Biomedical and Biopharmaceutical Research
Abbreviation: Biomed. Biopharm. Res.
Volume: 22: Issue: 01 |Year: 2025
Page Number: 753-765

TARGETED DRUG DELIVERY SYSTEM: RECENT DEVELOPMENT AND THERAPEUTIC APPLICATION

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Article Received:11-04-2025

Article Accepted:25-05-2025

ABSTRACT

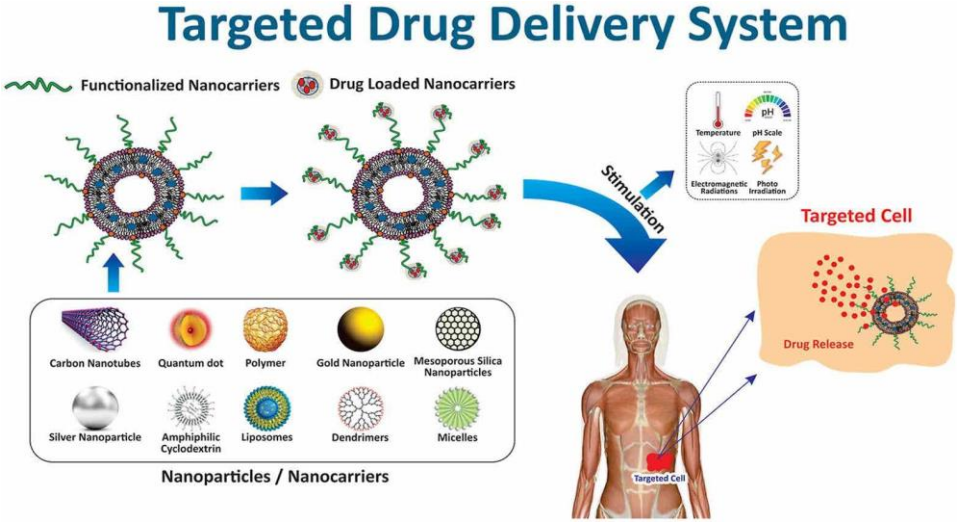
Background: More than a century back, Paul Ehrlich proposed the thought of a sedate working as a "enchantment bullet" that specifically disposes of infected cells without hurting the encompassing typical cells. Since at that point, much advance has been made in this field to broaden the scope for focused on conveyance of drugs. A major issue stay the poisonous impacts of focused on drugs on sound cells. In arrange to decrease the unfavorable impacts of chemotherapy on sound tissues, we overview the utilize of later medicate conveyance frameworks for focused on therapy.
Objective: The specific conveyance of the drugs to particular infected cells or tissues still could be a overwhelming assignment. In a perfect world, for target sedate conveyance frameworks, the framework ought to be made up of carriers and drugs, where carriers absolutely target the required sedate. This issue covers the later progressions in cutting edge procedures for such purposes.It envelops progresses, benefits and confinements in state of craftsmanship work of focused on medicate conveyance through hydrogels, microfluidics, nanoparticles, carbon nanotubes, polymeric micelles, liposomes, lipoprotein based sedate carriers and dendrites.

Keywords: Cancer treatment; sedate carriers; hydrogels; nanoparticles; polyoxometalate; focused on medicate conveyance.

INTRODUCTION

Focused on medicate conveyance may be a extraordinary frame of medicate conveyance framework where the medicament is specifically focused on or conveyed to as it were to the location of activity and not to the non-targeted organs or tissues or cells. Focused on sedate conveyance is additionally known as shrewd conveyance framework [1]. Targeted drug conveyance can be a sensibly satisfactory medicate conveyance framework that's supernatural pharmaceutical for the persistent. This commonplace sedate conveyance framework is supplemented by medicate retention a natural layer whereas the aiming discharge framework is that the medicate is discharged in an undetermined amount[2]. The framework comprises of a strategy that gives a certain sum of restorative specialist over a long period of time for a few time on the target ailing body zone and progresses the impact and diminishes side effect[1]. Targeted sedate conveyance has advanced a strategy of regulating drugs to patients in such arrangement grouping that increments the concentration of the medicate conveyed to target organs or tissues or cells, which in turn progresses proficiency treatment diminishing sedate side impacts management[3]. Targeted medicate conveyance framework is way better than traditional drug conveyance frameworks for three primary reasons .To begin with of all for pharmaceutical reasons. There's small in conventional pharmaceutical dissolvability and more prominent flimsiness of the drug compared to the target bunch sedate conveyance frameworks. Conventional medication too has its disadvantages retention, shorter half-life and requires a expansive sum Dissemination.The third reason is the pharmacodynamics properties. About drugs Customary drugs have moo specificity and moo restorative record compared to target [4].Currently, the center of cancer treatment advancement is the focused on dosing of drugs to attain restorative concentrations of anticancer specialists at the location of activity and to save typical tissue[5]. A focused on sedate conveyance framework is an amazing approach points at the pharmacologically and remedially dynamic part target a particular zone instead of focusing on a non-target and amasses in regions such as an organ or tissue target as it were the zone where pharmacological impacts are shown[6] . The organic impact of the sedate on the influenced individual depends on the pharmacological properties of the medicate. These effects are improved by intelligent between drugs and receptors within the web of medicate development. The viability of this drug-target interaction is diminished but the medicate is transported to its site of activity in a concentration and load that causes negligible impacts and maximal recuperating result Focused on sedate conveyance may be a helpful strategy that involves delivering a restorative operator to a interesting tissue without

