IJCRT.ORG ISSN : 2320-2882

INTERNATIONAL JOURNAL OF CREATIVE RESEARCH THOUGHTS (IJCRT)

An International Open Access, Peer-reviewed, Refereed Journal

Future Potential Of Nasopulmonary Drug Delivery System.

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Abstract:-

Nasal drug delivery system having a numerous benefits, including quick immersion, avoiding first-pass metabolism, and non-invasive administration, hence drawn a lot of attention. A introduction to nasal deconstruction and physiology is given in this review, along with a discussion of the variables affecting medicine immersion and bioavailability. The convenience of administration and bettered patient compliance are impoetant in the design of the nasal medicine delivery system, which remains the favoured route of medicine delivery in malignancy of colorful disadvantages. Remedy through intranasal administration has been an accepted form of treatment in the Ayurvedic system of Indian Medicine. Nasal medicine delivery has been around for centuries and employed both rest and recreation, and also for the treatment of colorful conditions such as migraine, decongestion, and in exigency. The route is accessible and popular. It has multitudinous advantages similar to direct delivery to the (Central Nervous System) CNS, high bioavailability, needles aren't used , and no special chops are needed to delivery the medicine.

Keywords: Nasopulmonary,Physiology,Absorption,Deconstruction,CNS,Bioavailability.

Introduction:-

The inhalation remedy has been used for thousand of times, albiet in a different form and use. Inhalation remedy was rehearsed by ancient societies in Egypt, Greece, India and People's Republic of China as substantiated by different vestiges displayed in galleries, that may be considered the first used inhalation bias. A feasible system for the effective administration of specific via the nasal route has surfaced in recent times, the Nasopulmonary medicine delivery system. With an emphasis on the system's possible uses and advantages, this through analysis attempts to identify the medicine delivery system's unborn prospects. One non-invasive way to deliver drug through the nose and into the lungs is through a nasal pulmonary medicine delivery system(NPDDS). Remedy through intranasal administration has been an accepted form of treatment in the A yurvedic system of Indian Medicine. In recent times, numerous medicines have been shown to achieve better systemic bioavailability through the nasal route than by oral administration. Currently, the inhalation remedy is the preferred option for lung condition like asthma, Cystic fibrosis, and Chronic Obstructive Pulmonary Disease(COPD). These original curatives allows the use of lower boluses and reduce systemic side goods. In the last two decades, a remarkable scientific interest in the technology for pulmonary delivery has been spiked by fact that the lungs can be used as a gate for systemic medicine delivery.

Advantages of NPDDS:

1. Drop dosing frequency.

2. Reduced rate of rise of medicine attention in the blood.

3. Enhanced bioavailability

4. To achieve a targeted medicine release.

5. Reduced side goods.

6. Better patient compliance.

Disadvantages of NPDDS:

1.Cure jilting.

2. Reduced eventuality for accurate cure adaptation.

3. Need of fresh patient education.

4. Stability problems.

Mechanism of Drug Delivery in Nasal Drug Delivery System:-

Medium of Drug Delivery in the Nasal Drug Delivery System-medicines are absorbed through the nasal route by passing through the nasal mucosa, largely passable and vascularized membrane that lines the nasal depression. The nasal mocosa is a endearing route surface area and direct access to the bloodstream. To effectively transfer specifics from the nasal depression into the systemic rotation or to specifics locales within the respiratory tract, the medium of medicine administration in nasal medicine delivery systems entails a number of pivotal process. The medicinal expression is generally scattered into the nasal as a liquid or as a greasepaint when administered. After that, the comes into contact with the nasal mucosa, which has a lot of blood vessels and a lot of area available for medicine penetration. There are two introductory styles that the medicine's patch can pass through the nasal mucosa.

Trans cellular Pathway:

This is the Favored route for lipophilic medicines, as they can dissolve in the lipid bilayer of cell membranes. They go straight through the nasal mucosa's lining epithelial cells.

Para cellular Route:

Most specifics that use this pathway are hydrophilic ones, meaning they have a hard time penetrating the cell membrane. They move via the voids created by the epithelial cells.

Sr. No.	Mechanism	Description
1	Trans cellular Pathway	Lipophilic drugs pass directly through the epithelial cell membranes.
2	Para cellular Pathway	Hydrophilic drugs pass through the spaces between epithelial cells.

