the relative thickness and degree of keratinization of these tissues, with the sublingual mucosa being relatively thin and non-keratinized, the buccal thicker and non-keratinized, and the palatal intermediate in thickness but keratinized.

Environment

The cells of the oral epithelia are surrounded by an intercellular ground substance, mucus, the principle components of which are complexes made up of proteins and carbohydrates. These complexes may be free of association or some maybe attached to certain regions on the cell surfaces. This matrix may actually play a role in cell-cell adhesion, as well as acting as a lubricant, allowing cells to move relative to one another. Along the same lines, the mucus is also believed to play a role in bioadhesion of mucoadhesive drug delivery systems.

Composition of Mucus Layer:

Mucus is a translucent and viscid secretion which forms a thin, contentious gel, mean thickness of this layer varies from about 50-450 µm in humans secreted by the globet cells lining the epithelia. It has the following general composition.

- Water -95%
- Glycoprotein and lipids – 0.5-3.00%
- Mineral salts – 1%
- Free proteins – 0.5-1.0% [1]

Functions of Mucus Layer:

1. Protective: resulting particularly from its hydrophobicity.
2. Barrier: The role of the mucus layer as a barrier in tissue absorption of the drugs and influence the bioavailability.
3. Adhesion: Mucus has strong adhesion properties.
4. Lubrication: It is to keep the mucus from the goblet cell is necessary to compensate for the removal of the mucus layer due to digestion, bacterial degradation and solubilisation of mucin molecules. [1]

Role of Saliva:

Saliva is composed of 99% water and is complex fluid containing organic and inorganic material. Secretion of saliva is highest during working hours.

1. Protective fluid for all tissues of the oral cavity.
2. Continuous mineralization / demineralization of the tooth enamel.
3. Moisten the oral cavity. [4]

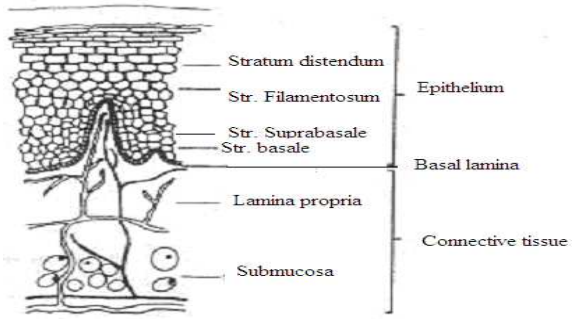

Fig 1: Structure Of Oral Mucosa [4]

THEORIES OF MUCOADHESION

There are six general theories of adhesion, which have been adapted for the investigation of mucoadhesion:-

The electronic theory suggests that electron transfer occurs upon contact of adhering surfaces due to differences in their electronic structure. This is proposed to result in the formation of an electrical double layer at the interface, with subsequent adhesion due to attractive forces.

The wetting theory is primarily applied to liquid systems and considers surface and interfacial energies. It involves the ability of a liquid to spread spontaneously onto a surface as a prerequisite for the development of adhesion. The affinity of a liquid for a surface can be found using techniques such as contact angle goniometry to measure the contact angle of the liquid on the surface, with the general rule being that the lower the contact angle, the greater the affinity of the liquid to the solid.

The adsorption theory describes the attachment of adhesives on the basis of hydrogen bonding and van der Waals' forces. It has been proposed that these forces are the main contributors to the adhesive interaction. A subsection of this, the chemisorptions theory, assumes an interaction across the interface occurs as a result of strong covalent bonding.

The diffusion theory describes interdiffusion of polymers chains across an adhesive interface. This process is driven by concentration gradients and is affected by the available molecular chain lengths and their mobilities. The depth of interpenetration depends on the diffusion coefficient and the time of contact. Sufficient depth of penetration creates a semi-permanent adhesive bond.

The mechanical theory assumes that adhesion arises from an interlocking of a liquid adhesive (on setting) into irregularities on a rough surface. However, rough surfaces also provide an increased surface area available for interaction along with an enhanced viscoelastic and plastic dissipation of energy during joint failure, which are thought to be more important in the adhesion process than a mechanical effect.

