Review Article

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Review on mucoadhesive Dental Gel

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ABSTRACT

Mucoadhesive drug delivery system interact with mucus layer covering the mucosal epithelial surface and mucin molecules and increase the residence time of the dosage form at the site of absorption. Periodontitis is inflammation of the supporting tissues of the teeth caused by specific microorganisms. Intra – periodontal pocket, mucoadhesive drug delivery systems have been shown to be clinically effective in the treatment of periodontitis.

Keywords: Mucoadhesive, Periodontitis, Dental gel.

INTRODUCTION

Teeth are important for proper digestion and nutrition since they break down food content. Dental disease may develop if teeth are not properly cared for. Dental disease is the most common chronic disease in the world, and it is a costly burden on health-care systems. Infections that cause inflammation and tissue damage in the structures around the teeth cause periodontal disease, also known as periodontitis. Local drug delivery to oral cavity tissues hasa variety of uses, including the treatment of periodontal disease such as periodontal abscess, chronic periodontitis, periapical granuloma, dental caries, and root caries[1]. The term "periodontal" means " about the tooth"[2]. Dental caries, also known as tooth decay or a cavity, is a bacterial infection that causes demineralization and erosion of hard tissues. It is caused by bacteria fragmenting food debris on the tooth surface, which produces acid[3]].

Adhesion is the molecular force of attraction that acts to bring two unlike bodies together in the region of touch. Where at least one of the adherents, such as mucosal membrane is biological. The materials are held together for an "extended period of time" by interfacial powers. A variety of bioadhesive systems have been developed. Bioadhesives systems have been used in dentistry for many years in the form of denture adhesives, stoma-based adhesives, and even surgical gloves. The bioadhesion process where the biological substrate is a mucosal surface is known as mucoadhesion.

Mucoadhesive macromolecules are hydrophilic macromolecules with various hydrogen bonding groups. They bindto the mucin layer of a biological membrane, allowing them to be used for therapeutic purposes, particularly delivery formulations that target specific sites such as the eyes, oral cavity, and gastrointestinal tract. Local distribution of mucoadhesive gel formulation can extend the formulation's residence time, improve patient compliance, and make administration easier.

GELS CRITERIA

The term gel represents a physical state with properties intermediate between those of solids and liquids. Herman in 1949 prompt a number of criteria for gels: They square measure mixture systems of at least 2 parts (The gelling agent and therefore the filling components). They exhibit characteristics of solid state.

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FORMULATION

The mucoadhesive dental gel was prepared using dispersion methodology. Different formulations deliberation desired quantity each was prepared. A blank formulation without the API was also prepared. Add desired quantity of drug with numerous concentration of carbopol 940 compound. Propanediol was used as a co-solvent whereas triethanolamine was used as a gelling agent. The formulations were ready in spherical glass jar[4].

MECHANISM OF MUCOADHESION

Diffusion theory, Electronic theory, Adsorption theory, Wetting theory, and Fracture theory have all been suggested to explain mucoadhesion. Wetting, interpenetration, and mechanical interlocking between the mucin and polymer are thought to be the three phases of mucoadhesion. However, since isoadhesion exists between intrinsically different mucosal surfaces and formulations, there has yet to be a clear explanation. A single, universal theory is impossible to account for all forms of adhesion observed. The first step is to make sure the adhesive and the substrate are in close proximity (mucous). This is a requirement for mucoadhesion to occur. It is accompanied by the formation of a physical or mechanical bond in the crevices of mucous caused by the deposition and inclusion of an adhesive substance, as well as chain entanglement between the polymer chains of both phases, also known as inter diffusion[5].

According to the electronic theory, mucoadhesion is caused by electron transfer between the mucoadhesive polymerand the mucin glycoprotein network, resulting in the creation of an electric double layer at the mucoadhesive interface. According to the Adsorption theory, mucoadhesive systems cling to tissues through secondary molecular interactions like Van der Waals forces and hydrogen bonding[6].

