REVIEW ARTICLE

ISSN:2394-2371
CODEN (USA):IJPTIL

RECENT ADVANCEMENTS AND NOVEL APPROACH THROUGH NASAL DELIVERY SYSTEMS- A REVIEW

Jigyasa Vindru, D. V. Gowda*, Anuj Gupta, Ashish

Dept. of Pharmaceutics, JSS University, JSS College of Pharmacy, SS Nagara, Mysore -570015, Karnataka, India

ABSTRACT

Mucosal delivery shows various benefits over other routes of drug administration. The present review outlines the different research works which has been done to safely deliver the drug through nasal cavity by various carriers like nanoparticles, microparticles, microemulsion etc. Nanoparticles show very promising results and prove to be very effective in drug delivery. Particle engineering plays important role in developing inhalable formulations which helps to develop the area of nasal drug delivery. This provide a lot of scope in research like targeting brain by using nasal drug delivery to effectively cross the BBB with undergoing degradation or in cancer therapy, vaccine delivery, systemic delivery in case of pain.

Keywords: - Nasal drug delivery, Nanoparticles, Inhalation, Microparticles, Microemulsion.

INTRODUCTION

Drug delivery through mucous membrane provides various alternatives to deliver the drug for systemic effect. Nasal route also considered as promising route for delivery of different drugs. It can be used to deliver both local and systemic effects like allergic or non-allergic rhinitis and other pulmonary diseases as it offers a highly vascularized epithelium which offers large surface area [1]. Delivery of drug through nasal route was recognized by ayurveda, in ayurvedic system it is known as “nasaya karama”. This nasaya karma has been practiced for thousands of years which provide a new lease of life [6]. The attainability of drug delivery by nasal route has received much attention from scientist because nasal delivery shows several benefits over oral route like poor bioavailability, slow absorption, drug degradation, avoids first pass metabolism [2]. It has been documented that nasal administration of steroids and hormones shows more absorption as compare to oral route so prove the potential of nasal delivery. Drugs

***Corresponding Author:**
Dr. D.V.Gowda, Professor
Dept. of Pharmaceutics,
JSS College of Pharmacy, JSS University,
Mysore-15, Karnataka, India.
E.Mail: dvgowdajssuni@gmail.com
Article Published: July-Sept 2016

with large molecules are poor candidates for the nasal drug delivery they show poor bioavailability [3]. On the other hand drug with small molecules show promising results. There are various types of delivery system that come into existence like nasal spray, nasal drops, nasal gels, nasal powder, liposomes, and nanoparticles. Drug can be deliver through nose by using inhalers. There are various types of inhalers that are used like nebulizers, pressurized metered dose inhaler, and dry powder inhalers. Drugs in liquid nasal sprays can be very well absorbed and liquid sprays are relatively simple and cost-effective but they have tendency to run down the esophagus which cause bad taste. Absorption of polar or large drugs are also difficult through liquid spray but use of dry powder formulations provide various advantages like better deposition and longer residence time in nasal cavity. This also improves stability and absorption. Spray drying is a technique to produce a formulation with unique particle size. It is method of producing dry powder from a liquid or slurry by the use of hot air. This method provide a consistent particle size which help to develop effective nasal preparation. But this process is not useful in case of thermal liable drugs. Spray dried powder are used to deliver the drug through various target sites but there are various challenges especially toxicity. Nasal drug delivery show various potential including the ability to target drugs across blood brain barrier. [1,2]

NASAL CAVITY- Anatomy and physiology

Nasal cavity is complex the basic function of the nose are heat and humidification of air before reaching the lungs. It performs functions like olfaction, filtration of inhaled particles and mucocilliary clearance. The nasal cavity is divided into two halves by the nasal septum and extends posteriorly to the nasopharynx, while the most anterior part of the nasal cavity, the nasal vestibule, opens to the face through the nostril. The atrium is an intermediate region between the vestibule respiratory regions. The respiratory region, the nasal conchae or turbinates, which occupies the major part of the nasal cavity, possesses lateral walls dividing it into 3 sections: the superior, middle and inferior nasal turbinates. These folds provide the nasal cavity with a very high surface area compared to its small volume. [3]

