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ADVANCEMENTS IN CARRIER-BASED DRUG DELIVERY SYSTEMS: A GATEWAY TO ENHANCED THERAPEUTICS

[1]Megha Hansan, [2]Afna S Kabeer,[3]Anudhanya Parengal

[1]Assitant Professor, Indira Gandhi Institute of Pharmaceutical Sciences, Perumbavoor, Ernakulam Dist,
[2&3] Indira Gandhi Institute of Pharmaceutical Sciences, Perumbavoor, Ernakulam Dist,
[1]Pharmaceutics department,
[1]Indira Gandhi Institute of Pharmaceutical Sciences, Perumbavoor, Ernakulam Dist,kerala

ABSTRACT

Carrier-based drug delivery systems have emerged as a transformative approach in the field of pharmaceuticals, offering innovative solutions to challenges associated with traditional drug formulations. Drug delivery systems are designed to improve the efficiency, targeting, and release of drugs within the body. Various carriers, such as nanoparticles, liposomes, micelles, and polymers, are often used to enhance drug delivery. These carriers can improve the solubility of drugs, protect them from degradation, and enable targeted delivery to specific tissues or cells**.** Carrier based drugs delivery system have a significant effort on the pharmacokinetic and pharmacodynamic effects which was produced by the encapsulated drug used in the patient therapy. This article explores the significance of carrier-based drug delivery systems, focusing on their diverse applications, advantages, and potential impact on improving therapeutic outcomes.

KEYWORDS: - Drug delivery system (DDS), Carrier based drug delivery (CBDDS), Site specific targeting, liposomes, micelles, nanoparticles, polymers, and dendrimers

INTRODUCTION

The landscape of drug delivery has witnessed a paradigm shift with the advent of carrier-based systems. Carrier based drug delivery system is the system in which the drug is encapsulated into a carrier, which slowly releases the encapsulated drug through various release mechanisms. Mainly it is an advanced version of targeted drug delivery system, which can stay over the carriers for a longer duration and able to maintain drug concentration in the therapeutic range for a prolonged duration as per the requirements and also delivering the molecules to the targeted site [1]. The aim of CBDDS is to minimize the degradation of drug and also to control the drug related toxicity to enhance drug bioavailability. the release of encapsulated drug from this

carrier system is by four major steps: (i) encapsulation of the drug in to the assigned or fabricated carrier system, (ii) delivery of the drug-carrier systems to the targeted site in the human body, (iii) carrier -drug complex entry in to the cell membrane, and (iv) release of the encapsulated drug from the carrier which favors a prolonged or constant release. Carrier based drug delivery system mainly increase patient convenience, safety, efficacy, faster the activity of drug reduces the toxicological effort and helps to determine the pharmacokinetic and pharmacodynamics of drug in the site[2-8].

A carrier-based drug delivery system is a strategy in pharmaceutical science and technology that involves the use of carrier materials to deliver therapeutic agents (drugs or bioactive molecules) to specific target sites within the body. The primary goal of this approach is to enhance the therapeutic efficacy of drugs while minimizing side effects associated with conventional drug administration [9,10]. Carriers can be designed to encapsulate, transport, and release drugs in a controlled manner, providing several advantages over traditional drug delivery methods. The carrier materials used in these systems can vary widely and include liposomes, micelles, nanoparticles, polymers, dendrimers, and other nanoscale or macromolecular structures. These carriers serve as protective vehicles for drugs, helping to overcome challenges such as poor drug solubility, rapid metabolism, and limited bioavailability [12,13].

ADVANTAGES OF CBDDS[14]

1. Targeted Delivery: One of the primary advantages is the ability to target specific tissues or cells. Carriers can be designed to accumulate preferentially in the desired site of action, reducing off-target effects and improving the therapeutic index.

2. Increased Drug Solubility: Carriers can enhance the solubility of poorly soluble drugs, improving their bioavailability. This is particularly important for drugs with low aqueous solubility, as it can enhance absorption and distribution in the body.

3. Prolonged Release: Carrier systems can provide controlled or sustained release of drugs over an extended period. This allows for a more consistent and prolonged therapeutic effect, reducing the frequency of dosing and improving patient compliance.

4. Protection of Drug Molecules: Carriers can protect drugs from degradation, metabolism, or elimination before reaching the target site. This protection can enhance the stability of the drug in the bloodstream and improve its overall pharmacokinetics.

5. Reduced Side Effects: By delivering drugs directly to the target tissue or cells, carrier systems can minimize exposure to healthy tissues and organs. This targeted delivery can reduce the occurrence of side effects associated with systemic drug administration.

6. Improved Bioavailability: Carrier-mediated drug delivery can enhance the bioavailability of drugs by improving their absorption and distribution. This is particularly important for drugs that have low oral bioavailability or undergo extensive first-pass metabolism.

7. Combination Therapy: Carriers can facilitate the co-delivery of multiple drugs, allowing for combination therapy. This is beneficial in cases where synergistic effects between different drugs are desired or when targeting multiple pathways is necessary for optimal therapeutic outcomes.

