Review Article

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Role of Mucoadhesive Microspheres as Intra-nasal Drug Delivery

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Abstract

Carrier technology offers a innovative method for medication distribution by connecting drugs to carrier particles like liposomes, nanoparticles, or microspheres. Microspheres, with their small size and effective characteristics, are crucial in this particle medication delivery method. Mucoadhesive microspheres achieve better drug absorption by sticking to the mucosal surface and releasing the medication over an extended period. Microspheres are spherical, freely flowing, made of natural or synthetic polymers with a particle size range of 1-1000µm. Due to their unique size-dependent property and ability to include medications in carriers, lipid microspheres offer potential for novel treatments. There are several methods for preparing microspheres and releasing the medication at the intended site of action in a steady and regulated way. Due to their enhanced half-life, oral delivery capabilities, and better therapeutic responses, microspheres have gained interest in targeting and treating various illnesses. This article reviewed about the mucoadhesive microspheres, its mechanism, preparation methods and also the recent trends being achieved on mucoadhesive microspheres.

Keywords: Mucoadhesive Microspheres, Carrier technology, Drug adsorption, Lipid microspheres, Oral delivery, Therapeutic

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1. Introduction

Nasal drug delivery has its roots in the previous topical administration of medications meant to have localized effects. Ayurvedic medicine, commonly known as "Nasya karma," recognizes nasal therapy as a legitimate kind of treatment. The nasal route was introduced in the early 1980s as a potentially effective systemic drug delivery option to replace other traditional drug delivery methods. With a highly vascularized epithelium and a porous endothelium membrane, the nasal route is a dependable, easy, and easily accessible method of absorbing drugs into the systemic circulation. This prevents the hepatic first pass clearance of the compound. Furthermore, dose reduction, a speedier commencement of pharmacological activity, a quicker attainment of therapeutic blood levels, and a reduced incidence of adverse effects are all made possible by intranasal drug delivery. Intranasal drug delivery systems incorporate microspheres to target particular areas for drug administration, increase stability, and enhance bioavailability. In comparison to solutions, microspheres can prolong the duration of medication residence in the cavity. By creating tight connections between the epithelial cells, they can potentially have a direct impact on the mucosa.

Microspheres can be defined as a structure consisting of a continuous phase of one or more miscible polymers in which drug particles are dispersed at the molecular or macroscopic level. Alternatively, they can be defined as a monolithic sphere or therapeutic agent distributed throughout the matrix either as a molecular dispersion of particles (1-3).

Microspheres are tiny, spherical particles with dimensions between 1 and 1000 µm. Microparticles are another term for microspheres. A wide range of synthetic and natural materials can

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be used to create microspheres. There are commercially available glass, polymer, and ceramic microspheres. Since the densities of solid and hollow microspheres range greatly, they have diverse uses. Generally, additives with hollow microspheres are used to reduce a material's density. Depending on their size and composition, solid microspheres can be used in a variety of ways (4-6). When microparticles were initially created in 1990, they were thought to be a potentially effective drug carrier system, particularly for incorporating the active ingredient and facilitating regulated and prolonged drug administration. An oral, topical, ocular, subcutaneous, intramuscular, intranasal, and especially parenteral mode of delivery have all been suggested as uses for microspheres as colloidal drug carriers (7, 8).

The two main types of polymers used to make microspheres are synthetic and natural polymers, which help carry active compounds. Natural polymers derived from sea brown algae are ethyl cellulose and sodium alginate. This is frequently used in oral and topical formulations since it is biocompatible, biodegradable, and non-toxic (7, 9). The main objective of a drug delivery system is to provide a therapeutic response with the fewest possible adverse effects. This is accomplished by delivering the medication to the body at a precise location at a predetermined rate and for a certain amount of time (4, 7). This article reviewed about the mechanism of mucoadhesion, mucoadhesive polymers utilized in formulating mucoadhesive microspheres, and its uses as intra nasal drug delivery.