In nasal vestibule the epithelial cells are stratified, squamous and keratinized with sebaceous gland. By its nature vestibule shows resistance to dehydration and limit permeation of substances. The atrium is a transitional epithelial region with stratified, squamous cells anteriorly. Pseudo- stratified columnar cells with microvilli posteriorly. Pseudo stratified columnar epithelial cell interspersed with goblet cells, seromucus ducts, the openings of sub-epithelial seromucus

glands cover the respiratory region (the turbinates).[16] Furthermore, many of these cells possess actively beating cilia with microvilli. Each ciliated cell contains about 100 cilia, while both ciliated and non-ciliated cells possess about 300 microvilli each.

The narrow anterior triangular dynamic segment of the nasal anatomy called the nasal valve is the primary flow-limiting segment, and extends anterior and posterior to the head of the inferior turbinate approximately 2–3 cm from the nostril opening . This narrow triangular-shaped slit acts as a dynamic valve to modify the rate and direction of the airflow during respiration. Anatomical studies describe the static valve dimensions as 0.3–0.4 cm^2. [18]

Specifically, particles larger than 3–10μm are efficiently filtered out and trapped by the mucus blanket. The nose also acts as an efficient "gas mask" removing more that 99 % of water-soluble, tissue-damaging gas like sulfur dioxide. Infective agents are presented to the abundant nasal immune system both in the mucous blanket, in the mucosa, and in the adjacent organized lymphatic structures making the nose attractive for vaccine delivery with potential for a longstanding combination of systemic and mucosal immune responses. [26, 3]

Nasal vasculature is richly supplied with blood. The cavity has relatively large surface area because of presence of nearly 400 microvilli. The total nasal secretion is about nearly 15ml per day in normal physiological condition [35]. These all factors provide large and rapid permeability of drug. [5]

RECENT APPROACHES IN NASAL FORMULATION

NANOPARTICLES

Today nanotechnology has been developing very fast; there are varieties of nanoparticles that are constructed as a drug delivery system. Nanoparticles show various advantages like improving the solubility, improving efficiency, protecting drug from enzymes [10]. This is because of small size, because of the tight junction of the mucosal membrane only smallest nanoparticles penetrate through the nasal mucosa [6]. Various types of nanoparticles have been generated like nanoparticles including liposomes, dendrimers, and polymer nanoparticles [10,31]. Nanoparticles which are larger than 20nm cross the mucosal membrane by endocytosis, carrier mediated or receptor mediated transport. In route nanoparticles forms droplets or aggregate which work by causing deposition in lungs based on their dimension. Particle size of nanoparticles greatly affect the retention time of nanoparticles in lungs [25]. There are various methods for the preparation of nanoparticles-

a. Emulsion cross- linking
b. Coacervation / precipitation
c. Spray drying

d. Emulsion- droplet coalescence method
e. Ionic gelatin
f. Reverse micellar method
g. Sieving method

Lipid Based Nanoparticles

These are the nano- carriers of submicron size consisting of monolayer of phospholipids with a hydrophobic centre. These carriers are able to deliver both hydrophilic and hydrophobic drugs, lipophilic drugs are incorporated into the lipid core and amphiphilic nature of some lipids helps to incorporate hydrophilic drugs. Solid nanoparticles show a great potential in local as well as systemic delivery of drug. These carriers are used in delivery of insulin without any stability issues and shows prolonged therapeutic effect. These lipid carriers can be formed by same lipids that form cell membrane this approach limits the toxicity and causes easy penetration [25, 36]. This also helps to target the blood brain barrier because of its lipophilic nature. These are various factors which should be keep in mind while going for solid-lipid nanoparticles –

- Solubility of drug in lipid
- Miscibility of drugs in lipid
- Physical and chemical structure of solid lipid matrix
- Lipid polymorphism

SLN increases the drug stability and enhances the bioavailability of drug [35, 36, 40].