Polymers are used as the adhesive component in bioadhesive formulations. These polymers are frequently water soluble, and when used dry, they draw water from the mucosal surface, resulting in a strong interaction. When these polymers are hydrated with water, they become viscous liquids, which increase their retention time over the mucosal surface and can contributeto adhesive interactions. Hydrogels (natural gums and cellulose derivatives, for example) are hydrophilic matrices that swell when placed in aqueous media. Since they are cross linked, they do not dissolve in water. As drugs are loaded into these hydrogels, chain ‘relaxation' occurs, and drug molecules are released through spaces or channels in the hydrogel network as water is absorbed into the matrix.

MUCOADHESIVE POLYMERS

For the localization of active agents to a selected location/site, mucoadhesive delivery systems are being explored.Polymers also played a key role in the development of such systems, permitting the active to pay longer at the required web site. Soluble and water-insoluble polymers frame mucoadhesive polymers. The adhesion of mucoadhesive polymers to the mucin-epithelial surface may be divided into 3 categories:

Sticky polymers that owe their mucoadhesion to their viscousness once placed in water.

Polymers that are in the main static in nature and cling by nonspecific, non-covalent interactions (althoughgas and hydrophobic bonding could also be significant).

Polymers that bind to a selected receptor web site on the self-adhesive surface of the tile. All 3 chemical compound sorts may be used for drug delivery.

Characteristics of an ideal mucoadhesive chemical compound :

- An ideal mucoadhesive chemical compound has the subsequent characteristic:
- They ought to not be harmful and may not be absorbed into the digestive tube.
- It should not cause irritation to the mucosa.
- It ought to ideally type a detailed non-covalent bond with the surfaces of mucin-epithelial cells.
- It will follow most tissues simply and have some site-specificity.
- It ought to be able to incorporate the medication on a daily basis and not impede it’s unharness.
- The chemical compound should not decompose throughout storage or throughout the indefinite quantityform's time period.
- The value of the chemical compound shouldn't be prohibitively high so as for the ready indefinite quantity type to be competitive[7] .

Classification of Mucoadhesive polymers

Based on origin :

a) SYNTHETIC MUCOADHESIVE POLYMERS:
   Cellulose derivatives, Poly (acrylic acid) polymers, Poly (hydroxyethyl methylacrylate), Poly (ethyleneoxide), Poly (vinyl pyrrolidone), Poly (vinyl alcohol).
b) NATURAL MUCOADHESIVE POLYMERS:
   Tragacanth, Sodium alginate, Karaya gum, Guar gum, Xanthan gum, Soluble starch, Gelatin, Pectin,Chitosan, etc.

Based on nature :

a) HYDROPHILIC POLYMERS:

The polymers among this class area unit soluble in water. Matrices developed with these polymers swell once place into associate aqueous media with consequent dissolution of the matrix. The polyelectrolytes extend bigger mucoadhesive property. E.g. poloxamer, hydroxypropylmethyl polyose, alkyl group polyose, poly (vinyl alcohol) and poly (vinyl pyrollidine), have conjointly been used for mucoadhesive properties.

b) POLYSACCHARIDES AND ITS DERIVATIVES:

Numerous polysaccharides and its derivatives like chitosan, alkyl polyose, mucopolysaccharide, group propyl group methylcellulose, group propyl group polyose, Xanthan gum, gellan gum, guar gum, and gum have found applications in ocular mucoadhesive delivery systems. Cellulose and its derivates are reported to have own surface active property additionally to its film forming capability. Cellulose derivatives with lower surface acting property are typically most popular in ocular delivery systems as they cause reduced eye irritation. Of the various cellulose derivates, atomic number 11 cellulose has been found to own wonderful ocular mucoadhesive property. Cationic cellulose derivatives (e.g. ion hydroxyethyl celluloses) are utilized in conjunction with varied anionic polymers for the event of sustained delivery systems.

c) HYDROGELS:

Hydrogels are outlined as three-dimensionally crosslinked compound chains that have the ability to hold water among its porous structure. The water holding capability of the hydrogels is chiefly owing to the presence of hydrophilic functional group, amino and carboxyl groups. Additionally to the drug targeting, mucoadhesive gel primarily based formulations for rising the bioavailability of the poorly water soluble drug. This was attributed to the increased retention time of the delivery system among the alimentary canal[8].

