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"A Perceptive Review on Advancement in Drug Delivery System".

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ABSTRACT:
Drug targeting to specific organs and tissues has become one of the critical endeavors of the century since the use of free drugs in conventional dosage forms generally involves difficulties in achieving the target site at the appropriate dose after or during a proper time period. Recent drug delivery systems (DDS) are formulated using advanced technology to accelerate systemic drug delivery to the specific target site, maximizing therapeutic efficacy and minimizing off-target accumulation in the body. As a result, they play an important role in disease management and treatment. This review explores the dynamic landscape of drug delivery systems, focusing on their profound impact on therapeutic efficacy and patient compliance. The integration of nanotechnology, RNA therapeutics, implantable devices, 3D printing, and artificial intelligence heralds a transformative era in precision medicine. Nanoparticles enable precise targeting, while RNA therapeutics offer molecular-level interventions. Implantable and injectable devices promise sustained release, enhancing patient compliance. 3D printing introduces personalized dosage forms, and artificial intelligence empowers data-driven adjustments to treatment plan.

KEYWORDS: 3D printing, Nanotechnology, Injectable devices, Drug delivery system, RNA therapeutics.

I. INTRODUCTION:

The search for new drug delivery approaches and new modes of action represent one of the frontier areas which involves a multidisciplinary scientific approach to provide major advances in improving therapeutic index and bioavailability at site specific-delivery. The hard to target tissues such as blood-brain barrier permeation limitation can now be overcome allowing the use of therapies otherwise excluded by conventional dosage forms . These new systems can hinder solubility problems, protect the drug from the external environment such as photodegradation and pH changes, while reducing dose dumping by controlling the release profile . Moreover, controlled targeting at the site of action and reduced time of exposure at non-targeting tissues increases the efficacy of treatments and reduce toxicity and side effects thus improving patient compliance and convenience.

Recently, several drug delivery systems (NDDS) have been developed using advanced systems for
more convenient, controlled, and targeted delivery.

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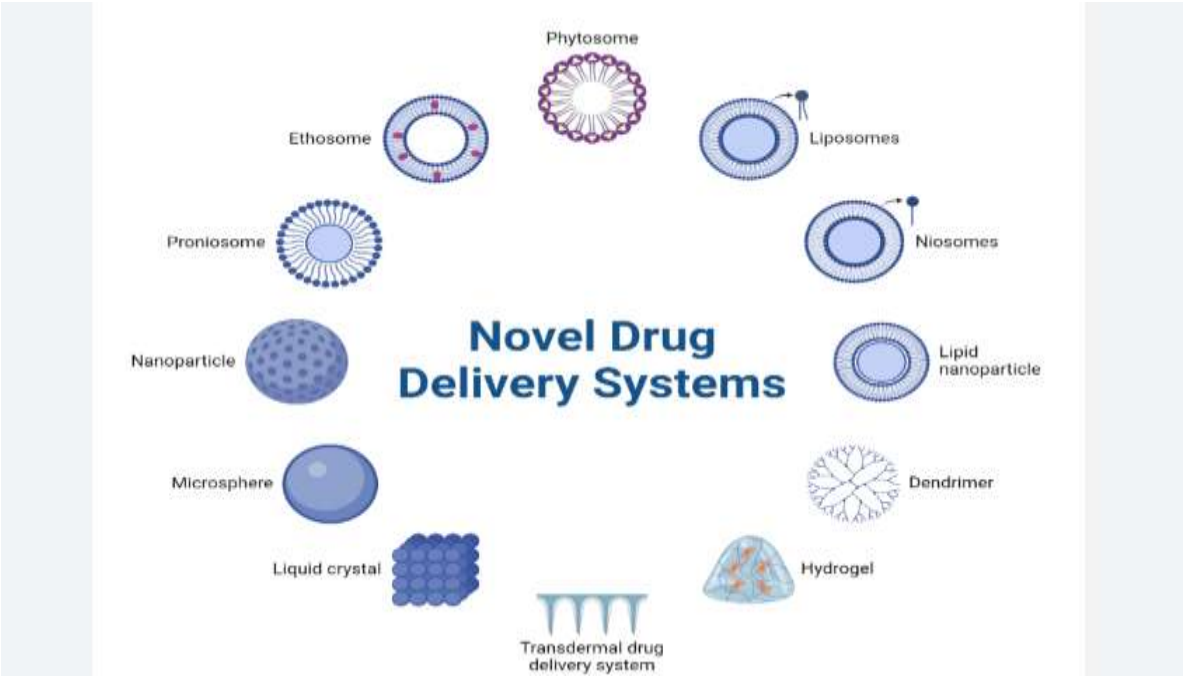

Fig.1 Novel Drug Delivery System.

