WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

A Review Article on Nasal Spray

[1]Mr. Nilesh Bhaskar Khairnar, [2]Ms. Rajeshwari K. Thokal, [3]Dr. Gajanan S. Sanap, [4]Nasal Spray

[1,2,3]LBYP college of Pharmacy, Pathri, Aurangabad – 431111, Maharashtra, India
[4]LBYP College of Pharmacy D Pharmacy (D Pharm & B Pharm) Pathri, Aurangabad – 431111, Maharastra, India

ABSTRACT:

For local, systemic, and central nervous system medication delivery, intranasal delivery is the preferred route of drug administration. Nasal spray is an increasingly popular dosage form for nasal drugs because to its benefits, including being affordable, convenient to use and carry, and highly patient compliant delivery. The pertinent features of nasal anatomy, physiology, histology, and the biological When developing a nasal spray formulation, physicochemical and pharmacological parameters must be taken into account. It makes intuitive sense to assume that this review will id in understanding nasal formulation and its in-vitro properties. Nasal spray, nasal drug delivery system, formulation, and in-vitro characterization are some of the keywords.

INTRODUCTION:

The use of intranasal medication delivery as a dependable and practical alternative to oral and parenteral methods is well known. For drug distribution, the nasal route is an option for drugs are delivered both locally and systemically. One example is Treatments typically employ local is nasal medication administration. Nasal -cavity-related conditions, like congestive, allergy, and rhinitis-related sinusitis conditions. medications, such as steroids, histamine blockers, anti-cholinergic drugs, and You can administer vasoconstrictors locally. Much attention has been paid in recent years to the idea of employing the nose as the body's entry point for drugs to take systemic effect attention. The nasal delivery also appears to be a good approach to get over the barriers for blood- a brain barrier (BBB) that permits direct medication delivery the central nervous system (CNS)-active bio phase compounds. It has also been regarded as one of vaccination administration.

Today, a variety of formulations are used to give medications via the nasal route, including nasal spray, nasal drops, nasal powder, and nasal gel nasal inserts, gels, etc. drug administration spray dose to be administered through the nose is a non-invasive technique that provides a quick medication onset due to the nasal spray's active ingredient affordable, simple to use/carry, and self-administrable Patient compliance is very high. hence, nasal medication Delivery is becoming a common method of drug administration. is itation and has much room for growth [1]

Devices with special is designs that can deliver sprays or powders to the olfactory just recently have become available area of the nose, making it possible to deliver the medication that enters the brain directly. First, systemic drug delivery dense vascularization the nasal mucosa. it seems that way A particularly attractive alternative to conventional medication Oral in activator [12] The current review describes the key parameters influencing nasal drug distribution, as well as the morphological, physiological, and histological characteristics of the nasal cavity features of medication formulations and drug attributes decisively ascertain nasal pharmacokinetics preparations. Also, this article analyses nasal parameters for spray formulation, excipients, Characterization and its impact on important in-vitro tests.

Despite the obvious advantages of intranasal administration of drugs The nasal cavity has many restrictions drug absorption such as low intrinsic permeability hydrophilic molecules, peptides, proteins and nucleotides, rapid mucociliary clearance and enzymatic degradation [13,14]

in vitro models of the nasal cavity are commonly used to study the intranasal cavity. Nasal administration of drugs has been around for decades and is a common route of administration. Local action therapy for diseases such as allergic rhinitis, sinusitis, congestion, etc. and is increasingly used for systemic administration. B. Migraines, pain, use and research such as dosing [15]. Looking to the future, we have a strong interest in developing new treatment of central nervous system disorders such as Alzheimer's disease and Parkinson's disease by nasal administration. A variety of factors influence the delivery of therapeutic agents through nasal sprays. Or aerosols, and in vitro studies are often performed during research into new nasal therapies It is used to guide research and development **a**natomical Deposition of intranasal therapy[16] This approach serves as an in vitro tool. It mimics the anatomy of the human nasal cavity. This review article sheds light on nose development Casts and how they are used to support drug development.