8. Minimized Drug Interactions: By encapsulating drugs within carriers, the potential for drug-drug interactions can be reduced. This is especially important when combining multiple medications, as it helps maintain the stability and efficacy of each drug.

9. Tailored Release Profiles: Carriers can be designed to release drugs in response to specific stimuli, such as changes in pH, temperature, or enzyme activity. This enables the development of smart drug delivery systems that release the drug at the desired location and under specific conditions.

10. Improved Drug Stability: Carriers can protect drugs from environmental factors, such as light and oxidation, which can lead to degradation. This improved stability contributes to the overall shelf life of the drug formulation.

11. Enhanced Cellular Uptake: Certain carriers, such as nanoparticles, can facilitate the internalization of drugs into target cells, improving their intracellular concentration and therapeutic effects.

DISADVANTAGES OF CBDDS[15]

1. Complexity and Cost: Developing and manufacturing carrier systems can be complex and expensive. The production of specialized carriers, such as liposomes or nanoparticles, often involves intricate processes and may require sophisticated technology, leading to increased production costs.
2. Limited Loading Capacity: Carriers have a finite capacity to carry drugs. Loading too much drug substance may affect the stability of the carrier or result in a less efficient drug release. This limitation can impact the overall therapeutic efficacy of the system.
3. Biocompatibility Concerns: Some carrier materials may elicit immune responses or cause toxicity issues. The body's immune system may recognize carriers as foreign entities, leading to clearance or adverse reactions. Ensuring the biocompatibility of carriers is crucial to avoid unintended side effects.
4. Drug Leakage: There may be a risk of premature drug release or leakage from the carrier before reaching the target site. This premature release can reduce the concentration of the drug at the intended site of action and may lead to suboptimal therapeutic outcomes.
5. Storage and Stability Issues: Maintaining the stability of carrier-mediated drug delivery systems during storage and transportation can be challenging. Changes in temperature, pH, or other environmental factors may affect the integrity of the carriers and the encapsulated drugs.
6. Tissue-Specific Challenges: Achieving precise targeting to specific tissues or cells can be difficult. The carrier system may not always effectively navigate through biological barriers or reach the desired site of action, limiting its efficiency in certain cases.

7. Regulatory Hurdles: The approval process for carrier-mediated drug delivery systems can be more challenging than for traditional drug formulations. Regulatory agencies may require extensive testing to ensure the safety and efficacy of these systems before they can be approved for use.
8. Patient Compliance: The administration of carrier-mediated drug delivery systems may be more complex than conventional methods, impacting patient compliance. Complicated administration procedures, frequent dosing, or specific requirements for storage and handling can pose challenges for patients.
9. Variable Response: The response to carrier-mediated drug delivery systems can vary among individuals. Factors such as patient physiology, variability in drug metabolism, and individual immune responses can influence the effectiveness of the delivery system.
10. Limited Applications: Carrier systems may not be suitable for all types of drugs or therapeutic applications. The design of an effective carrier depends on the properties of the drug and the intended target, limiting the broad applicability of these systems.

CLASSIFICATION OF CBDDS[16-21]

Carrier-based drug delivery systems can be classified mainly into 5 types (i) based on the type of carrier, (ii) the mechanism of drug release, (iii) based on its target Application, (iv) Based on Nature of Payload and (v) based on administration route

1. **Based on Carrier Type:**

• Liposomal Drug Delivery Systems: Liposomes are vesicles composed of lipid bilayers that can encapsulate both hydrophilic and hydrophobic drugs. They are widely studied for their biocompatibility and ability to enhance drug solubility.

• Polymeric Drug Delivery Systems: Polymers, either natural or synthetic, can be used to create drug carriers. Examples include micelles, nanoparticles, and nanocapsules. Polymeric carriers offer versatility and controlled release properties.

• Dendrimer-Based Drug Delivery Systems: Dendrimers are highly branched macromolecules that can be used to create nanoscale carriers. Their well-defined structure allows for precise control over drug loading and release.

• Protein-Based Drug Delivery Systems: Proteins, such as albumin, can serve as carriers for drug delivery. These systems are often biocompatible and can be designed for targeted drug release.

• Nucleic Acid-Based Drug Delivery Systems: Some carriers are designed to deliver nucleic acid-based drugs, such as siRNA or mRNA, to specific cells or tissues. Examples include lipid nanoparticles and viral vectors.

2. **Based on Mechanism of Drug Release:**

• Sustained/Controlled Release Systems: These systems release drugs gradually over an extended period, maintaining therapeutic levels and reducing the frequency of administration.

• Stimuli-Responsive Systems: Carriers that respond to specific stimuli, such as changes in pH, temperature, or enzymatic activity, triggering controlled drug release at the target site.

- Triggered Release Systems: Release of the drug is triggered by an external stimulus, such as light, magnetic fields, or ultrasound.

