Review Article

A review on mucoadhesive polymer used in nasal drug delivery system

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Abstract

This update review is on mucoadhesive polymers used in nasal dosage forms. The nasal mucosa provides a potentially good route for systemic drug delivery. One of the most important features of the nasal route is that it avoids first-pass hepatic metabolism, thereby reducing metabolism. The application of mucoadhesive polymers in nasal drug delivery systems has gained to promote dosage form residence time in the nasal cavity as well as improving intimacy of contact with absorptive membranes of the biological system. The various new technology uses in development of nasal drug delivery dosage forms are discussed. The various dosage forms are vesicular carriers (liposome, noisome), nanostructured particles, prodrugs, *in situ* gelling system with special attention to *in vivo* studies.

Key words: *In vivo*, mucoadhesive polymers, nasal drug delivery system

INTRODUCTION

Drugs have been administrated nasally for therapeutic and recreational purpose since ancient times. Psychotropic drugs and hallucinogens were snuffed for these purposes by the Indian of South America, and this practice is currently widespread among abusers of cocaine and heroin. The interest in and importance of the systemic effects of the drugs administrated through the nasal route have expanded over recent decades.

Nasal administration offers an interesting alternative for achieving systemic drug effects to the parenteral route, which can be inconvenient or oral administration, which can result in unacceptably low bioavailabilities. The nasal epithelium is a highly permeable monolayer, the sub mucosa is richly vascularized, and hepatic first-pass metabolism is avoided after nasal administration. Other attractive features include the rather large surface area of the nasal cavity and the relatively high blood flow, which promotes rapid absorption.[1] Furthermore, self-medication is easy and convenient.

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Advantages of Nasal Route

Systemic nasal absorption of drug is a new attractive alternative to parenteral drug delivery system, as it offers the following advantages:[2]

- Transnasal delivery provides direct entry of drug into systemic circulation, e.g., Thiomeerosal, Amastatin, Puromycin, Nifedipine, etc.
- Unlike the skin, nasal mucosa is not constructed from the keratinized stratum corneum. The subepithelial layer of the nasal mucosa with numerous microvilli is highly vascularized, with large and fenestrated capillaries facilitating rapid absorption.
- The rate and extent of absorption as well as plasma concentration *vs* time profiles are comparable with I.V. administration.
- Avoidance of first pass elimination, gut wall metabolism, and destruction in gastrointestinal tract.
- Various nasal drug delivery systems are available for user-friendly noninvasive painless application.

Limitation of Nasal Drug Delivery System

There is risk of local side effects and irreversible damage of the cilia on the nasal mucosa, both from the drug substances and from the constituents added to the dosage forms.[2]

- Certain compounds when used as absorption enhancers may disrupt and even dissolve the nasal membrane in high concentration.

- Nasal atrophic rhinitis and severe vasomotor rhinitis can reduce the capacity of nasal absorption, e.g., Caerulein.
- There could be mechanical loss of the dosage form into the other parts of the respiratory tract like lungs.
- Untoward immunogenic effects might arise with the route.

Low bioavailability results from enzymatic degradation and metabolism at mucosal site and low residence time.

The Nasal Cavity

The nasal cavity has an important protective function in that it filters, warms, and humidifies the inhaled air before it reaches the lower airways. Any inhaled particles or microorganisms are trapped by the hairs in the nasal vestibule or by the mucus layer covering the respiratory area of the nasal cavity. Due to the mucociliary clearance mechanism, layer will gradually carry such particulates to the back of the throat, down the esophagus, and further into the gastrointestinal tract. Furthermore, the nasal layer mucosa has a metabolic capacity that will help convert endogenous materials into compounds that lies beneath are more easily eliminated.[3]

Nasal Anatomy and Physiology

The nostrils are a pair of nasal cavities divided by a nasal septum; their total volume is approximately 15 cc^3, with a total surface area of 150 cm^2. These nasal cavities are covered by a mucosa with a thickness of 2 to 4 mm, whose function in human beings is 20% olfactory and 80% respiratory. The nasal epithelium has a relatively high permeability, and only two cell layers separate the nasal lumen from the dense blood vessel network in the lamina propria cavity which is lined with three types of epithelia: Squamous, respiratory, and olfactory [Figure 1].[4,5]