NOVEL MUCOADHESIVE POLYMERS

In novel mucoadhesive polymer cases, existing mucoadhesive polymers have been modified, while inothers, new materials are developed.

Lectins

Lectins are proteins which have the ability to reversibly bind with specific sugar/carbohydrate residues and are found in both animal and plant kingdom in addition to various microorganisms[9-11]. Many lectins have been found to be toxic and immunogenic which may lead to systemic anaphylaxis in susceptible individuals on subsequent exposure[12]. The specific affinity of lectins towards sugar or carbohydrate residues provides them with specific cyto-adhesive property and is being explored to develop targeted delivery systems. Lectins extracted from legumes have been widely explored for targeted delivery systems. The various lectins which have shown specific binding to the mucosa include lectins extracted from *Ulex europeaus* I, soybean, peanut and *Lens culnarius*[13]. The use of wheat germ agglutinin has been on the rise due to its least immunogenic reactions, amongst available lectins, in addition to its capability to bind to the intestinal and alveolar epithelium and therefore it could be used to design oral and aerosol delivery systems[14].

Thiolated polymers

These are thiomers, a special type of multifunctional polymer that is created by adding a thiol group to anexisting polymer. Free thiol groups on the polymeric backbone characterize these hydrophilic macromolecules. Thiomers can form intra- and interchain disulphide bonds within the polymeric network, improving the cohesive properties and stability of drug delivery systems like matrix tablets significantly. Thiomers, through a thioldisulphide exchange reaction and an oxidation mechanism, have the best mucoadhesive properties of all the polymeric excipients tested so far due to the formation of strong covalent bonds with mucus glycoproteins. 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[15].

BIOADHESIVE NANOPOLYMERS AS DRUG CARRIERS

The use of nanometer-scale particles or devices to diagnose and treat diseases at the molecular level is referred to as nanomedicine. Mucoadhesive nanopolymers appear to be a promising solution to the problem of topical drug bioavailability, particularly in the ocular drug delivery system. The possible entrapment of particles inthe ocular surface mucus layer and the interaction of bioadhesive polymer chains with mucin, which increases the precorneal resident time of the particular drug, are the justifications for the development of particulate systems for the delivery of ophthalmic drugs[16].

Alginate-Polyethylene Glycol Acrylate (Alginate - PEGAC)

Alginate-polyethylene glycol acrylate (alginate-PEGAc), a novel mucoadhesive polymer with an alginate backbone and acrylated polyethylene glycol, is synthesized. This polymer combines alginate's resilience, simplicity, and gelation capacity with PEG's characteristics and acrylate functionality to produce mucoadhesion properties.

PEG's ability to interpenetrate the mucus surface, combined with a Michael-type addition reaction between an acrylate end group on a polymer and the sulphide end group of the mucin-type glycoprotein, results in a close bond to the mucus. It has also developed a number of other multifunctional biomaterials for a range of biotechnological and medical applications[17].

Poloxomer

Poloxomer gels are investigated as they're reported to indicate phase transitions from liquids to mucoadhesive gels at body temperature and can thus enable in-situ gelation at the location of interest.

Pluronics and combination

Pluronics have additionally been with chemicals combined with poly(acrylic acid)s to supply systems with increased adhesion and retention within the bodily cavity. dihydroxyphenylalanine (DOPA), associate amino acid foundin membrane adhesive macromolecule that's believed to lend to the adhesive method, has additionally been combined with pluronics to boost their adhesion.

OTHER NOVEL MUCOADHESIVE POLYMERS

The incorporation of ethyl radical hexyl acrylate into a polymer with carboxylic acid so as to provide an additional hydrophobic and plasticized system. this might scale back association rate whereas allowing optimum interaction with the membrane surface, and conjointly the mucoadhesive force was found to be larger with the chemical compound than with poly (acrylic acid) alone. chemical group monooleate/water liquid crystalline phases have in addition been found to be mucoadhesive using a vary of membrane surfaces, although themechanism will take issue somewhat from that of various mucoadhesives[18].