1.1. Advantages of mucoadhesive microspheres as intra-nasal delivery

1. After the particle size is reduced, the poorly soluble drug becomes more soluble.
2. The effects of microsphere therapy are long lasting and continuous.
3. Decrease the dose and toxicity.
4. Reduce the frequency of dosages to improve the compliance of patients.
5. More effective use of the medication will increase its bioavailability and lower the frequency and severity of side effects (1, 10).

1.2. Disadvantages of mucoadhesive microspheres as intra-nasal delivery

1. The cost of the ingredients and processing for the controlled release preparation is much higher than for regular formulations.
2. Various factors, such as meals and the pace of transit through the stomach, can affect the release rate of the controlled release dosage form.
3. Since controlled release formulations often have larger drug loads, any compromise to the dosage form's release properties might potentially be hazardous.
4. These kinds of dosage formulations shouldn't be eaten or crushed (1, 10).

2. Mucoadhesion

A phenomenon known as "bioadhesion" occurs when two materials are held together by interfacial forces, at least one of which is biological in nature. The adherence of the polymers to the mucosal layer's surface is referred to as “mucoadhesion” (11, 12).

2.1. Mucous membrane

The wet coverings that line the walls of several bodily cavities, including the respiratory and gastrointestinal systems, are called mucous membranes.

It is the goblet cells that produce mucus. Mucus may be found in three different forms: suspended, gel-like, or luminally soluble. It can also be found adhering to the mucosal surface (as shown in Figure 1). All mucus gels are primarily composed of lipids, water, inorganic ions, and mucin glycoprotein. Mucus acts as both a lubricant and a barrier of defense (11, 13).

2.2. Mechanism of mucoadhesion

The drug's attachment to the mucosal layer in conjunction with an appropriate carrier is known as mucoadhesion. The intricate process of mucoadhesion entails the wetting, adsorption, and penetration of polymer chains. The process by which certain macromolecules adhere to the mucous tissue's surface is still poorly understood. To improve surface contact and create intimate contact, the mucoadhesive must extend throughout the substrate. This will help the chains in the adhesive diffuse throughout the mucus (11, 14).

A mucoadhesive must have the greater attraction force in order to overcome the repulsion force. The dosage type and method of administration have the potential to assist each stage. For instance, the attraction of the surface water might

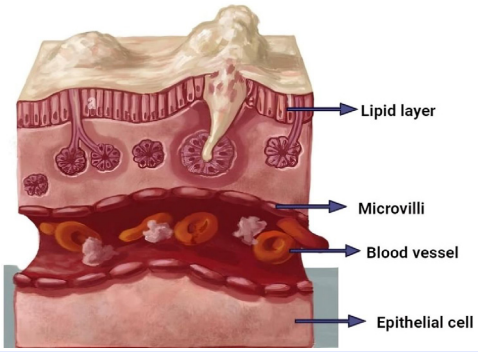

Figure 1. Structure of mucous membrane.

induce the substrate to absorb a partly hydrated polymer. The two stages of the mucoadhesion process are commonly referred to as the contact stage and the consolidation stage (Figure 2). The first stage is characterized by the contact between the mucoadhesive and the mucus membrane, with spreading and swelling of the formulation, initiating its deep contact with the mucus layer (15).

2.3. Theories of mucoadhesion

Theories involved in mucoadhesion are as follows (11, 16)

2.3.1. The electronic theory

This hypothesis states that during the transmission of electrons between the mucoadhesive and mucosal membranes, an electrical double layer is produced.

2.3.2. The adsorption theory

According to this idea, intermolecular interactions such as hydrogen bonding and Vander Waal's forces cause the mucoadhesive to be adsorbed on the mucosal surface.

2.3.3. The diffusion theory

According to this idea, the polymer chains that are present on the mucoadhesive surface diffuse, establishing a network structure between the mucosal and mucoadhesive surfaces.