3. Based on Target Application:

- Cancer Targeted Drug Delivery Systems: Designed to selectively deliver anticancer drugs to tumor tissues while minimizing exposure to healthy tissues.
- Brain-Targeted Drug Delivery Systems: Formulations designed to overcome the blood-brain barrier and deliver drugs to the central nervous system.
- Ocular Drug Delivery Systems: Carriers designed for targeted delivery of drugs to the eyes, addressing challenges such as short residence time and limited penetration.
- Pulmonary Drug Delivery Systems: Systems tailored for targeted drug delivery to the lungs, commonly used for the treatment of respiratory diseases.
- Intracellular Drug Delivery Systems: Carriers designed to facilitate the internalization of drugs into specific cells or cellular compartments.

4. Based on Nature of Payload:

- Small Molecule Drug Delivery Systems: Targeted delivery of conventional small molecule drugs using carriers.
- Biological Drug Delivery Systems: Carriers designed for the delivery of biologics, such as proteins, peptides, nucleic acids, and vaccines.

5. Based on Administration Route:

- Oral Drug Delivery Systems: Designed to improve the oral bioavailability of drugs, overcome gastrointestinal challenges, and provide targeted delivery.
- Injectable Drug Delivery Systems: Formulations for parenteral administration, including intravenous, intramuscular, and subcutaneous routes.

CARRIER BASED DRUG TARGETTING

❖ LIPOSOMAL DRUG DELIVERY SYSTEMS

Liposomes, phospholipid-based vesicles with a unique structure, have emerged as versatile carriers in drug delivery. Liposomes, first discovered in the 1960s, it have captivated the attention of researchers for their unique bilayer structure resembling biological membranes. It mainly composed of amphiphilic phospholipids, it also provide a biocompatible and flexible platform for drug encapsulation and delivery. The lipid bilayer structure of liposomes, consisting of hydrophilic heads and hydrophobic tails, imparts them with the ability to encapsulate both hydrophilic and hydrophobic drugs. This feature allows liposomes to serve as carriers for a diverse range of therapeutic agents (21,23).The advantages of liposomal drug delivery follow, emphasizing their biocompatibility, ability to encapsulate a variety of drugs, and targeted delivery potential. It protects the drugs from degradation, enhance drug solubility, and offer controlled release mechanisms (25). Their versatility makes them suitable for various administration routes, including intravenous, oral, and topical applications. Specific applications of liposomes, showcasing their efficacy in cancer treatment, infectious diseases, and inflammatory conditions.

Liposomal formulations have demonstrated the ability to improve drug pharmacokinetics, reduce side effects, and enhance therapeutic outcomes. Some commonly available liposomal drug delivery systems with their composition, features and applications are listed below [26,27,28]

1. **Conventional Liposomes:**

- Composition: Composed of natural or synthetic phospholipids and cholesterol, forming a lipid bilayer structure.
- Features: Biocompatible, versatile, and capable of encapsulating both hydrophobic and hydrophilic drugs.
- Applications: Used for a broad range of therapeutic agents and drug delivery applications.

2. **PEGylated Liposomes (Stealth Liposomes):**

- Composition: Surface-modified with polyethylene glycol (PEG).
- Features: Increased circulation time in the bloodstream, reduced clearance by the immune system (Stealth effect).
- Applications: Enhances drug delivery to target tissues by avoiding rapid recognition and elimination.

3. **Cationic Liposomes:**

- Composition: Contain positively charged lipids.
- Features: Interact with negatively charged cell membranes, facilitating cellular uptake.
- Applications: Commonly used for nucleic acid delivery in gene therapy.

4. **Long-Circulating Liposomes:**

- Composition: Modified for prolonged circulation.
- Features: Utilize surface modifications to avoid uptake by the reticuloendothelial system (RES).
- Applications: Enhance drug bioavailability and increase the therapeutic window.

5. **Immunoliposomes:**

- Composition: Liposomes conjugated with antibodies or ligands.
- Features: Target specific cells or tissues expressing corresponding antigens.
- Applications: Precision targeting in cancer therapy and other diseases.

6. **pH-Sensitive Liposomes:**

- Composition: Designed with pH-responsive components.
- Features: Drug release triggered by changes in pH, such as in acidic tumor environments.
- Applications: Targeted drug delivery to specific tissues with varying pH levels.

7. **Thermosensitive Liposomes:**

- Composition: Altered lipid composition for temperature sensitivity.
- Features: Drug release triggered by changes in temperature, often used in hyperthermia treatments.
- Applications: Controlled drug release in response to temperature variations.

8. **Multifunctional Liposomes:**

- Composition: Engineered with multiple functionalities.
- Features: Combine features like targeting ligands, imaging agents, and therapeutic payloads.
- Applications: Comprehensive platforms for diagnostics and therapeutics.

9. Janus Liposomes:

- Composition: Liposomes with asymmetric structures.
- Features: Dual functionality, often with different properties on each side.
- Applications: Improved drug loading and release characteristics.

10. Stimuli-Responsive Liposomes:

- Composition: Designed to respond to specific stimuli (e.g., temperature, pH, enzymes).
- Features: Controlled drug release in response to external or internal triggers.
- Applications: Tailored drug delivery based on the physiological conditions of the target site.