Bacterial adhesions

Bacteria are able to adhere to epithelial surfaces of the enterocytes with the help of fimbriae. Fimbriae are long, glycoprotein like proteins found on the surface of the many bacterial strains. Their presence has been correlative with pathogenicity, e.g. adherence of E. coli to the comb border of animal tissue cells mediate by K99 fimbriae could be a necessity for resulting production and cellular uptake of E. coli cytotoxin. Thus, the DDS supported bacterial adhesion factors may well be associate degree economical mechanism to extend adhesion of bio adhesivemicrospheres to epithelial surfaces. Another study investigating the importance of microorganism adhesions has been allotted victimised as “invasin”, that could be a membrane super molecule from Yersinia pseudo tuberculosis. Cellular uptake of polymeric nanospheres functionalized with invasion has been ascertained using confocal laser scanning microscopy.

Amino acid sequences

Certain amino acid sequences have complementary elements on the cell and tissue layer surfaces and once connectedto micro particles will promote binding to specific cell surface glycoproteins. The cell surface glycoproteins square measure altered within the presence of disease conditions and these altered protein sequences are often targeted by the drug delivery device.

Antibodies

Antibodies may be created against selected molecules present on membrane surfaces. due to their high specificity, protein may be a rational selection as a compound matter for planning site specific mucoadhesives. This approach may be helpful for targeting medicine to growth tissues. (Table:1)

Table:1 Related research on mucoadhesive polymers and delivery systems[19,20,21,22]

Bioadhesive Polymer(s) Studied	Investigation Objectives
HPC and CP	Preferred mucoadhesive strength on CP, HPC, and HPC-CP combination.
HPC and CP	Measured bioadhesive property using peritoneal membrane
CP, HPC, PVP, CMC	Studied inter polymer complexation and its effect on bioadhesive strength
CP and HPMC	Formulation and evaluation of buccoadhesive controlled delivery systems
HPC, HEC, PVP and PVA	Tested mucosal adhesion on patches with two-ply laminates with an impermeable backing layer and hydrocolloid polymer layer
HPC and CP	Used HPC-CP powder mixture as peripheral base for strong adhesion andHPC-CP freeze dried mixture as core base

CP, PIP and PIB	Used a two roll milling method to prepare a new bioadhesive patch formulation
Xanthum gum and Locust beam gum	Hydrogel formation by combination of natural gums
Chitosan, HPC, CMC, Pectin, Xanthumgum and Polycarbophil	Evaluate mucoadhesive properties by routinely measuring the detachment force form pig intestinal mucosa
Hyaluronic acid benzyl esters,Polycarbophil and HPMC	Evaluate mucoadhesive properties
Hydroxyethyl cellulose	Design and synthesis of a bilayer patch(polytef-disk) for thyroidgl and diagnosis
Polycarbophil	Design of unidirectional patch for oral mucosal delivery of peptide drugs
Poly (acrylic acid) and Poly(methacrylicacid)	Synthesized and evaluated cross linked polymers differing in charge densities and hydrophobicity
Number of polymer including HPC,HPMC, CP, CMC	Measurement of bioadhesive potential and to derive meaningful on the structural requirement for bioadhesion
Poly(acrylic acid-co-acrylamide)	Adhesion strength to gastric mucus layer as a function of cross linking agent, degree of swelling and carboxyl group density
Poly(acrylic acid-co-methylmethacrylate)	Effects of polymer structural features on mucoadhesion
HEMA copolymerized with polymeg (polytetramethylene glycol)	Bioadhesive buccal hydrogel for controlled release delivery of buprenorphine
Poly(acrylic acid-co-butylacrylate)	Relationship between structure and adhesion for mucoadhesive polymers
CMC, Carbopol974P, Carbopol EX-55, Pectin(low viscosity), chitosan chloride	Mucoadhesive gels for intraoral delivery
CMC, CP, Polyethylene oxide, Maleic anhydride and Tragacanth	Buccal mucoadhesive device for controlled release anticandidal device - CMC tablets yielded the highest adhesive force.
HPMC and Polycarbophil (PC)	Buccal mucoadhesive tablets with optimal blend ratio of 80:20 PC to HPMC yielding the highest force of adhesion