Table1:The list of mechanism of nasal drug delivery system.

The various marketed drug products widely used in the treatment of nasal delivery via different types of mechanism pathways discussed in the given Table 2 as below followings:

Table2: The list of marketed products depends on their mechanism of absorption.

Sr. No.	Marketed Nasal Drug	Therapeutic Users	Mechanism Of Absorption
1	Oxymetazoline (Afrin)	Nasal decongestant	Transcellular and paracellular
2	Sumatriptan (Imitrex Nasal Spray), Desmopressin (DDAVP)	Treatment of Migraine, diabetes insipidus (DI) treatment	Transcellular
3	Azelastine (Astelin), Fluticasone propionate (Flonase)	Allergy medication	Transcellular and paracellular
4	Nitroglycerin (NitroMist), Morphine (Rylomine)	Treatment of angina, pain, seizure emergencies,	Transcellular

TYPES OF INHALER:

1)Dry powder inhalers (DPIs):

Dry powder inhalers (DPIs) fall into two main types, passive or active, based on the airflow source for powder aerosolization. They are also classified into single-dose reusable, multidose, and single-use devices. DPIs are categorized based on dose capacity, patient involvement in powder aerosolization, and the mechanism of powder dispersion. Concerning dose capacity, they are classified into single-unit dose, multi-unit dose, and multi-dose reservoirs.

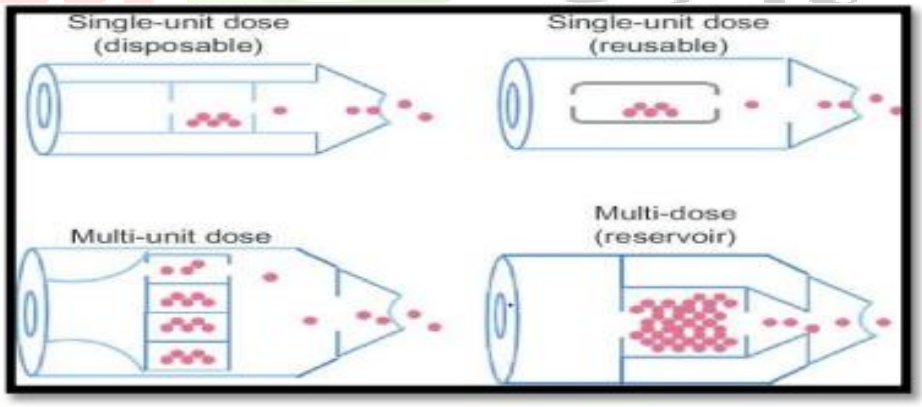

Figure 1: Dry powder inhaler devices classified by the number of doses.

2)Pressurized metered dose inhalers (pMDIs):

Pressurized metered dose inhalers (pMDIs) are sometimes regarded as outdated devices, with fairly minor advancements over the once 50 times(Year). Nonetheless, the recent introduction of compact and convenient breath actuated, breath-coordinated, and velocity-modifying device hardware has successfully addressed issues pertaining to actuation coordination, inefficient fine particle range, and limited delivered dose.

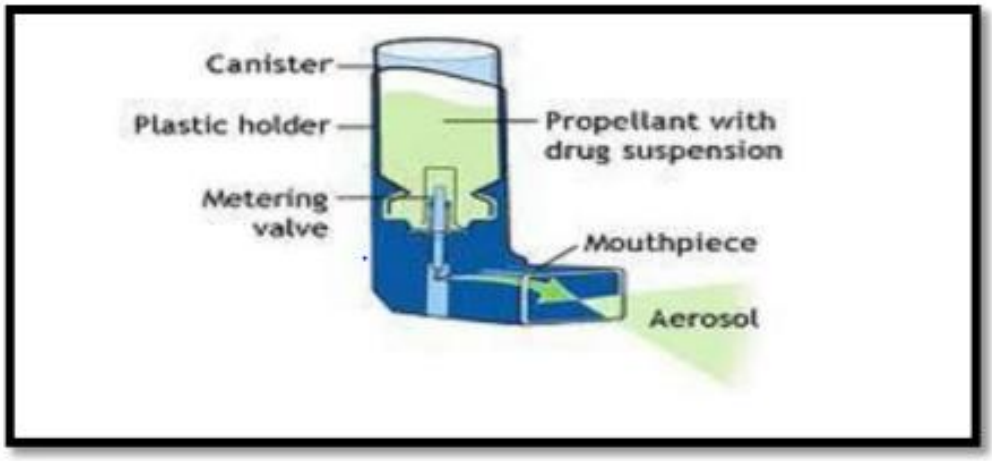

Figure 2: Pressurized metered dose inhalers (pMDIs)