Drug delivery system has its own peculiarities that determine its release rate and mechanism. This is largely due to the differences in the physical, chemical, and morphological characteristics which will ultimately affect their affinities for various drug substances. Studies on these have identified diffusion, chemical reaction, solvent reaction, and stimuli control as major release mechanisms. For instance, since most cancer cells can proliferate the porous blood vessels and lymphatic system, the drug can easily permeate through this opening to reach the target tissues. This is referred to as Enhanced Permeability and Retention (EPR) . EPR is a passive diffusion mechanism well researched and applied in the delivery of many chemotherapeutic agents. Although EPR is a controversial concept, this effect has been observed by many researchers in various types of human tumors and is the basis for the use of nanomedicine in cancer treatment. Though it has a drawback of lack of selectivity and increased toxicity . Active targeting overcomes the lack of specificity and selectivity found in passive targeting. It involves attaching to the carriers, certain ligands, and molecules that can actively bind to the surface of target tissues. This prevents uptake by non-target cells thereby reducing side effects and toxicity. Selectivity of ligands to target cells, immunogenicity, and chances of lysosomal degradation after macrophage endocytosis still pose solid challenges to the full development of actively targeting Drugs. These delivery systems can also reach the target cells through the control of one or more physical or chemical properties in the process of responsive stimuli targeting. These physical properties include pH, temperature, ultrasound, magnetic and electric field.

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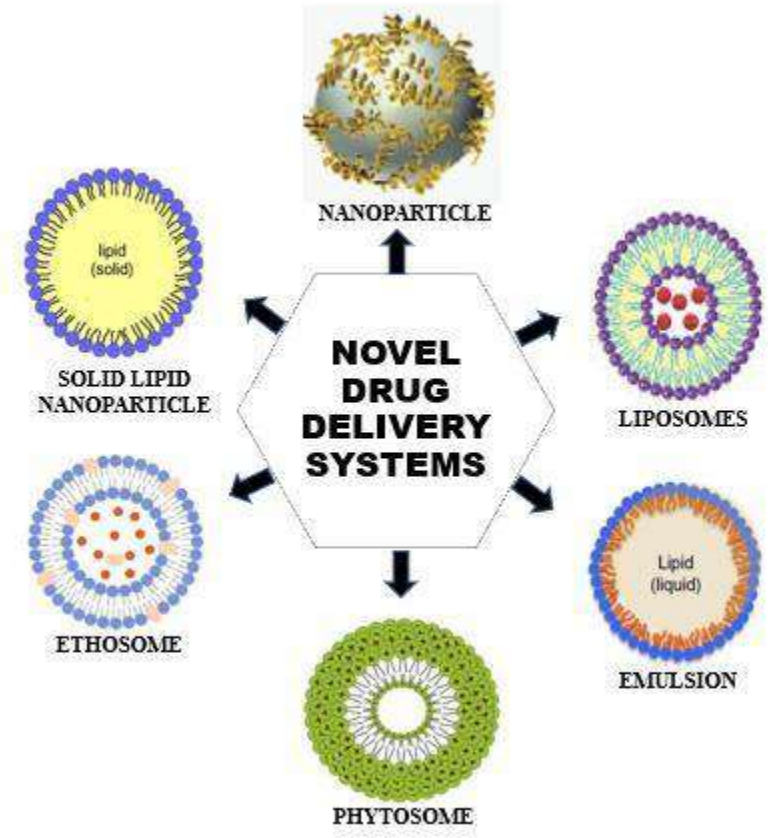