❖ POLYMERIC DRUG DELIVERY SYSTEMS

Polymeric drug carrier systems represent a cutting-edge approach in drug delivery, offering a versatile and dynamic platform for enhancing the efficacy of therapeutic agents. Polymeric drug carrier systems, characterized by their tunable properties and biocompatibility, have emerged as pivotal tools in the field of pharmaceutical sciences. Polymeric drug carrier systems lies the ability of polymers to serve as carriers for therapeutic agents (29). This versatility of polymeric carriers enables their adaptation to different drug delivery routes and therapeutic needs Polymeric drug delivery systems can be classified based on various criteria, including the type of polymer used, and based on structure [30,31,32].

1. Based on Polymer Type:

- Natural Polymers: Derived from natural sources, such as proteins (e.g., albumin, gelatin) or polysaccharides (e.g., chitosan, hyaluronic acid). These polymers often exhibit good biocompatibility.
- Synthetic Polymers: Man-made polymers designed for specific drug delivery applications. Examples include poly(lactic-co-glycolic acid) (PLGA), polyethylene glycol (PEG), and polyvinyl alcohol (PVA). Synthetic polymers offer precise control over properties like degradation rate and mechanical strength.
- Semi-synthetic Polymers: Polymers derived from both natural and synthetic sources. For instance, cellulose derivatives like hydroxypropyl cellulose (HPC) or hydroxypropyl methylcellulose (HPMC) are semi-synthetic polymers used in drug delivery

2. Based on Structure:

- Micelles: Self-assembling structures formed by amphiphilic block copolymers. In aqueous solutions, these polymers can organize into micellar structures, encapsulating hydrophobic drug molecules within their cores.
- Nanoparticles: Solid colloidal particles with a size range typically between 1 and 1000 nanometers. Nanoparticles can be made from various polymers and offer a versatile platform for drug delivery33,34.
- Hydrogels: Three-dimensional networks of hydrophilic polymers that can absorb and retain large amounts of water. Hydrogels are suitable for sustained drug release due to their ability to swell and release the incorporated drug over time.
- Dendrimers: Hyperbranched polymers with a tree-like structure. Dendrimers offer precise control over size and molecular weight, making them suitable for drug delivery applications35.

❖ DENDRIMER-BASED DRUG DELIVERY SYSTEMS

Dendrimer-based drug delivery systems have emerged as innovative and promising platforms in pharmaceutical research, providing a unique combination of structural precision and versatility. Dendrimers are synthetic, highly branched macromolecules with a well-defined three-dimensional structure. The term "dendrimer" is derived from the Greek word "dendron," meaning tree, which describes their tree-like or branched architecture(36). Dendrimers are designed with a central core, from which successive layers of branched, repeating units radiate outward, creating a symmetric and controlled structure. This unique architecture distinguishes dendrimers from linear polymers which offer advantages such as controlled drug release, enhanced solubility, and the ability to encapsulate both hydrophobic and hydrophilic drugs, making them promising candidates for targeted drug delivery. It find applications in various areas, including drug delivery, imaging, and diagnostics, catalysis, and materials science (37,38). Their controlled and tunable structure, along with their ability to encapsulate or bind other molecules, makes them valuable tools in the development of advanced materials and technologies.The classification of dendrimer-based drug delivery systems can be based on various criteria, including their composition, generation, and functionalization.(39,40)

1. **Based on Composition:**

- Polyamidoamine (PAMAM) Dendrimers: One of the most studied dendrimer types, PAMAM dendrimers are characterized by amine groups at their periphery. They can be modified for drug encapsulation and surface functionalization.
- Poly(propyleneimine) (PPI) Dendrimers: PPI dendrimers have a similar structure to PAMAM but are built from different monomers. They have primary amines at their periphery and have been explored for drug delivery applications.
- Poly(L-lysine) (PLL) Dendrimers: PLL dendrimers are composed of lysine residues and have been investigated for nucleic acid delivery due to their positively charged nature.

2. **Based on Generation:**

- First Generation (G1), Second Generation (G2), etc.: Dendrimers are often synthesized in generations, each generation representing a layer of branching. Higher-generation dendrimers have more branches and, consequently, more functional groups for drug loading.

3. **Based on Surface Functionalization:**

- Hydroxyl-Terminated Dendrimers: Dendrimers with hydroxyl groups at the periphery, which can be utilized for drug conjugation or other modifications.
- Carboxyl-Terminated Dendrimers: Dendrimers with carboxyl groups at the periphery, offering additional functionalization options.
- Amine-Terminated Dendrimers: Dendrimers with primary amine groups at the periphery, allowing for interactions with negatively charged entities.

• PEGylated Dendrimers: Dendrimers modified with polyethylene glycol (PEG) to improve biocompatibility and reduce immunogenicity.

• Targeting Ligand-Conjugated Dendrimers: Dendrimers functionalized with targeting ligands (e.g., antibodies, peptides) to enhance specificity for certain cells or tissues.

4. Based on Drug Encapsulation:

• Dendrimer-Doxorubicin Conjugates: Doxorubicin, an anticancer drug, has been conjugated to dendrimers to enhance its delivery and reduce side effects.