2.3.4. The wetting theory

Applicable to liquids, this theory suggests that there will be a higher affinity for adhesion the smaller the contact angle of the liquid on the substrate surface.

2.3.5. The mechanical theory

This theory explains how the diffusion of liquid adhesives into the microcracks and imperfections on the mucoadhesive substrate leads to mucoadhesion and the creation of an interlocking structure.

2.3.6. The cohesive theory

This hypothesis states that the primary cause of the mucoadhesion phenomenon is like-molecule intermolecular interactions.

3. Polymers used in Formulating Mucoadhesive Microspheres

Mucoadhesive polymers are used to create mucoadhesive microspheres. Mucoadhesive polymers can come from synthetic or natural sources.

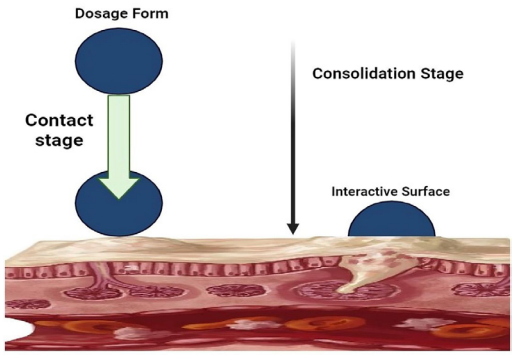

Figure 2. Process of mechanism of mucoadhesion.

Three main groups of mucoadhesive polymers that stick to the mucin-epithelial interface are easily distinguishable:

Polymers that exhibit stickiness upon immersion in water and subsequently acquire mucoadhesion.

Polymers that stick together mainly by electrostatic interactions that are nonspecific and noncovalent.

polymers on the tile self-surface that attach to a particular receptor location (11, 17).

Following is a list of some mucoadhesive polymers used in formulating mucoadhesive microspheres (Table 1).

4. Methods for preparation of mucoadhesive Microspheres

The various methods for preparation of mucoadhesive microspheres include following.

4.1. Emulsion solvent evaporation techniques

This method involves dissolving the medication in a polymer that has already been dissolved in chloroform, and then adding the resultant solution to an aqueous phase that contains 0.2% sodium PVP as an emulsifying agent. After 500 rpm of agitation, the drug and polymer (eudragit) were separated into fine droplets, which solidified into stiff microspheres through solvent evaporation. The droplets were then collected by filtration, cleaned with demineralized water, and dried at room temperature for 24 h (1, 18).

4.2. Emulsion cross-linking method

This procedure involved dissolving the drug in an aqueous gelatine solution that had been heated to 400C for one hour beforehand. Drop by drop, the solution was added to the liquid paraffin while the mixture was stirred at 1500 rpm for 10 minutes at 35 °C. This produced an emulsion, therefore more stirring was carried out for 10 minutes at 15 °C. Following three separate washes with acetone and isopropyl alcohol, the resulting microspheres were allowed to air dry and then dispersed in 5 mL of aqueous glutaraldehyde-saturated toluene solution at room temperature for three hours to facilitate cross-linking. Next, they were treated with 100 mL of 10 mm glyciene solution containing 0.1% w/v of tween 80 at 37 °C for ten minutes in order to block unreacted glutaraldehyde (18).

4.3. Coacervation Phase separation method

For the purpose of microencapsulating a medication, researchers have looked at the usage of cellulose acetate phthalate and cellulose acetate as polymers with organic solvents. Liquid paraffin that has already included polysorbate is mixed with the drug to create microspheres. To make polymer solution, dissolve polymer in organic solvent and stir continuously until solvent evaporates at room temperature. This is done for each dosage combination (1, 19).

4.4. Ionic gelation method

Using this method, an alginate/chitosan particulate system for Nateglinide release was created. A two percent (w/v) sodium alginate aqueous solution was mixed with varying percentages (w/v) of nateglinide. After agitating the mixture to get the whole solution, it was added dropwise to an acetic acid solution containing Ca^{2+} and chitosan solution. The produced microspheres were left in the original solution for six and twenty-four hours to allow for internal gellification, and then they were filtered to separate. In an acidic pH, the drug did not release; however, the full release was achieved at pH 7.4 (1, 3).