II. DRUG DELIVERY SYSTEM CLASSIFICATION:

In recent years, drug delivery systems have seen significant advances in the pursuit of optimizing treatment outcomes and increasing patient satisfaction. These innovations aim to address the challenges associated with traditional drug administration methods, such as oral tablets and injectable tablets, by offering a more precise, targeted and convenient way to patience. This comprehensive review examines the main drug delivery systems, including oral, parenteral, transdermal, inhalation, and newer approaches such as nanoparticles and liposomes. It describes their methods, benefits and potential impact on health care. 3.1. Oral Drug Delivery Systems Oral drug delivery is the most common method and is preferred due to its simplicity, patient acceptance and non-invasiveness. Recent innovations in oral drug delivery systems have focused on overcoming the challenges associated with variable absorption rates, intestinal permeability, and the need for consistent dosing. Enteric-coated formulations: These compounds prevent elimination in the stomach and ensure that drugs are released into the intestines. This approach is especially important for drugs that affect stomach acid or enzymes. Enteric coating improves the bioavailability and efficacy of the drug by protecting the drug from early degradation (Katona et al, 2022). Gastrointestinal systems: their purpose is to prolong the residence time of the stomach and ensure the continuous release of the substance. Floating and paralyzing systems are common strategies. These systems increase drug absorption, especially for drugs that have an absorption window in specific parts of the gastrointestinal tract (Streubel, Siepmann, & Bodmeier, 2006).

2.1 Nanoparticle-based carriers:

Nanoparticle-based oral drug delivery involves encapsulation of drugs in nanoscale carriers such as liposomes and polymeric nanoparticles. This approach improves the drug's solubility, stability and bioavailability. Nanoparticles protect drugs from enzymatic degradation and facilitate targeted delivery to specific tissues

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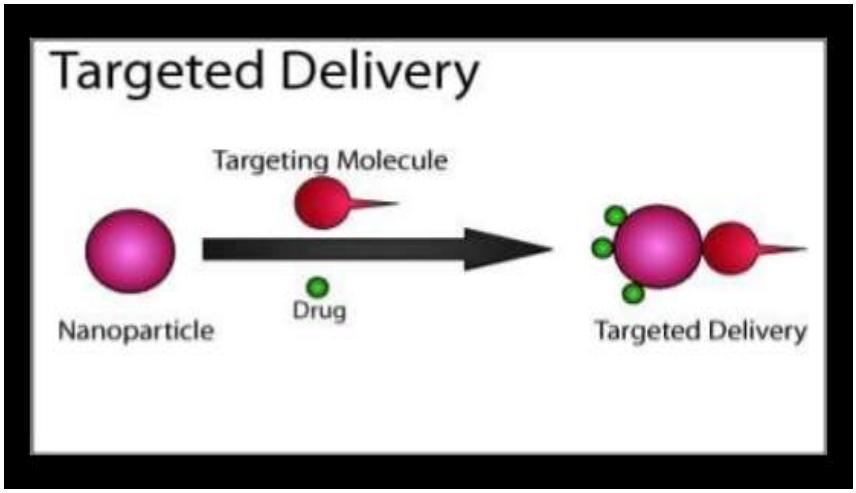

Fig.2 Targeted Delivery

2.2 Injectable drug delivery system :

Injectable drug delivery systems are essential for rapid and accurate drug administration. Advances in this field focus on controlled-release formulations, biodegradable polymers, and new injection devices to improve patient safety and compliance.

