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Recent Advancements In Site Specific Mucoadhesive Drug Delivery Systems and Polymers

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ABSTRACT

Mucoadhesive dosage forms may be designed to enable prolonged retention at the site of application, providing a controlled rate of drug release for better therapeutic results. Mucoadhesive drug delivery systems are used to prolong the residence time of the dosage form at the site of application or absorption and to facilitate intimate contact of the dosage form with the underlying absorption surface to improve and enhance the bioavailability of drug. Some of the promising plymers that have been commonly used in these systems include polycarbophil, carbopol, lectins, chitosan, carboxymethylcellulose, pectin, carragenan, alginic acid, polylysine, polybrene, polyethylene glycol, polyvinyl pyrrolidone , dextran etc. Now scientists are developing mucoadhesive micro and nanoparticulate systems by using novel mucoadhesive polymers for better therapeutic results and site specific targeting with lesser side effects. Improvements in mucoadhesive based oral delivery and, in particular, the development of novel, highly-effective and mucosa-compatible polymers, are creating new commercial and clinical opportunities for delivery of narrow absorption window drugs at the target site to maximize their efficacy. This review is an effort to provide information on such mucoadhesive drug delivery systems that are developed for oral, buccal, nasal, rectal and vaginal routes for both systemic and local effect.

Keywords: Mucoadhesive; gastroretentive; bioavailability; micro and nanoparticulte; polymers.

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INTRODUCTION

Mucoadhesion can be defined as the ability of synthetic or biological macromolecules to adhere to mucosal tissues such as the mucosa of the stomach, small intestine, nasal, buccal etc. The concept of mucoadhesion has gained considerable interest to develop novel, highly efficient dosage forms especially for oral drug delivery[1]. To increase the residence of drug formulations at or above the absorption window main approaches used are bioadhesive microspheres that have a slow intestinal transit; the gastroretentive dosage system, which is based on multiparticulates or large single unit systems and floating drug delivery systems. Among these, mucoadhesive drug delivery systems have several advantages like localization at a given target site, prolonged residence time at the site of drug absorption, and an intensified contact with the mucosa increasing the drug concentration gradient leads to enhancement in bioavailability and reduction in dosing frequency[2]. Different types of polymers have been investigated for potential use as mucoadhesives. These include synthetic polymers such as poly (acrylic acid) (PAA), hydroxypropyl methylcellulose and poly(methylacrylate) derivatives, as well as naturally occurring polymers such as hyaluronic acid, tragacanth, chitosan etc [3]. The development of novel, advanced and mucosa-compatible polymers, are providing new commercial and clinical opportunities for delivery of drugs with narrow absorption window at the target site. The tailored polymers offer better opportunities for and broader applicability to highly variable and challenging drugs and therapy of various gastrointestinal disorders[4]. Significant efforts have been devoted to use the potentials of nanotechnology in drug delivery since it offers a suitable means of site-specific and/or time controlled delivery of small or large molecular weight drugs and other bioactive agents. Mucoadhesive nanoparticulate drug delivery system prolongs the residence time of dosage form at the site of application or absorption. They facilitate an intimate contact of the dosage form with the underlying absorption surface and thus improve the therapeutic performance of the drug. Nanoparticle drug carriers that can shield drugs from degradation and deliver them to intended sites may enable more efficient and sustained drug delivery to the gastrointestinal track. Recently to overcome the short residence time of topical drugs, the sustained release mucoadhesive chitosan-dextran sulfate nanoparticles nanoparticles were developed[5,6]. Table (1) summarizes various mucoadhesive drug delivery systems from different routes.