Table 1. List of mucoadhesive polymers (17).

S. No.	Synthetic Polymers	Natural Polymers
1.	Hydroxy propyl methyl cellulose (HPMC)	Chitosan
2.	Poly vinyl pyrrolidone (PVP)	Sodium alginate
3.	Poly vinyl alcohol (PVA)	Guar gum
4.	Sodium carboxy methyl cellulose (Na CMC)	Xanthan gum
5.	Hydroxyl ethyl cellulose (HEC)	Soluble starch
6.	Hydroxy propyl ce (HPC)	Lecithin
7.	Methyl cellulose (MC)	Gelatin

4.5 Multiple emulsion method

This method produced oral controlled release drug administration for a variety of medications. Initially, the medication powder was mixed with methyl cellulose and then emulsified in an ethyl cellulose solution in ethyl acetate. After that, an aqueous medium was used to reemulsify the original emulsion. Discrete microspheres generated during this phase under optimal conditions (3).

4.6. Emulsion solvent diffusion method

Emulsion solvent diffusion method was used to create floating microparticles of ketoprofen in order to increase the residence period in the colon. The drug polymer combination was first dissolved in a 1:1 mixture of ethanol and dichloromethane. The mixture was then gradually added to a solution of sodium lauryl sulphate (SLS). For one hour at room temperature and 150 rpm, the solution was agitated using a propeller-style agitator. In a desiccator set to room temperature, the resulting floating microspheres were so cleaned and dried. The microparticles listed below were collected and sieved (3).

5. Use of Microspheres as Nasal Drug Delivery

Microspheres used in nasal medication delivery systems are water-insoluble, but water is absorbed into the sphere's matrix, causing it to inflate and gel. Formulation include starch, dextran, albumin, and hyaluronic acid. These microspheres enhance the bioavailability of peptides and proteins and have been beneficial for low-molecular-weight medications. Mucoadhesion, the long-term attachment of materials to a mucus layer, is another factor that improves the absorption of hydrophilic medicines. Mucoadhesive microparticles, drug and excipient particles the size of microns, can transfer drugs more effectively than liquid formulations or pure medication. Mucoadhesive polymers, such as cellulose, carbomer, alginate, degradable starch microspheres, and cationic polymer chitosan, have been investigated for better formulation of mucoadhesive microspheres.

Bioadhesion refers to the bonding of a synthetic or biological macromolecule to a biological tissue, such as the continuous mucus layer or epithelial cell layer. Insulin and water-insoluble cellulose derivatives have been combined in dry powder formulations for nasal delivery of peptides and proteins, resulting in water absorption, inflated, and gel formation. These formulations have been used to deliver medications like beclomethasone, oxymetazoline, and interferon via the nasal route (20-23).

6. Feasible Nasal Drug Delivery

The nose is a potentially useful drug delivery organ due to its simple accessibility and accessible surface area. The creation of pharmaceutical products is a crucial undertaking that is closely linked to their intended therapeutic uses (24). When developing a product, factors need to be taken into account based on whether the product is meant for:

6.1. Local delivery:

When compared to the oral route of administration, nasal distribution has the lowest possibility for systemic side effects, making it suitable for local (or topical) therapy. As a result, nasal administration of relatively modest dosages is efficacious with little systemic adverse effects. Decongestants for cold-related nose symptoms, along with antihistamines and corticosteroids for allergic rhinitis, are well-known therapeutic groups of medications supplied (25, 26).