• Dendrimer-Antisense Oligonucleotide Conjugates: Dendrimers have been explored for the delivery of nucleic acid-based therapeutics, such as antisense oligonucleotides.

5. Based on Core Structure:

• Janus Dendrimers: Dendrimers with two distinct halves or surfaces, each serving a different function.

• Dendrimer Nanoparticles: Larger dendrimer structures that may have a core-shell structure, combining dendrimers with other nanomaterials.

6. Based on Stimuli-Responsive Properties:

• pH-Responsive Dendrimers: Dendrimers designed to release drugs in response to changes in pH, such as those found in tumor microenvironments.

• Temperature-Responsive Dendrimers: Dendrimers that exhibit changes in their properties or drug release behavior in response to variations in temperature.

❖ PROTEIN-BASED DRUG DELIVERY SYSTEMS

Proteins, the building blocks of life, have become pivotal in the design of innovative drug delivery systems. Protein-based drug delivery systems harness the inherent properties of proteins, such as biocompatibility, specificity, and structural diversity. Protein-based drug delivery systems encompass various types of carriers and platforms that utilize proteins or protein-derived components for the delivery of therapeutic agents(41). some common types of protein-based drug delivery systems are listed below :

1. Protein Nanoparticles:

• Albumin Nanoparticles: Albumin, a naturally occurring protein, is commonly used as a carrier for drug delivery. Albumin nanoparticles can encapsulate a variety of drugs and have applications in cancer therapy and other diseases.

• Ferritin Nanocages: Ferritin is a protein that forms nanocages, and it has been explored as a carrier for drug delivery. The hollow structure of ferritin can be loaded with therapeutic agents.

• Hemoglobin-based Nanocarriers: Hemoglobin, the oxygen-carrying protein in red blood cells, can be used as a basis for nanocarriers. Hemoglobin nanoparticles have been investigated for oxygen delivery and drug delivery applications.

2. Protein-Drug Conjugates:

• Antibody-Drug Conjugates (ADCs): ADCs combine monoclonal antibodies with potent cytotoxic drugs. The antibody targets specific cells, and upon internalization, the attached drug is released, leading to targeted therapy, primarily used in cancer treatment.

• Enzyme-Prodrug Systems: Enzymes can be conjugated to prodrugs, and the enzyme's activity at the target site converts the prodrug into its active form. This approach allows for localized drug activation.

• Protein-Polymer Conjugates: Conjugation of proteins with polymers can enhance their stability and improve drug release characteristics. This strategy is employed to extend the circulation time of therapeutic proteins.

3. Protein-based Micelles:

• Micelles formed by Protein-Polymer Conjugates: Amphiphilic protein-polymer conjugates can self-assemble into micelles in aqueous solutions. These micelles can encapsulate hydrophobic drugs in their cores.

4. Protein-Coated Nanoparticles:

• Protein-Coated Liposomes: Liposomes, vesicles with lipid bilayers, can be coated with proteins to enhance their stability and improve their pharmacokinetics. Protein-coated liposomes are employed for drug delivery, especially in cancer treatment.

• Protein-Stabilized Gold Nanoparticles: Gold nanoparticles coated with proteins can be used for drug delivery and imaging applications. The protein coating provides stability and allows for functionalization with targeting ligands.

5. Protein-Engineered Drug Delivery Systems:

• Designed Proteins for Drug Delivery: Researchers are engineering proteins specifically for drug delivery purposes. These engineered proteins may have enhanced binding affinities, stability, and controlled release properties.

6. Milk Proteins for Drug Delivery:

• Casein Micelles: Casein, a milk protein, has been investigated for drug delivery applications. Casein micelles can encapsulate hydrophobic drugs and have potential in oral drug delivery.

7. Virus-Like Particle (VLP) Platforms:

• VLPs for Vaccine Delivery: Virus-like particles, composed of viral structural proteins without genetic material, have been explored for vaccine delivery. These protein-based carriers mimic viruses and can elicit an immune response.

❖ NUCLEIC ACID-BASED DRUG DELIVERY SYSTEMS

Nucleic acid-based drug delivery systems represent a revolutionary frontier in pharmaceutical research, leveraging the power of genetic materials for targeted therapeutic interventions. Nucleic acid-based drug delivery refers to the development and implementation of delivery systems designed to transport nucleic acids, such as DNA, RNA, and small RNA molecules (e.g., siRNA, miRNA), to specific cells or tissues for therapeutic purposes(42). Nucleic acids play a crucial role in the regulation of cellular functions, and

manipulating their expression or structure can be harnessed for treating various diseases, including genetic disorders, cancers, and viral infections(43). The primary goal of nucleic acid-based drug delivery is to overcome the inherent challenges associated with the delivery of nucleic acids into cells, ensuring their safe and effective delivery to the target site. These challenges include issues such as enzymatic degradation, poor cellular uptake, and potential immunogenicity. By employing specialized delivery systems, researchers aim to protect nucleic acids from degradation, enhance their cellular uptake, and achieve targeted delivery to specific tissues or cells(44). The key components and strategies involved in the nucleic acid-based drug delivery are enlisted below,