Inhalable Nanoparticulate Powders

There are various parameters that affect the formulation like particle size, size distribution, particle morphology, surface morphology, electrical charge density, hygroscopicity. Patient related factor like breathing pattern and disease state. Nanoparticles within the size range of 200nm are effective in mucous preparation. Dry powder chitosan nanospheres show promising result in nasal drug delivery because of the nano size of chitosan which adheres very well to mucous [31]. Spray drying is considered as one of the important technique to prepare nanoparticles for inhalation; this is easy process through which liquid droplets convert into the powder. Sham et al invented this technique to formulate the nanoparticles into the carrier for nasal delivery [52]. DPI's provide various advantages like higher dose can be deliver, provide chemical stability as compare to liquids [8,1].

It is very difficult to maintain the particles in dry state; any type moisture can cause aggregation of particles which effect the formulation. There are various techniques to reduce the particle size in the minimal range, improve dispersibility, sustained release. Such techniques are:

1. Surface modification to protect nanoparticle from deterioration.

2. Preparation of large hollow particles for deep lung deposition.
3. Encapsulation of nanoparticles within microparticles to prevent aggregation.
4. Preparation of effervescent particles for the improvement of dispersion.[33, 31, 32]

There are various advantages offers by powder drugs like delivery of poor water soluble drugs and protein-peptide drugs. There are very less choices for non-respirable carriers in DPI formulations. Carriers approved by FDA –

- Lactose
- Mannitol
- Glucose
- Erthritol
- Sorbitol
- Dextrose etc.

DPIs have good encapsulating ability, no hand-lung inhalation coordination, and long term stability, improved tolerability, easy to use and non- invasive [8, 12].

COLLOIDAL DISPERSIONS

It is a type of colloidal system for the drug delivery. It is a heterogeneous system consisting of dispersed phase which can be solid or liquid drug dispersed into dispersion medium. This is a suitable method for the water insoluble drug by formation of aerosols which is formed by dispersion of hydrophobic drug in water by sonication [19]. These aerosols can be administered into lungs by inhalation. Colloidal dispersion is a process that is cheaper and faster as compare to all other techniques. It is important that size range colloidal dispersion should be in range of 40- 60µ. If particle size is very small less than 10µ; this particle size can be carried out by the air streams into the bronchial region whereas larger particles remain deposited in the nose [19, 52, 23].

MICROPARTICLES

Microparticles are the drug delivery system that are in the range of 1-10µm [17] and is used to prolong the drug delivery, to improve the bioavailability, enhance the stability and to target the drug at specific site. These are prepared by using polymer with different coat- drug ratio by using different methods like:

a. Single/ double emulsion solvent evaporation
b. Spray drying
c. Ionotropic gelatin
d. Coacervation
e. Air suspension and polymerization[16]

There are various natural or synthetic polymers that are used in formation of nanoparticles such as poly (lactic-co-glycolic) acid, chitosan, poly (lactic) acid. Properties of polymeric microparticles like morphology, particle size, porosity easily meet the requirement for nasal delivery. [17]

Microparticles are generally use because they do not form aggregates under force and deposit deep inside the lungs. There are various examples through which improved activity of drugs are monitored; insulin and corticosteroids are formed by entrapping within microparticles. Insulin microparticles shows prolong residence time for 6-48 hours compare to free insulin [27,28].

MICROEMULSION

These preparations are spontaneous formations which are also called as miscellar emulsion. Particle size range varies between 1nm- 100nm in diameter. Microemulsions are optically isotropic and composed of oil, water and surfactant. They can be water in oil or oil in water; they show thermodynamic stability, elegant appearance and good penetration through the membrane [7, 33].

There are various advantages offered by microemulsion-

a. Shows rapid absorption
b. Onset of action is fast.
c. It avoids first pass metabolism.
d. It reduces the risk of over dosing.
e. It in non- invasive process.
f. Self medication is possible.
g. Improved patient compliance.

There are various drugs which are used as API in microemulsion like clonazepa, zolmitriptan, sumatriptan, ziprasidone and carbamazepine etc. Carbamazepine loaded microemulsion and mucoadhesive microemulsion were prepared for intranasal drug delivery. Vyas et al observed that there is rapid and large transfer of drug occur in rat brain following intra nasal administration of mucoadhesive microemulsion of drugs like zolmitriptan and sumatriptan. Mukesh et al study shows that risperidone was effectively delivered to the brain through mucoadhesive emulsion of risperidone by intranasal route [11, 30, 29].

