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Review Paper

Targeted Drug Delivery System: Carriers and Strategies

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ABSTRACT

Targeted drug delivery systems represent a revolutionary approach in modern pharmacology, designed to enhance therapeutic efficacy while minimizing adverse effects. The causes for adopting such systems stem from the limitations of conventional drug administration, including poor bioavailability, systemic toxicity, and non-specific distribution. By directing drugs specifically to diseased cells or tissues, targeted delivery offers significant advantages such as reduced side effects, improved patient compliance, and enhanced treatment outcomes, though challenges like high cost, complexity, and potential immune reactions remain. An ideal targeted drug delivery system should exhibit biocompatibility, stability, controlled release, and the ability to bypass biological barriers. Carriers play a pivotal role in drug targeting, with diverse nanostructures such as niosomes, nanotubes, nanoparticles, liposomes, and dendrimers serving as vehicles to encapsulate and transport drugs effectively. Each carrier type offers unique properties in terms of stability, drug-loading capacity, and release mechanisms. In conclusion, targeted drug delivery systems hold immense promise in transforming therapeutic practices by achieving site-specific action, reducing systemic toxicity, and improving overall treatment efficiency. Continued advancements in nanotechnology, biomaterials, and molecular biology are expected to overcome current limitations and expand the clinical applications of these systems, such as enhancing the precision of drug delivery to specific tissues and improving patient outcomes in various diseases. As researchers explore innovative strategies and materials, the integration of real-time monitoring and feedback mechanisms may further optimize these systems, potentially allowing for adjustments in drug delivery based on patient responses and improving the effectiveness

INTRODUCTION

1.1 Targeted Drug Delivery System:

Targeted drug delivery is considered an effective and innovative system for administering medication to patients. In conventional drug delivery, the process occurs through absorption

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across biological membranes. In contrast, targeted release systems are designed to discharge the drug in a controlled and specific manner, ensuring precise dosage at the intended site [1, 2].

The effectiveness of this drug-receptor binding is compromised unless the drug reaches the target location at an optimal concentration and rate, ensuring minimal side effects while maximizing therapeutic benefits [3].

These challenges fall under pharmacokinetics-the way drugs move through and interact with the body [4]. This not only enhances effectiveness but also minimizes harm to healthy tissues. For these reasons, targeted drug delivery systems are considered a more efficient, safer, and smarter approach compared to conventional drug delivery methods [4, 5].

The following design factors must be considered when establishing a targeted release system: the disease, the targeted site, the drug's adverse effects, the drug's delivery channel, and the drug's qualities [6, 7, 4].

First, the drug must be properly loaded into a suitable carrier. Next, this carrier should be able to avoid the body's natural defenses and degrading secretions, allowing it to circulate longer and reach the intended destination. Since different areas of the body have unique needs, the choice of delivery system depends on the route being used [8,9].

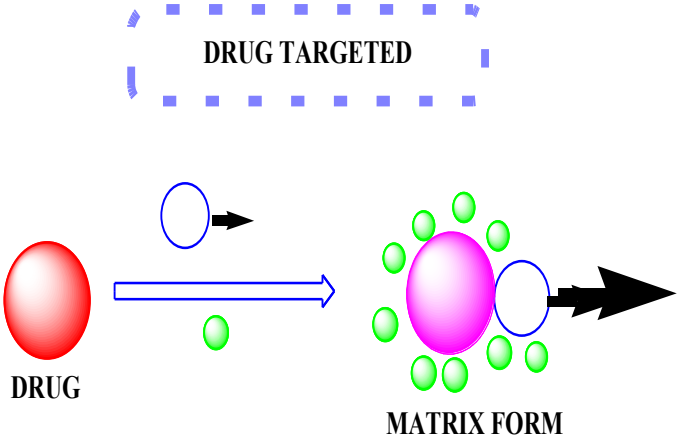

Figure 1 : Drug Targeting

1.2 Scheme and Rationale for Drug Targeting:

Core principle: deliver a high drug concentration to the target organ/tissue/cells while keeping levels low in healthy sites, to maximize therapeutic effect and minimize side effects, dose, and off-target interactions [10].