Table (1): Various mucoadhesive drug delivery systems from different routes:

Type of dosage forms	Route of administration	Examples	References
Tablets	Oral, buccal, vaginal, rectal	Theophyline, Metronidazole , declofenac	44, 45, 46
Ointment	Ocular,buccal, vaginal, rectal	Zinc oxide, terameprocol, Benzyl nicotinate, sulphadicramide.	47, 48, 49, 50
Gel	Ocular,buccal, vaginal, rectal	Benzdamine, Insulin, Amphotericin, Quinene	51, 52, 53, 54
Patch	buccal, vaginal,	Miconazole, Insulin, Ciprofloxacin	55, 56, 57
Film	buccal, vaginal	Theophylline, chlorpromazine, Fentanyl	58, 59, 60
Microspheres	Oral , nasal, ocular	Metoclopramide, Insulin,	61, 62
Nanoparticles	Oral , nasal, ocular	Natamycin,	63, 64

Rationale behind controlled–drug delivery:

Controlled drug delivery is the use of formulation components and devices to release a therapeutic agent at a predictable rate *in vivo.* The basic underlying principle of controlled drug delivery is to alter the pharmacokinetic and pharmacodynamics of pharmacologically active moieties by using novel drug delivery systems or by modifying the molecular structure and/or physiological parameters inherent in a selected route of administration. Primary objective is that the duration of drug action more important to design properly for desired delivery. Controlled drug delivery ensure safety and to improve efficiency of drugs as well as patient compliance.[4].

Various novel mucoadhesive drug delivery systems

- Mucoadhesive oral drug delivery Systems

  Types of oral mucoadhesive drug delivery systems:

  1. Mucoadhesive gastroretentive drug delivery
  2. Mucoadhesive buccal drug delivery
- Mucoadhesive ocular drug delivery Systems
- Mucoadhesive vaginal drug delivery Systems
- Mucoadhesive nasal drug delivery Systems
- Mucoadhesive rectal drug delivery Systems

General characteristics of mucosa and mucus:

The tissue layer responsible for formation of the adhesive interface is mucus. Mucus is a translucent and viscid secretion which forms a thin, continuous gel blanket adherent to the mucosal epithelial surface. The mean thickness of this layer varies from about 50 to 450 micro-meters in humans [7].

The composition of mucus varies widely depending on animal species, anatomical location and

the normal or pathophysiological state of the organism [8]. It is secreted by the goblet cells lining the epithelia or by special exocrine glands with mucus cells acini [3]. The lubrication properties of mucus secretions are a result of their viscous and gel forming properties and general stickiness [9].

General composition of mucus:

- Water 95%
- Glycoproteins and lipids 0.5-5%
- Mineral salts 1%
- Free proteins 0.5-1%

Mucus glycoprotiens are high molecular weight proteins possessing attached oligosaccharide units. These units contain an average of about 8-10 monosaccharide residues of five different types. They are:

1) L-fructose
2) D-galactose
3) N-acetyl-D-glucosamine
4) N-acetyl-D-galactosamine
5) sialic acid

In humans the only important sialic acid is N-acetylneuramic acid although in animals a number of other sialic acids occur, including N-glycollyneuramic acid and various O-substituted derivates. Amino acids principally found in mucus are serine, proline and threonine [3].

Mucoadhesive oral drug delivery Systems

Oral absorption of drugs:

A drug given orally must encounters with low pH and numerous GI secretions, including potentially degrading enzymes in stomach. Peptide drugs (e.g-insulin) are particularly susceptible to degradation and are not used orally. Oral drugs absorption involves transport across membranes of the epithelial cells in the GI tract. The oral mucosa is highly vascularized and therefore any drug diffusing into the oral mucosal membranes has direct access to the systemic circulation via capillaries and venous drainage [9, 10, 11]. Oral Absorption is affected by luminal pH along the GI tract, surface area per luminal volume, blood perfusion, the presence of bile and mucus, and the nature of epithelial membranes. The oral mucosa has a thin epithelium and rich vascularity, which favor absorption; however, contact is usually too short for substantial absorption. The drugs which are placed between the gums and cheek (buccal administration) or under the tongue (sublingual administration) is retained longer, so enhance