6.2. Systemic delivery:

Compared to oral and intravascular modes of administration, intranasal administration of medications is a more efficient way to ensure systemic availability of the medication. Compared to oral and parenteral delivery, it offers quicker and longer drug absorption. Analgesics, cardiovascular medications like propranolol and carvedilol, hormones like levonorgestrel, progesterone, and insulin, anti-inflammatory medications like indomethacin and ketorolac, and antiviral medications (acyclovir) are among the therapeutic groups of pharmaceuticals administered. Zolmitriptan and sumatriptan are two examples of medications that are sold on the market to treat migraines and cluster headaches, respectively (24, 27).

6.3. Nasal vaccines:

Since the nasal mucosa is the first place the body comes into touch with inhaled antigens during inhalation, its utility in vaccination—primarily against respiratory infections—has been well studied. Indeed, nasal vaccination can raise systemic levels of particular immunoglobulin G and nasal secretory immunoglobulin A, making it a viable substitute for the traditional parenteral approach. Intranasal vaccinations against influenza A and B viruses, proteosoma influenza, adenovirus-vectored influenza, native Group B meningococcal infection, attenuated respiratory syncytial virus, and parainfluenza virus are examples of vaccines that are effective against humans (24, 28).

6.4. Central nervous system delivery through nasal route

The medications can be administered to the brain via the intranasal method. Drugs are transported from the nasal pathway to the central nervous system via the olfactory neuroepithelium. There have been reports of drug administration by nasal route into CNS for Alzheimer's disease, brain tumors, epilepsy, pain, and sleep disturbances (29, 30).

7. Mwchanism of Nasal Drug Absorption

Basically two main mechanisms have been considered out of sever mechanism proposed. The first one involves the aqueous route of transport, which is also known as the paracellular route (31, 32).

Key features of paracellular mechanism:

- Paracellular route is slow and of passive transport.
- The molecular weight of substances that are soluble in water and intranasal absorption have an inverse log-log relationship.
- A drug having a molecular weight more than 1000 Daltons was shown to have poor bioavailability.

Drugs that exhibit a rate dependence on lipophilicity are transported by the second method, which is also referred to as the transcellular process (or) pathway and includes transport via a lipoidal pathway (31, 33, 34).

8. Factors affecting Nasal Drug Absorption

Various factors affecting bioavailability of nasal administered drugs nasally are as follows (35):

8.1. Biological factors

8.1.1. Structural features

The nasal cavity is divided into five sections: the nasal vestibule, atrium, respiratory area, olfactory region, and nasal posterior. The permeability is influenced by these structures as well as the kind, density, and quantity of cells that are present there. Combining medications with absorption enhancers increases the amount of chemicals that go through (36).

8.1.2. Biochemical changes

The nasal mucosa acts as an enzymatic barrier to the administration of medications due to the abundance of several enzymes, including as peptidases, proteases, and oxidative and conjugative enzymes. These enzymes cause the medicines to break down in the nasal mucosa, which produces the pseudo-first-pass effect. Alcohols, nicotine, nasal decongestants, and cocaine are all metabolized via the p450 dependent monoxygenase system. The pre-systemic breakdown and consequent decreased penetration of several peptide medications, including desmopressin, insulin, calcitonin, and LHRH, were caused by protease and peptidase. Many strategies have been employed to combat these degradations. Protease and peptidase inhibitors, such as puromycin, amastatin, bacitracin, and boroleucin, are among them (35).

8.2. Physiological factors:

8.2.1. Nasal secretions

The anterior serous and seromucus glands secrete secretions into the nose. The amount of mucus produced each day is around 1.5-2 liters (37).

8.2.2. Blood supply and neural regulation

The nasal mucosa has a high permeability. The increase and decrease in the quantities of medicine absorbed are regulated by high blood supply resulting from parasympathetic stimulation, which causes congestion, and low blood supply resulting from sympathetic stimulation, which causes relaxation. We may infer from the aforementioned findings that parasympathetic activation is the cause of a compound's enhanced permeability (38).