The fracture theory differs a little from the other five in that it relates the adhesive strength to the forces required for the detachment of the two involved surfaces after adhesion.[5]

MECHANISMS OF MUCOADHESION

The mechanism of mucoadhesion is generally divided in two steps,

1. Contact stage
2. Consolidation stage

The first stage is characterized by the contact between the mucoadhesive and the mucous membrane, with spreading and swelling of the formulation, initiating its deep contact with the mucus layer. In some cases, such as for ocular or vaginal formulations, the delivery system is mechanically attached over in other cases, the deposition is promoted by the aerodynamics of the organ to the membrane, the system is administered, such as for the nasal route.

In the consolidation step, the mucoadhesive materials are activated by the presence of moisture. Moisture plasticizes the system, allowing the mucoadhesive molecules to break free and to link up by weak van der Waals and hydrogen bonds. Essentially, there are two theories explaining the consolidation step:

1. The diffusion theory
2. The dehydration theory. [6]

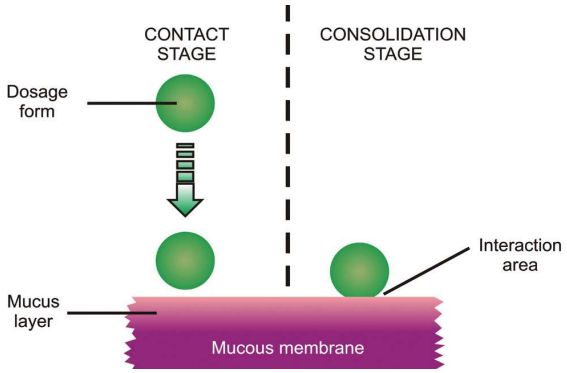

Fig 2: Two steps of mucoadhesion [6]

According to diffusion theory, the mucoadhesive molecules and the glycoproteins of the mucus mutually interact by means of interpenetration of their chains and the building of secondary bonds. For this to take place the mucoadhesive device has features favouring both chemical and mechanical interactions. According to dehydration theory, materials that are able to readily gelify in an aqueous environment, when placed in contact with the mucus can cause its dehydration due to the difference of osmotic pressure.

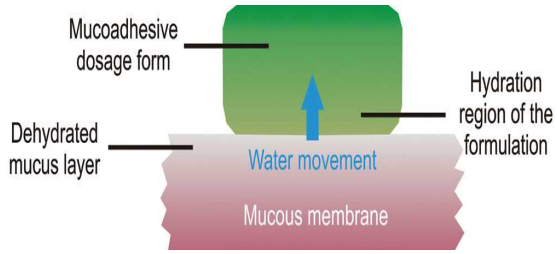

Fig 3: Dehydration theory of mucoadhesion [6]

FACTORS AFFECTING MUCOADHESION [1]

Based on the theories of the adhesion, it can be summarized

FACTORS	PROPERTIES	COMMENTS
a. Polymer related factors	1. Molecular weight	The mucoadhesive force increases with molecular weight of polymer, up to 1, 0000 and beyond this level there is no much effect.
	2. Concentration of active polymers	For solid dosage forms such as tablets showed that the higher the polymer concentration the stronger the mucoadhesion. There is an optimum concentration of polymer corresponding to the best mucoadhesion.
	3. Flexibility of polymer chain	Flexibility is an important factor for interpenetration and enlargement.
b. Environment related factors	1.pH	pH influences the charge on the surface of both mucus and the polymers.
	2.Applied strength	To place a solid mucoadhesive system, it is necessary to apply a defined strength.
	3. Initial contact time	The mucoadhesive strength increases as the initial contact time increases.
	4. Swelling	Swelling depends on both polymers concentration and on presence of water.
c. Physiological Variables	1.Mucin turn over	a. The mucin turnover is expected to limit the residence time of the mucoadhesive on the mucus layers.
	2.Diseased state	b. Mucin turnover results in substantial amounts of soluble mucin molecules. Physicochemical properties of mucus are known to change during diseased states, such as common cold, gastric ulcers, ulcerative colitis, cystic fibrosis, bacterial and fungal infections of the female reproductive tract and inflammatory conditions of the eye.