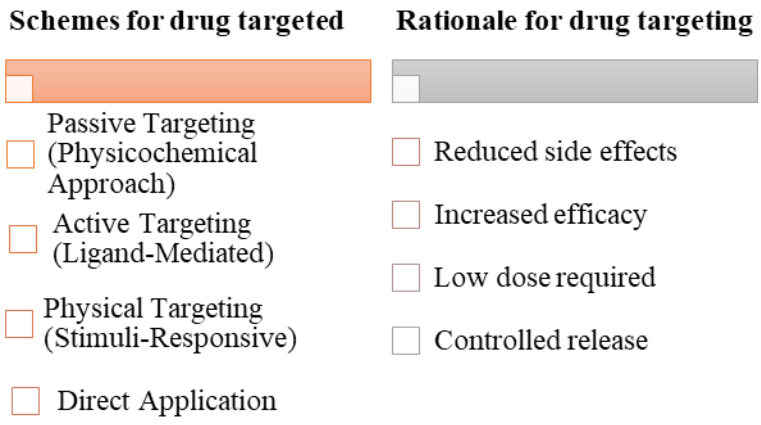

Figure 2 : Scheme and Rationale For Drug Targeting

1.3 Reasons For Site-Specific Delivery Of Drugs:[11]

- Drug instability in traditional dosage forms
- Low solubility and absorption
- Elevated membrane binding
- Instability in biological systems
- Short half-life
- Large volume of distribution
- Insufficient specificity

1.4 Causes of using the targeted drug delivery systems:[12]

There are several reasons for the application of a targeted drug delivery system, as conventional drugs may:

- Break down easily, making them less stable.
- Not be absorbed well by the body.
- Have short-lived effects due to a short half-life.
- Spread widely once in the body, leading to a large volume of distribution.
- Lack selectivity, allowing them to act on unintended targets.
- Have a narrow margin of safety, meaning the difference between an effective dose and a harmful one is small.

2. CHARACTERISTICS OF TARGETED DRUG DELIVERY

Targeted drug delivery aims to concentrate a drug at a specific site (organ, tissue, cell, or organelle) while minimizing exposure to healthy tissue, thereby improving efficacy and reducing side effects [13,14].

- Ideal carriers should meet the following criteria:
- They should be biochemically inert.
- They should be non-immunogenic.
- They must be chemically and physically stable both in vitro and in vivo.
- The amount of drug released should be therapeutic.
- There should be minimal drug leakage during transit.
- Carriers should be easily removed from the body or biodegradable.
- The delivery system should be affordable, reproducible, and easy to set up.
- The drug should have a wide margin of safety, or the system must minimize risks if the margin is narrow.
- During transportation, there should be as little drug loss as possible [15-17].

3. ADVANTAGE AND DISADVANTAGE OF TARGETED DRUG DELIVERY SYSTEM

Table 1 : Advantage and Disadvantage of Targeted Drug Delivery System

Advantages of drug targeting:-[18]	Disadvantages of drug targeting:-[19]
1. Simplified Drug Administration Protocol 2. Reduced Drug Toxicity 3. Effective Response with a Smaller Dose 4. Avoidance of First-Pass Metabolism 5. Improved Absorption at the Target Site 6. Stable Plasma Concentration 7. Enhanced Patient Compliance 8. Prolonged Drug Action 9. Reduced Frequency of Administration 10. Minimized Systemic Distribution 11. Better Therapeutic Index 12. Improved Treatment of Chronic Diseases 13. Lower Risk of Drug Resistance	1. Rapid Drug Elimination 2. Immune Response to Carriers 3. Insufficient Localization at Tumor Tissue 4. Diffusion and Redistribution of Released Drugs 5. High Expertise Required 6. Toxicity at Target Site 7. Difficulty in Product Stability 8. High Cost of Development 9. Limited Availability of Suitable Carriers 10. Complex Regulatory Approval 11. Risk of Premature Drug Release 12. Patient-Specific Variability

	13. Potential for Accumulation in Non-Target Organs

4. STRATEGIES FOR DRUG TARGETING

There are several strategies for drug targeting as shown by Figure 3 which include:

Figure 3: Strategies for Drug Targeting

Table 2 : Strategies of Drug Targeting with Examples:-[34-39]

Strategy	Principle	Mechanism	Examples
Passive targeting	Drug accumulates at diseased site due to physiological factors (EPR effect)	Leaky tumor vasculature, poor lymphatic drainage, nanoparticle size (10–200 nm)	Doxorubicin loaded in Doxil; PLGA nanoparticles carrying paclitaxel
Active targeting	Surface-modified carrier binds to specific receptors overexpressed on target cells	Ligand–receptor interaction (antibody, peptide, folate, transferrin)	Trastuzumab conjugated nanoparticles for HER2+ breast cancer
Inverse targeting	RES (reticuloendothelial system) uptake is avoided to increase circulation time	Surface modification (e.g., PEGylation) to evade macrophage uptake	PEGylated liposomes like Doxil
Physical targeting	Drug delivery controlled by external physical stimuli	Magnetic field, ultrasound, hyperthermia, light Local tumor therapy	Magnetic nanoparticles guided by external magnet; gold nanoparticles activated by NIR light
Ligand-Mediated Targeting	Specific ligand attached to carrier to recognize target cell receptors	Folate receptor, transferrin receptor, integrins	Folic acid-coated liposomes; transferrin-conjugated nanoparticles for brain targeting
Dual Targeting	Combines two targeting mechanisms (e.g., passive + active)	EPR effect + ligand-mediated binding	Folate-targeted PEGylated liposomes delivering paclitaxel
Double Targeting	Targets two different receptors or tissues simultaneously	Two ligands attached to same carrier	Nanoparticles conjugated with folate + transferrin

4.1 Passive targeting

Pharmaceutical methods of administration that target the medicine to the systemic circulation are commonly referred to as passive targeting [20]. The enhanced permeation and retention (EPR) effect is the name given to this phenomenon [21]. Opsonins immediately coat the nanoparticle's surface and deliver it to the liver, spleen, and RES organs [22, 23].