Advantages of Nasal Drug Delivery system [2]:

1. From the perspective of patients, intranasal administration has a number of practical benefits (primarily non-invasiveness) pleasant, painless, and easy medication delivery acceptable profile)

2. Quick absorption of drugs.

3. Rapid start of action.

4. There is no hepatic first-pass metabolism.

5. Larger drug molecules' bioavailability can be enhanced through absorption a strategy or enhancement.

6. A smaller drug has better nasal bioavailability molecules. [2]:

Limitations:

1. The relatively small area available for drug absorption limits the dose.

2. There is a finite amount of time for drug absorption.

3. Drug effectiveness is hampered by nasal disease absorption.

4. The substances that increase absorption are nasal medication delivery system toxicity in histology that is yet unclear established.

5. There is less surface area for absorption compared to GIT.

6. Nasal sensitivity

7. Some surfactants used to enhance chemicals may destabilize and even dissolve a membrane high level of focus.

Nasal Anatomy and Physiology [3, 4]:

Nasal depression is lined with mucus and hairs which are involved in those functions, gobbled patches and pathogens. Also resonance of produced sounds mucus MMC [immunological conditioning and metabolism of endogenous substances are also essential functions of nasal structures. The mortal nasal depression has a total volume of 15- 20 mL and a total face area of roughly 150 cm2 The nasal halves correspond of four areas(nasal entranceway, patio, respiratory region and olfactory region) that are distinguished according to their anatomic and histological characteristics(Figure 1; Table 1).

1) Nasal vestibule

In this area of nasal depression, there are nasal hairs, also called vibrissae, which filter the gobbled patches. Nasal vestibular characteristics are desirable to go high resistance again poisonous environmental substances

2) Atrium

Between the nasal vestibule and the respiratory region, there is an atrium. A stratified squamous epithelium makes up its anterior part, and the by pseudo stratified columnar cells in the posterior region showing off microvilli.

3) Respiratory region

Divided into upper, middle and lower nasal turbinate protruding from the sidewall. These special structures are Humidification and temperature control of the inhaler air. Between them there is a space called a way these are the passages through which the air flow is created Ensure intimate contact with inhaled air the mucosal surface of the respiratory tract lower and middle

The tract receives the nasolacrimal ducts and sinuses these are air-filled pockets inside the bone around the face and nasal cavities. Nose the most important airway mucosa Sections are formed for systemic delivery of drugs via epithelium, basement membrane, and lamina exclusive use Nasal discharge is essential for many people Physiological functions.

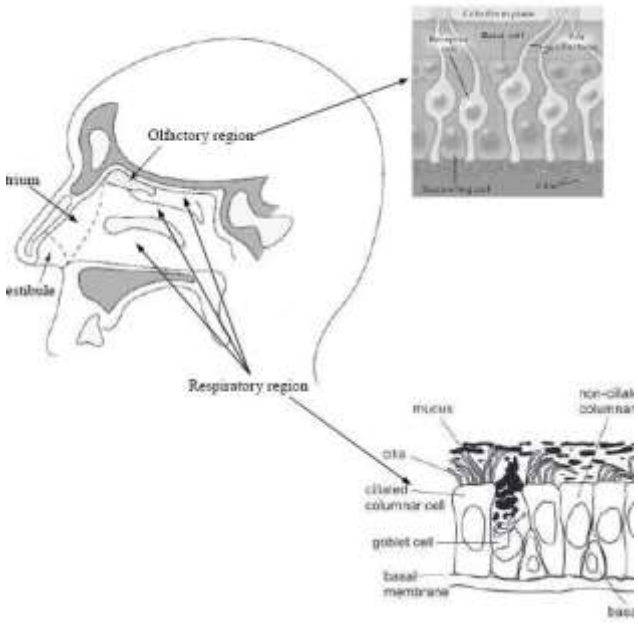

Fig-1: Anatomy and histology of human nasal cavity.

4) Olfactory region

The olfactory region is located on the roof of the Extends a short distance under the nasal cavity and nasal septum and side walls. Its epithelium is the only part central nervous system directly exposed to the outside world Surroundings. Similar to respiratory epithelium, the sense of smell is also pseudo stratified, but included Special olfactory receptor cells important for odors Perception.

Different factors affecting nasal drug absorption [4-5]

Various factors affect nasal bioavailability drugs administered as follows

A) Biological factors

1) Structural features there are 5 different sections nasal cavity: nasal vestibule, vestibule, respiratory cortex, olfactory area and nasal pharynx. These structures and cell type, cell density and number Presence in this area affects transparency. Absorption enhancers used with drugs Increases compound penetration.