LIPOSOMES

Liposomes are artificially prepared spherical vesicles composed of lamellar phase lipid bilayer. It consists of aqueous compartment where drug can be kept [52]. Membrane of liposomes can easily dissolve hydrophobic chemicals so they can be used to deliver both hydrophilic and hydrophobic molecules. To deliver the drug to the site of action lipid bilayer membrane of liposomes fuses with the other bilayer such as cell membrane and cause the delivery of drug from liposome [42]. Liposomes are very useful as carrier in nasal drug delivery because of its nature, they consist of biogenic phospholipids, biocompatible and non-immunogenic [43]. Liposomes show promising results in case of nasal drug delivery of various drug molecules; proteins and peptides can be deliver through nasal passage by using liposomes. Firstly it provides protecting effect on proteins they have ability to cause mucosal

disruption. Positively charged liposomes have capability to increase the residence time of drug in negatively charged surface [50]. Liposomes were investigated for nasal delivery of insulin. Many drugs can be given through nasal route which are degraded by GI tract; for example salmon calcitonin which is widely used because of its tolerance and affectivity. But as other peptides salmon calcitonin is also degraded by the enzymes present in GI tract because of its bioavailability gets reduced through oral route. So it can be delivered by nasal route using liposomes as carrier [44].

Liposomes in vaccine delivery-

Liposomes offer various advantages in delivery of vaccines like it provide protection to antigen during transit and increase facilitation of antigen uptake by M cells. As liposomes are biocompatible and biodegradable, easy to prepare, characterize hence these are prove to be very effective in immune response antigen [46].

CONCLUSION

The intranasal route is an interesting alternative route for drug administration with enormous advantages such as muco-adhesion, increase in residence time of drug, inhibition of enzymatic degradation and enhanced penetration of drug. All these advantages provide lots of potential for administration several drugs like vaccines, anti-cancer drugs and drugs which act on CNS. Although there are various challenges also which are related with understanding of anatomy and physiology of nasal cavity which are not widely understood that limits the potential and efficacy of nasal drug delivery system. With these understandings this route provides various future opportunities for research and development of new system.

REFRENCES:

1. Couckea. D, Schotsaert. M, Libert. C, Pringels. E, Verva. C et, Foreman.P, Saelens X, Remon JP “Spray-dried powders of starch and crosslinked poly(acrylic acid) as carriers for nasal delivery of inactivated influenza vaccine” Vaccine 27 (2009) 1279–1286.
2. Chen KH, Sabatino M, Albertini B, Passerini N, Kett VL “The effect of polymer coatings on physicochemical properties of spray-dried liposomes for nasal delivery of BSA.” Europoean Journal of Pharmaceutical Science 50 (2013) 312-322.
3. Illum L, “Nasal drug delivery: new developments and strategies” Research focus DDT Vol. 7, No. 23 December 2002.
4. Pascual J, PhD; Mateos V, MD; Roig.C, MD, PhD; Sanchez-del-Rio R, MD; D. Jim´enez, MD, PhD “Marketed Oral Triptans in the Acute Treatment of Migraine:A Systematic Review on Efficacy and Tolerability”. ISSN 0017-8748 doi: 10.1111/j.1526-4610.2007.00849.x Journal

compilation 2007 American Headache Society Published by Blackwell Publishing.