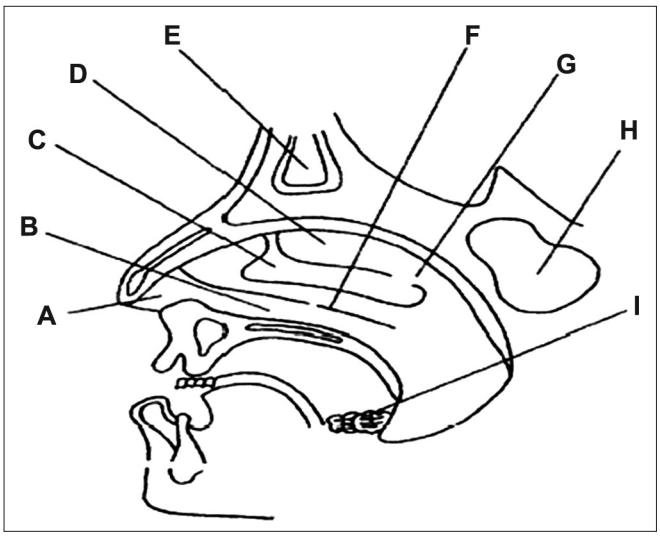

Figure 1: Lateral wall of the nasal cavity. (A) Squamous epithelium, (B) inferior turbinate, (C) middle turbinate, (D) superior turbinate, (E) frontal sinus, (F) respiratory epithelium, (G) olfactory epithelium, (H) sphenoidal sinus, and (I) faucial tonsil

The mucosa in the anterior part of the nose is squamous and without cilia. Within the anterior nostrils, a transitional epithelium is found that precedes the respiratory epithelium. The olfactory epithelium is present in the posterior part of the nasal cavity. The epithelium contains ciliary cells that produce a unidirectional flow of mucus toward the pharynx.[6] A drug deposited posteriorly in the nose is cleared more rapidly from the nasal cavity than a drug deposited anteriorly, because clearance is slower at the anterior part of the nose than in the more ciliated posterior.[7]

Nasal Mucosal

The nasal lining has the same lining as the rest of the respiratory tract with pseudostratified ciliated columnar epithelium. There are up to 200 cilia per cell whose tips lie in the superficial gel layer [Figure 2]. At the anterior end of the inferior and middle turbinate, which is the area which has most contact with inspired air, there can be metaplasia with cuboidal cells which have no cilia.

VARIOUS DOSAGE FORMS GIVEN BY NASAL ROUTE

Solution and Sprays

The drug solutions are nasally administered as nasal drops, sprays, and as metered dose nebulizer. The dose of the active ingredient administered depends upon the volume of drug and the concentration of drug in the formulation. The therapeutic levels of nitroglycerine, 3 ng/ml in central venous blood, 1.7 ng/ml in arterial blood, and 0.4 ng/ml in peripheral venous blood were achieved within 2 minutes following intranasal administration of 0.8 mg/ml of nitroglycerine in normal saline. The effect of formulation variables such as dose of active ingredient, pH of the solution, and its osmolarity on nasal absorption has been reported by various researchers.[8]

Suspensions

Suspensions for nasal administration are prepared by suspending the micronized drug in a liquid diluent or carrier suitable for application to the nasal mucosa. The

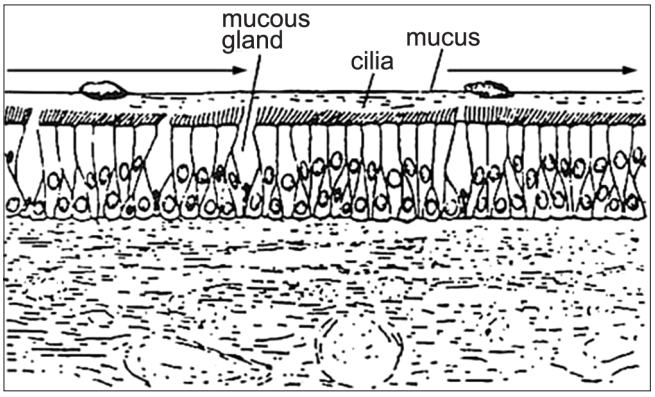

Figure 2: Structure of nasal mucosa

preparation of suspension form gave a better insulin uptake and blood glucose reduction compared with that from the solution.[9]