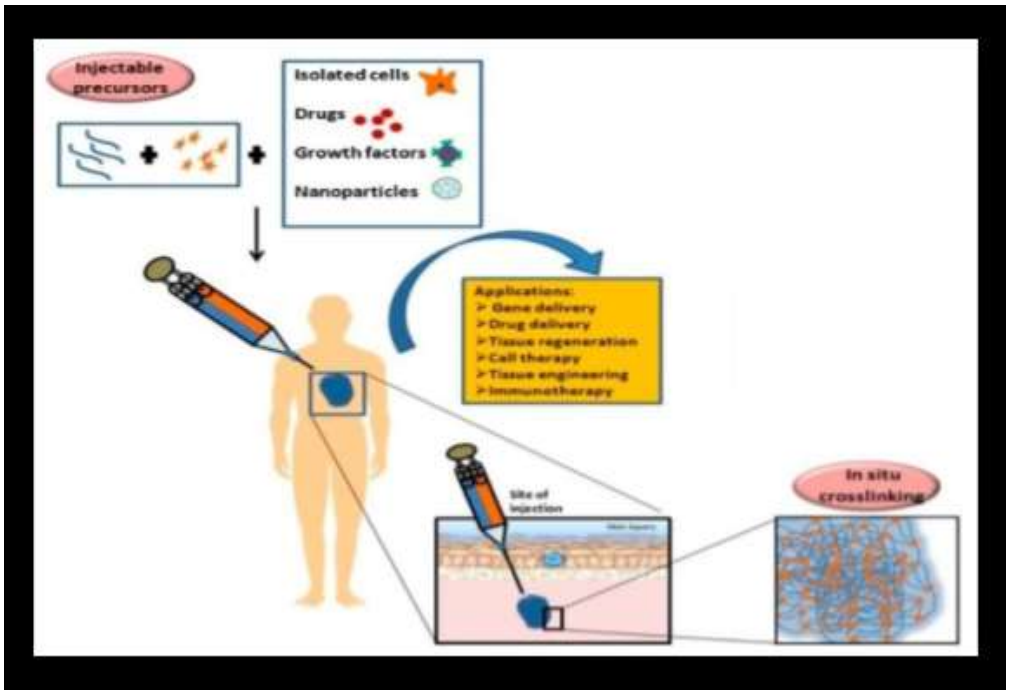

Fig.3 Injectable drug delivery system

2.2.1 Controlled manufacturing and delivery:

The purpose of controlled manufacturing and delivery is to increase the long-term release of the drug and reduce the frequency of injections. This is especially true for older situations. These structures use different methods such as controlled diffusion, controlled osmotic and matrix delivery to achieve therapeutic effects

2.2.2 Biodegradable polymers:

These polymers play an important role in injectable drugs. These polymers are reduced to non- toxic products, eliminating the need for

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removal or extraction after the release of the drug. Biodegradable microspheres and implants provide drug delivery while reducing the risk of side effects (Z. Zhang, Ortiz, Goyal, & Kohn, 2014).

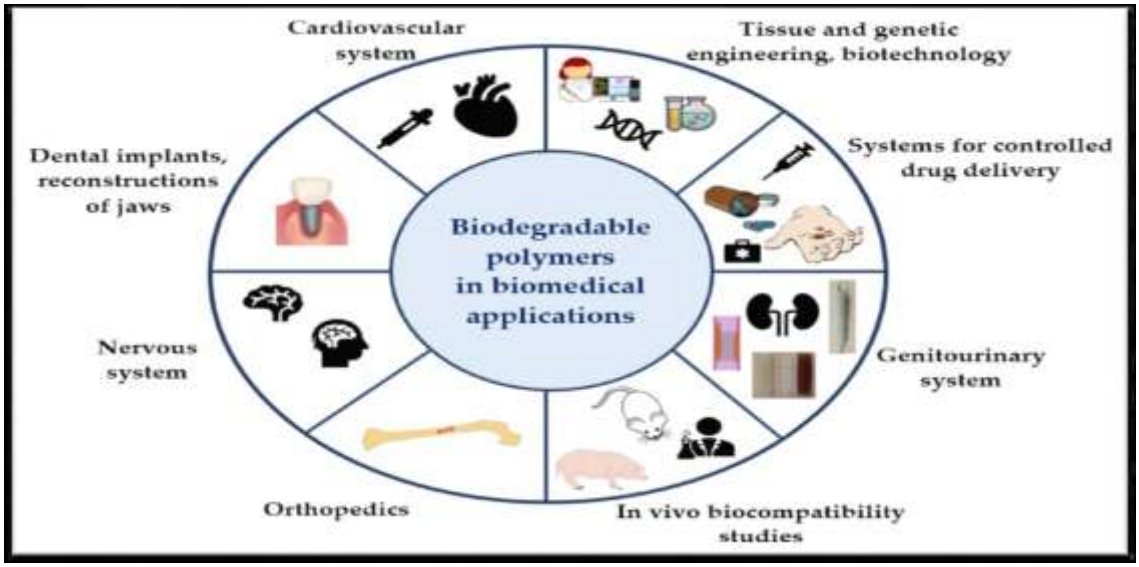

Fig.4 Biodegradable polymers in application

2.2.3 Microneedle Technologies:

Emerging as a minimally invasive method of drug delivery. Microneedles, usually hundreds of micrometers to a few millimeters long, are inserted painlessly into the skin to deliver medication. This approach is particularly relevant for vaccines, insulin, and other pharmaceuticals (Ingroll et al., 2021; Richter-Johnson, Kumar, Konara, de Toit, & Pillai, 2018). 3.3. Transdermal drug delivery systems Transdermal drug delivery systems offer a non-invasive and controlled method and avoid the initial transfer associated with oral administration. These systems deliver drugs continuously through the skin and ensure long-term therapeutic results.