Table 1: Commercial Mucoadhesive Drug Delivery System [7]

DRUG	MUCOADHESIVE POLYMERS	APPLICATION SITE	NAME & FORM
1) Triamcinolone acetonide	Hydroxypropyl cellulose, cabopol 934	Oral cavity	Attach tablet
2) Nitroglycerin	Synchron (modified HPMC)	Buccal	Susadrintablet
3) Prochlorperazine Maleate	Ceronia, Xanthum Gum	Buccal	Buccastem tablet
4) Beclomethasone dipropionate	Hydroxypropyl cellulose	Oral cavity	Salcoat powder spray
	Sodium CMC, pectin, and gelatin inpoly-ethylene mineral ail base	Oral cavity	Oral base gel
	Sodium CMC ,pectin, and gelatin in polyisobutylene spread ontopolyethylene film	Oral cavity	Orahesive bandage
5) Beclomethasone dipropionate	Hydroxypropyl cellulose	Oral cavity	Rhinocort powder
	Polyacrylic acid	Vaginal	Raplens gel
6) Aluminium hydroxide	Sucrose octasulfate	GIT ulcers	Sucralfate
7) Fantanyl citrate	HPMC, Chitosan	Oral cavity	Fentora tablets
8) Nitroglycerine	Carbopol, HPMC K15M, K4M	Oral cavity	Nitrostat tablet
9) Miconazole	Na CMC, HEC	Oral cavity	Loramyc
10) Testosterone	HPMC,PVA,Chitosan PC and EudragitR S-100 (Polymethacrylic acid-co-methyl methacrylate)	Oral cavity	Striant SR
12) Buprenorphine	Gelatin and CP 934P CP 934P, Polyisobutylene, and Polyisoprene	Oral route	Subutex tablets

MUCOADHESIVE POLYMERS

Mucoadhesive drug delivery systems are based on the adhesion of a drug/ carrier to the mucous membrane. To promote this adherence a suitable carrier is required.

Ideal Characteristics of Mucoadhesive Polymers:

A mucoadhesion promotoing agent or the polymer is added to the formulation which helps to promote the adhering of the active pharmaceutical ingredient to the oral mucosa. The agent can have such additional properties like swelling so as to promote the disintegration when in contact with the saliva.

1) Polymer must have a high molecular weight up to 100.00 or more. This is necessary to promote the adhesiveness between the polymer and mucus.
2) Long chain polymers-chain length must be long enough to promote the interpenetration and it should not be too long that diffusion becomes a problem.
3) High viscosity.
4) Degree of cross linking- it influences chain mobility and resistance to dissolution. Highly cross linked polymers swell in presence of water and retain their structure. Swelling favours controlled release of the drug and increases the polymer/mucus interpenetration
5) Spatial conformation.
6) Flexibility of polymer chain- this promotes the interpenetration of the polymer within the mucus network.
7) Concentration of the polymer- an optimum concentration is required to promote the mucoadhesive strength. It depends however, on the dosage form.
8) Charge and degree of ionization- the effect of polymer charge on mucoadhesion was clearly shown by Bernkop-Schnurch and Freudl. Cationic chitosan HCl showed marked adhesiveness when compared to the control. The attachment of EDTA an anionic group increased the mucoadhesive strength significantly. DTPA/chitosan system exhibited lower mucoadhesive strength than cationic chitosan and anionic EDTA chitosan complexes because of low charge. Hence the mucoadhesive strength can be attributed as anion>cation>non-ionic.
9) Optimum hydration- excessive hydration leads to decreased mucoadhesive strength due to formation of a slippery mucilage.
10) Optimum pH – mucoadhesion is optimum at low pH conditions but at higher pH values a change in the conformation occurs into a rod like structure making those more available for inter diffusion and interpenetration. At very elevated pH values, positively charged polymers like chitosan form polyelectrolyte complexes with mucus and exhibit strong mucoadhesive forces.
11) It should non toxic, economic, biocompatible preferably biodegradable. [8]

Various mucoadhesive polymers can broadly be categorized as follow:

Synthetic polymers:

1. Cellulose derivatives (Methylcellulose, Ethyl cellulose, Hydroxyl ethyl cellulose, Hydroxyl propyl cellulose, Hydroxy propyl methylcellulose, Sodium carboxy methylcellulose).
2. Poly (Acrylic acid) polymers (Carbomers, Polycarbophil).
3. Poly hydroxyl ethyl methylacrylate.
4. Poly ethylene oxide.
5. Poly vinyl pyrrolidone.
6. Poly vinyl alcohol.

Natural polymers:

Tragacanth, Sodium alginate, Guar gum, Xanthum gum, soluble starch, Gelatin, Chitosan

Mucoadhesive polymers can also classify into following categories:

Traditional non-specific first-generation mucoadhesive polymers

First-generation mucoadhesive polymers may be divided into three main subsets, namely:

1) Anionic polymers,
2) Cationic polymers,
3) Non-ionic polymers.