Powders

Powder dosage forms of drugs for nasal administration offer several advantages over liquid formulations. In the powder form, the chemical stability of the drug is increased, a preservative in the formulation is not required, and it is possible to administer larger doses of drugs. Powder form is suitable for number of non-peptide drugs and is well suited for peptide drugs.[10]

Polymer-based powder formulations show no adhesion until their absorption of mucus occurs on the nasal mucosa surface. This allows easy application to the nasal cavity by metered dose in sufflation even if the polymer is highly mucoadhesive.[11] In addition, liquid preparations are more easily cleared to the nasopharynx and oropharynx from where they enter the posterior part of the tongue.[12]

Therefore, administration of nasal powders may increase patient compliance, especially if the smell and taste of the delivered drug is unacceptable. After getting in contact with the nasal mucosa, polymer-based powders are believed to form a viscous gel following absorbing water from the nasal mucus [Figure 2]. Then, the free polymer chains penetrating into the tissue crevices can hold back the ciliary movement, which will increase the retention time of the drugs in the nasal cavity.[13]

Dry powder formulations can also avoid the utilization of preservatives and freeze storage, because they do not support microbial growth and are more stable than solution. For these reasons, the dried powder is the most commonly studied formulation for the nasal drug delivery, including small hydrophobic drugs, peptide drugs, and vaccine.[14] prepared dry powder nasal influenza vaccine formulation by using spray-freeze-drying method; the results indicated that the powders were amorphous and more stable with respect to liquid formulations. *In vivo* experiments demonstrated that the powders significantly increased residence time in rats and elicit enhanced serum and mucosal antibody response.

Nasal Particulate Drug Delivery System

Nasal particulate systems using mucoadhesive polymers as carriers include microparticle/sphere and nanoparticle. Particulate drug carrier systems administered through nasal mucosa may protect the drug from enzymatic degradation, increase the drug dissolution rate, intensify the contact of the formulation with the mucosa, enhance the uptake by the epithelium, and act as a controlled release system resulting in prolonged blood concentrations.[15,16] Among the polymers widely used as nasal drug particulate carrier, the positively charged polymers such as chitosan and aminated gelatin are most attractive because of their hydrogel nature which leads to opening of the tight junctions and their intimate contact with the negatively charged mucosa membrane.[17] *In vivo* evaluation in rabbits has proved that chitosan nanoparticles were able to improve the nasal absorption to a great extent compared with chitosan solution due to the intensified contact of the nanoparticle with the nasal mucosa as compared with chitosan solutions.[18]

It has been believed that nanoparticles possess superiority over microspheres as nasal drug carrier because their larger surface area results in more intimate contact with the mucosa, which leads to higher local concentration gradient.[19]

Moreover, nanoparticles cross the mucosal epithelium better than microspheres do. Microparticles smaller than 10 μm administered intranasally are believed to be taken up by the M-cells overlaying the nasal-associated lymphoid tissue (NALT) and transported to sub-mucosal layers. However, in case of the nanoparticles, besides the M-cell-associated phagocytosis, the epithelial cells are also involved in the transport of nanoparticles by internalization.[20]

Recent study by showed that FITC-albumin-loaded chitosan nanoparticles, when administered in the nasal cavity, were able to cross the mucosal layer, taken up by rat nasal epithelia and NALT cells. This property of nanoparticles provides a good indication of their potential as gene and vaccine carriers.[21]

Teijeiro-Osorio *et al*. found that the transfection efficiency of the nanoparticles loaded with pSEAP (100-200 nm) was higher than the naked DNA (control).[22]

Recently, many studies confirmed that association of vaccines to the nanoparticulate systems has shown to enhance the antigen uptake by nasal lymphoid tissues.[23]

SEMI-SOLID DOSAGE FORMS

A gel is a soft, solid or solid-like material consisting of two or more components, one of which is a liquid, present in substantial quantity. A gel should, on a time scale of seconds, not flow under the influence of its own weight. The solid-like characteristics of gels can be defined in terms of two dynamic mechanical properties: An elastic modulus, G′(ù), which exhibits a pronounced plateau extending to time at least of the order of second; and a viscous modulus, G″(ù), which is considerably smaller than G′(ù). The first biological uses of gels (polymerized methyl methacrylate) were presented by the institute for Macromolecular Chemistry in Prague in 1960 and involved the manufacturing of contact lenses, arteries, etc.