2) Biochemical changes: enzyme barrier Medication administration is for the nasal mucosa presence of numerous enzymes, including Oxidase and conjugation enzymes, peptidases, etc. protease. this involved proteases and peptidases deterioration and later lower Penetration of various peptide drugs such as calcitonin, Insulin, LHRH. to overcome these Degradation using protease and peptidase inhibitors bacitracin, amastatin boroleucine, puromycin, etc.

B) Physiological factors

1) Blood supply and neuro modulation

The nasal mucosa is a highly permeable area. Expensive Therefore, blood supply by stimulation of the parasympathetic nerve Sympathetic congestion and decreased blood supply Stimulation relaxes and regulates ups and downs Amount of drug penetrated.

2) Viscosity of nasal secretions: viscous surface layer the sol mucus layer inhibits ciliary movement too thin and mucociliary clearance is compromised. The layer is too thick because it has lost contact with Jill. Impairment of the drug impairs drug penetration. mucociliary clearance by varying contact time drugs and mucous membranes.

• Drug solubility in nasal secretions: for penetrating of drug dissolution is required. a drugs must have appropriate physicochemical effects Dissolving properties in nasal secretions. • Nasal PH values Fluctuations in pH are observed.5.5 to 6.5 in adults and 5.0 to 7.0 in infants. The lower the nasal pH value, the greater the drug penetration under such conditions, as the drug's PKA Penetrant molecules exist as connective tissue species.

3) Mucociliary

clearance (MCC) and ciliary stroke Whenever a substance is administered through the nose, it is Cleared from nasal cavity by MCC at ~21 min Because mucociliary clearance is the normal defense Mechanism of the nasal cavity to expel substances Adheres to nasal mucosa and clears with GIT Drainage into the nasal pharynx drug permeation Improved by increasing contact time with drug Mucous membranes, due to the reduction of MMC.

4) Pathological conditions mucociliary dysfunction, hypo secretion or hyper secretion, Irritation of the nasal mucosa occurs due to illness Common cold, rhinitis, atrophic rhinitis, etc. nasal polyposis, and drug penetration are affected.

5) Environmental conditions

A gradual decline in MCC rate occurs It was predicted to be linear at a temperature of 24°C. Increased ciliary beat frequency occurs with increasing at temperature.

C) Physicochemical properties of drug:

1) molecular weight and size: drug permeation molecular weight, molecular size, hydro philicity and lipo philicity of compounds. For Compound 1 kda, bioavailability may be direct Predicted from knowledge of MW. in general, The bioavailability of these large molecules is 0.5% to 5%. Physico chemical properties of drugs does not significantly affect the penetration of the drug LT 300There it penetrates almost watery Membrane channel. In contrast, for connections At MW 300 Da, the permeability is very sensitive.

2) Solubility: The main factors that determine the absorbance of A drug that crosses biological membranes is the solubility of the drug. Nasal discharge is more watery, so medication Must have suitable water solubility Better resolution. Fewer lipophilic drugs Solubility in aqueous secretions water soluble Drugs are absorbed by passive diffusion and lihpo philicity Drugs by active transport according to solubility.

3) lipophilicity: Penetration of compound usually rises through the nasal mucosa with increasing in lipophilia. It seems that the nasal mucosa are predominantly lipophilic and serve lipid domains Critical role in these barrier functions Membrane, slightly hydrophilic feature. Systemic bioavailability of many drugs In such cases, excessive hydrophilicity reducesa prodrug approach is beneficial.

4) pka and partition coefficient: According to pH classification Theoretically, integrated seeds are better absorbed in comparison The same facts apply in this case. absorption through the nose. Have an ongoing relationship Between pka and nasal absorption of these drugs.

5) Polymorphism is important Parameters in the development of nasal drops it's administered in particulate form. Polymorphism is known to affect medicines and their dissolution immersion through natural membranes is affected by Polymorphism. This factor should be precisely consil Considered in Dosage Form Development Nasal delivery

D) Physicochemical properties of formulation:

1) Physical form of expression liquid phrasings are less effective than greasepaint forms When administering insulin to rabbits totally hamstrung Nasal medicine delivery with density was observed tradition. Viscous phrasings help minimize watery nose.