Of these, anionic and cationic polymers have been shown to exhibit the greatest mucoadhesive strength. Consequently, such charged polymeric systems will now be examined in more depth.

Anionic polymers are the most widely employed mucoadhesive polymers within pharmaceutical formulation due to their high mucoadhesive functionality and low toxicity. Typical examples include poly (acrylic acid) (PAA) and its weakly cross-linked derivatives and sodium carboxymethylcellulose (NaCMC). PAA and NaCMC possess excellent mucoadhesive characteristics due to the formation of strong hydrogen bonding interactions with mucin.

Polycarbophil (Noveon) and Carbomers (Carbopol), PAA derivatives have been studied extensively as mucoadhesive platforms for drug delivery to the GI tract.

Cationic Polymers

Of the cationic polymer systems, undoubtedly chitosan is the most extensively investigated within the current scientific literature. Chitosan is a cationic polysaccharide, produced by the deacetylation of chitin, the most abundant polysaccharide in the world, next to cellulose. The intriguing properties of chitosan have been known for many years with many medicine. [9]

Novel second-generation mucoadhesive

The major disadvantage in using traditional non-specific mucoadhesive systems (first generation) is that adhesion may occur at sites other than those intended. Unlike first-generation non-specific platforms, certain second-generation polymer platforms are less susceptible to mucus turnover rates, with some species binding directly to mucosal surfaces; more accurately termed “Cytoadhesives”.

Lectins

The most widely investigated of such systems in this respect are lectins. Lectins belong to a group of structurally diverse proteins and glycoproteins that can bind reversibly to specific carbohydrate residues. After initial mucosal cell-binding, lectins can either remain on the cell surface or in the case of receptor-mediated adhesion possibly become internalised via a process of endocytosis.

Table 2: Various Properties and characteristics of bioadhesive polymers are discussed below:-[10]

Bioadhesives	Properties	Characteristics
Polycarbophil (polyacrylicacidcrosslinked with divinylglycol)	Mw 2.2×105 η 2000–22,500 cps (1% aq. soln.) κ 15–35 mL/g in acidic media (pH 1–3) 100 mL/g in neutral and basic media φ viscous colloid in cold water Insoluble in water, but swell to varying degrees in common organic sol-vents, strong mineral acids, and bases.	Synthesized by lightly crosslinking of 0.5–1% w/w divinyl glycol Swellable depending on pH and ionic strength. Swelling increases as pH increases. At pH 1–3, absorbs 15–35 ml of water per gram but absorbs 100 ml per gram at neutral and alkaline pH. Entangle the polymer with mucus on the surface of the tissue Hydrogen bonding between the nonionized carboxylic acid and mucin.
Poly (Hydroxy butyrate), Poly (e-caprolactone) and copolymers.	Biodegradable Properties can be changed by chemical modification, copolymerization and blending.	Used as a matrix for drug delivery systems, cell microencapsulation.
Carbopol/carbomer (carboxy polymethylene) empirical formula: (C3H4O2)x (C3H5 –Sucrose)y	Pharmaceutical grades: 934 P, 940 P, 971 P and 974 P. Mw 1×106–4×106 η 29,400–39,400 cps at 25 °C with 0.5% neutralized aqueous solution. κ 5 g/cm3 in bulk, 1.4 g/cm3 tapped. pH 2.5–3.0 φ water, alcohol, glycerine White, fluffy, acidic, hygroscopic powder with a slight characteristic odour.	Synthesised by cross-linker of allyl sucrose or pentaerythritol. Excellent thickening, emulsifying, suspending, gelling agent. Common component in bioadhesive dosage forms. Gel looses viscosity on exposure to sunlight. Unaffected by temp. Variations, hydrolysis, oxidation and resistant to bacterial growth. It contributes no off-taste and may mask the undesirable taste of the formulation. Incompatible with phenols, cationic polymers, high concentration of electrolytes and resorcinol.
Hydroxypropyl cellulose partially substituted polyhydroxy propylether of	Grades: Klucel EF, LF, JF, GF, MF and HF	Best pH is between 6.0 and 8.0. Solutions of HPC are susceptible to shear, heat,