absorption and bioavailability[12]. Relatively large epithelial surface, thick mucous layer and short transit time of the stomach limits its absorption. Mainly absorption occurs in the small intestine and its gastric emptying is often the rate-limiting step. Food, especially fatty food, lowers gastric emptying rate and enhance drug absorption, that's why some drugs absorbed better in empty stomach. Drugs that affect gastric emptying (e.g, parasympatholytic drugs) affect the absorption rate of other drugs. Food may enhance the extent of absorption for poorly soluble drugs (eg, griseofulvin), reduce it for drugs degraded in the stomach (eg, penicillin G), or have little or no effect. Due to the large surface area and high permeability, the drugs are absorbed primarily in the small intestine, and acids, despite their ability as un-ionized drugs to readily cross membranes, are absorbed faster in the intestine than in the stomach. The intraluminal pH is 4 to 5 in the duodenum but becomes progressively more alkaline, approaching pH 8 in the lower ileum. Gastro- intestinal microflora may also reduce absorption in some cases. Decrease in blood flow may lower the concentration gradient across the intestinal mucosa and reduce absorption by passive diffusion. Intestinal transit time can also affect drug absorption, especially for drugs that are absorbed by active transport (eg, B vitamins), that dissolve slowly (eg, griseofulvin), or that are polar (ie, with low lipid solubility; eg, many antibiotics) [13,14.]

Oral mucosal membrane

The epithelium of stomach, small intestine, large intestine and bronchi consist of single layer and multiple layers in case of esophagus . The upper layer contains goblet cells, which secrete mucus directly onto the epithelial surface. Mucus is a viscous and gelatinous secretion, consist glycoproteins, lipids, inorganic salts, and up to 95% water[15]. Mucus is secreted either constantly or intermittently and its volume changes by the influence of external and internal factors [16] .

Glycoproteins (mucins) are the most important components of mucus and are responsible for its gelatinous structure, cohesion, and antiadhesive properties [17]. The different sites at which mucus is secreted, glycoproteins usually have similar structure and are highly glycosylated protein molecules. The terminal domains of the glycoprotein (C- and N-) are consist more than 10% cysteine. These domains, leads to the formation of large mucin oligomers due to the formation disulfide linkage [18,19]. Mainly protein part consists of a repeating sequence of serine, threonine, and proline residues. Oligosaccharide chain are attached to 63% of the protein core, at every third residue within the glycosylated areas and results in formation of more than 200 carbohydrate chains per glycoprotein molecule [20]. Each carbohydrate side chain contains from

two to twenty sugar residues and account for more than 80% of the molecular weight of the molecule [19].

Mucoadhesive gastroretentive drug delivery

Amongst the various approaches for achieving a prolonged and predictable drug delivery in the Gastro intestinal tract (GIT) is to control the gastric residence time. Dosage forms with a prolonged gastric residence time, (*e.g.*, gastro retentive dosage forms) like mucoadhesive, floating and particulate drug delivery systems will provide advanced and better therapeutic opportunities. Among the various approaches, mucoadhesive drug delivery systems have emerged as an efficient means for enhancing the bioavailability of drugs having narrow absorption window by increasing the gastric residence time [1,13]. The medications that are included in the category of narrow absorption window drugs are mostly associated with improved absorption at the jejunum and ileum due to their enhanced absorption properties, e.g. large surface area, in comparison to the colon or because of the enhanced solubility of the drug in the stomach as opposed to more distal parts of the gastrointestinal tract [20]. It was suggested that compounding narrow absorption window drugs with gastro retentive properties would enable an extended absorption phase of these drugs. For example, drugs that are absorbed in the proximal part of the gastrointestinal tract and drugs that are less soluble in or are degraded by the alkaline pH may benefit from prolonged gastric retention.

In addition, for local and sustained drug delivery to the stomach and proximal small intestine to treat certain conditions, prolonged gastric retention of drugs offer numerous advantages including improved bioavailability and therapeutic efficacy, and possible reduction of dose size. It has been suggested that prolonged local availability of antibacterial agents may augment their effectiveness intreating *H. Pylori* related peptic ulcers [13,21,22].