Gelation occurs through the cross-linking of polymer chains, something that can be achieved by (i) covalent

bond formation (chemical cross-linking) or (ii) non-covalent bond formation (physical crosslinking). Gels have been used for the delivery of drugs for both systemic and local actions (see the review by Peppas *et al*.). Many different methods using gels have been reported, including subcutaneous delivery for sustained release, buccal delivery, deliveries to the stomach, colon, rectum, vagina, and nasal.

Gel formulations with suitable rheological properties increase the contact time with the mucosa at the site of absorption. The increased contact time is caused by the mucoadhesive properties of the polymer in the gel and by the rheological properties of the formulation reducing the clearance by the nasal and ocular protective mechanisms.[24-26]

MECHANISM OF MUCOADHESION

The process of mucoadhesion following nasal administration relates to the interaction between the mucoadhesive polymer and the mucus secreted by the sub-mucosal glands.[27] The sequential events that occur during the mucoadhesion include the proper wetting and swelling of the polymer, and intimate contact between the polymer and the nasal mucosa. Then, the swelled mucoadhesive polymer penetrates into the tissue crevices followed by the interpenetration between the polymer chains and protein chains of the mucus [Figure 2].

To obtain sufficient absorption of drugs, first, the formulation should spread well on the nasal mucosa. Therefore, the spreadability is very important for the liquid mucoadhesive formulation, so do the flowability and wettability for the solid mucoadhesive formulation.[28]

Hydration of the polymer (swelling) plays a very important role in mucoadhesion, through which the polymer chains are liberated and interact with the biological tissue.[29] During hydration, there is a dissociation of hydrogen bonds of the polymer chains. When the polymer–water interaction becomes greater than the polymer–polymer interaction, adequate free polymer chains will be available for interaction between the polymer and biological tissue. There is a critical degree of hydration required for optimum mucoadhesion. The incomplete hydration due to the lack of the water leads to incomplete liberation of the polymer chains. On the other hand, an excessive amount of water will weaken the mucoadhesive bonds by over diluting the polymer solution.[30] The polymer chains penetrating into the tissue crevices can hold back the ciliary movement, which will increase the retention time of the drugs in the nasal cavity. Furthermore, the existence of the mucoadhesive carrier also reduces the contact between the drugs and the enzymes existing in the mucosa. These both can enhance the intranasal absorption of hydrophilic drugs (the comparison of ordinary intranasal formulation with mucoadhesive intranasal formulation is showed in Figure 1). Apart from these, the dehydration of the epithelial cells after hydration may also temporarily open the tight junctions between the epithelial cells and improve the paracellular absorption of macromolecular drugs. This function of the mucoadhesive polymer is very important for the enhancement of the intranasal absorption of macromolecules weighting above 1 000 Da.[31] Mucoadhesion can slow down the mucociliary clearance, but with time, mucus production will lead to the inordinate swelling of the mucoadhesive polymer and the reduction of the mucoadhesion bond strength, allowing a recovery of normal mucociliary movement rate and the clearance of the polymer from the mucosa.

Although many references indicate that the mucoadhesive polymer are effective on enhancing the intranasal absorption of macromolecular drugs, very few papers focus on the changes of gel structure and rheology of the mucus caused by the mucoadhesive polymer, to what extent the interaction between the polymer and the mucus influences the release of the drugs including in the disease condition. Disease conditions can affect mucoadhesion due to their influence on either mucus production or ciliary movement, and then may result in undesired drug release. Thus, a good understanding of the nature of mucus in these diseases is imperative in designing a good nasal drug delivery system. Mucoadhesive capabilities of polymers should be studied under such disease conditions during the product development.