8.2.3. Mucociliary clearance

Mucociliary clearance, the nasal cavity's natural defense system, removes chemicals sticking to the nasal mucosa and clears them in the GIT by draining into the nasopharynx. This process takes around 21 minutes for any drug supplied nasally to be cleansed from the nasal cavity by MCC. greater contact time between the drug and mucous membrane results in decreased MMC, which inhibits drug penetration; on the other hand, greater MCC increases drug permeability.

8.2.4. Pathological conditions

Diseases including the common cold, rhinitis, atrophic rhinitis, and nasal polyposis can cause mucociliary dysfunction, hypo- or hypersecretions, irritation of the nasal mucosa, and this might impact medication penetration (37).

8.2.5. Environmental conditions

It has been shown that there is a linear increase in ciliary beat frequency with temperature, with a moderate drop in the rate of MCC occurring at 24 °C.

8.2.6. Membrane permeability

The most crucial element influencing medication absorption via the nasal route is membrane permeability. Due to their limited membrane permeability, big molecular weight medications and water-soluble medications like peptides and proteins are absorbed by endocytic transport in smaller quantities (39).

8.3. Physicochemical properties of drugs

8.3.1. Solubility

Drugs solubility is a key element in influencing medication absorption across biological membranes. Given the higher aqueous nature of nasal secretions, a medication should have the right aqueous solubility for better dissolution. Drugs that are lipophilic are less soluble in aqueous secretions. Depending on their solubility, medications that are soluble in water are absorbed by passive diffusion, while pharmaceuticals that are lipophilic are absorbed via active transport.

8.3.2. Molecular weight and size

The molecular weight, molecular size, hydrophilicity, and lipophilicity of the chemical all affect drug permeability. With knowledge of MW, bioavailability for substances 1 kDa may be precisely calculated. These big compounds have a bioavailability that typically falls between 0.5% and 5%. Drug LT 300 Da's physicochemical characteristics have little effect on how well it permeates the membrane; instead, it largely does so through the aqueous channels. On the other hand, the rate of penetration is quite sensitive for molecules with MW 300 Da (40).

8.3.3. Lipophilicity

When a compound's lipophilicity increases, its permeability through the nasal mucosa often rises as well. Despite having certain hydrophilic qualities, it appears that the nasal mucosa is mostly lipophilic in nature, and the lipid domain is crucial to the barrier function of these membranes. Excessive hydrophilicity reduces the systemic bioavailability of many medications; in these situations, a prodrug strategy is helpful.

8.3.4. pKa and partition coefficient

Unionized species are absorbed more effectively than ionized species, according to the pH partition principle, and nasal absorption is no exception. There is a steady correlation between these medications' nasal absorption and pKa. Increases in the medications' lipophilicity or partition coefficient result in higher drug concentrations in biological tissues. The rate at which aminopyrine was absorbed rose as pH rose and was found to closely match the expected profile. Partition coefficient has a major role in controlling nasal absorption (41).

8.3.5. Polymorphism

One crucial factor in the creation of nasal medication products that are delivered as particulates is polymorphism. Drug absorption via biological membranes and drug dissolution are both known to be impacted by polymorphism. This issue needs to be carefully taken into account when developing the dose form for nasal distribution.

8.3.6. Physical state of drug

Two of the most crucial characteristics of particulate nasal medication products are particle size and drug shape. It is important to regulate these two factors in order to get the right medi-

cation dissolution characteristics in the nostrils. Avoiding particles smaller than 5 microns is advised since they might enter the lungs through inhalation. Particles in the 5–10 micron range are often deposited in the nasal cavity.

8.3.7. Chemical state of drug

The chemical form of the medicine when it is administered to the nasal mucosa determines how well it is absorbed. One potential solution to enhance medication absorption in cases when desired absorption qualities are not being met is to chemically modify the drug molecule by including a bio-cleavable lipophilic component. The creation of drug products must overcome several extra hurdles presented by the prodrug strategy. It is necessary to thoroughly assess the prodrug's toxicity (42).