Certain types of drugs can benefit from using gastric retentive devices. These include:

1. Drugs with a narrow absorption window e.g- Aclyovir, gabapentin,furosemide, biphosphonates, metformin captopril, baclofin.
2. Drugs that are primarily and rapidly absorbed in the stomach or drugs that are poorly soluble at an alkaline pH e.g- Salicylic acid, aspirin, thiopental, secobarbital and antipyrine.
3. Drugs that degrade in the colon.
4. Drugs acting locally in the stomach e.g- Cemitidine, lansoprozole , misoprstol, omeproazole , Pentagastrin , propanthelin, suclralfate, clarithromycin, amoxicillin, metronidazole.

Mucoadhesive buccal drug delivery

Mucosal delivery of drugs *via* the buccal route is still very challenging in spite of extensive clinical studies. Buccal drug delivery is an important route of drug administration. Local drug delivery to oral cavity play a important role in treatment of toothache, periodontal diseases, dental caries, bacterial and fungal infections and aphthous stomatitis. The buccal route has high acceptance due to avoidance of first pass metabolism and possibility of being accessible for controlled drug release. These regions consist of a non-keratinized epithelium, resulting in a somewhat more permeable tissue than the skin. Therefore, drugs with a short biological half life requiring a sustained release effect and exhibiting poor permeability, sensitivity to enzymatic degradation, or poor solubility may be good candidates to be delivered via the oral cavity Buccal administration is viable alternative for peptide delivery based on excellent site specificity, avoidance hepatic first-pass metabolism, and protection from degradation in the stomach and the intestine. Furthermore, the oral mucosa is less prone to irritation or damage than, e.g., nasal mucosa.[23,24,25]**.** Inflammatory periodontitis disease can be treated by the combination of mechanical and intraperiondontal pocket chemotherapeutic agents in form mucoadhesive parches and syringeable semisolid formulations [26].

Buccal drug absorption

There are two permeation pathways for passive drug transport across the oral mucosa: paracellular and transcellular routes. Permeants can use these two routes simultaneously, but one route is usually preferred over the other depending on the physicochemical properties of the diffusant. Since the intercellular spaces and cytoplasm are hydrophilic in character, lipophilic compounds would have low solubilities in this environment. The cell membrane, however, is rather lipophilic in nature and hydrophilic solutes will have difficulty in permeating through the cell membrane due to a low partition coefficient. Therefore, the intercellular spaces pose as the major barrier to permeation of lipophilic compounds and the cell membrane acts as the major transport barrier for hydrophilic compounds. Since the oral epithelium is stratified, solute permeation may involve a combination of these two routes. The route that predominates, however, is generally the one that provides the least amount of hindrance to passage [8,27].

Various buccal mucoadhesive dosage forms

1) Buccal tablets
2) Buccal films
3) Buccal patches

4) Buccal gels and ointments

Mucoadhesive vaginal drug delivery

The conventional preparations, have very short residence time due to the self-cleaning action of the vaginal tract, so require frequent dosing to ensure the desired therapeutic effect. The vaginal mucoadhesive drug delivery systems are highly suitable for treatment of local conditions like contraception and sexually-transmitted diseases [28]. To prolong the drug residence time in the vaginal cavity, mucoadhesive systems have been explored in the form of semi-solid and solid dosage forms

Vaginal drug absorption

Vaginal route is an important site of drug administration for both local and systemic diseases. For drugs that are susceptible to gut or hepatic metabolism or which cause GI side effects, vaginal drug delivery may provide many advantages over the other routes of administration due to its large surface area, rich blood supply, avoidance of the first-pass effect, relatively high permeability to many drugs. The vagina is a fibro-muscular tube connecting the uterus to the exterior of the body. The surface area of the vagina is increased by numerous folds in the epithelium and by microridges covering the epithelial cell surface [29]. Various mucoadhesive systems developed by the use of different types of polymer and absorption promoters like itraconazole vaginal cream containing cyclodextrins and other ingredients [30].