Abbreviations: CP = Carbopol 934P, HPC = Hydroxy propyl cellulose, PVP = Poly(vinyl pyrrolidone), CMC = Sodium carboxymethyl cellulose, HPMC = Hydroxy propyl methyl cellulose, HEC = Hydroxy ethyl cellulose, PVA= Poly(vinyl alcohol), PIB = Poly(isobutylene), PIP = Poly(isoprene)

PERMEABILITY

The oral mucosae are a form of leaky epithelia that lies somewhere between the epidermis and the intestinal mucosa. The permeability of the buccal mucous membrane is measured to be 4-4000 times larger than that of the skin. Because of the complex structures and functions of the different oral mucosae, there are significant variations in permeability between different regions of the oral cavity, as shown by the large range in this recorded value. The permeabilities of the oral mucosae decrease in order of sublingual greater than buccal, buccal greater than palatal, and buccal greater than palatal[23].

The sublingual mucosa is thin and nonkeratinized, the buccal mucosa is thicker and nonkeratinized, and thepalatal mucosa are moderate in thickness but keratinized. The permeability barrier in the oral mucosa is thought to be caused by intercellular content derived from so-called "membrane coating granules" (MCG)[24]. This barrier can be found in the superficial layer's outermost 200 meters. A variety of very high molecular weight tracers, such as horseradish peroxidase[25] and lanthanum nitrate, have been used in permeation studies[26]. These tracers only penetrate the epithelium's outer layer or two of cells when added to the epithelium's outer surface. They permeate up to, but not into, the epithelium's outermost cell layers when added to the submucosal surface. According to these results, flattened surface cell layers appear to be the primary barrier to permeation, while more isodiametric cell layers appear to be relatively permeable. Apart fromthe

MCGs, the basement membrane can also be a barrier to permeation, but the outer epithelium is still thought to be the rate limiting stage in mucosal penetration. The basement membrane's structure isn't thick enough to keep even relatively large molecules out. (Table:2)

Table 2: List of compounds used as oral mucosal permeation enhancers

Permeation Enhancer
23-lauryl ether
Aprotonin
Azone
Benzalkonium chloride
Cetylpyridinium chloride
Cetyltrimethylammonium bromide
Cyclodextrin
Dextran sulphate
Lauric acid
Lauric acid/Propylene glycol
Lysophosphatidylcholine
Menthol
Methoxysalicylate
Methyloleate
Oleic acid
Phosphatidylcholine
Polyoxyethylene
Polysorbate 80
Sodium EDTA
Sodium salicylate
Sodium taurodeoxycholate
Sulfoxides

Advantage of Mucoadhesive drug delivery system

Increases absorption and, as a result, the therapeutic effectiveness of the medication by prolongingthe residence time of the dosage type at the site of absorption.

Very good accessibility

Fast absorption due to abundant blood supply and high blood flow rates - Increased drug bioavailability due to the avoidance of first-pass metabolism - In the acidic world of the GIT, the drug isshielded from degradation.

Patient compliance is improved; drug administration is simplified; and the mucosal surface allowsfor a quicker onset of action.

Limitation of Mucoadhesive drug delivery system

- The drugs having bitter taste cannot be formulated
- The drugs which irritate oral mucosa, cause allergic reactions and discoloration of teeth cannot be formulated
- If formulation contains antimicrobial agents, affects the natural microbes in the buccal cavity
- The patient feels discomfort in eating, drinking, speaking.
- Only the drugs which are absorbedby means of passive diffusion can be administered by buccal route
- Drugs which are unstable at buccal pH cannot be administered by this route
- Sometimes, the degradation of moisture sensitive drugs may take place by saliva[27]

EVALUATION OF FORMULATED TOOTH GEL:[28]

Physical examination

(Color, Odor, Taste, Smoothness, Relative Density)

- Formulated tooth gel was evaluated for its color. The visually color was checked.
- Odor was found by smelling the product.

- Taste was checked manually by tasting the formulation.
- The Smoothness was tested by rubbing the gel formulation between the fingers.
- Relative density was verify by weight in gram taken in 10 ml formulation and 10 ml H_2O using RD bottle.