2.2.4 Liquid patches:

An adhesive system that contains drugs that are delivered continuously to the skin. These patches are effective and provide long-lasting relief with minimal side effects. It is often used for pain management, hormone therapy and smoking cessation (Dhiman, Singh and Rehni, 2011).

Fig.5 Liquid patches

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2.2.5 Microneedle Implants:

They combine the benefits of percutaneous delivery with the precision of mimicroneedling. These patches have small needles that can be inserted painlessly into the skin to deliver drugs, including macromolecules that are not well absorbed in traditional transdermal patches

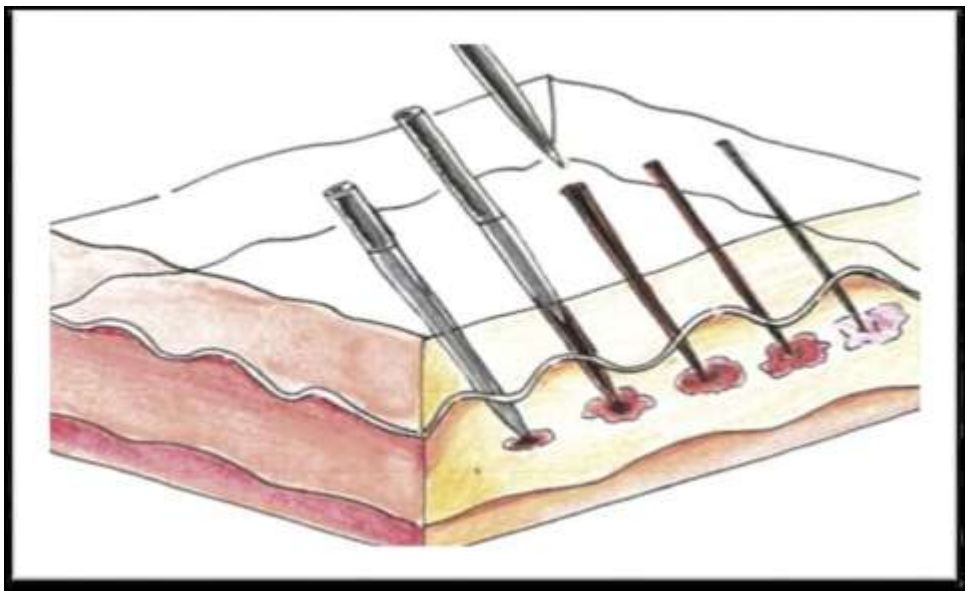

Fig.6 Microneedle implant

2.3 Inhalational drug delivery system:

Inhalational drug delivery is very effective for respiratory and systemic diseases, allowing rapid absorption and delivery to the lungs. Advances in drugs focus on improving the efficiency of delivery devices and improving the production of various drugs.