4.2 Active targeting

This method involves identifying a targeting ligand and attaching it to the receptors in the target cells on the drug delivery system's surface [24]. The targeting ligands consist of albumin proteins, antibodies, and bioadhesive nonionic surfactants [25].

This active targeting approach has different levels [24, 25]:

- First-order targeting
- Second-order targeting
- Third-order targeting

4.3 Inverse targeting

The goal of inverse targeting is to prevent the reticuloendothelial system (RES) from passively absorbing the drug delivery mechanism [26,27] . This technique can be accomplished by injecting large amounts of a blank drug delivery system or large molecules of dextran sulfate to saturate the RES and suppress the defense mechanism, thereby suppressing the normal absorption function of the RES [28].

4.4 Dual targeting

Dual targeting increases the therapeutic impact of medication delivery by using a mixture of encapsulated medicines in the carrier [29].

4.5 Double targeting

Double targeting is a type of dual-location targeting (spatial) and action-phase targeting (temporal) [30]. When temporal and spatial methodologies are combined to target a carrier system, it may be called double targeting [31].

4.6 Physical targeting

Physical targeting uses environmental changes such as pH, system temperature, light intensity, magnetic fields, electric fields, or ionic strength, along with other specific stimuli like glucose or gas concentrations, to deliver the drug carrier to a predefined location [32].

4.7 Ligand-mediated targeting

This drug targeting method requires specific receptors to take up both natural low-density lipoprotein (LDL) particles and synthetic microemulsions containing LDL particles with attached Apo proteins [33].

5. CARRIERS OF DRUG TARGETING

5.1 Vesicular system

5.1.1 NIOSOMES:

Niosomes are vesicular systems formed from non-ionic surfactants, capable of encapsulating both hydrophilic and lipophilic drugs. Unlike liposomes, they exhibit greater stability due to the intrinsic properties of their surfactant components. Their versatility has made them valuable carriers for the targeted delivery of antiviral, antibacterial, antifungal, anti-inflammatory, and anticancer agents [40,41].

Their amphiphilic nature enables them to encapsulate both types of drugs: hydrophilic compounds within the aqueous core and hydrophobic molecules within the non-polar bilayer region. This dual entrapment capacity makes niosomes effective carriers for a wide range of therapeutic agents [42].

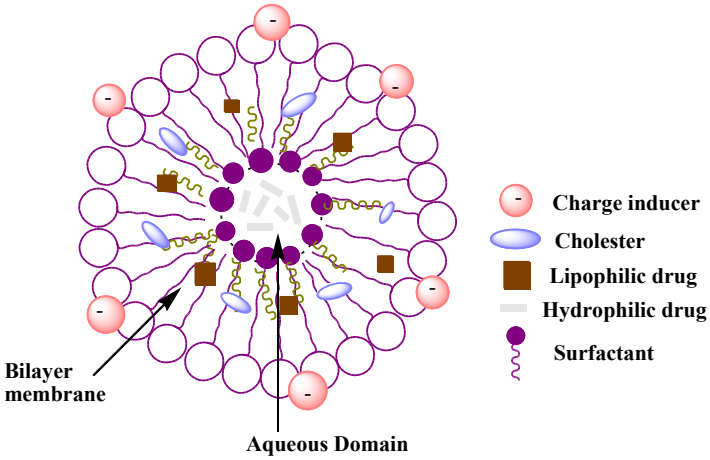

Figure 4 : Structure of Niosomes

- **Method of preparatiion of Niosomes:-**

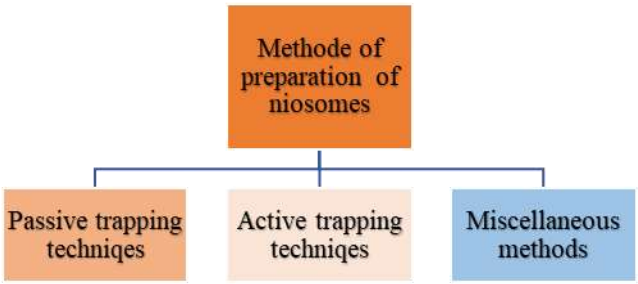

Figure 5 : Method of preparation of Niosomes

i. Ether Injection Method

- Niosomes are produced by gradually adding a surfactant solution (dissolved in diethyl ether) into warm water maintained at 60 °C.
- The ether mixture is injected into the aqueous drug solution using a 14-gauge needle.
- As the ether vaporizes, single-layer vesicles are formed.The resulting vesicles typically range in size from 50 to 1000 nm, depending on the preparation conditions [43,44,45].