3)Nebulizers**:**

There are two types of nebulizers, jet and ultrasonic, that differ in the force used to generate the aerosol from the respective liquid. Depending on the model and the manufacturer, nebulizers generate 1–5 µm droplets. Nebulizers do not require patient coordination between inhalation and actuation, thus they are useful for pediatric, elderly, ventilated, non-conscious patients, or those who are unable to use pMDIs or DPIs.

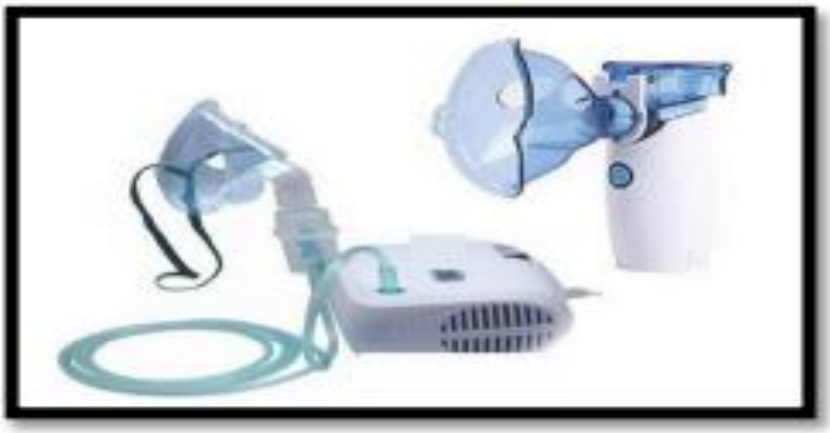

Figure 3: Nebulizer Machine

Transepithelial Transport of Drugs:

Transepithelial transport of drugs is a vital aspect of pharmacokinetics, encompassing the movement of drugs across epithelial cell layers lining various biological barriers, such as the gastrointestinal tract, blood-brain barrier, and renal tubules. This transport is pivotal for drug absorption, distribution, and elimination within the body. Passive diffusion is a primary mechanism where drugs move from areas of high to low concentration, crossing epithelial membranes based on their physicochemical properties. Active transport involves carrier proteins to move drugs against concentration gradients, often requiring energy. Facilitated transport utilizes specific carriers to enhance the movement of certain drugs across epithelia.

Example:

1. Peptide and Protein Drugs

- Insulin (nasal or pulmonary delivery)
    - Transported via transcytosis or paracellular routes.
- Calcitonin (nasal spray)
    - Delivered across the nasal epithelium via paracellular pathways with absorption enhancers.

2. Antidiabetic Drugs

- Metformin (oral)
    - Absorbed via organic cation transporters (OCTs) on intestinal epithelium.

3. Antiviral Drugs

- Zidovudine (AZT)
    - Transported via carrier-mediated epithelial transporters.

4. Anticancer Drugs

- 5-Fluorouracil (topical, GI)
    - Absorbed through passive diffusion and sometimes via nucleoside transporters.

Nasal Cavity Anatomy:

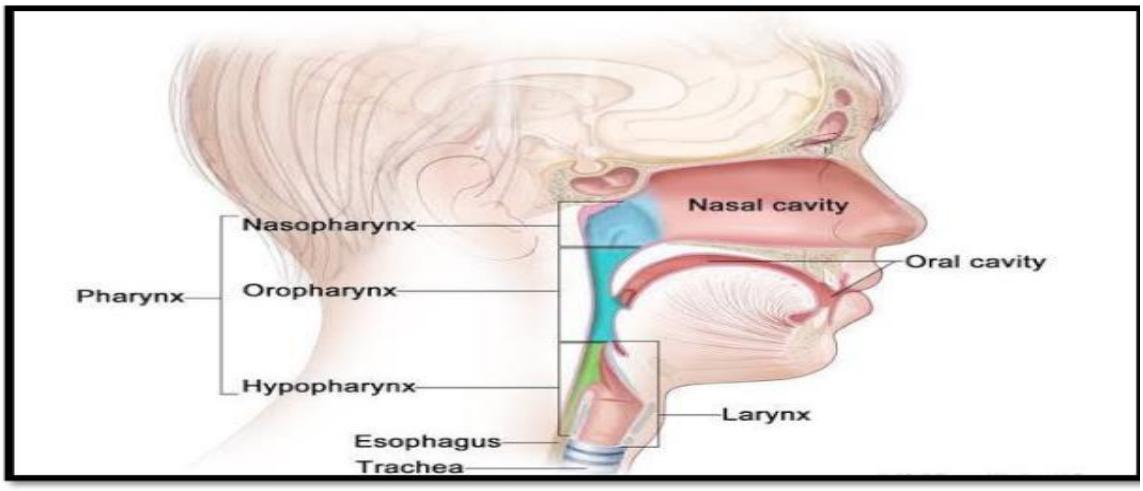

Figure 4: The nasal cavity is a large region located above the mouth.

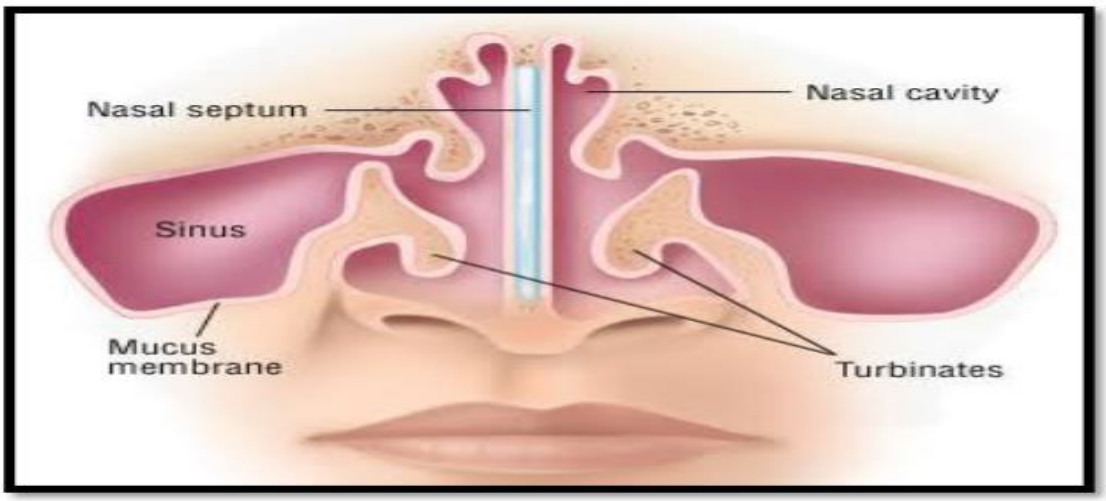

Figure 5: The nasal cavity is divided by the nasal septum

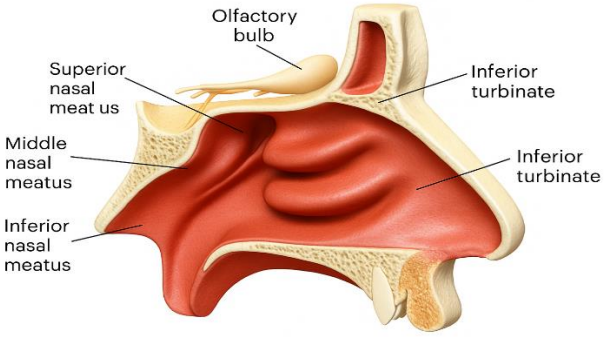

Figure 6: Cut-away view showing the location of turbinates in the nasal cavity

Innovative Drug Delivery Tools and Innovations:

A number of innovative drug delivery tools and technologies have been created to improve medication delivery to the pulmonary and nasal areas. The following are some of them, as examples, that are covered below:

i)Micro-fluidic Systems-Based Nasal Sprays:

Nasal spray devices with micro-fluidic systems incorporated provide optimal medication deposition and absorption in the nasal cavity through precise control over droplet size and distribution.