8.4. Physicochemical properties of formulation

8.4.1. pH

The pH partition hypothesis determines the degree of drug ionization, hence formulation pH is relevant. A suitable pH should be achieved for nasal formulation in order to minimize irritation, achieve effective absorption, and stop the growth of harmful germs. The ideal pH range for a formulation is 4.5 to 6.5. The nasal surface has a pH of 7.39, whereas the nasal secretions have a pH of 5.5–6.5 in adults and 5.0–6.7 in newborns and kids.

8.4.2. Physical form of the formulation

When it comes to taking drugs through the nose, the formulation's physical shape is crucial. Insulin is more effectively administered to rabbits in powder form than in liquid form. A less effective systemic nasal medication distribution was noted when the formulation was more viscous. Researchers discovered that adding a viscous substance to desmopressin results in somewhat longer-lasting effects, but does not increase its overall bioavailability. Viscous mixtures might be useful in reducing nasal drip.

8.4.3. Osmolarity

Since the nasal mucosa is often affected by formulation tonicity, an isotonic formulation is recommended. Researchers looked at how formulation osmolarity affected rats' ability to absorb secretin through their noses. They discovered that the sodium chloride concentration in the formulation had an impact on every nasal mucosal cell and that the absorption peaked at 0.462 M concentration of sodium chloride. Epithelium cell shrinkage was seen at this dosage. Therefore, tonicity affects medication absorption as well (43).

8.4.4. Viscosity

A greater formulation viscosity lengthens the period of contact between the medication and the nasal mucosa, which extends the time for penetration.

8.4.5. Volume of solution and drug concentration

The amount of administration and the degree of absorption are not always correlated. Clement investigated the impact of three cetrizine nasal spray concentrations on the medication's clinical effectiveness. The findings demonstrated that when the medication concentration was reduced to just 0.125%, the patients' experiences on 16.7%, 30.8%, 42.9%, and 26.7% of days seemed to improve. The effectiveness decreased at 0.250%, the greater concentration (44).

9. Strategies to Improve Nasal Drug Absorption

To counter many other barriers present in nasal cavity which interfere with absorption of various drugs, some methods to be deployed to improve nasal drug absorption.

Nasal enzymes inhibitors: Many types of enzyme inhibitors are used to reduce drug metabolism in the nasal cavity, which reduces the activity of the enzymes present in the nasal cavity, such as peptidase and protease, which are employed as inhibitors to create peptide and protein molecules (35).

Permeation enhancers: Many types of permeability enhancers, such as phospholipids, cyclodextrins, bile salts, surfactants, and fatty acids, have been studied to increase nasal absorption (44).

Particulate drug delivery: Drugs are encapsulated in carriers to increase the drug's ability to remain in the nasal cavity and to keep it out of the nasal environment. Microspheres, liposomes, nanoparticles, and niosomes are a few instances of carriers (45).

Bioadhesive polymers: Bioadhesive poly-

mers are utilized to enhance the drug's nasal residency and absorption. By creating an adhesive force between the formulation and the nasal mucosa, they enhance the drug's retention period inside the nasal cavity and reduce the amount of formulation mucociliary evacuation (46).

Modifying drug structure: One of the most profitable approaches to increase nasal absorption is to modify the drug's structure without affecting its pharmacological action. In this case, altering physiochemical characteristics like solubility, pKa, molecular weight, and size is advantageous for medication absorption by the nose. The duration of effect, length of therapy, and the specific medication molecule's therapeutic necessity all influence nasal formulation design. The nasal route allows for both conventional release and controlled release medication administration. Depending on whether a medicine is delivered locally or systemically, different pharmaceutical excipients are needed (47).

10. Role of Mucoaadhesive Microspheres in Nasal Delivery

Modern pharmaceutical formulations (Table 2) have shown a considerable deal of interest in novel drug delivery mechanisms in recent years. Researchers and academics are becoming increasingly interested in mucoadhesive microspheres as a medication delivery technology due to its benefits of controlled and prolonged release action and adaptability (48).