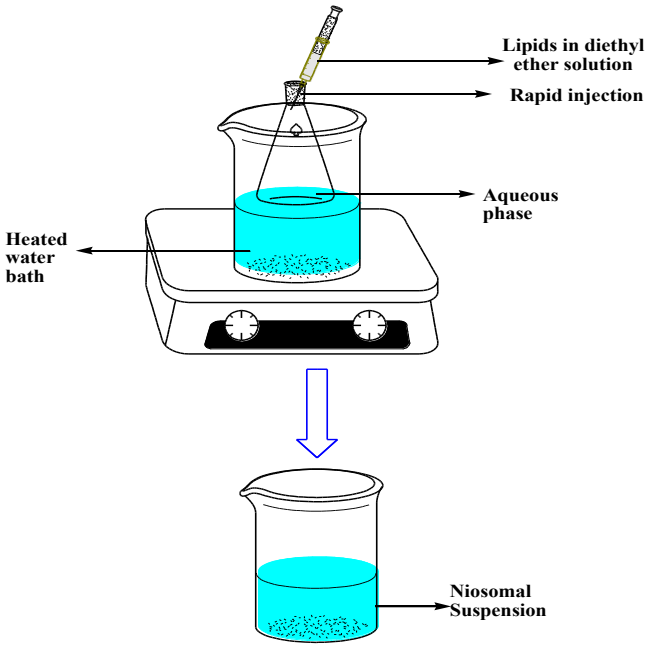

Figure 6: Niosome preparation by ether injection method

ii. The Bubble Method

- A bubbling unit is used for temperature control, employing a round-bottom flask with three necks placed in a water bath.
  - The first neck is connected to a water-cooled reflux system.
  - The second neck holds a thermometer for monitoring.
  - The third neck is attached to a nitrogen supply.
- At 70 °C, cholesterol and surfactant are dispersed in a buffer solution with a pH of 7.4.
- The dispersion is mixed for 15 seconds using a high-shear homogenizer.
- Nitrogen gas is then introduced to generate bubbles at 70 °C, facilitating niosome formation [46].

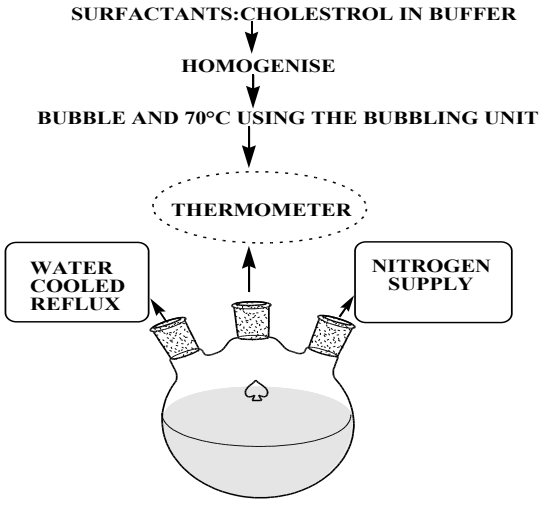

Figure 7:- The Bubble Method

iii. Sonication

- A mixture containing the drug solution, surfactant, and cholesterol in buffer is prepared.

- Niosomes are generated by sonicating this mixture at 60 °C for 3 minutes using a titanium probe sonicator [47].

5.1.2 Liposomes:

Liposomes are tiny vesicles with a bilayer structure made from natural phospholipids [48,49]. Both hydrophilic and lipophilic medications can be trapped within the phospholipid bilayers or the aqueous space [50,51]. The drug's chemical and physical characteristics, as well as the lipid composition, determine the percentage of entrapped drug. Huwyler et al. investigated tumor-targeting using liposomal anti-tumor drugs [52,53].