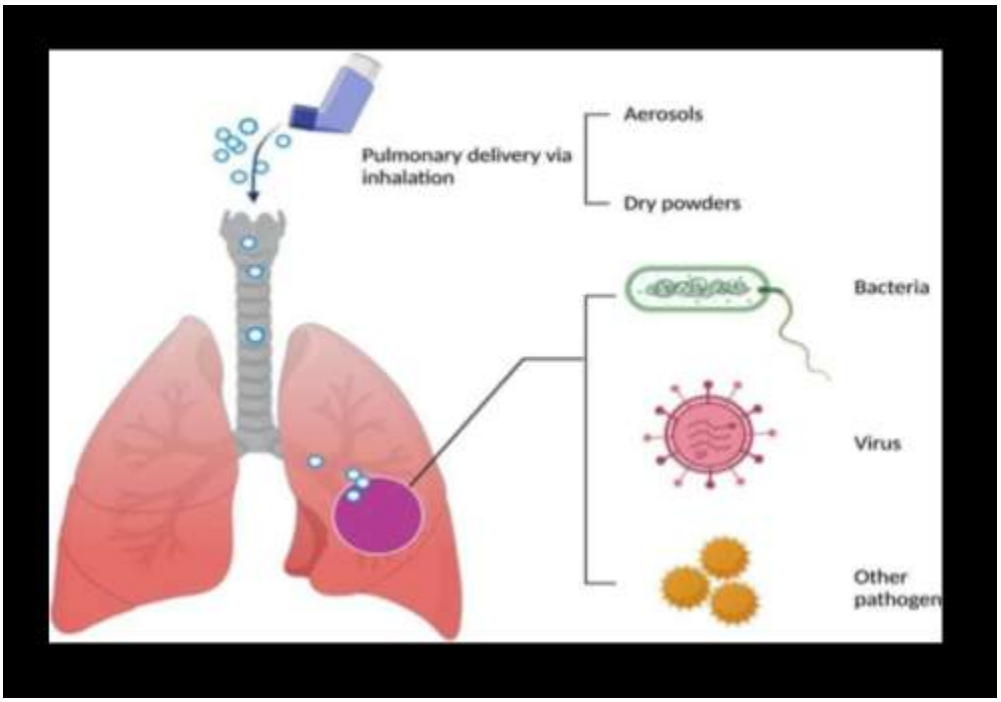

Fig.7 Inhalation drug delivery system

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2.3.1 MDIs (Metered-dose inhalers):

MDIs deliver a precise dose of medicine in aerosol form, allowing patients to inhale the medicine into their lungs. Propagation-related MDIs are widely used for bronchodilators and anti-inflammatory drugs. Improvements in non-invasive technologies aim to reduce environmental impacts (Newman, 2005).

2.3.2 Dry powder inhalers (DPIs):

DPIs deliver drugs in powder form that are activated when the patient inhales.These units are preferred because of their ease of use and lack of speed. DPI is effective against many drugs, including corticosteroids and bronchodilators. Nebulizers: Nebulizers turn liquid medications into a fine mist that patients inhale through a mask or mouth. These devices are often used for patients with severe respiratory disease who would find it difficult to use an MDIS or DPI. Advances in nebulizer technology aim to increase the efficiency of drug delivery

Novel Approaches

Novel drug delivery approaches leverage nanotechnology and liposomal carriers to enhance drug solubility, stability, and targeted delivery. These systems can revolutionize personalized medicine by enabling precise drug delivery to specific cells or tissues.

2.3.3 Nanoparticles:

Nanoparticles, typically in the range of 1 to 100 nanometers (Scott, Ewim, and Eloka-Eboka, 2022), can encapsulate drugs, protecting them from degradation and improving bioavailability (Mendoza-Munoz, Urbán-Morlán, Leyva-Gómez, de la Luz Zambrano-Zaragoza, and Quintanar-Guerrero, 2021). These carriers can passively target diseased tissues through the enhanced permeability and retention (EPR) effect or be actively targeted using ligands.

2.3.4 Liposomes:

Liposomes are lipid-based vesicles that encapsulate hydrophobic and hydrophilic drugs. Liposomal formulation increases drug stability, improves solubility and controlled release. Liposomes can also be modified for drug delivery by attaching specific linkers (Grimaldi et al., 2016).