cellulose HPC (cellulose 2-hydroxypropyl ether) empirical formula: (C15H28O8)n	Mw 6×104–1×106 η 4–6500 cps with 2.0% aq. soln. pH 5.0–8.0 ρ 0.5 g/cm3 in bulk Soluble in water below 38 °C, ethanol, propylene glycol, dioxane, methanol, isopropyl alcohol, dimethyl sulphoxide, dimethyl formamide etc. Insoluble in hot water White to slightly yellowish, odourless powder.	bacterial, enzymatic and bacterial degradation. It is inert and showed no evidence of skin irritation or sensitization. Compatible with most water-soluble gums and resins. Synergistic with CMC and sodium alginate. Not metabolized in the body. It may not tolerate high concentrations of dissolved materials and tend to be salting out. It is also incompatible with the substituted phenolic derivatives such as methyl and propyl parahydroxy benzoate. Granulating and film coating agent for tablet Thickening agent, emulsion Stabilizer, suspending agent in oral and topical solution or suspension
Hydroxypropylmethyl Cellulose HPMC (cellu-lose2-hydroxypropylmethyl ether) empirical formu-la: C8H15O6 – (C10H18O6)n –C8H15O5	Methocel E5, E15, E50, E4M, F50, F4M, K100, K4M, K15M, K100M. Mw 8.6×104 η E15–15 cps, E4M–400 cps and K4M–4000 cps (2% aqueous solution.) φ Cold water, mixtures of ethylene chloride and isopropyl alcohol. Insoluble in alcohol, chloroform and ether. Odorless, tasteless, white or creamy white fibrous or granular powder.	Mixed alkyl hydroxyalkyl cellulosic ether Suspending, viscosity-increasing and film-forming agent Tablet binder and adhesive ointment in-gradient E grades are generally suitable as film formers while the K grades are used as thickeners. Stable when dry. Solutions are stable at pH 3.0 to 11.0 Incompatible to extreme pH conditions and oxidizing materials.
Xantham gum Xantham gum is an anionic poly-saccharide derived from the fermentation of the plant bacteria *Xanthamonas campestris*	It will dissolve in hot glycerine. Solutions are typically in the 1500 to 2500 cps range at 1%; they are pseudoplastic and especially shear-thinning. In the presence of small amounts of salt, solutions shows good viscosity stability at elevated temperatures.	Xantham gum is more tolerant of electro-lytes, acids and bases than most other organic gums. It can, nevertheless, be gelled or precipitated with certain polyvalent metal cations under specific circumstances.
Carrageenan an anionic polysaccharide, ex-tracted from the red seaweed *Chondrus Crispus*.	Available in sodium, potassium, magnesium, calcium and mixed cation forms. Three structural types exist: Iota, Kappa, and Lambda, differing in solubility and rheology. The sodium form of all three types is soluble in both cold and hot water. Other cation forms of kappa and Iota are soluble only in hot water. All forms of lambda are soluble in cold water.	All solutions are pseudoplastic with some degree of yield value. Certain ca-Iota solutions are thixotropic. Lambda is non-gelling, Kappa can produce brittle gels; Iota can produce elastic gels. All solutions show a reversible decrease in viscosity at elevated temperatures. Iota and Lambda Carrageenan have excellent electrolyte tolerance; kappa's being somewhat less. The best solution stability occurs in the pH 6 to 10. It is compatible with most non-ionic and anionic water-soluble thickeners. It is strongly synergistic with locust bean gum and strongly inter-active with proteins. Excellent thermoreversible properties. Used also for microencapsulation.
Chitosan a linear poly-saccharide composed of randomly distributed β-(1-4)-linked D-glucosamine (deacetylated unit) and N-acetyl-D glucosamine (acetylated unit).	Prepared from chitin of crabs and lobsters by N deacetylation with alkali. Φ dilute acids to produce a linear polyelectrolyte with a high positive charge density and forms salts with inorganic and organic acids such as glutamic acid, hydrochloric acid, lactic acid, and acetic acid.	Mucoadhesive agent due to either secondary chemical bonds such as hydrogen bonds or ionic interactions between the positively charged amino groups of chitosan and the negatively charged sialic acid residues of mucus glycoproteins or mucins. Biocompatible and biodegradable. Excellent gel forming and film forming abilility.
Sodium Alginate consists chiefly of the alginic ac-id, a polyuronic acid composed of β-D-mannuronic acid resi-dues. Empirical formula: (C6H7O6Na) an anionic polysaccharide extracted principally from the giant kelp *Macrocystis Pyrifera* as alginic acid and neutralized to sodium salt.	Purified carbohydrate product ex-tracted from brown seaweed by the use of dilute alkali. Occurs as a white or buff powder, which is odourless and tasteless. pH 7.2 φ Water, forming a viscous, colloidal solution. Insoluble in other organic solvents and acids where the pH of the result-ing solution and acids where the pH of the	Safe and nonallergenic. Incompatible with acridine derivatives, crystal violet, phenyl mercuric nitrate and acetate, calcium salts, alcohol in concentrations greater than 5%, and heavy metals. Stabilizer in emulsion, suspending agent, tablet disintegrant, tablet binder. Excellent gel formation properties Biocompatibility Solutions show fair to good tolerance of water miscible solvents (10–30% of volatile solvents; 40–70% of glycols)