2) pH The degree of medicine ionization is determined by pH Because it's a distributive thesis, it's related to the expression pH value. Nasal phrasings should be acclimated consequently avoid vexation, achieve effective immersion, To help the growth of pathogenic bacteria. Ideal The pH of the expression should be acclimated between4.5 and6.5.

3) Osmolarity tradition pressure has a big impact Nasal mucosa is generally an isotonic expression preferabl.

Mechanism of drug absorption:[19]

In the first step of absorption, the absorbed drug must be absorbed It moves from the nasal cavity to the mucus layer small However, uncharged drugs can cross the mucus layer Larger, more charged drugs struggle a lot pass/cross. mucin is the main protein in mucus Tendency to bind to solutes and obstacles diffusion. Additional structural changes in mucus Environmental influences (temperature and pH) changes**.**

Formulation of nasal spray [6]:

Contains nasal drops Therapeutic Active Ingredients (Pharmaceuticals)

Dissolved or suspended in a solution or mixture of Auxiliaries (e.g. preservatives, viscosity modifiers, emulsifier, buffer) reduced pressure A dispenser that dispenses a spray containing a metered amount Dose of active substance. Dosage can be administered through a spray pump. A nasal spray unit can be constructed Can dispense up to unit doses or hundreds Metered spray of drug-containing formulations material. Nasal spray is applied to the nasal cavity for local and/or systemic effects. Similar, but Many features, some aspects to other drugs Nasal sprays can be unique (e.g. formulation, container Closed system, manufacturing, stability and drugs product). Dosing and nebulizing (e.g. opening,nozzles, jets) pump mechanisms and components are used Reproducible delivery of drug formulations and these Can consist of many parts with different designs dimensionally precisely controlled composition. Dispersion requires energy Formulated as a spray. This is usually achieved By passing the formulation through the nose actuator and the opening. Formulation and container Closure Systems (Containers ,Closures, Pumps, Everything Protective packaging) make medicine together product. Design of container closure system Affects drug dosing performance Both solution and suspension formulations can be used.

Formulated in a nasal spray.

Fig-2: Nasal spray (Dymista®)

IDEAL DRUG CANDIDATE FOR NASAL DELIVERY [20,21,22]

 Sufficient water solubility to provide the required dose in a volume of 25–150 µl

Formulations administered through the nostrils.

 Adequate nasal absorption properties.

 No nasal irritation from medicine.

 Adequate clinical justification for nasal dosage forms rapid initiation of action.

 Low dose a single dose is usually less than 25 mg.

 No toxic nasal metabolites, no unpleasant odors/odors associated with drugs.

 Adequate stability.

1) Active Pharmaceutical Ingredient

An ideal nasal drug candidate should have thes the following attributes:

• Sufficient water solubility to provide. Dosage required in volumes of 25-150 ml Prescription.

• Adequate nasal absorption properties.

• No nasal irritation from drugs.

• Appropriate clinical justification for nasal administration form Rapid initiation of action.

• Low dose. A single dose is usually less than 25 mg.

• No toxic nasal metabolites.

• No unpleasant odors/fragrance medicine.

2) **Excipients used in nasal spray formulations [7]**

There are different types of excipients used in the nose pharmaceutical formulation commonly used and frequently added Auxiliaries are as follows.

a**) Buffers:**

Nasal secretions can change pH Potentially Influencing Dosage Concentration of non-ionized drug available absorption. Therefore the proper expression May require buffer capacity to maintain pH in situ. Examples of buffers used in nasal spray sodium phosphate, sodium citrate citric acid.

b) Solubilizers:

Water solubility of drugs Nasal administration of drugs always has limitations Solved. conventional solvents or co-solvents glycol, small amounts of alcohol transcutol (di ethylene glycol mono ethyl) ether), medium chain glycerides, labrasol (saturated polygly colized C8-C10 glycerides) It can be used to improve drug solubility Other connections are available and welcome to use Surfactants such as HP–s- or cyclo dextrin cyclo dextrins that act as biocompatibility Combination with solubilizers and stabilizers Lipophilic absorption enhancer In these cases, their effect on nasal irritation is considered

c) Preservatives:

Most nasal formulations are Water-based, requires preservatives Prevents the growth of microorganisms. parabe, phenyl Ethyl alcohol, benzalkonium chloride, EDTA Benzoyl alcohol is also part of it preservatives commonly used in the nose pharmaceutical formulation.

d) Antioxidants:

Small amount Antioxidants may be needed to prevent drugs oxidation. Commonly used antioxidants are sodium bisulfite, butylated hydro xytoluene, sodium metabi sulfite and tocopherol. Normally, Antioxidants do not affect drug absorption or absorption cause nasal irritation.

e) Humectants

Due to allergies or chronic diseases Illness can cause scabs and dehydration mucous membrane. Certain preservatives/ Antioxidants can also cause sinus infections Irritation, especially when used at high altitudes Amount of money. Sufficient intranasal fluid It is essential to prevent dehydration therefore, moisturizers can be added in particular Gel-based nasal product. avoid moisturizers Does not affect nasal irritation and medicine absorption. A common example is Glycerin, sorbitol, mannitol.

f) Surfactants

Incorporation of surfactants into Nasal dosage forms can change that Permeability of the nasal mucosal Facilitate the absorption of drugs through the nose

g) Bioadhesive polymers

Connection can interact with biological matter by interfacial forces and pinning such material for a long time called bio adhesive polymers.you too called muczoal adhesive biomaterials mucous membrane. of bio adhesive strength Polymer materials depend on properties polymer, surrounding medium (pH), swelling and physiological factors (mucin turnover, disease state). from security (nose Stimulus) combination use perspective Using a carrier is of te recommended.

Synthetic Polymers [17]

a) N-isopropylacrylamide copolymer [17] Poly (N-isopropylacrylamide) is a LCST, a non-biodegradable polymer at 32°C in water The cross linked gel of this material collapses around this temperature.

h) Penetration enhancer

Chemical intrusion Enhancers are widely used in nasal sprays delivery.

Table 2: Commonly utilized excipients

on such material for prolonged periods of time is called as bioadhesive polymer. They are also

enhancers are widely used in the nasal drug delivery.

Table 2: Commonly utilized excipients

Sr. No.	Category	Role	Example
1	Isotonicity adjustment	Used to adjust the tonicity of the formulation	Sodium chloride, Dextrose
2	pH adjustment	Used to adjust pH same to physiological conditions and maximize drug stability	Sodium hydroxide, hydrochloric acid sulphuric acid
3	Purging	Purging used to reduce oxidation	Nitrogen
4	Antimicrobial preservative	To avoid the microbial growth in the formulation	Benzalkonium chloride, ethanol, propylene glycol, Beczoyl Alcohol, chlorobutanol, Methyl paraben
5	Buffer component	It gives the buffer capacity to formulation at desire Ph	Sodium citrate, Sodium Phosphate
6	Surfactant	Increases suspendability and stability of suspension	Polysorbate 80,20
7	Cation chelating agent	Forms chelate with ions present in the formulation and increases the stability	Disodium EDTA
8	Suspending Agents	Increases viscosity and suspendability of suspension	CMC, Na CMC
9	Co-Solvent	Helps to improve solubility	Alcohol, PEG 400, Propylene Glycol
10	Humactant	Used to maintain humidification in the formulation	Glycerin

3) Metered-dose spray pumps

Metered spray pumps have been around since then. Introduced about 40 years ago, nose was dominant drug delivery market. The pump normally supplies 100 Offers a lot of volume, with µl per spray (25-200 µl) Reproducibility of emitted dose and plume shape in vitro test. Particle size and plume shape may vary within certain limits, Pump characteristics, formulation, opening method Actuator and applied force conventional spray The pump replaces the expelled liquid with air, So preservatives need preservatives pollution. However, driven by research a reference to the possible adverse effects of preservatives; Pump manufacturers develop various sprays A system that does without preservatives. More recently, side action pumps have been developed.

Characterization of Nasal Spray [6-8]:

1) pH :

For both solution and suspension nasal sprays test the pH of the formulation,

Corresponding acceptance criteria are defined. Of Healthy human volunteers, full pH range

The front of the nose was 5.17 to 8.13, rear is 5.20 to 8.00 and the average human baseline nasal pH is approximately 6.3. Therefore, stability can be achieved by proper pH selection Wording. However, the pH of the formulation to prevent this, keep close to the human nasal mucosa (5.0-6.5).sneeze.