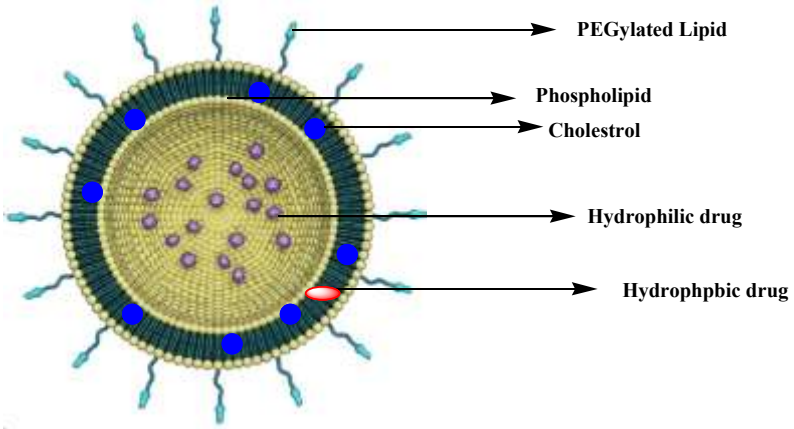

Figure 10 : Structure of Liposomes

➢ **Preparation of Liposomes:-**

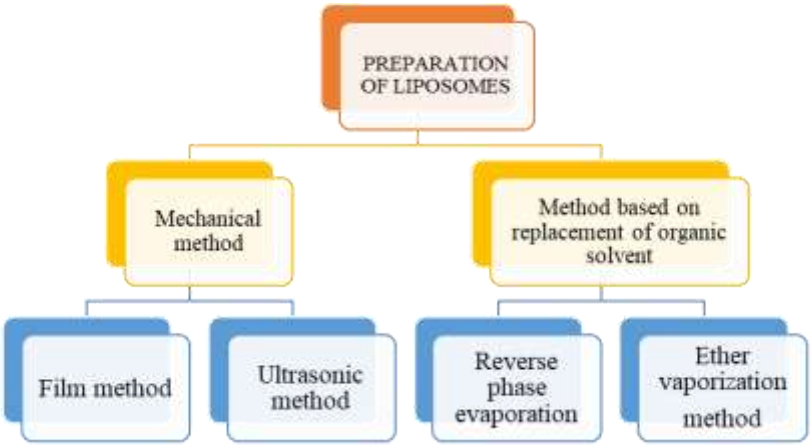

Figure 11 : Preparation of Liposome

1. Mechanical method

✓ **Thin Film method:**

Although the original Bangham et al. approach is currently the most straightforward way to make liposomes, it has certain drawbacks due to its poor encapsulation efficiency. This method creates liposomes by hydrating a thin lipid film in an organic solvent, which is subsequently removed by vacuum-induced film deposition. An aqueous buffer is used to hydrate the solid lipid mixture after all of the solvent has been removed. Lipids hydrate and swell on their own to produce liposomes. A population of MLVs with a diameter of more than one micrometer is produced by this procedure [54].

2. Metod based on replacement of organic solvent

✓ **Ether vaporization method:**

This technique, known as the ether vaporization method, is used in pharmaceutics for the

preparation of emulsions. It depends on the swift evaporation of a volatile solvent to create small droplets of the dispersed phase. Based on the solvent chosen, it falls into two categories [55,56,57]:

i. Infusion of Ethanol

In this approach, ethanol is initially mixed with the oil phase (drug or lipid material). The ethanolic mixture is then gradually introduced into the aqueous phase containing an emulsifying agent while stirring continuously. As ethanol diffuses out and partially evaporates, fine droplets form, leading to the creation of an emulsion [58].

ii. Injection of Ether

In this method, ether (a highly volatile solvent) containing the oil phase is injected into the aqueous phase. Because of ether's low boiling point, it quickly evaporates, causing the creation of very fine droplets and thus forming an emulsion. The rapid solvent evaporation contributes to reducing globule size [59].

5.2 Polymeric system

5.2.1 Dendrimers:

Synthetic particles with a specific diameter are called dendrimers [60]. They are made up of polymer layers encircling a central core [61]. The medication may bind to the dendrimers at a number of different locations on their surface [62]. They are employed in medical imaging and gene transfection [63].

Mechanism of Action Dendrimers: [64-67]

Dendrimers like PAMAM encapsulate or conjugate drugs, circulate systemically, and target cells via passive (EPR effect) or active (ligand-based) mechanisms.

Once internalized, they escape endosomes, release drugs intracellularly, achieve site-specific therapy with reduced toxicity, and are eliminated through renal excretion or biodegradation.

5.2.2 Hydrogels:

Hydrogels are hydrophilic polymeric networks that can absorb large amounts of water and undergo appropriate swelling and shrinking to provide controlled medication delivery. They are exceptionally appealing biocompatible drug delivery vehicles because of their porosity and compatibility with aqueous environments [68].

