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NANOCARRIER BASED INTRANASAL DRUG DELIVERY SYSTEM

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ABSTRACT

In the recent years, Intranasal drug delivery is emerging as a reliable and promising pathway to deliver a wide range of therapeutic agents. Though the oral delivery is most convenient route of administration , as it is having some complications to certain drugs, an alternative way to those drugs is intranasal administration. Intranasal drug delivery is non - invasive and promising options to bypass blood-brain barrier (BBB) to reduce the systemic actions and lower the drug dose. In this article we will discuss about the nanoparticles based intranasal drug delivery that transports nose - via - brain. The aim of this study was to design and characterize the nanoparticles for intranasal drug delivery system. On the other hand, the nanoparticulate systems usage for vaccine delivery provide the beneficial effects, by achieving the good immune response. In this review we will mainly focus on the anatomical and cellular structure of nasal cavity and absorption surface. Furthermore, we are giving an overview on the recent advances in nasal delivery and mechanism of drug transport. Therefore, the drugs used for nasal delivery has the higher bioavailability and lesser side effects which are more helpful to lessen the neurodegenerative disorders (NDD).

Keywords: Intranasal administration, non - invasive, nanoparticles and Blood brain barrier.

INTRODUCTION

In the past years we have been studied about the drug administration through oral route as well as parenteral administration. Here we introduce the intranasal route of administration which has recently growing interest. The nasal formulations and new technologies are introduced inorder to decrease the side effects[1]. It is the easiest way i.e., nose to brain targetting with higher bioavailability and it is direct brain targetting which donot have any blood stream clearance and invasive methods. Hence we can say here that the intranasal administration is non - invasive and it can pass the BBB. It may potentially increases the CNS bioavailability of drugs. As it is passing the BBB the endothelial cells of it is connected by tight junctions which can prevent the leakage of substances from blood into brain[2].

The brain diseases such as Alzhiemers, schizophrenia, parkinsons disease are major brain diseases which donot have the particular drug to administer that leads to death in major cases. Even the disorders related to brain are not been fully clarified yet[3]. The brain disorders have the symptoms such as oxidative stress , mental toxicity , blood pressure etc. Here the oxidative stress is mainly due to the reactive oxygen spieces excessive production. So here we come to know that the antioxidant therapy is the forbidden thing in the treatment of neurodegenerative disorders (NDD)[4]. It is been surrounded by both *in vivo*and invitro studies. Here the lipid nanoparticles can improve the nose - to - brain drug delivery even faster when compared to other carrier particles because of their biodegradability[5] and bioacceptability and also rapid uptake by the brain. When compared to the drug solutions the nanosized carrier particles could increase the intranasal administration of drugs [6].

ANATOMY

Anatomically the nasal cavity is present between the base of the skull and roof of the mouth. It is comprised of two symmetrical cavities , which is divided by the septum which lies along the mid - saggital plane[7]. The cavities are lined with layer of mucosa and total area of both cavities is ~150cm 2. Furthermore it is divided into 3 regions,

1. Vestibular region
2. Respiratory region
3. Olfactory region

1. VESTIBULAR REGION

This is the first region which is also known as nasal vestibule. It has the area of 0.6cm 2. The vestibular region is covered by stratified squamous and keratinized epithelium with sebaceous glands. In this region the particles which are inhaled are gets filtered by the nasal hairs , also known to be vibrissae[8].

2. RESPIRATORY REGION

It is also known as conchae. It is the largest area of ~130cm 2 and is vascular. It is the cavity and it is divided into superior , middle and inferior cavities which are evolved or projected from the lateral wall[9]. This respiratory region consists of pseudostratified epithelium has 4 dominated cell types. They are goblet cells , ciliated columnar cells , basal cells and non - ciliated columnar cells[10]. It also consists of mucous glands and sebaceous glands.

The main physiology of this respiratory region involves the basal cells which are situated on the basal membrane , the goblet cells are mostly responsible for the secretion of mucus. These cells helps to prevent drying of mucosa by trapping of moisture and facilitates active transport. It consists of cilia which is responsible for increase in the respiratory surface area. The nasal secretion is a complex mixture consists of water of 95 % , mucin of 2% , salts of 1% and other proteins such as albumin, lysozymes, immunoglobulins, lactoferrin of 1% and <1% lipids[11].

3. OLFACTORY REGION

This region consists of the neuroepithelium it is the only part of CNS that is directly exposed to external environment. The drug is absorbed and reaches brain by crossing BBB. As same as respiratory region even it contains pseudostratified epithelium and also it consists of different olfactory cells[12].

MECHANISM OF NOSE - TO - BRAIN TRANSPORT

The mechanism of transport involves 2 pathways and the movement of molecules from nasal cavity to the brain takes place. When the molecules once delivered to the cerebrum and pons they disperse throughout the brain[13].