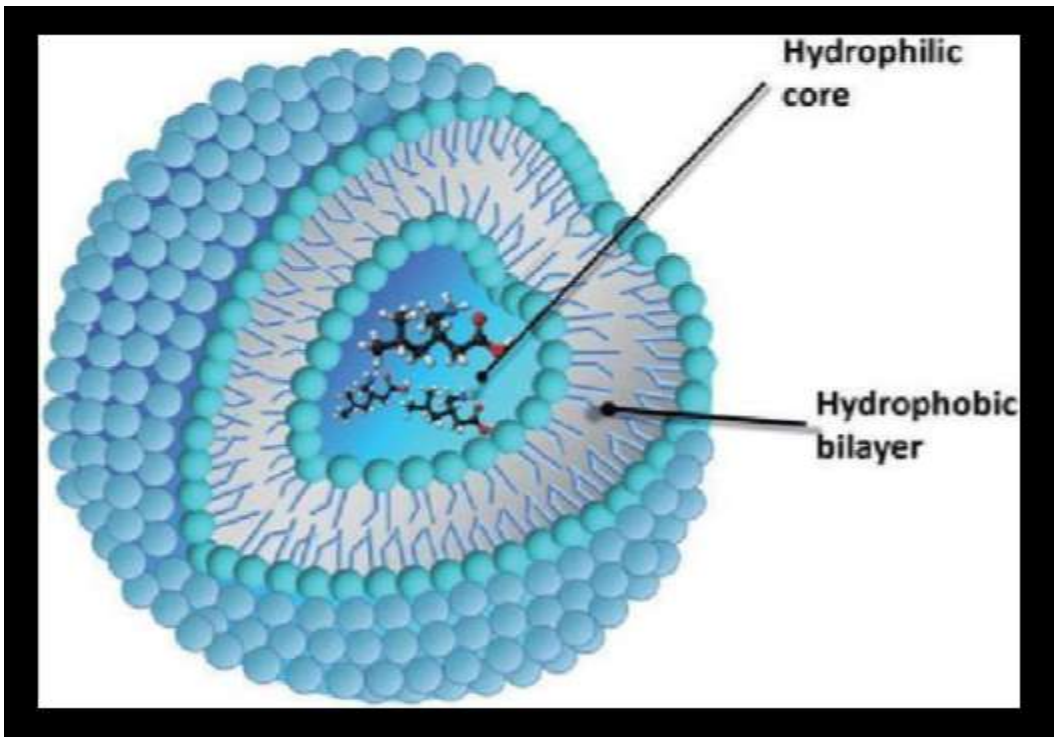

Fig.8 Liposomes

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III. FUTURE SCOPES IN NDDS:

Novel-Drug Delivery Systems (NDDS) are an exciting and rapidly evolving field with significant potential for future advancements. Here are some key areas where NDDS are expected to make a substantial impact:

1. **Cancer Treatment**: NDDS can enhance the delivery of chemotherapeutic agents directly to tumor sites, improving efficacy and reducing side effects. This targeted approach is particularly promising for treating various cancers.
2. **Chronic Disease Management**: NDDS can provide controlled and sustained release of drugs, which is beneficial for managing chronic conditions like diabetes, cardiovascular diseases, and neurological disorders.
3. **Personalized Medicine**: With advancements in nanotechnology, NDDS can be tailored to individual patients' needs, allowing for personalized treatment plans that optimize therapeutic outcomes.
4. **Gene Therapy**: NDDS can be used to deliver genetic material to specific cells, offering potential treatments for genetic disorders and enabling advancements in gene therapy
5. **Infectious Diseases**: NDDS can improve the delivery of antibiotics and antiviral drugs, enhancing their effectiveness and potentially reducing the development of drug resistance.
6. **Colon-Targeted Drug Delivery**: NDDS are being developed to target diseases affecting the colon, such as ulcerative colitis, Crohn's disease, and colon cancer. These systems can deliver drugs directly to the affected area, minimizing systemic side effects.

The future of NDDS looks promising, with ongoing research and development likely to bring about innovative solutions for various medical challenges.

IV. APPLICATION:

Drug delivery systems (DDS) are specialized technologies designed to apply medical agents to specific areas of the body, increasing the effectiveness, safety and availability of treatment. The application of DDS is increasing in various pharmaceuticals, which provide solutions while minimizing side effects.

1. Oral drug delivery:

- Improve bioavailability DDS can increase the bioavailability of poorly soluble drugs, or permanent in the intestinal tract. Methods such as encapsulation in liposomes or solid lipid nanoparticles protect the drug from degradation and improve absorption.
- Peptide and protein drugs: DDS helps orally deliver bioactive substances such as insulin that are broken down in the intestinal tract. Formulations such as enteric-coated capsules or nanoparticles are used to bypass the tumor and deliver the drug into the intestine.

2. Transdermal delivery:

- Pain management: Drugs such as fentanyl are injected into the skin to provide pain relief without an injection. or oral injection.
- Hormone replacement therapy: Patches are used to release hormones such as estrogen or testosterone in hormone replacement therapy, which provides a drug-free delivery method. and consistency.

3. Medication for inhalation:

- Respiratory disease: DDS allows direct delivery of drugs to the lungs, which are used to treat the disease asthma, chronic obstructive pulmonary disease (COPD) and other useful factors. Breathing techniques It is a common device for delivering corticosteroids and other drugs for delivering inhalers and nebulizers.

4. Vaccines:

- Helper System: DDS in vaccines help to increase the immune response by delivering antigens to cells prevent. Nanoparticles and emulsions are used to improve the stability and potency of vaccines.

New Features:

- Personalized Medicine: DDS is designed to tailor treatment based on the patient's genetic makeup, allowing for precise dosing and better results.
- Nanomedicine: Nanotechnology is rapidly being used in DDS, allowing the design of multiple nanoparticles that can detect, deliver drugs, and monitor the strength of treatment.