5. Parvathi.M "Intranasal drug delivery to brain- An overview", International Journal of Research in Pharmacy and Chemistry. ISSN: 2231□2781.
6. Kushwaha KS, Keshari R.V and Rai AK "Advances in nasal trans-mucosal drug delivery" Journal of Applied Pharmaceutical Science 01 (07); 2011: 21-28.
7. Rajput A.P, Prakash V.P, Motilal C.P, Prakash C.S, Tukaram B.D, "Nose to brain delivery of Ziprasidone microemulsion: Design and Characterization." International Research Journal of Pharmacy ISSN 2230-8407.
8. Duan. J, Vogt F, Xiaojian D, Mansour HM Design, "Characterization, and aerosolization of organic advanced spraydried moxifloxacin and ofloxacin dipalmitoylphosphatidylcholine (DPPc) microparticulate/nanoparticulate powders for pulmonary inhalation aerosol delivery." International Journal of Nanomedicine
9. Agnihotri SA, Mallikarjuna NN, Aminabhavi TM. Recent advances on chitosan-based micro-and nanoparticles in drug delivery. Journal of controlled release. 2004 Nov 5;100(1):5-28.
10. Gao H. Progress and perspectives on targeting nanoparticles for brain drug delivery. Acta Pharmaceutica Sinica B. 2016 Jul 31;6(4):268-86.
11. Patel RB, Patel MR, Bhatt KK, Patel BG. Formulation consideration and characterization of microemulsion drug delivery system for transnasal administration of carbamazepine. Bulletin of Faculty of Pharmacy, Cairo University. 2013 Dec 31;51(2):243-53.
12. Muralidharan P, Malapit M, Mallory E, Hayes D, Mansour HM. Inhalable nanoparticulate powders for respiratory delivery. Nanomedicine: Nanotechnology, Biology and Medicine. 2015 Jul 31;11(5):1189-99.
13. Vehring R. Pharmaceutical particle engineering via spray drying. Pharmaceutical research. 2008 May 1;25(5):999-1022.
14. Baltzley S, Mohammad A, Malkawi AH, Al-Ghananeem AM. Intranasal drug delivery of olanzapine-loaded chitosan nanoparticles. AAPS PharmSciTech. 2014 Dec 1;15(6):1598-602.
15. Kozlovskaya L, Stepensky D. Quantitative analysis of the brain-targeted delivery of drugs and model compounds using nano-delivery systems. Journal of Controlled Release. 2013 Oct 10;171(1):17-23.
16. Kozlovskaya L, Abou-Kaoud M, Stepensky D. Quantitative analysis of drug delivery to

the brain via nasal route. Journal of controlled release. 2014 Sep 10;189:133-40.

17. Van Woensel M, Wauthoz N, Rosière R, Amighi K, Mathieu V, Lefranc F, Van Gool SW, De Vleeschouwer S. Formulations for intranasal delivery of pharmacological agents to combat brain disease: a new opportunity to tackle GBM?. Cancers. 2013 Aug 14;5(3):1020-48.
18. Djupesland PG. Nasal drug delivery devices: characteristics and performance in a clinical perspective—a review. Drug delivery and translational research. 2013 Feb 1;3(1):42-62.
19. Menaka M, Pandey VP, Smith AA. Colloidal Dispersions As A Potential Nasal Drug Delivery System For Ondansetron Hydrochloride–In Vitro And In Vivo Properties. Asian Journal of Pharmaceutical and Clinical Research. 2013 Dec 29;1(2):72-5.
20. Saluja V, Amorij JP, Kapteyn JC, de Boer AH, Frijlink HW, Hinrichs WL. A comparison between spray drying and spray freeze drying to produce an influenza subunit vaccine powder for inhalation. Journal of Controlled Release. 2010 Jun 1;144(2):127-33.
21. Hoppentocht M, Hagedoorn P, Frijlink HW, de Boer AH. Technological and practical challenges of dry powder inhalers and formulations. Advanced drug delivery reviews. 2014 Aug 30;75:18-31.
22. Longest PW, Golshahi L, Behara SR, Tian G, Farkas DR, Hindle M. Efficient Nose-to-Lung (N2L) Aerosol Delivery with a Dry Powder Inhaler. Journal of aerosol medicine and pulmonary drug delivery. 2015 Jun 1;28(3):189-201.
23. Coucke D. *Development of a platform for nasal delivery of peptides and vaccines using powder carriers based on starch/poly (acrylic) acid* (Doctoral dissertation, Ghent University).
24. Majithiya RJ, Ghosh PK, Umrethia ML, Murthy RS. Thermoreversible-mucoadhesive gel for nasal delivery of sumatriptan. AAPS PharmSciTech. 2006 Sep 1;7(3):E80-6.
25. Kuzmov A, Minko T. Nanotechnology approaches for inhalation treatment of lung diseases. Journal of Controlled Release. 2015 Dec 10;219:500-18.
26. Chaturvedi M, Kumar M, Pathak K. A review on mucoadhesive polymer used in nasal drug delivery system. Journal of advanced pharmaceutical technology & research. 2011 Oct;2(4):215.
27. Giri TK, Choudhary C, Alexander A, Badwaik H, Tripathi DK. Prospects of pharmaceuticals and biopharmaceuticals loaded microparticles prepared by double emulsion technique for controlled delivery.