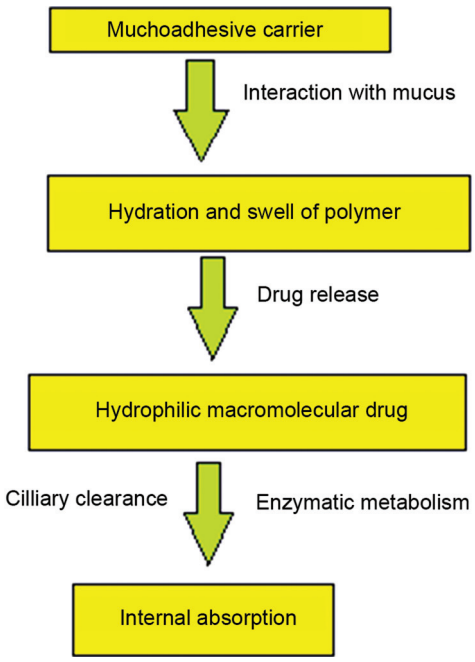

Figure 3: Schemated of the mucoadhesive internal drug delivery system

MUCOADHESIVE POLYMERS USED IN NASAL DRUG DELIVERY

Cellulose Derivatives

There are many pharmaceutical grade derivatives of cellulose widely used in different administration routes. Several cellulose derivatives have proved to be effective on enhancing the intranasal absorption of drugs, including soluble cellulose derivatives such as hydroxypropyl methylcellulose, hydroxypropyl cellulose (HPC), methylcellulose (MC), and carboxymethyl cellulose (CMC), and insoluble cellulose derivatives such as ethylcellulose and microcrystalline cellulose (MCC).

Cellulose derivatives can markedly prolong the residence time of drugs in the nasal cavity due to their desirable mucoadhesive property.[32] Additionally, due to their high viscosity following hydration in the nasal cavity, the celluloses can sustain the release of drugs.[33] For these reasons, using celluloses as absorption enhancer can lead to improved intranasal absorption and increased bioavailability. Many references show that the celluloses are effective on increasing the intranasal bioavailability of small hydrophobic as well as hydrophilic macromolecular drugs [Table 1]. For example, administered nasally with CMC, apomorphine can obtain a relative bioavailability of 102% compared with subcutaneous injection in rabbits.[34] Another study reported that an absolute bioavailability up to 90.77% could be achieved for ketorolac tromethamine administered with MCC.[35] The peptide drugs, leuprolide and FD-4, when dosed with MCC/HPC through nasal route, reached an absolute bioavailability of 34.9% and 35.5% in rabbits, respectively.[36]

Sometimes, combination of the celluloses with other absorption enhancer would obtain the better effectiveness than using the polymer alone.[37] reported that the intranasal absolute bioavailability of ciprofloxacin in rabbits using MC and HEC alone as enhancer is only 18.2% and 19.46%, respectively. When combining with the Tween 80, the bioavailability increased to 22.35% and 25.39%, respectively.[39] In another study by on the intranasal delivery of dopamine, the combination of the HPC and azone leaded to an absolute bioavailability of almost 100%, while it was only 25% for using HPC alone.[38]

Table 1: Summary of some nasal drug delivery studies where cellulose derivatives were employed

Mucoadhesive polymer	Drug	Dosage form	Reference
CMC	Apomorphine	Powder	Ugwoke MI *et al*.[7]
MCC	Ketorolac acid	Spray	Quadir M *et al*.[44]
MCC/HPC	Leapralide	Powder	Suzuki Y *et al*.[28]
HPC	Dopamine	Liquid	Ikeda K *et al*.[38]
HPC	Metaclopramide	Gel	Zaki NM *et al*.[32]

Polyacrylates

Polyacrylates have been investigated very frequently in many drug administration routes, like nasal drug delivery systems, due to their excellent mucoadhesive and gel-forming capability. Among the pharmaceutical polyacrylates, carbomers, and polycarbophil, which differ in the cross-linking condition and viscosity, are widely used in the nasal mucoadhesive drug delivery systems.[39]

Polyacrylates, capable of attaching to mucosal surfaces, can offer the prospects of prolonging the residence time of drugs at the sites of drug absorption, and ensure intimate contact between the formulation and membrane surface. Studies by Ugwoke *et al*. in rabbits reported that the use of Carbopol 971P in nasal dosage forms increases their residence time in the nasal cavity. The percentage of the formulations cleared from the nasal cavity at 3 hours was 24% for Carbopol 971P, while it was 70% for lactose. Sustained release of drugs can also be obtained by using polyacrylates in nasal formulation, which result in a more stable blood concentration-time curve. Table 2 shows the use of polyacrylates in nasal drug delivery system.[34,40]

Another research by Ugwoke *et al*. showed that the Tmax of the Carbopol 971P-containing formulation of apomorphine was 52.21 minutes, which represented a 5-fold improvement compared with that of the lactose-containing formulation, while the Cmax of the Carbopol 971P-containing formulation was 330.2 ng/ml, lower than that of the lactose-containing formulation, which was 450.7 ng/ml.[34,41]

Besides the mucoadhesion capability, polyacrylates may also temporarily open the tight junctions between the epithelial cells during the swelling progress in the nasal cavity and improve the paracellular absorption of drugs.[42]

An absolute bioavailability of 14.4% in rabbits was reported for intranasal insulin formulation containing Carbopol 974P.