Table : 3 Common targeted applications

Targeted Area	Mechanism / Benefit	Commerical example
Cancer	Provides high local drug concentration at tumor site; may respond to tumor microenvironment (pH, enzymes, etc.).	Eligard (Prostate Cancer)[69]
Ophthalmic	Extends drug residence time on ocular surface or within vitreous cavity; sustained anti-inflammatory effect.	Dextenza (Post – operative pain/inflammation)[70]

5.3 Biological carriers:-

5.3.1 Monoclonal Antibodies

Monoclonal antibodies are highly specific proteins that bind to unique antigens, making them powerful tools for detecting and neutralizing pathogens or toxins. They are widely used in assays to measure targets, kill microbes, and clump or precipitate antigens [71].Monoclonal antibodies (mAbs) are a single type of identical immunoglobulin directed against a particular epitope (antigenic determinant) and are produced by clones of a single parent B-cell or a single hybridoma cell line. A hybridoma cell line is formed by the fusion of one B-lymphocyte and one myeloma cell. Some myeloma cells naturally produce single mAb antibodies [72].

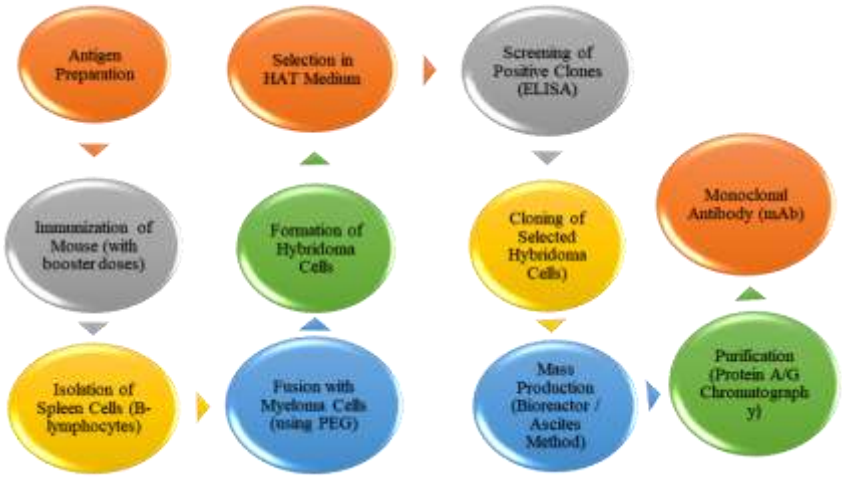

Figure 12 :Production of Monoclonal Antibodies

5.3.2 Erthyrocytes:-

Human erythrocytes, also known as red blood cells (RBCs), are enucleated, biconcave disk-shaped cells. RBCs have a plasma membrane surface area of about 160 µm[73], a diameter of about 7 µm, and a thickness of about 2 µm. The most prevalent component of blood are erythrocytes; approximately 4–5 million RBCs are present in 1 µL of human blood.

Human erythrocytes have a half-life of 100–120 days. The erythrocyte membrane contains a variety of receptors, proteins, and functional groups that serve as binding sites for drugs, particular ligands, and antibodies[74,75].

5.4 Inorganic Nanoparticles

5.4.1 Gold Nanoparticles

Alzheimer's disease has been targeted with β-amyloid peptides and gold nanoparticles [76]. Additionally, these nanoparticles have demonstrated promise in treating Parkinson's disease when combined with L-Dopa [77]. Metal-based nanoparticles are excellent candidates for use as nanomaterials in medicine due to their physical, chemical, optical, thermal, and biological properties [78].

Examples:-

I. Doxorubicin-Loaded Gold Nanoparticles (Cancer Targeting)[79]

Drug: Doxorubicin

Targeting Ligand: Folic acid

Target Site: Folate receptor–overexpressing cancer cells (e.g., breast, ovarian cancer)

Mechanism: AuNPs conjugated with folic acid bind specifically to folate receptors.

⬇

Drug released inside tumor cells.

Outcome: Enhanced cytotoxicity, reduced systemic toxicity

5.5 Particulate system:-

5.5.1 Polymeric Nanoparticles:

Nanoparticles can significantly enhance the effectiveness of drugs by offering better protection and enabling targeted delivery to specific sites in the body[80,81]. Several types of nanoparticles have demonstrated potential in drug delivery, including polymer-based, inorganic, and lipid-derived particles[82,83].

Biodegradable polymeric nanoparticle:-

When considering biomolecules such as proteins and peptides for oral vaccination, biodegradable polymers play a crucial role by either protecting these compounds from the harsh acidic environment of the stomach or providing sustained

release. This protection can help reduce the frequency of doses, whether maintenance or booster doses[84].

Example:- Examples of synthetic biodegradable polymers include:-

- poly(d,l-lactide) (PLA),
- co-polymer poly(lactide-co-glycolide) (PLGA),
- poly(d,l-glycolide) (PLG),[85]

Mechanisms of polymeric nanoparticles:-

Mechanisms of drug release of polymeric nanoparticles the polymeric drug carriers deliver the drug at the tissue site by any one of the three general physicochemical mechanisms.

(1) By the swelling of the polymer nanoparticles by hydration followed by release through diffusion.

(2) By an enzymatic reaction resulting in rupture or cleavage or degradation of the polymer at site of delivery, there by releasing the drug from the entrapped inner core.