2) Osmolality

For preparations containing means to combat for isotonic or labeled products Tonicity should be the osmotic pressure of the formulation Tested and checked upon release. More data from animal models Bioavailability of salmon calcitonin from nasal spray 100 or 600 osmalarity formulation mos mol/kg compared to isotonic formulations. Other Studies show that hypotonic nasal sprays multation improved drug permeability through the nose mucous membrane have some existing commercial products reported osmotic pressures ranging from 300 to 700mol/kg.

3**) Viscosity**

For formulations containing active ingredient contributions For viscosity, test this parameter When released and confirmed stable. contact time Increases between drug and nasal mucosa The formulation becomes more viscous time to penetrate. high viscosity Formulation interferes with normal nciliary motility and/or increase the permeability of MCC drug.

4) Impurities and Degradation Products

Content of impurities and decomposition products must be determined by validated analysis procedure or procedure. Acceptance criteria are Single and global contamination and degradation settings product. all relevant impurities occurring at concentrations of Report 0.1% or more as appropriate ICH Contamination Policy.

5) Preservatives and Stabilizing Excipients Assay

Preservatives, antioxidants, chelating agents or Other stabilizing excipients (e.g. benzalko niumchloride, pheny lethyl alcohol,edetate) can be used prescription, there should be a specific assay for it Components with associated acceptance criteria. Acceptance criteria for the chemical composition of Preservatives from release to release the shelf life of the product should be included in the medicine Product specifications.

6) Pump Delivery

Tests to assess reproducibility between pumps regarding and evaluating drug performance

Delivery from the pump must take place. Of General Acceptance Criteria for Pump Spray Weight You must check the weight of each spray Weight up to 10% of your target weight. Within 15% of target weight and average.

7) Spray Content Uniformity (SCU)

Spray is delivered by nasal actuator Active ingredients must be thoroughly analyzed Multiple spray contents from start to finish Single container, sub container, and sub Pharmaceutical batches. This test should provide one overall performance evaluation of the batch, Recipes, manufacturing processes, pumps. This test helps demonstrate the uniformity of Dosing per spray, in line with label claims Delivered from the nasal actuator by a suitable number of (n = 10 from the beginning, n = 10 from the end) container from one batch. Main purpose Make sure the SCU is in the same container and between them multiple containers in batches. to accept Batch the amount of active substance per measurement Do not exceed 80-120% of label claim ≥ 2 out of 20 measurements 10 containers, none The measured value is outside 75-125% of the measured value. label claims and each start and average Final decision is not outside the 85-115% range of label claims.

8) Spray Pattern and Plume Geometry

Characterization of spray patterns and plumes Shape matters when evaluating performance pump. Various factors can affect the spray pattern and plume shape (including size and shape) Nozzle, pump type, dosage Characterization of chambers and formulations.

9) Droplet Size Distribution

DSD of nasal spray is an important parameter because it significantly affects the in vivo deposition of Intranasal medicine. Click here for droplet size primarily influenced by design and handling. operating parameters, devices and formulation, and the main average droplet size is 30–120 μm. If the droplets are too large (> 120 μm) deposits occur mainly in the anterior tooth region part of the nose, and if the droplets are too small (<10μm), which can be inhaled and enter the lungs should be avoided for safety reasons.

10) Particle Size Distribution

For Suspended Nasal Spray, Specifications should include testing and acceptance criteria for Particle size distribution of active material particles in formulations. e.g. microscope evaluation You can use and provide such a check Information and data about the presence of large particles, changes in drug particle morphology, Degree of aggregate and crystal growth.

Advances [10-11]

1) Systemic delivery

Intranasal administration of drugs advantages over oral and intravascular administration, Such as rapid and prolonged drug absorption. Example For systemic delivery, includes commercially available products Contains the active ingredients zolmitriptan and sumatriptan. treatment of migraines and cluster headaches. Even if other drugs, such as pain relievers (morphine), cardiovascular drugs such as propranolol and carvedilo, levonor gestrel, progesterone and insulin, anti anti-inflammatory agents such as indomethacin and ketorolac, and antiviral drugs (acyclovir).