Various mucoadhesive vaginal drug delivery systems are given below:

1) Mucoadhesive gels
2) Mucoadhesive tablets
3) Mucoadhesive films
4) Emulsion type mucoadhesive systems
5) Pessaries or suppositories

Mucadhesive nasal drug delivery

The nasal mucosa provides a promising route for systemic delivery of drugs including biopharmaceuticals. Nasal mucoadhesive drug delivery systems are used for the delivery of organic molecules, antibiotics, proteins, vaccines and DNA. Nasal drug delivery avoids first-pass hepatic metabolism which provide fast onset of action in management of chronic situations like cardiac arrest, epileptic seizures, severe nausea and vomiting [31]. Despite the potential advantages, there are certain factors like mucociliary clearance, mucous and epithelial barriers and enzymic activity, leads to poor bioavailability of drugs administered intranasally. Thus mucoadhesive agents make intimate contact with the mucin of mucosa, thereby,

prolonging residence time of the drug in nasal cavity, which leads to improved drug absorption [32, 33, 34].

Nasal mucosal drug absorption

With a surface area of 150 cm^2, a highly dense vascular network, and a relatively permeable membrane structure, the nasal route has good absorption potential. This large mucosal surface covered with a rich vascular bed of highly permeable capillaries creates an opportunity for intranasal drug delivery. Thus nasal mucosal absorption provide drug directly into the blood stream [35].

Various mucoadhesive nasal drug delivery systems are given below:

1) Nasal gels
2) Micoemusions
3) Mucoadhesive nanoparticles

Mucoadhesive ocular drug delivery

The poor bioavailability of ocular drug delivery systems is due to the continuous formation of tears and blinking of eye lids which leads to rapid removal of the drug from the ocular cavity. Opthalmic dosage forms can be improved by increasing the time the active ingredients remain in contact with eye tissues. The mucoadhesive polymers used for the ocular delivery include thiolated poly(acrylic acid), poloxamer, celluloseacetophthalate, methyl cellulose, hydroxy ethyl cellulose, poly(amidoamine) dendrimers, poly(dimethyl siloxane) and poly (vinyl pyrrolidone) mucoadhesive dosage forms that have been developed are liquid systems, in situ gelling systems, dispersed, systems and solid systems [36]. Recently micro and nanoparticulate drug delivery systems gain most of the attention among scientists. Formulations like bioadhesive sulfacetamide sodium microspheres to increase residence time on the ocular surface and to enhance treatment efficacy of ocular keratitis and bioadhesive DNA nanocarrier made of hyaluronan (HA) and chitosan (CS), specifically designed for topical ophthalmic gene therapy [37, 38].

Corneal drug absorption

Mucin is secreted by conjunctival globlet cells, but there are no globlet cells on the cornea. On this basis, a mucoadhesive polymer will firmly attach to conjunctival mucus [39, 40]. Drugs administered by instillation must penetrate the eye primarily through cornea.

Cornea is a lipid-water-lipid sandwich like structure and consist of three basic layers: Epithelium-lipophilic , Stroma-hydrophilic, Endothelium-lipophilic .Most effective penetration is obtained with drugs having both lipophilic and hydrophilic properties [41].

Rectal drug delivery systems

Rectal drug administration is used in situations when patients are vomiting or suffering from nausea. The first-pass elimination of drugs is also partially avoided by rectal administration and furthermore the rectum environment is quite constant with respect to pH; composition, volume and viscosity of fluid; and less influenced by food. The function of the rectum is mostly concerned with removing water. Surface area without villi gives it a relatively small surface area for drug absorption [42]

Various drug delivery systems and mucoadhesive polymers have been explored for drug delivery through rectum. Hydrogels administered rectally have proven to be useful for drug delivery [42]. The hydrogels using hydroxy ethyl methacrylate cross-linked with ethylene glycol dimethacrylate are studied by many scientists for rectal drug delivery. Recently scientists developed thermoreversible flurbiprofen liquid suppository base composed of poloxamer and sodium alginate for the improvement of rectal bioavailability of flurbiprofen [43]

Mucoadhesive polymers

Mucoadhesive polymers have several advantages when compared to conventional drug carriers, including localization at the specific target site, prolonged residence time and increase drug uptake. Polymers have played an important role in designing the systems which increase in residence time of the drug at the target site. Table (2) summarizes list of mucoadhesive polymers used in different drug delivery systems.