(3) Dissociation of the drug from the polymer and its deadsorption/release from the swelled nanoparticles[86].

Example:-

- Poly(lactic-co-glycolic acid)
- Chitosan nanoparticle

5.6 Solid lipid nanoparticles (SLNs) :-

Solid lipid nanoparticles (SLNs) are lipid nanoparticles which use a solid matrix as their fundamental structure. The production of these particles uses solid lipids to form oil-in-water nanoemulsions [86].Recent research developed SLNs which contained ciprofloxacin (CIP) as an antibacterial agent through the process of ultrasonic melt emulsification[87].

Targeting principle:- Solidified Core Lipid carriers enhance poor solubility drugs, thus enabling sustained release[88].

Example:- SLN-based doxorubicin and curcumin carriers[89].

5.7 Micelles:-

Micelles form when amphiphilic molecules create self-assembled nanoparticles through their spontaneous organization in water. The hydrophobic core of micelles can hold poorly water-soluble medications which results in enhanced stability and improved solubility[90].

Targeting principle:- Hydrophobic drugs can be dissolved using self-assembling amphiphilic block copolymers[91].

Example:- Genexol-PM® (paclitaxel loaded micelles)[92].

5.8 Carbon nanotubes:-

Nanostructures with a cylindrical shape composed of carbon atoms, capable of loading drugs and crossing cell membranes. Enhanced drug capacity, stability, targeted drug delivery[93].

The research examines two main points: the effect of biocompatibility and toxicity which includes pulmonary and hepatic toxicity, and the potential danger of organ accumulation[94].

Targeting principle:- Functionalized CNTs therefore have a very large surface area that can be used to convey genes or drugs to the inside of cells [95,112].

Drug-loading strategies:- Adsorption(combining with some chemical bonds-funtional groups), covalent functionalization, encapsulation[96,97]

Release triggers:- pH, NIR light, enzymatic[98,99]

Example:- CNT–doxorubicin conjugates[100]

5.9 Quantum dots:-

Quantum dots (QDs) are semiconductor nanoparticles that range in size from 1 to 10 nm [101,102].

Their compact size is responsible for their long photostability, great brightness, and restricted emission spectrum[103,104,105] . QDs are employed

in biomedicine, optoelectronics, electronics, and catalysis [106-107].

QDs are divided into two categories based on their composition: compound semiconductors like CdSe, CdTe, lead sulfide (PbS), lead selenide (PbSe), and carbon compounds, or single-element materials like silicon and germanium[108,109].

Example:-

- Doxorubicin-loaded ZnO quantum dots coupled with chitosan and folate
  Efficient drug entrapment (~99%).
- used for imaging and targeted cancer treatment[110,111].

6. APPLICATION OF TARGETED DRUG DELIVERY SYSTEM

6.1 Cancer Therapy (Oncology)[113,114,115]

This technology is being evaluated for cancer therapy. Nanoshells are tuned to absorb infrared rays when exposed from a source outside the body and get heated and cause destruction of the tissue. This has been studied in both in vitro and in vivo experiments on various cell lines[116].

6.2 Diagnostic Applications:

Monoclonal antibodies have revolutionized the laboratory diagnosis of various diseases. For this purpose, MAbs may be employed as diagnostic reagents for biochemical analysis or as tools for diagnostic imaging of diseases[117].

(A) MAbs in Biochemical Analysis

(B) MAbs in Diagnostic Imaging[118]

6.3 Cardiovascular Diseases :-

Cardiovascular applications, targeted delivery systems frequently make use of particular markers expressed in diseased vessels or combine magnetic guidance for targeted medication administration. The creation of injectable systems that react to particular pathological conditions, like pH shifts or cardiovascular disease-related enzyme levels, have made more accurat e therapeutic measures [119,120].

6.4 Infectious Diseases :-

Targeted delivery systems have profoundly influenced the management of infectious diseases by facilitating more efficient delivery of antimicrobial agents. These systems can improve drug penetration into infected tissues and intracellular pathogens, potentially addressing antimicrobial resistance mechanisms[121,122].

6.5 Inflammatory Diseases:-

Targeted drug delivery systems improve treatment of inflammatory diseases by directing drugs precisely to affected tissues.

In rheumatoid arthritis, they enhance drug accumulation in inflamed joints using passive and active targeting[123].

Inflammation-responsive carriers release drugs selectively at disease sites, boosting efficacy.

Long-acting formulations reduce dosing frequency and improve patient compliance[124].

For inflammatory bowel disease, colon-specific systems protect drugs until reaching inflamed tissue, minimizing side effects[125].

6.6 Neurological Disorders

The management of neurological diseases poses distinct challenges because of the blood-brain barrier. Targeted delivery mechanisms tailored for central nervous system applications have demonstrated advancements in improving drug delivery to the brain. These mechanisms frequently utilize specific targeting ligands that aid in crossing the BBB via receptor-mediated transcytosis [126].