1) Mucoadhesive microspheres provide a special delivery method for several drugs. Without a doubt, mucoadhesion has entered a new field with the introduction of these new specific targeting compounds (lectins, trimers, etc.). Researchers and pharmaceutical companies are investigating the possibility of using more complex molecules, proteins, peptides, and DNA, as well as DNA, in the future to advance technology in the constantly changing field of drug delivery.

Table 2. List of some marketed nasal formulations.

S. No.	Product	Drug	Medical benefits	Manufacturer
1.	Solspre Isotonic Nasal spray	Sodium Chloride	Cold Sinusitis Allergies	Abbott India Ltd.
2.	Netiwash Nasal Rinse Sachet	Sodium Bicarbonate Sodium Chloride	Nose inflammation Allergic rhinitis	Sunways India Pvt. Ltd.
3.	Bresol Ns Nasal Solution	Parnayavarni, Tailaparna, Yashtimadhu	Allergies Stuffy nose	Himalaya Wellness company
4.	Nasivion Nasal Solution	Oxymetazoline Hydrochloride	Cold Allergies Fever	Procter and gamble Health Ltd.
5.	Neilmed Nasogel	Sodium Hyaluronate Sodium Chloride Sodium Bicarbonate	Dry nose Moisturize Cleanse	Neilmed
6.	Naselin saline spray	Sodium Chloride	Cleanse Blocked nose	Vivimed Labs Ltd.
7.	Nasowash sachets	Sodium Chloride	Cleanse Stuffy nose	Cipla Ltd.
8.	Nasomist Nasal spray	Sodium Chloride	Cold Nasal crusting	Meridian Enterprises Pvt. Ltd.
9.	Nironet Nanogel	Sodium Bicarbonate	Nose irritation	Zydus Candila
10.	Otrivin Oxy Nasal spray	Oxymetazoline Hydrochloride	Nasal decongestant	GSK consumer Pvt. Ltd.

2) Mucoadhesive microspheres provide a vast applications in drug delivery through nasal region. Because of its controlled drug dosing and long lasting effect of that particular drug.
3) Mucoadhesive microspheres provide the benefit of targeted treatment. Adhering to certain mucosal surfaces allows medications to be delivered directly and specifically to the site of action.
4) The objective of the development of mucoadhesive microspheres is to improve their mucus penetration capacities and bioadhesive qualities. Through improved mucosal surface contact and mucus barrier removal, these microspheres can achieve longer residence times, higher retention, and improved medication absorption.
5) Combination therapy, in which many medications or therapeutic agents are administered concurrently, can make use of mucoadhesive microspheres. Combining many medications or active ingredients into a single microsphere formulation can enhance therapy, provide synergistic effects, and streamline treatment plans.

11. Conclusion

The nasal cavity, with its large surface area and vascularized mucosa, can absorb drugs directly into the systemic circulation, bypassing first-pass metabolism. All varieties of microspheres that have been employed as nasal medication delivery systems are insoluble in water, but they ultimately take in water and absorb it into their matrix, which causes the spheres to swell. Mucoadhesive microspheres have shown great promise as drug delivery vehicles for intra-nasal administration because of their capacity to stick to the nasal mucosa, increasing absorption and extending drug residence duration. Improved bioavailability, fewer doses required, and less systemic adverse effects are just a few of its benefits. They also offer regulated medication release, guaranteeing maintenance of therapeutic doses. All things considered, mucoadhesive microspheres are a useful method of improving nasal medication delivery, with prospective uses in a number of therapeutic domains, including the treatment of allergies, central nervous system diseases, and vaccine administration. This could facilitate pharmaceutical manufacturing and drug delivery challenges. With growing interest in nasal drug delivery, it is expected to see a range of novel nasal products reach the market soon.

Conflict of Interest

The authors declare no conflict of interest.

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