An ideal polymer for a bioadhesive drug delivery system should have the following characteristics [65, 66]:

1. The polymer and its degradation products should be nontoxic and nonabsorbable.
2. It should be nonirritant.
3. It should preferably form a strong noncovalent bond with the mucus or epithelial cell surface.
4. It should adhere quickly to moist tissue and possess some site specificity.
5. It should allow easy incorporation of the drug and offer no hindrance to its release.
6. The polymer must not decompose on storage or during the shelf life of the dosage form.
7. The cost of the polymer should not be high so that the prepared dosage form remains competitive.

Mucodhesive polymers that adhere to the mucin-epithelial surface divided into three broad classes [67, 68]:

a) Polymers that swells when placed in water and owe their mucoadhesion to stickiness.

Examples -Polyacrylic acid, poly(methylacylates), polycarbophil, carbopol, polyox etc.

b) Polymers that adhere through nonspecific, noncovalent interactions that are primarily electrostatic in nature (mainly hydrogen and hydrophobic bonding).

Examples- Poly(methyl vinyl ether-co-malic anhydride etc.

c) Polymers that bind to specific receptor site at the mucosal membrane

Examples- Lectins, thiolated polymers etc.

Table 2: A list of mucoadhesive polymers used in different drug delivery systems:

Synthetic polymers	Natural polymers
(a) **Cellulose derivatives** methylcellulose, ethylcellulose, hydroxy-ethylcellulose, Hydroxyl propyl cellulose, hydroxy propyl methylcellulose, sodium carboxy methylcellulose	(a) Tragacanth (b) Sodium alginate (c) Karaya gum (d) Guar gum (e) Xanthan gum
(b**) Poly (acrylic acid) polymers** carbomers, polycarbophil	(f) Lectin (g) Soluble starch
(c) Poly (hydroxyethyl methylacrylate)	(h) Gelatin
(d) Poly (ethylene oxide)	(i) Pectin
(e) Poly (vinyl pyrrolidone)	(j) Chitosan
(f) Poly (vinyl alcohol)	

Novel and new generation mucosa compatible polymers

Mucoadhesive site-specific drug delivery is important in targeting different regions of GIT using more selective compounds capable of distinguishing between the types of cells found in different areas of the GIT. The term "cytoadhesion," is specifically based on certain materials that can reversibly bind to cell surfaces in the GIT. New generation of mucoadhesives function with greater specificity because they are based on receptor-ligand-like interactions in which the molecules bind strongly and rapidly directly onto the mucosal cell surface rather than the mucus itself. One such class of compounds that has these unique requirements are called lectins[69].

Lectin-Based Delivery

Lectins are proteins or glycoproteins have the ability to bind specifically and reversibly to carbohydrates. They exist in either soluble or cell-associated forms and possess carbohydrate-selective and recognizing parts. Lectins have the capacity to recognize cell-surface carbohydrates; this includes their applicability in various biological processes, such as phagocytosis, cell activation, and cell adhesion. Lectin-based drug delivery systems have applicability in targeting epithelial cells, intestinal M cells, and enterocytes. The intestinal epithelial cells possess a cell surface composed of membrane-anchored glycoconjugates. It is these surfaces that could be targeted by lectins, thus enabling an intestinal delivery concept[69,70].

The novel polymers 'Thiomers'

Thiolated polymers, or thiomers, interact with cysteine-rich subdomains of mucus glycoproteins forming disulfide bonds between the mucoadhesive polymer and the mucus layer. The formation of disulfide bonds between thiomers and mucus glycoproteins has been studied by applying various analytical approaches. Owing to the immobilization of thiol groups on already well-established mucoadhesive polymers, their mucoadhesive properties are strongly enhanced [71]. Covalent bonds are believed to be formed not only between thiomer and mucus, but also within the thiomer itself. This theory was confirmed by the decrease in free thiol groups within thiomers resulting in an increase in viscosity [72]. Inter- and intramolecular disulfide bonds improve the cohesive properties of the thiolated polymer compared to the unmodified polymer. Table 3 summarizes various thiolated polymers used in drug delivery.