7. CHALLENGES AND LIMITATIONS OF TARGETED DRUG DELIVERY SYSTEMS (TDDS)

Targeted drug delivery systems are designed to deliver drugs specifically to diseased tissues or cells. However, several scientific and technological challenges limit their clinical effectiveness.

I. Biological Barriers:-

A key challenge is the existence of biological obstacles that hinder drug delivery systems from accessing the intended site.

Such barriers consist of the blood–brain barrier (BBB), the thick tumor extracellular matrix, and the immune system's clearance mechanisms. These obstacles decrease the effectiveness of nanoparticle or carrier build-up within the target tissue[127].

II. Rapid Clearance by the Immune System:-

The reticuloendothelial system (RES), particularly in the liver and spleen, commonly identifies nanoparticles and other carriers as foreign particles. This leads to rapid removal from circulation and reduces drug delivery to the target tissue[128].

III. Limited Targeting Efficiency:-

Drug delivery systems often face the challenge of limited targeting efficiency. Even when advanced ligand-mediated strategies are employed- such as using antibodies, peptides, or receptor-specific molecules to guide carriers toward diseased tissues—the majority of the administered therapeutic agents fail to reach the intended destination [129].

IV. Toxicity and Safety Issues:-

Nanocarrier-based drug delivery systems often encounter significant toxicity and safety challenges that hinder their progress toward widespread clinical application. Certain classes of nanomaterials-such as dendrimers, quantum dots, and specific synthetic polymers-have been reported to induce adverse biological effects. These may include direct cytotoxicity, unintended immunogenic responses, or the potential for long-term accumulation within vital organs and tissues[130].

V. Stability and Drug Leakage:-

One of the persistent challenges in nanomedicine is the issue of stability and drug leakage from carrier systems. Drug delivery vehicles such as liposomes, polymeric nanoparticles, and other nanoscale formulations are often prone to structural instability, which can manifest in several problematic ways. For instance, premature drug leakage may occur during storage or upon exposure to biological fluids, leading to a significant reduction in the amount of therapeutic agent available at the intended site of action[131].

VI. High Production Cost and Complex Manufacturing:-

High production costs and complex manufacturing processes frequently hinder the development of advanced targeted drug delivery systems. Unlike conventional pharmaceutical formulations, these innovative nanocarriers demand sophisticated preparation methods that involve multiple stages of synthesis, functionalization, and Only through such innovations can the balance between affordability and therapeutic sophistication be achieved , paving the way for broader accessibility and real-world application [132].

VII. Regulatory and Clinical Translation Challenges:-

Only a limited number of targeted nanomedicines have successfully progressed into clinical practice, largely because the pathway to regulatory approval is highly demanding. Before such therapies can be authorized , they must undergo extensive investigations into safety, pharmacokinetics, and potential toxicity. These studies are not only rigorous but also require significant financial

investment and long periods of evaluation. As a result, the overall process becomes both costly and time-consuming, slowing down the translation of promising nanocarrier technologies from the laboratory to real-world medical use [133,134].

CONCLUSION

Targeted Drug Delivery Systems (TDDS) represent a major advancement in pharmaceutical science, designed to deliver drugs directly to diseased tissues while minimizing exposure to healthy cells. The central aim is to improve therapeutic efficacy and reduce side effects by using strategies such as passive targeting, which exploits physiological features like the enhanced permeability and retention (EPR) effect, and active targeting, which employs ligands such as antibodies or peptides to bind specifically to target cells. The choice of drug carriers is critical, with liposomes, polymeric nanoparticles, dendrimers, and lipid-based nanoparticles widely used for their ability to encapsulate drugs, protect them from degradation, and enable controlled release. These carriers also enhance drug solubility, stability, and bioavailability, making them versatile tools in modern medicine.

The efficiency of TDDS depends on several factors, including the physicochemical properties of the drug, particle size, surface charge, ligand–receptor interactions, and biological barriers such as the immune system or blood–brain barrier. Proper optimization of these parameters ensures precise targeting and sustained therapeutic outcomes. Recent advances in nanotechnology and biotechnology have introduced innovations like stimuli-responsive nanoparticles, surface-modified carriers, and gene delivery systems, which expand the potential of TDDS in treating complex diseases such as cancer, neurological disorders, and genetic conditions.

Looking ahead, TDDS are expected to play a pivotal role in personalized and precision medicine, offering tailored treatments for individual patients. Despite challenges in large-scale production, regulatory approval, and long-term safety, ongoing research in nanomedicine and biomaterials promises safer and more efficient drug delivery platforms. Overall, TDDS hold immense promise for revolutionizing disease management and improving patient outcomes.

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