Saudi Pharmaceutical Journal. 2013 Apr 30;21(2):125-41.

28. El-Sherbiny IM, McGill S, Smyth HD. Swellable microparticles as carriers for sustainpulmonary drug delivery. Journal of pharmaceutical sciences. 2010 May 1;99(5):2343-56.
29. Rassu G, Soddu E, Cossu M, Brundu A, Cerri G, Marchetti N, Ferraro L, Regan RF, Giunchedi P, Gavini E, Dalpiaz A. Solid microparticles based on chitosan or methyl-β-cyclodextrin: A first formulative approach to increase the nose-to-brain transport of deferoxamine mesylate. Journal of Controlled Release. 2015 Mar 10;201:68-77.
30. El-Sherbiny IM, El-Baz NM, Yacoub MH. Inhaled nano-and microparticles for drug delivery. Global cardiology science & practice. 2015;2015.
31. Kulvanich P. Preparation and in vivo absorption evaluation of spray dried powders containing salmon calcitonin loaded chitosan nanoparticles for pulmonary delivery. Drug design, development and therapy. 2013;7:861-73.
32. Yasir M, Sara UV. Solid lipid nanoparticles for nose to brain delivery of haloperidol: in vitro drug release and pharmacokinetics evaluation. Acta Pharmaceutica Sinica B. 2014 Dec 31;4(6):454-63.
33. Rassu G, Soddu E, Cossu M, Brundu A, Cerri G, Marchetti N, Ferraro L, Regan RF, Giunchedi P, Gavini E, Dalpiaz A. Solid microparticles based on chitosan or methyl-β-cyclodextrin: A first formulative approach to increase the nose-to-brain transport of deferoxamine mesylate. Journal of Controlled Release. 2015 Mar 10;201:68-77.
34. Olkhovyk O, Batykefer L "Orally inhaled and nasal drug products" Ondrug delivery.
35. Arora P, Sharma S, Garg S. Permeability issues in nasal drug delivery. Drug discovery today. 2002 Sep 15;7(18):967-75.
36. Chirio D, Gallarate M, Peira E, Battaglia L, Muntoni E, Riganti C, Biasibetti E, Capucchio MT, Valazza A, Panciani P, Lanotte M. Positive-charged solid lipid nanoparticles as paclitaxel drug delivery system in glioblastoma treatment. European Journal of Pharmaceutics and Biopharmaceutics. 2014 Nov 30;88(3):746-58.
37. Rahisuddin SP, Garg G, Salim M. Review on nasal drug delivery system with recent advancement. Int J Pharm Pharm Sci. 2011;3(2):6-11.
38. Danielsson, I.; Lindman, B. Colloids Surf. A 1981, 3, 391.
39. Bhople N. Nasal dosage forms and devices for intranasal drug delivery.