2**) Vaccines**

Immunization,especially use against respiratory diseases Infectious diseases are widely appreciated. Can increase systemic levels of certain immunoglobulins G and nasal secretory immunoglobulin A. Human efficacy of intranasal vaccines includes: influenza A and B viruses, proteosomal influenza, Adenovirus-vectored influenza, group B meningococcus native attenuated respiratory syncytial virus and parainfluenza 3 virus.

3**) Liposomes**

Liposomal medicine delivery systems include several Advantages similar as lower effective encapsulation Large motes with a wide range of hydrophilicity and pKa values. in fact they were set up ameliorate nasal immersion of peptides similar as insulin, Increases membrane permeability of calcitonin. This was attributed to increased nasal traffic protection of peptides, reprised peptides Enzymatic declination and mucous membranes inhibition. also, liposomal medicine delivery systems It has also been reported to be useful in influenza vaccines. Non-peptide medicines similar as nifedipine.

4) Microsphere

Microspheres are generally grounded on mucoal dhesives Benefit Polymers(Chitosan, Alginate) For intranasal administration of medicines. microbeads too Can also cover medicines from enzymatic metabolism Maintains medicine release and prolongs its action. gelatin microspheres as a nasal medicine delivery system for Insulin has shown significant hypoglycemic goods when Rats were cured intranasally in dry greasepaint form.

5) CNS delivery through nasal route

Two extracellular transport pathways May underlie the drug's rapid entry into the brain May occur within minutes of intranasal medication management. Based on first extracellular transport Intranasally administered substances can be routed first Crossing the gap between olfactory neurons Olfactory epithelium that is then transported in the olfactory bulb.

A second pathway based on extracellular transport Substances administered intranasally may be transported along the trigeminal nerve he bypasses the BBB.after arrival Olfactory bulb substance of trigeminal nerve area May spread to other areas of the brain Can also be facilitated by perivascular pumps Driven by the pulsation of arteries.delivery of medicines to Remains a challenge in the central nervous system 'CNS' Development of therapeutics against central targets Due to the impermeable nature of the drug Blood-brain barrier (BBB). BBB is Substrate penetration based on multiple properties, Lipophilicity, molecular size, specificity, etc. accommodates a variety of ATP-dependent transport systems.

In vitro drug release studies[18]

Medicine release studies are performed on in situ phrasings intended for oral or optical administration A plastic dialysis cell is used. A cell consists of two half- cells, the patron. chambers and open chambers. Both half- cells are cellulose membrane. The sol form of the expression is placed in the distribution cube. also shake the assembled cell horizontally in the incubator**.**

CONCLUSION:

Consider potential nose benefits Range should be considered for dosing method of new nasal products coming to market in the near future. They don't just contain local medicines Not only for treatment, but also for systemic protection Infection. Direct targeting drug development brain to achieve good therapeutic effect CNS with reduced systemic side effects. nasal medicine Shipping may be affected by several factors .biological factors, physiological

factors, Physicochemical properties of drugs, physic chemistry Formulation properties .nasal spray medicine Contains dissolved or suspended active substances Solutions or mixtures of non-pressurized excipients A dispenser that dispenses a spray containing a metered amount Dose of active substance.key characterization Nasal spray testing includes spray pattern, droplet size Distribution, spray content and uniformity depend on it Formulation and device characteristics.

ACKNOWLEDGEMENT:

I would like to express my genuine thanks Dr. Gajanan Sanap, Principal, LBYP college of Pharmacy, for giving me this opportunity to carry out my study in the LBYP (Afflicted University DBATU) Maharashtra, India.

REFRENCES

1. Sharma PK, Chaudhari P, Kolsure P, Ajab A, Varia N. Recent trends in nasal drug delivery system - an overview. 2006; 5(4), 56-69.

2. Rahisuddin, Sharma P. K., Garg G; Review on nasal drug delivery system with recent advancemnt; Int J Pharm Pharm Sci; 2011; 3(2), 6-11

3. Putheti R., Patil M. C., Obire O.; Nasal Drug delivery in Pharmaceutical and biotechnology: present and future; e-Journal of Science & Technology; 2009; (3), 1-19.

4. Romeo V. D, Meireles J, Sileno A. P.,Pimplaskar H. K., Behl C. R. Effects of physicochemical properties and other factors on systemic nasal delivery; Adv Drug Deliv Rev, 1998; 29: 89-116.