Callens and Remon reported that the effect of Carbopol on the mucosa is negligible and reversible, no change of

Table 2: Summary of the studies on the use of polyacrylates in nasal drug delivery

Mucoadhesive polymer	Drug	Dosage form	Reference
Carbopol971P	Apomorphine	Powder	Ugwoke MI *et al*.[34]
Carbopol934P	Levonorgestrol	Liquid	Shahiwala A *et al*.[27]
Carbopol981P/Dm B-cd	Metaclopramide	Powder	Quadir M *et al*.[44]
Carbopol934/HPC	Metaclopramide	Powder	Callens C *et al*.[43]

the epithelium barrier was observed even after a 4-week administration of Carbopol-based powder formulation in rabbits.

Starch

The starch is one of the most widely used mucoadhesive carrier for nasal drug delivery, which has been reported to be effective on improving the absorption of both small hydrophobic drugs and hydrophilic macromolecular drugs [Table 3]. Maize starch is the most preferred class for pharmaceutical purpose, among which the drum-dried waxy maize starch, due to its better bioadhesive property, has been considered as the best one compared with starch processed through other methods.[43]

Starch can be used as nasal drug carriers in the form of powder microspheres nanoparticles [Table 3] among which the degradable starch microspheres (DSM), also known as SpherexR, is the most widely used and also the first example of mucoadhesive microparticulate nasal delivery system. These microspheres are prepared by an emulsion polymerization technique, in which the starch is cross-linked with epichlorohydrin and can incorporate molecules weighting less than 30 kDa[44] have observed that the half-life of clearance for DSM was prolonged to 240 minutes as compared with 15 minutes for the liquid and powder control formulations.[45]

Chitosan

Chitosan [2-amino-2-deoxy-(1→4)-β-d-glucopyranan] is a linear cationic polysaccharide which is obtained by a process of deacetylation from chitin, an abundant structural polysaccharide in shells of crustacea, such as lobsters, shrimps, and crabs. Due to the NH_2 groups resultant from the deacetylation process, chitosan is insoluble at neutral and alkaline pH. However, it can form water-soluble salts with inorganic and organic acids including glutamic acid, hydrochloric acid, lactic acid, and acetic acid. Toxicity tests have revealed that the LD50 of chitosan in mice exceeds 16 g/kg (Paul and Garside, 2000). Because of its low cost, biodegradability, and biocompatibility, chitosan has been increasingly applied as pharmaceutical excipients in oral, ocular, nasal, implant, parenteral, and transdermal drug delivery.[46]

Table 3: Summary of some nasal drug delivery studies where starch and other carbohydrates were employed

Mucoadhesive polymer	Drug	Dosage form	Reference
DSM	Apomorphine	Powder	Ugwoke MI *et al*.[34]
DSM/STDHF	Gentamicin	Powder	Illum L *et al*.[45]
DDMW	HGS	Powder	Illum L *et al*.[45]

Chitosan and its derivatives have been shown to be active in enhancing the intranasal drug absorption due to their excellent mucoadhesive properties. It was also confirmed that coating micro- and nanoparticulates with chitosan could improve drug adsorption to mucosal surfaces.[47] Table 4 shows various chitosan derivatives used in nasal drug delivery system.