- Paracellular pathway
- Transcellular pathway

1. PARACELLULAR PATHWAY

The hydrophilic drugs are transported via the paracellular pathway which moves the drug through tight junctions of nasal epithelium. It is the first mechanism[14]. The poor bioavailability was observed with a molecular weight greater than 1000Da for some drugs. The lipophilic drugs like propanolol , progesterone , pentazocine and fentanyl are used for efficient absorption[15].

2. TRANSCELLULAR PATHWAY

It is the second mechanism. The nasal administration transports nasal epithelium through the transcellular pathway through which it goes by active transport by p - glycoproteins and peptides. Here the lipophilic drugs will be transported. Furthermore , the drugs need to cross the blood brain barrier to reach the brain [16].

NANOPARTICULATE CNS DELIVERY THROUGH NASAL ROUTE

From the past few decades, to the nasal nanotechnology much attention has be given. In the nasal nanotechnology, the nanocarriers include nanoemulsions, liposomes, polymeric nanoparticles and solid lipid nanoparticles these can efficiently transport the drug delivery system[17]. In general when compared to intranasal delivery through novel nanotechnology has the greater rate of flow i.e., which can easily transport to the brain and can cross the BBB. In the nanocarrier based particles the poorly distributed drug will be inserted and it comes to contact with 3 different areas[18]

1)Nasal mucosa the residence time increases, the mucoadhesive and viscosity also increases.

2) Olfactory nerve fibres which easily promotes drug from nasal cavity to the CNS.

3) The drug will interact with the BBB at the endothelial cells to cross the barrier and shows the therapeutic effects to the brain diseases.

The nanocarrier molecules, due to its small size can easily penetrate from nose - to - brain pathways and can cross BBB. The nanocarrier based systems have the different targetting ligands and those will bind to the specific receptors which shows the therapeutic effects

and also enchancement of brain selectivity and affinity[19]. The usage of nasal nanotechnology is even more safety and afficacy[20].

NOVEL NANOTECHNOLOGY

NANOPARTICLES

The better drug or vaccine deliver now - a - days explored as nanoparticulate system which can be delivered through intranasal administration[21]. The size range of nanoparticles is also in the nanosize range. As like the microparticles, nanoparticles also improves the drug metabolism and drug solubility. As the size range of nanoparticles are too less the bioavailability will be increases and is better one when compared to normal drug delivery rather than nanoparticulate drug delivery[22]. Generally nanoparticles are made up of polymers and lipids or in some cases both because to produce the sustained and controlled drug release and forms the controlled nanostructure[23].

LIPID BASED NANOPARTICLES

Lipid nanoparticles are solid matrix structures that are developed as an alternative to the nanoemulsions, nanogels and polymeric nanoparticles[24].The size range of SLN are also very less like the nanoparticles i.e., from 1 - 1000nm[25]. As the surface of the solid lipid nanoparticles consists of physiological lipids and surfactants there are generally considered as safe within the body. Generally the widy used lipids are triglycerides , monoglycerides , diglycerides , fatty acids and waxes[26]. These solid lipid nanoparticles are advance delivery system. These can minimize or avoid the limitation of polymeric nanoparticulate systems. Here it comprises of 2 generations. The first generation comprises of SLN and the second generation includes the Nanostructured lipid carriers (NLC)[27]. NLC are identified because to overcome the limitations of first generation. The lipid matrix which can improve the protein stability and also by avoiding the proteolytic degradation after administration[28].

RECENT ADVANCES

ANTIBODIES MEDIATED DRUG DELIVERY

This recent advancement about antibodies becomes the most popular over the last decade , but due to having its large size it is restricted to cross the BBB and also of low permeability and also limited the potential towards antibody mediated therapy for neurodegenerative disorders[29].

GENE VECTORS TUMORS

The administration of gene vectors to intranasal cavity restricts the blockage of BBB so that it can easily pass through the BBB and shows therapeutic actions in the brain[30].

STEM CELL THERAPIES

Stem cells are most forbidden treatment options for many diseases due to having the ability to replace dead cells in damaged areas. Now-a-days many markets of nasal preparations are delivered with pump sprays. They are most easy for the patients to use and are liable[31].

CONCLUSION

In this article the topics we have discussed are related to intranasal administration by using nanoparticles for brain targetting which are used to treat neurodegenerative disorders. Readers will gain the outlines of nasal cavity and many of the approaches here in reviewed are still at a basic level. The advantages of intranasal delivery are numerous and non - invasive. It bypass the BBB and delivers the drug directly into the CNS. These nanoparticulate carriers have the promising and advanced characters of enhanced therapeutic efficacy, enhanced targetting abilities and enhanced bioavailability. Furthermore because of growing demand of nasal drug products in global pharmaceutical marks, the pharmaceutical companies are investing a huge amount of money. However, it was also stated that intranasal route presents several limitations which must be overcome to develop successful nasal medicine. Finally the SLN and NLC for intranasal route of drug administration becomes the better option for delivery in the treatment of diseases.

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