Thiolated Chitosans

Various properties of chitosan are improved by the immobilization of thiol groups. Due to the formation of disulfide bonds with mucus glycoproteins, mucoadhesive property get enhanced. Thiolated chitosan polymers offer advantage of high mucoadhesive, controlled release and permeation enchancing properties leading to strongly improved therapeutic potential of drugs.

Table 3: Thiolated polymers, which are interesting candidates for mucoadhesive drug delivery are given.[72]

Polymer	Mucoadhesive Potential
Chitosan–iminothiolane	250-fold improved mucoadhesive properties
Poly(acrylic acid)–cysteine	100-fold improved mucoadhesive properties
Poly(acrylic acid)–homocysteine	Approximately 20-fold improved mucoadhesive properties
Chitosan–thioglycolic acid	Tenfold improved mucoadhesive properties
Poly(methacrylic acid)–cysteine	Improved cohesive and mucoadhesive properties
Sodium carboxymethylcellulose–cysteine	Improved mucoadhesive properties
Alginate–cysteine	Fourfold improved mucoadhesive properties

Current scenario and future developments in mucoadhesive drug delivery systems

Currently mucoadhesive nanoparticulate systems were developed for the controlled and targeted delivery of drugs Nanoparticles generally vary in size from 10-1000nm. Biodegradable nanoparticles have been used frequently as drug delivery vehicles due to its better encapsulation efficiency, control release and less toxic properties. They offer several advantages like enhanced biocompatibility, high drug/vaccine encapsulation, and improved release profiles for the drug (73). Synthetic nanoparticles typically feature hydrophobic, charged and/or hydrogen bonding surfaces and are, therefore, likely to be strongly

mucoadhesive due to interactions with periodic exposed hydrophobic domains or negatively charged glycosylated segments along mucin fibers.The average pore size of viscoelastic mucus is around 150 ± 50 nm. Thus, mucoadhesive nanoprticles can easily penetrate in to the mucus and leads to the effective drug delivery at the target site. Commonly used materials for formulating nanoparticles are poly(lactide-co-glycolide) (PLGA) and Pluronics and chitosan . PEG coatings have been widely used in the development of polymeric drug carriers, including particles composed of biodegradable polyesters and polyanhydrides. PEG coatings reduce aggregation and enhance the blood circulation times of biodegradable nanoparticles designed for drug delivery . Nanoparticles size range up to 200 nm in diameter that are coated with a dense layer of non-mucoadhesive PEG polymers and mucoadhesive polymer, chitosan composed drug carriers readily penetrate nasal mucus. The development of polymeric particles with improved mucus penetration capability should encourage the commercial development of new generations of nanoparticle based drug delivery systems . The use of mucoadhesive nanopaticles delivery system for peptide/poorly absorbable drugs is one of the areas that need to be explored in the future leads to enhancement of bioavailability and site specific targeting. (74, 75).

CONCLUSION

The mucoadhesive dosage forms offer prolonged contact at the site of administration, drug targeting potential, low enzymatic activity, and better patient compliance. Development of novel mucoadhesive delivery systems are being undertaken so as to understand the various mechanism of mucoadhesion and improved permeation of active agents. The formulation of mucoadhesive drug delivery system depends on the selection of suitable polymer with excellent mucosal adhesive properties and biocompatibility. Now scientists are looking beyond traditional polymers, in particular next-generation mucoadhesive polymers (lectins, thiols, etc.); these polymers offer greater attachment and retention of dosage forms at the target site. The various sites where mucoadhesive polymers have played an important role includes buccal cavity, nasal cavity, rectal lumen, vaginal lumen and gastrointestinal tract, providing systemic as well as local benefits. Many new potential mucoadhesive nanoparticulate systems are being investigated which may increase mucus penetration and site specific targeting.

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