40. Yasir M, Sara UV. Solid lipid nanoparticles for nose to brain delivery of haloperidol: in vitro drug release and pharmacokinetics evaluation. Acta Pharmaceutica Sinica B. 2014 Dec 31;4(6):454-63.
41. Prajapati N, Srivastava P, Bhargava S. Recent advances in nasal drug delivery using natural polymers. Current drug therapy. 2012 Sep 1;7(3):170-8.
42. Mao Y, Li X, Chen G, Wang S. Thermosensitive Hydrogel System With Paclitaxel Liposomes Used in Localized Drug Delivery System for In Situ Treatment of Tumor: Better Antitumor Efficacy and Lower Toxicity. Journal of pharmaceutical sciences. 2016 Jan 31;105(1):194-204.
43. Chono S, Fukuchi R, Seki T, Morimoto K. Aerosolized liposomes with dipalmitoyl phosphatidylcholine enhance pulmonary insulin delivery. Journal of Controlled Release 137 (2009) 104–109.
44. Chena M, Li X.R, Zhou Y.X, Yang K.W, Chen XW, Deng Q, Liu Y, Ren L. Improved absorption of salmon calcitonin by ultraflexible liposomes through intranasal delivery. Peptides 30 (2009) 1288–1295.
45. Amina M, Jaafari M R, Tafaghodi M. Impact of chitosan coating of anionic liposomes on clearance rate, mucosal and systemic immune responses following nasal administration in rabbits. Colloids and Surfaces B: Biointerfaces 74 (2009) 225–229.
46. Tiwari S, Verma SK, Agrawal GP, Vyas PV. Viral protein complexed liposomes for intranasal delivery of hepatitis B surface antigen. International Journal of Pharmaceutics 413 (2011) 211– 219.
47. Reddy S.C. Formulation and evaluation of dry powder for inhalation of anti-inflammatory drug.
48. Yang ZZ, Zhang YQ, Wanga ZZ, Wua K, Lou JN, Qi XR. Enhanced brain distribution and pharmacodynamics of rivastigmine by liposomes following intranasal administration. International Journal of Pharmaceutics xxx (2013) xxx–xxx.
49. Law S.L, Huang K.J, Chou H.Y. Preparation of desmopressin-containing liposomes for intranasal delivery. Journal of Controlled Release 70 (2001) 375–382.
50. Chen K.H, Sabatino. M.D, Albertini B, Passerini N, Ket V.L. The effect of polymer coatings on physicochemical properties of spray-dried liposomes for nasal delivery of BSA. European Journal of Pharmaceutical Sciences 50(2013) 312-322.
51. Vinogradov S.V. Colloidal microgels in drug delivery applications. Curr Pharm Des. 2006 ; 12(36): 4703–4712.

52. Sham JO, Zhang Y, Finlay WH, Roa WH, Löbenberg R. Formulation and characterization of spray-dried powders containing nanoparticles for aerosol delivery to the lung. Int J Pharm. 2004;269(2):457–467.
53. Dhuria SV, Hanson R, FreyII WH. Intranasal delivery to the central nervous system: mechanism and experimental considerations. J Pharm Sci 2010; 99:1654-1673.

Table 1: Advantages and Limitation of Nasal Delivery

Advantages	Limitation
a. **Avoids degradation of drug in GIT.**	Volume of dose restricted to 25-200µl.
b. **Avoids first pass metabolism.**	Compounds with high molecular weight cannot be delivered.
c. **Shows better absorption.**	Large interspecies variability is observed.
d. **Shows higher bioavailability in lower doses of drug.**	Mucocilliary clearance affects the permeability of drug.
e. **Non-invasive route.**	Irritation of nasal mucosa.
f. **Self medication possible.**	Enzymatic barrier to permeability of drug.
g. **No complex formulation required.**	Adversely affected by pathological condition.

Table 2: Drug made into nanoformulation as dry powder inhalers

DRUG	CLASS	CONDITION	ROUTE OF ADMINISTRATION
Vancomycin	Antibiotic	Infection	DPI
Clarithromycin	Antibiotic	Infection	DPI
Cyclosporine A	Immunosuppressant	Lung transplant	DPI
Doxorubicin	Anticancer agent	Lung cancer	DPI
Ofloxacin	Antimicrobial	Infection	DPI
Budesonide	Glucocorticoid	Asthma and COPD	DPI

Table 3: Patents in nasal drug delivery

Publication Number	Publication Type	Application Number	Publication Date	Filing Date	Inventors
US20010055569 A1	Application	US 09/841,228	Dec 27/2001	Apr 24/2001	Stanley Davis, lisbeth IIIum
US6241969 B1	Grant	US 09/105,838	Jun 5/2001	Jun 26/1998	Zahir Saidi, Boris Klyaschitsky
US5690954	Grant	US 08/412,094	Nov 25/ 1997	Mar 28/1995	Lisbeth lllum
US5874064A	Grant	US 08/739,308	Feb 23/1999	Oct 29/1996	David Edwards