Example:

1. **Opti Nose Delivery System**

- **Technology**: Uses breath-powered microfluidic delivery.
- **Use**: Approved for delivering drugs like sumatriptan (for migraines).
- **Benefit**: Ensures deep nasal deposition, bypassing the nasal valve.

2. **Nemera's Unidose Nasal System**

- **Technology**: Microfluidic platform for single-use drug delivery.
- **Use**: Emergency treatments like naloxone (opioid overdose).
- **Benefit**: Portable, easy-to-use, precise dosage.

ii)Nasal Powder Inhalers:

When it comes to medication stability and patient convenience, nasal powder inhalers are a better option than liquid nasal sprays. They administer powdered formulations straight to the nasal mucosa.

Example:

1. **Insulin Nasal Powder (in development)**

- **Developers:** Various companies like Diasome, Nastech.
- **Use:** Non-invasive insulin delivery.
- **Status:** Clinical trials; some discontinued due to bioavailability issues.
- **Benefit:** Alternative to subcutaneous insulin.

2. **Dry Powder Naloxone Nasal Inhalers**

- **Use**: Emergency treatment for opioid overdose
- **Technology**: Powder-based formulation for rapid onset
- **Status**: Under research; some prototypes under regulatory evaluation
- **Advantage**: Long shelf life, no refrigeration needed

iii)Drug distribution Systems with Nanotechnology:

By delivering medications to particular areas of the nasal cavity with controlled release and targeted distribution, nanoparticle-based nasal drug delivery systems enhance bioavailability and therapeutic efficacy.

Examples:

1. **Solid Lipid Nanoparticles (SLNs)**

- **Example:** SLN-based formulations for curcumin, insulin, and antiretrovirals.
  - **Use:** Enhancing bioavailability of poorly soluble drugs.
  - **Benefit:** High stability, controlled release, and biocompatibility.

2. **Nanoemulsions**

- **Example**: Nasally administered nanoemulsions for vaccines or CNS drugs.
  - **Use:** Intranasal vaccines (e.g., influenza) or brain-targeted delivery.
  - **Benefit:** Enhanced mucosal absorption and targeting.

iv)Nasal inserts and implants:

These non-invasive, easy alternatives to regular dosage are inserted inside the nasal cavity to allow sustained medication release over an extended period of time.

Examples:

1. Lyophilized Nasal Inserts

Example: Chitosan-based inserts with propranolol.

- **Use:** Systemic delivery for hypertension.
- **Technology:** Mucoadhesive polymer (e.g., chitosan, HPMC).
- **Benefit:** Extended residence time, controlled drug release.
- **Status:** Experimental/academic research.

2. Thermosensitive Nasal Gels (Implant-like behavior)

Example: Poloxamer-based gel inserts for midazolam.

- **Use:** Seizure treatment.
- **Function:** Becomes a gel at body temperature, acts like an implant.
- **Benefit:** Prolonged mucosal contact, rapid onset.
- **Status:** In development.

v)Vibrating mesh devices for nasal aerosols:

By producing small aerosol particles with a limited size distribution, vibrating mesh technology improves medication absorption and deposition in the nasal cavity.

Examples:

1.Mesh Nebulizer-Enhanced Nasal Delivery for Vaccines

- **Example:** Studies using vibrating mesh devices for intranasal COVID-19, flu, or TB vaccines.
- **Goal:** Improve deposition in the upper respiratory tract or olfactory region.
- **Technology:** Customized vibrating mesh devices for fine-particle targeting.

APPLICATIONS OF NASOPULMONARY DRUG DELIVERY SYSTEMS :

Because they may effectively target both the upper and lower respiratory tract, nasopulmonary drug delivery systems have great potential for a variety of therapeutic applications. Local delivery to the nose and lungs NPDDS is a useful tool for treating a range of respiratory disorders, including infections, allergies, COPD and asthma, by delivering medications locally to the nose and lungs.

i) Systematic delivery:

NPDDS can also be used to administer medications in a way that distributes them throughout the body by absorbing them into the bloodstream. This may be helpful for administering medications that must be administered fast or that are poorly absorbed from the stomach.

Example:

1. Intranasal Oxytocin

- **Use:** Autism, anxiety, social disorders (experimental).
- **Form:** Nasal spray or device-delivered liquid.
- **Mechanism:** Delivered to brain via systemic/olfactory pathways.
- **Outcome:** Influences mood, behavior, and social bonding.
- **Status:** Clinical trials / research.