Advances in drug delivery systems have revolutionized medicine by improving the targeting, effectiveness and safety of treatments

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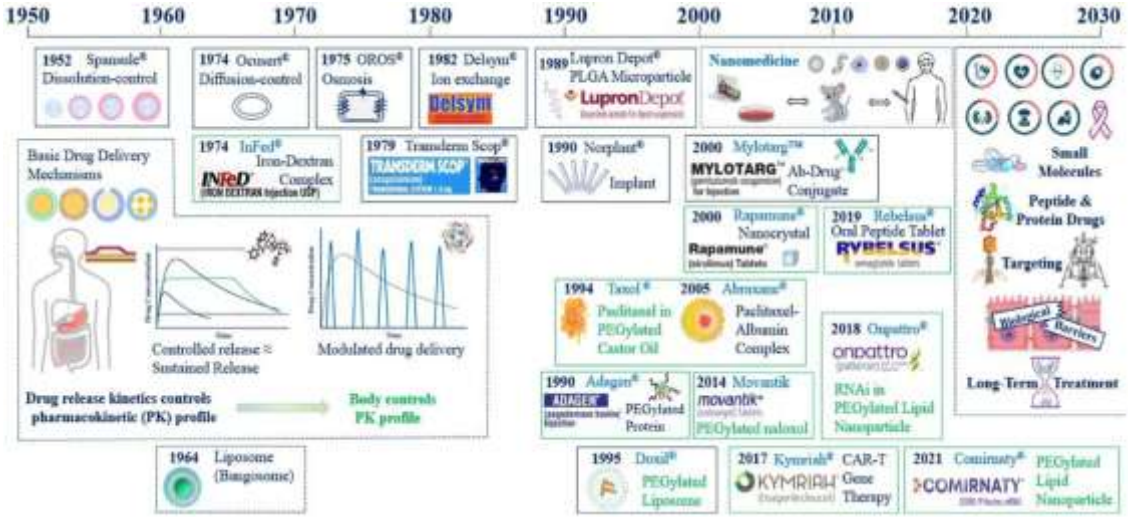
and offering new hope for treating complex diseases and chronic diseases.

V. FUTURE TRENDS IN NDDS:

1. **Nanotechnology and Nanomedicine:** Nanoparticles are being increasingly used for their ability to deliver drugs precisely to targeted sites, enhancing the efficacy and reducing side effects. This includes the use of liposomes, dendrimers, and polymeric nanoparticles.
2. **Personalized Medicine**: Tailoring drug delivery systems to individual patient profiles is becoming more common. This approach ensures that patients receive the most effective treatment based on their unique genetic makeup and disease characteristics.
3. **Biologics and Gene Therapies**: The rise of biologics and gene therapies has led to the development of novel drug delivery methods that can effectively transport these complex molecules to their intended targets.
4. **Smart Drug Delivery Systems:** These systems can respond to specific physiological conditions or external stimuli (like pH, temperature, or light) to release drugs at the right time and place.
5. **Implantable Devices**: These devices offer sustained release of medications over extended periods, improving patient compliance and ensuring a steady therapeutic effect.
6. **Advanced Materials**: The use of advanced materials such as hydrogels, biodegradable polymers, and stimuli-responsive materials is enhancing the precision and control of drug delivery.
7. **Integration with Technology:** The convergence of drug delivery with technologies like artificial intelligence, machine learning, and wireless electronics is paving the way for more sophisticated and efficient delivery systems.

These trends are poised to revolutionize the pharmaceutical industry, offering more effective, patient-centered therapies for a wide range of medical conditions.



EVOLUATION OF DRUG DELIVERY SYSTEM FROM: 1950 TO 2020.

VI. CONCLUSION:

We assume that the ongoing research and development in novel drug delivery systems hold great potential for revolutionizing the way we administer medications, ultimately leading to better health outcomes and improved quality of life for patients worldwide. Novel drug delivery systems (NDDS) represent a significant advancement in the field of pharmaceuticals, offering innovative methods to enhance the efficacy, safety, and patient compliance of therapeutic treatments. By utilizing cutting-edge technologies such as nanomedicine, lipid nanoparticles, and targeted delivery mechanisms, NDDS can improve the bioavailability and targeted release of drugs, minimizing side effects and maximizing therapeutic benefits.These systems are particularly promising for treating complex diseases, where traditional drug delivery methods fall short. The development of NDDS is a multidisciplinary effort, combining insights from polymer science,

molecular biology, and pharmaceutics to create more effective and patient-friendly treatments.

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