5. Pagar S. A., Shinkar D., Saudagar R.; A Review on Intranasal Drug Delivery System; J. Adv. Pharm. Edu. & Res.; Oct-Dec 2013; 3 (4), 333-346.

6. Guidance for Industry Nasal Spray and Inhalation Solution, Suspension, and Spray Drug Products —Chemistry, Manufacturing, and Controls Documentation, Center for Drug Evaluation and Research; 2002.

7. Kulkarni, V., Brunotte, J., Smith, M., and Sorgi, F.; Investigating influences of various

excipients of the nasal spray formulations on droplet size and spray pattern; poster at AAPS Annual meeting.

8. Djupesland P., Nasal drug delivery devices: characteristics and performance in a clinical perspective-a review; Drug Deliv. and Transl. Res.; 2013; 3;42–62.

9. Sabrina T., Klaus W., Rene S., Hartwig S.; Analytical Challenges and Regulatory Requirements for Nasal Drug Products in Europe and the U.S.; Pharmaceutics; 2014; 6, 195219.

10. Ibrahim A., Alsarra A.Y., Hamed., Fars K.A., and Gamal M., Maghraby E. Vesicular Systems for Intranasal Drug Delivery, K.K. Jain (ed.), Drug Delivery to the Central Nervous System, Neuromethods 45, DOI 10.1007/978-1-60761-529-3-8.

11. Muhammad U. Ghori, Mohammed H. Mahdi, Alan M. Smith, Barbara R. Conway; NasalDrug Delivery Systems: An Overview; American Journal of Pharmacological Sciences, 2015; 3(5); 110-119.

12. Laurent Salade∗, Nathalie Wauthoz, Jonathan Goole, Karim Amighi.

13. lim ST, Forbes B, Brown MB, Martin GP. Physiological factors affecting nasal drug delivery. In: Touitou E, Barry BW, editors. Enhancement in drug delivery. Boca Raton: CRC Press; 2007.

14. Pillon DJ, Arnold JJ, Meezan E. Nasal delivery of peptides. In: Touitou E, Barry BW, editors. Enhancement in drug delivery. Boca Raton: CRC Press; 2007.

15. Williams, G.; Suman, J. Repurposing CNS drugs: Opportunities and challenges via the nose. In RDD Asia 2016; Dalby, R.N., Peart, J., Young, P.M., Traini, D., Eds.; DHI Publishing: River Grove, IL, USA, 2016; pp. 37–44.

16. Le Guellec, S.; Ehrmann, S.; Vecellio, L. In vitro—In vivo correlation of intranasal drug deposition. Adv. Drug Deliv. Rev. 2021, 170, 340–352. [CrossRef] [PubMed]

17. Shaikh RG, Shah SV, Patel KN, Patel PA. A Review on Polymers used in In-Situ gel drug delivery system. International Journal for Pharmaceutical Research Scholars (IJPRS), 2012; 1(2): 17-29.

18. Raval Sanjay, Vyas Jigar, Parmar Vijay, Raval Dhaval. A Review on In-Situ Polymeri Drug Delivery System. International Journal of Drug Formulation and Research, Jul-Aug 2011; 2(4): 143-168.

19. Carlfors J, Edsman K, Petersson R, Jornving K. Rheological evaluation of Gelrite® in situ gels for ophthalmic use. Eur J Pharm Sci, 1998; 6: 113-119.

20. L. Karpagavalli, B. Senthilnathan, A. Maheswaran and N. Narayanan, "An Outlook on In-Situ Mucoadhesive Gel for Nasal Delivery" International Journal of Pharmacy and Pharmaceutical Research, 2015; 4(1): 113-128.

21. Sheetal b. Gondkar 1, jayesh k. Kakad2, ravindranath b. Saudagar Formulation and evaluation of nasal in-situ gel of losartan Potassium" International journal of universal Pharmacy and bio sciences, 2015; 4(4): 34-57.

22. Inayat Bashir Pathan, Vijay Chudiwal, Irfan.farooqui, Prakash Shingare, "Formulation design and evaluation of nasal in situ gel as a novel vehicle for Azelastine hydrochloride" International Journal of Drug Delivery, 2013; 5: 284-290.