1. Carriers: These are vehicles or carriers that encapsulate or complex with nucleic acids, providing protection and facilitating their delivery. Common carriers include lipid nanoparticles, polymeric nanoparticles, viral vectors, and peptides.
2. Protection: Nucleic acids are vulnerable to degradation by nucleases in the extracellular environment. Delivery systems are designed to shield nucleic acids from enzymatic degradation until they reach their intended target.
3. Cellular Uptake: Achieving efficient internalization of nucleic acids into target cells is crucial for their therapeutic efficacy. Various delivery systems are designed to enhance cellular uptake and promote endosomal escape.
4. Targeting: To ensure specificity and reduce off-target effects, delivery systems may be engineered to target specific cells or tissues. This can be achieved through surface modifications or the use of ligands that recognize specific cellular receptors.
5. Release: Controlled release of nucleic acids at the target site is essential for therapeutic efficacy. Strategies involve designing delivery systems that respond to specific stimuli, such as changes in pH or the presence of enzymes, to trigger the release of nucleic acids.

Different Types of Nucleic Acid-Based Drug Delivery Systems (45):

1. Lipid Nanoparticles for RNA Delivery:

- Composition: Lipid-based carriers encapsulate nucleic acids, protecting them from degradation.
- Features: Efficient intracellular delivery, especially for RNA-based therapeutics.
- Applications: mRNA vaccines, siRNA delivery for gene silencing.

2. Polymeric Nanoparticles for Gene Delivery:

- Composition: Biodegradable polymers form nanoparticles for nucleic acid encapsulation.
- Features: Controlled release and protection of genetic material.
- Applications: Gene therapy, DNA vaccination.

3. Viral Vectors for Gene Transfer:

- Types: Adenoviruses, lentiviruses, adeno-associated viruses.
- Features: Natural viral vectors modified for safe gene delivery.
- Applications: Gene therapy for genetic disorders.

4. Peptide-Based Nucleic Acid Delivery:

- Composition: Short peptides designed for nucleic acid binding and cellular uptake.
- Features: Low immunogenicity, targeted delivery.
- Applications: siRNA and antisense oligonucleotide delivery.

MARKETED VAIABLE FORMULATION OF CBDDS

Some examples of carrier-mediated drug delivery systems that have been developed and which are widely available in the market which comes under each category are listed below (46).

1. Liposomes:Example: Doxil (liposomal doxorubicin) - Liposomes are spherical vesicles composed of lipid bilayers. Doxil is used in the treatment of various cancers, and the liposomal formulation helps to enhance drug delivery and reduce toxicity.
2. Polymeric Micelles:Example: Genexol-PM (paclitaxel-loaded polymeric micelles) - Polymeric micelles are formed by self-assembly of amphiphilic block copolymers. Genexol-PM is used for the treatment of breast and lung cancers.
3. Nanoparticles:Example: Abraxane (albumin-bound paclitaxel nanoparticles) - Nanoparticles can be made from various materials, and in this case, albumin is used to deliver paclitaxel. Abraxane is indicated for the treatment of breast cancer.
4. Polymeric Nanoparticles:Example: Depo-Provera (medroxyprogesterone acetate-loaded polymeric nanoparticles) - Polymeric nanoparticles can be used for sustained release of drugs. Depo-Provera is a contraceptive injection that uses polymeric nanoparticles.
5. Dendrimers:Example: VivaGel (dendrimer-based nanogel) - Dendrimers are highly branched macromolecules that can be used for drug delivery. VivaGel is a dendrimer-based nanogel used for topical prevention of HIV and herpes simplex virus.
6. Exosome-Based Delivery:Example: Codiak's exoSTING - Exosomes, naturally occurring extracellular vesicles, can be engineered for drug delivery. Codiak's exoSTING utilizes exosomes to deliver a STING agonist for cancer immunotherapy.

CONCLUSION:

Carrier-based drug delivery systems represent a frontier in pharmaceutical research and development, offering a multifaceted approach to drug delivery challenges. It is also a transformative paradigm in pharmaceutical sciences, offering innovative solutions to longstanding challenges in drug development and delivery. The fundamental strength of carrier-based drug delivery lies in its ability to enhance the precision of therapeutic interventions. Through the strategic encapsulation of pharmaceutical agents within carriers such as nanoparticles, liposomes, and polymers, drugs can be shielded from degradation, optimized for bioavailability, and precisely targeted to specific tissues or cells. This level of precision not only improves the therapeutic efficacy of drugs but also mitigates off-target effects, paving the way for more tolerable and patient-centric treatments. Moreover, carriers facilitate the delivery of a diverse range

of therapeutic agents, including small molecules, nucleic acids, and proteins, broadening the scope of treatable diseases.