Transparency

- Approximately 5 ml of formulated gel was taken in the 10 ml test tube and its transparency was checked by visually.

pH

A pH meter was used to calculate the pH of the prepared gel. 1 g gel was distributed in 100 mL filtered water in this process. The electrode was cleaned with double distilled water, dried with tissue paper, and calibrated with a regular buffer solution at 4.0, 7.0, and 9.0 before being used. The pH readings were taken three times and the average valueswere determined.

Homogeneity

By applying normal force at 27±20C, the tooth gel can extrude a homogeneous mass from the transparent collapsible tube or any suitable jar. Furthermore, the bulk of the contents must extrude from the container's crimp and be rolled out in a gradual manner.

Determination of sharp and edge abrasive particles

Extrude the material onto the butter paper until it is 15-20 cm long, then repeat the procedure for at least ten collapsible tubes. For the presence of sharp and hard tipped abrasive particles, press the contents of the entire lengthwith your finger tip. Such particles are not permitted in dental gel.

Viscosity

It was determined by using suitable viscometer (Brookfield) with 2 number spindles.

Microbial growth

Nutrient agar media was used in this process. The blank and sample petriplates were used, and the formulated gelsample was placed in a cross pattern on the sample plate aseptically. Up to 15 days, the microbial growth was monitored continuously.

The power to foam the foamability of formulated tooth gel was assessed by mixing a small amount of formulationwith water in a measuring cylinder and shaking it for ten times. The total amount of foam was calculated.

Determination of moisture and volatile matter

- Take 5 g of formulation placed in a porcelain dish containing 6-8 cm in diameter and 2-4 cm depth in it. Dry thesample in oven at 1050C.
- Calculation % by mass=100MI/M MI-Loss of mass(g) on drying M- Mass (g) of the material taken for the test.

Extrudability

The formulated gel was filled into a regular capped collapsible aluminium tube and crimped to the end in this process. The tube weights were kept track of. The tubes were clamped in place between two glass slides. The slideswere covered with 500 g until the cap was removed. The extruded gel was collected and measured in its entirety. The extruded gel's percentage was measured.

Spreadability

In this technique, slip and drag characteristic of gel involve. Formulated gel (2g) placed on the bottom slide underneath study. The formulated gel placed (Sandwich like) between this slide and another glass slides for 5 min toexpel air and to supply an identical film of the gel between slides. Excess of the gel was scrapped off from the sides. the highest plate was then subjected to drag of 80 g with the assistance of string connected to the hook and also the time (Sec) needed by the highest slide to hide a distance of seven.5 cm was noted. A short interval indicated higher spreadability.

Formula was used to calculate spreadability:

$$S=M \times L/T$$

Where, S= Spreadability M= Weight within the pan (tied to the higher slide) L= Length moved by the glass slide T=Time (Sec) taken to separate the higher slide from the bottom slide.

Stability study

It study was performed as per ICH guidelines. The formulated gel was crammed in collapsable tubes and keep attotally different temperature and humidity conditions, 25ºC±2ºC / hour ± 5-hitter RH, 30ºC±2ºC / 65th ± 5-hitter RH, 40ºC±2ºC / 75%±5% RH for pH of 3 months and studied for appearance, hydrogen ion concentration and spreadability.

MARKETED AVAILABLE TOOTH GEL

- Forever Bright **Toothgel**
- Aloe Vera **Tooth gel**
- Herbal **Tooth gel**
- Forever bright Aloe Vera **Toothgel**

CONCLUSION

Gels are becoming more common as a result of their increased stability and ability to provide managed release overother semisolid preparations

such as creams, ointments, pastes, and so on. The gel formulation may have better absorption properties, increasing the drug's bioavailability. A thorough investigation into the gel formulation's stability characteristics over a long period of time may open the door to its therapeutic use in patients. Since the polymer is water soluble, it forms a water washable gel and has a greater chance of being used as a topical drug delivery dosage form. The main advantage of topical drug delivery is that it allows for the accumulation of high local drug concentrations within the tissue and its vicinity for improved drug action. This is mainly advantageous when drugs with a short biological half-life and a limited therapeutic window are being used.

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