2.Intranasal Insulin (Experimental/Clinical Trials)

- **Use:** Alzheimer's disease, cognitive disorders (not for diabetes control).
- **Mechanism:** Insulin reaches systemic circulation and bypasses the blood–brain barrier via olfactory pathway.
- **Outcome:** Improves memory and cognitive performance.
- **Status:** Investigational.

ii)Treatment of Respiratory Disorders:

A novel and promising method for treating respiratory conditions is the use of nasopulmonary drug delivery devices, or NPDDS. With the use of NPDDS, medications can be administered straight to the lungs and nose, where they can act locally or enter the bloodstream.

Examples:

1. Salbutamol (Albuterol)

- **Use:** Asthma, COPD (acute bronchospasm).
- **Class:** Short-acting β2-agonist (SABA).
- **Delivery:** Inhalers (MDI, DPI), nebulizers.
- **Outcome:** Rapid bronchodilation and symptom relief.

2. Budesonide

- **Use:** Asthma, COPD.
- **Class:** Inhaled corticosteroid (ICS).
- **Delivery:** Inhaler (DPI or MDI), nebulized suspension.
- **Outcome:** Reduces inflammation and prevents exacerbations.

iii)Drug delivery to Brain:

Drug delivery directly to the brain is another application for NPDDS. This may be helpful in the treatment of illnesses such brain tumors, Parkinson's disease, and Alzheimer's disease. Nasopulmonary plays a significant part in the treatment of numerous diseases by delivering drugs through the nasal route.

Examples:

1. Intranasal Insulin

- **Use**: Alzheimer's disease, cognitive impairment.
- **Mechanism**: Intranasal → olfactory/trigeminal pathways → direct access to CNS.
- **Form**: Liquid spray or gel formulations.
- **Outcome**: Enhances memory and cognitive performance.
- **Status**: Clinical trials (e.g., using devices like Impel NeuroPharma's POD system).

2. Focused Ultrasound (FUS) with Microbubbles

- **Use**: Brain tumors, Alzheimer's, Parkinson's.
- **Mechanism**: Temporarily disrupts BBB using focused ultrasound + IV microbubbles.
- **Outcome**: Enables local drug delivery to targeted brain regions.
- **Status**: Clinical trials (e.g., Insightec FUS system).

iv)Asthma :

A range of asthma treatments, including bronchodilators, corticosteroids, and anti-inflammatory agents, can be administered via NPDDS.

Examples:

1.Theophylline

- **Class:** Methylxanthine.
- **Use:** Rarely used today; oral bronchodilator for maintenance.
- **Form:** Tablet or sustained-release capsule.

2.Cromolyn Sodium

- **Class:** Mast cell stabilizer.
- **Use:** Preventive treatment (especially in children).
- **Form:** Nebulizer solution.
- **Note:** Less commonly used due to ICS preference.

CONCLUSION:

With Nasopulmonary drug delivery system many benefits are associated with the nasopulmonary route, such as non-invasive administration, quick absorption, and avoidance of first-pass metabolism. In addition, the nasal cavity's abundant blood supply and vast surface area make it a perfect delivery channel for systemic medications. Leveraging the rich vascularization and large surface area of the nasal mucosa and lungs, these systems enable rapid onset of action, enhanced bioavailability, and targeted delivery both for local respiratory conditions and systemic therapies. The inhaler's structure and design play a pivotal role in determining aerosol deposition in the lungs. Dry Powder Inhalers (DPIs) are gaining popularity due to ease of use and powder stability. Pressurized Metered-Dose Inhalers (pMDIs) face challenges in formulation and design. Nebulizers are undergoing modifications to enhance versatility. Despite advancements, no single device meets all requirements for delivering drugs with diverse properties. Medical professionals must comprehend each inhaler's capabilities, aligning them with the patient's needs based on health conditions to achieve optimal therapeutic outcomes. Nasopulmonary delivery is especially valuable for treating diseases such as asthma, COPD, migraines, diabetes, and neurodegenerative disorders, offering alternatives to oral or injectable routes. As research continues to address challenges like mucociliary clearance, enzymatic degradation, and formulation stability, nasopulmonary systems are poised to become a cornerstone in modern, patient-friendly drug delivery strategies.

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