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REFERENCE

1. Mainardes RM, Silva LP. 2004. Drug delivery systems: past, present, and future, Curr Drug Targets, 5:449–455.
2. Greish, K.; Fang, J.; Inutsuka, T.; Nagamitsu, A.; Maeda, H. 2003. Macromole-cular therapeutics - Advantages and prospects with special emphasis on solid tumor targeting. Clinical Pharmacokinetics, 42, 1089-1105.
3. Maeda, H.; Fang, J.; Inutsuka, T.; Kitamoto, Y. 2003.Vascular permeability enhancement in solid tumor: Various factors, mechanisms involved and its implications. Int. Immunopharm., 3, 319-328.
4. Maeda, H.; Wu, J.; Sawa, T.; Matsumura, Y.; Hori, K. 2000.Tumor vascular permeability and the EPR effect in macromolecular therapeutics: A review. J. Contr. Rel., 65(1-2), 271-284.
5. Park, J.W. 2002. Liposome-based drug delivery in breast cancer treatment. Breast Cancer Res, 4, 93-97.
6. Duncan, R .1999. Polymer conjugates for tumor targeting and intracytoplasmic delivery. The EPR effect as a common gateway? Pharm. Sci. Technol. Today, 2, 441-449.
7. Sapra, P.; Allen, T.M. 2003. Ligand-targeted liposomal anticancer drugs. Progress in Lipid Res., 42, 439-462.
8. Allen, T.M.; Sapra, P.; Moase, E.; Moreira, J.; Iden, D. 2002. Adventures in targeting. J. Liposome Res., 12, 5-12.
9. Torchilin, V.P. 2000. Drug targeting. Europ. J. Pharm. Sci, 11, S81-S91.
10. Lasic, D.D. 1996. Liposomes in drug delivery. In: Vesicles, Rosoff, M. Ed.; Marcel Dekker: New York, Basel, Hong Kong; Surfactant Science Series; Vol. 62, pp 447-476.
11. K. Rani, S. Paliwal.2014. A review on targeted drug delivery: its entire focus on advanced therapeutics and diagnostics Scholars J. Appl. Med. Sci., 2 ,pp. 328-331
12. Desai P, Date A, Patravale B.2012. Overcoming poor oral bioavailability using nanoparticle formulations-opportunities and limitations. Drug Discov Today Technol.; 9:87–95.
13. Gursoy RN, Benita S. 2004. Self-emulsifying drug delivery systems (SEDDS) for improved oral delivery of lipophilic drugs. Biomed Pharmacotherapy.; 58:173–82.
14. MuÈller RH, Mader K, Gohla S. 2000. Solid lipid nanoparticles (SLN) for controlled drug delivery–a review of the state of the art. Eur J Pharm Biopharm.;50(1):161–177.
15. Beloqui A, Solinis MA, Rodriguez-Gascon A, Almeida AJ, Preat V. 2016. Nanostructured lipid carriers: Promising drug delivery systems for future clinics. Nanomedicine.;12(1):143–161
16. Verma, R.K. 2001.Garg, S. Drug delivery technologies and future directions. Pharm. Technol.25, 1–14.