Soane *et al*. reported that chitosan microspheres and solutions resulted in three- and eight-fold longer clearance half-lives compared with sodium pertechnetate solution in sheep nasal cavity, respectively.[6,48] In addition, many studies have proved that chitosan and its derivatives could transiently open the tight junctions between the cells and lead to the paracellular transport of drugs.[49] and Chung *et al*. have observed interpenetration of thermo-sensitive gels of insulin in nasal delivery by cross linking of chitosan. The preparation shows sustained release of insulin and improved pharmacological efficiency.[50]

Chemical and biological properties of chitosan, such as mucoadhesion and ability in enhancing nasal absorption, are determined by the types of derivatives, degree of deacetylation, and molecular weight, because chitosan is only soluble in acidic environment in which the amino groups at the C-2 position are protonated. At neutral pH, most chitosan molecules will lose their charge and precipitate from solution.[50]

Recent studies have shown that only protonated, soluble chitosan can trigger the opening of tight junctions and thereby facilitate the paracellular transport of hydrophilic mannitol.[51]

To improve the poor water solubility of chitosan, some derivatives were synthesized, such as trimethyl chitosan.[52] Thanou *et al*. reported that the trimethyl chitosan was soluble and effective on enhancing intranasal absorption even at neutral pH.[53] N-trimethyl chitosan hydrochlorides are more mucoadhesive than unmodified chitosans and show a higher bioavailability *in vivo* compared with the unmodified chitosans.[54]

Table 4: Summary of the recent nasal drug delivery studies where chitosan derivatives were employed as absorption enhancer

Mucoadhesive polymer	Drug	Dosage form	Reference
Chitosan	Tetramethyl pyrazine	Liquid	Mei D *et al*.[55]
Chitosan	Insulin	Liquid	Illum L *et al*.[46]
Chitosan	Levonorgestrol	Liquid	Shahiwala A *et al*.[27]
Chitosan	FD-4	Liquid	Miyamoto M *et al*.[17]
Chitosan	Metaclopramide	Liquid	Zaki N M *et al*.[32]

Mei *et al*. reported that the permeation-enhancing effect of chitosan increased with increasing molecular weight up to Mw 100.[55]

Tengamnuay *et al*. suggested that chitosans should differ in their molecular weight by at least two-fold in order to have a clearly differentiating effect on the nasal absorption enhancement of a kyotorphin analogue.[22]

On the contrary, Zaki *et al*. found that there is no significant difference between the constants of intranasal absorption for metoclopramide HCl administered with chitosan high weight (600 kDa) and low weight (150 kDa) even though they differ in molecular weight by four-fold.

Due to the positive charge of chitosan in a weak acidic environment, it can also be applied to deliver the negatively charged DNA through nasal mucosa and protect them from nuclease degradation.[35]

Compared with viral vectors, this alternative vector markedly reduced the safety risks that meanwhile result in high transfectability. Recently, many studies show that nasal immunization with chitosan plus inactive vaccine is a potentially effective, easily administered form of vaccination.[56] *Bordetella pertussis* filamentous hemagglutinin and recombinant pertussis toxin have shown to induce very strong systemic and mucosal immune reactions against the antigens when intranasally administrated with chitosan.[57]

Read *et al*. confirmed that the standard inactivated trivalent influenza vaccine administered intranasally in combination with chitosan glutamate (0.5%, w/w) could induce both systemic and local immune responses, and the results were not statistically different from those obtained following administration of the commercial influenza vaccine by the intramuscular route.

Bacon *et al*. have reported that chitosan solutions are able to enhance both the mucosal and systemic immune responses against influenza virus vaccines. Only in mice which received chitosan/vaccine formulation intranasally, high IgA titers in nasal washings could be found. This was not observed in mice receiving the antigen through subcutaneous injection.[58]

CONCLUSION

With advantages such as mucoadhesion, an increase in the residence time of the polymer, penetration enhancement, and enzymatic inhibition, mucoadhesive polymers will undoubtedly be utilized for the nasal delivery of a wide variety of therapeutic compounds. This class of polymers has enormous potential for the delivery of therapeutic macromolecules, genes, and vaccines. Unfortunately, only a few studies have been conducted with new generation mucoadhesive polymers for nasal drug delivery, and very few papers focus on the changes of structure and rheology of the mucus caused by the mucoadhesive polymer, to what extent the interaction between the polymer and the mucus influences the release of the drugs including in the disease condition. With recent advancements in the fields of biotechnology and cytoadhesion, the authors believe that there will be both academic and industrial efforts to explore this new area of nasal drug delivery, and it might not be too far-fetched to envisage more and more nasal products that employ mucoadhesive polymers. The authors believe that there will be both academic and industrial efforts to explore this new area of nasal drug delivery, and more nasal products that employs mucoadhesive polymers.

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