	resulting solution falls below 3.0.	Compatible with most water-soluble thickeners and resins.

Thiolated polymers:

The presence of free thiol groups in the polymeric skeleton helps in the formation of disulphide bonds with that of the cysteine-rich sub-domains present in mucin which can substantially improve the mucoadhesive properties of the polymers (e.g. poly (acrylic acid) and chitosan).Various thiolated polymers include chitosan–iminothiolane, poly(acrylic acid)– cysteine, poly (acrylic acid)–homocysteine, chitosan–thioglycolic acid, chitosan–thioethylamidine, alginate–cysteine, poly (methacrylic acid)– cysteine and sodium carboxymethylcellulose–cysteine.

Polyox WSR

A class of high molecular weight polyethylene molecular weight polyethylene oxide homopolymers having the following properties,

- Water soluble hydrophilic nature
- Functional group for hydrogen bonding
- Biocompatible and non toxic
- High molecular weight

Novel polymers

-Tomato lectin showed that it has binding selectivity to the small intestine epithelium.

-A new class of hydrophilic pressure sensitive adhesives (PSA) have been developed by corium technologies. Complex have been prepared by non covalent hydrogen bonding crosslinking of a film forming hydrophilic polymer with a short chain plasticizer having reactive OH groups at chain ends. [8]

Table 3: REPORTED MUCOADHESIVE / BUCCAL DOSAGE FORMS

DRUG	DOSAGE FORMS	POLYMERS	REFRENCES
1. Tramadol HCL	Microspheres	Carbopol, Sodium alginate	Gonjari *et al*, 2009
2. Flufenamic	Films	Chitosan	Mura *et al*, 2010
3. Ondansteron	Tablets	Carbopol, Sodium alginate, Gelatin	Kotagale *et al*, 2010
4. Domeperidone	Tablet	Taro gum	Arora *et al*, 2011
5. Glibenclamide	Films	HPMC, PVP, Carbopol	Indira *et al*, 2012
6. Gliclazide	Microspheres	Tamarind seed polysaccharide and alginate	Pal *et al*, 2012
7. Indomethacin	Tablets	Carbopol, Xanthum gum	Ikeuchi *et al*, 2012

RECENT ADVANCES IN MUCOADHESIVE DRUG DELIVERY SYSTEM

Mucoadhesive Polymers

Diverse classes of polymers have been investigated for potential use as mucoadhesive. PAA has been considered as a good mucoadhesive. PAA is copolymerised with polyethylene glycol (PEG) or poly (vinyl pyrrolidone) (PVP) to improve these properties.

Devices

Several laminated devices have been developed to achieve sustained drug release. It can be classified as:-

- Monolithic (or matrix) systems where the drug is dissolved or dispersed in the polymer system – diffusion of drug from the drug/polymer matrix controls the overall rate of its release from the device.
- Reservoir (or membrane) systems where diffusional resistance across a polymeric membrane controls the overall drug release rate.[11]

CONCLUSION

The phenomenon of mucoadhesion can be used as a model for the controlled drug delivery approaches for

a number of drug candidates. There is no doubt that the oral route is the most favoured and probably most complex route of drug delivery. The buccal mucosa offers several advantages for controlled drug delivery for extended periods of time. The mucosa is well supplied with both vascular and lymphatic drainage and first-pass metabolism in the liver and pre-systemic elimination in the gastrointestinal tract are avoided.

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