17. Betz, M.; García-González, C.; Subrahmanyam, R.; Smirnova, I.; Kulozik, U. 2012. Preparation of novel whey protein-based aerogels as drug carriers for life science applications. J. Supercrit. Fluids, 72, 111–119.
18. Franzè, S.; Musazzi, U.M.; Minghetti, P.; Cilurzo, F. 2019.Drug-in-micelles-in-liposomes (DiMiL) systems as a novel approach to prevent drug leakage from deformable liposomes. Eur. J. Pharm. Sci., 130, 27–35.
19. Li, C.; Wang, Y.; Du, Y.; Qian, M.; Jiang, H.; Wang, J.; Murthy, N.; Huang, R. 2018. Side effects-avoided theragnostic achieved by biodegradable magnetic silica-sealed mesoporous polymer-drug with ultralow leakage. Biomaterials, 186, 1–7.
20. Patra, H.K.; Dasgupta, A.K.; Sarkar, S.; Biswas, I.; Chattopadhyay, A. 2011. Dual role of nanoparticles as drug carrier and drug. Cancer Nanotechnology, 2, 37–47.
21. Kim B.Y., Rutka J.T., Chan W.C. 2010. Nanomedicine. N. Engl. J. Med.;363:2434–2443.
22. Allen T.M., Cullis P.R. 2004.Drug delivery systems:entering the mainstream. Science.;303:1818–1822.
23. Khater D., Nsairat H., Odeh F., Saleh M., Jaber A., Alshaer W., Al Bawab A., Mubarak M.S. 2021. Design, preparation, and characterization of effective dermal and transdermal lipid nanoparticles: a review. Cosmetics.;8
24. Yezhelyev M.V., Gao X., Xing Y., Al-Hajj A., Nie S., O'Regan R.M. 2006. Emerging use of nanoparticles in diagnosis and treatment of breast cancer, the Lancet. Oncology;7:657–667.
25. Sahoo S.K., Labhasetwar V.2003.Nanotech approaches to drug delivery and imaging. Drug Discov. Today.;8:1112–1120.
26. Nsairat H., Khater D., Odeh F., Al-Adaileh F., Al-Taher S., Jaber A.M., Alshaer W., Al Bawab A., Mubarak M.S. 2021.Lipid nanostructures for targeting brain cancer. Heliyon;7
27. Celia C., Paolino D., Santos H.A. 2021. Advanced nanosystems for clinical translation. Adv. Ther.;4:2000215.
28. Haley B., Frenkel E. 2008. Nanoparticles for drug delivery in cancer treatment. Urol. Oncol.;26:57–64.
29. Doane T.L., Burda C. 2012. The unique role of nanoparticles in nanomedicine: imaging, drug delivery and therapy. Chem. Soc. Rev.; 41:2885–2911.
30. Peer D., Karp J.M., Hong S., Farokhzad O.C., Margalit R., Langer R. 2007. Nanocarriers as an emerging platform for cancer therapy. Nat. Nanotechnol.;2:751–760.
31. Vithani, K.; Goyanes, A.; Jannin, V.; Basit, A. W.; Gaisford, S.; Boyd, B. J. J. P. R. 2019. An Overview of 3D Printing Technologies for Soft Materials and Potential Opportunities for Lipid-Based Drug Delivery Systems. Pharm. Res, 36(1), 1–20.
32. Boyd, B. J.; Bergström, C. A.; Vinarov, Z.; Kuentz, M.; Brouwers, J.; Augustijns, P.; Brandl, M.; Bernkop-Schnürch, A.; Shrestha, N.; Préat, V. J. E. J. O. P. S., et al. 2019 Successful Oral Delivery of Poorly Water-Soluble Drugs Both Depends on the Intraluminal Behavior of Drugs and of Appropriate Advanced Drug Delivery Systems. Eur. J. Pharm. Sci.,137
33. Tiwari, G.; Tiwari, R.; Bannerjee, B.; Bhati, L.; Pandey, S.; Pandey, P.; Sriwastawa, S. K. I. 2012. Drug Delivery Systems: An Updated Review. Int. J. Pharmaceutical Investigation, 2(1), 2.
34. Calixto, G. M. F.; de Annunzio, S. R.; Victorelli, F. D.; Frade, M. L.; Ferreira, P. S.; Chorilli, M.; Fontana, C. R. J. A. P. 2019. Chitosan-Based Drug Delivery Systems for Optimization of Photodynamic Therapy: A Review. AAPS Pharm. Scitech, 20(7), 1–17.
35. Castro, E.; Kumar, A. J. N. I. D. D. 2013. Nanoparticles in Drug Delivery Systems. Nanomedicine in drug delivery., 1, 1–22.
36. Chauhan A.S., Diwan P.V., Jain N.K., Tomalia D.A. 2009. Unexpected in vivo anti inflammatory activity observed for simple, surface functionalized poly(amidoamine) dendrimers. Biomacromolecules;10:1195–1202.

37. Chauhan A.S., Sridevi S., Chalasani K.B., Jain A.K., Jain S.K., Jain N.K., Diwan P.V.2003. Dendrimer-mediated transdermal delivery: Enhanced bioavailability of indomethacin. J. Control. Release,90:335–343.
38. Tomalia D., Baker H., Dewald J., Hall M., Kallos G., Martin S., Roeck J., Ryder J., Smith P. 1985. A New Class of Polymers: STARBURST®-Dendritic Macromolecules. Polym. J,17:117–132.
39. Tomalia D., Naylor A.M., Goddard W.A.1990. III STARBURST Dendrimers: Molecular Level Control of Size, Shape, Surface Chemistry, Topology and Flexibility from Atoms to Macroscopic Matter. Angew. Chem. Int. Ed. Engl.;29:138–175.
40. Yandrapu S.K., Kanujia P., Chalasani K.B., Mangamoori L., Kolapalli R.V., Chauhan A. 2013. Development and optimization of thiolated dendrimer as a viable mucoadhesive excipient for the controlled drug delivery: An acyclovir model formulation. Nanomedicine.;9:514–522.
41. Tekade R.K., Tekade M., Kumar M., Chauhan A.S. 2015. Dendrimer-stabilized smart-nanoparticle (DSSN) platform for targeted delivery of hydrophobic antitumor therapeutics. Pharm. Res.,32:910–928.
42. Anderson, E. J. 2020.Safety and immunogenicity of SARS-CoV-2 mRNA-1273 vaccine in older adults. New Engl. J. Med. 383, 2427−2438.
43. Sahin, U. 2020. COVID-19 vaccine BNT162b1 elicits human antibody and TH1 T-cell responses. Nature 586, 594−599.
44. Rossi, J. J. & Rossi, D. 2020. Oligonucleotides and the COVID-19 pandemic: a perspective. Nucleic Acid Ther. 30, 129–132
45. Aiuti, A. 2009. Gene therapy for immunodeficiency due to adenosine deaminase deficiency. N. Engl. J. Med. 360, 447–458.
46. Hisham , Mridul M, and Fiza BA.2017.morphous and Crystalline Particulates: Challenges and Perspectives in Drug Delivery Current Pharmaceutical Design, 23, 112