coming to it to the final portion of the body[7]. The assets that are utilized have to be be biodegradable or eco-friendly, and Exits the body easy without any issues. It ought to be simple to prepare the dispersion system, or in a way that's relatively straightforward, simple to reproduce, and reasonable. Employing a focused on sedate conveyance framework is predominant to. There are three primary reasons for this. One reason is pharmaceutical in nature. Conventional pharmaceuticals show restricted solubility and have a more noteworthy number of helpful attributes. Targeted medicate conveyance is comparatively more steady than precariousness. Conventional drugs have moo assimilation rates within the body. Shorter half-life and tall measurement required[8].



ADVANTAGES[3,9]

1. Medication organization conventions can be pre-digested Poisonous quality is decreased by sedate convey goal that diminishes destructive framework effects
2. The pharmaceutical can be managed in a littler dosage makes a swell impact Shirking of essential digestion system within the liver.
3. Improve target retention atoms such as peptides and particles.
4. The measurement is lower compared to conventional pharmaceutical dissemination framework.
5. There is no most extreme and least plasma concentration.
6. Selective focusing on of irresistible cells which compared to typical cells.

DISADVANTAGES[3,10]

1. Immune response IV overseen working frameworks.
2. Inadequate localization of target frameworks to tumor cells.
3. Dissemination and redistribution of discharged drugs.
4. Requires exceptionally progressed innovation formulation
5. Requires generation, capacity, administration
6. Accumulation of drugs within the target range can cause side effects of harmfulness.
7. Difficulty in keeping up solidness of dose frame.

1.) IDEAL CHARACTERISTICs [11]

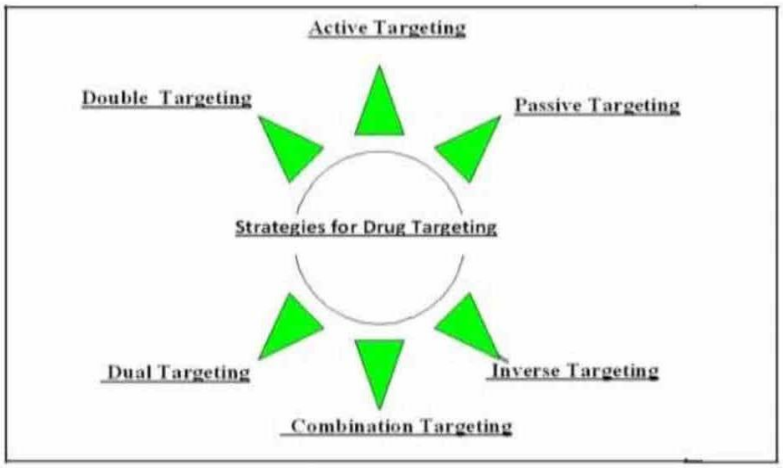
1. The framework must be physically and chemically steady in vivo and in vitro.
2. The framework ought to be non-immunogenic and biochemically dormant.
3. The framework must pass and assimilate organic membranes.
4. Arrangement of the conveyance framework ought to be straightforward or sensibly straightforward, reproducible and cost-effective compelling.

CLASSIFICATION OF TARGETED DRUG DELIVERY SYSTEM:-

As of now, focused on medicate conveyance can be separated into two wide categories zones: systemic focusing on and

intracellular focusing on Systemic focusing on circulation and extravasation, can be assist classified as ligand-receptor interceded and locally actuated sedate conveyance [12]

1. CLASSIFICATION BASED ON STRATERGIES OF DRUG TARGETING:-



1. **ACTIVE TARGETING**:

Using this method, the drug-bearing carrier system travels to a designated location based on surface modifications rather than RES's organic absorption. One method of surface modification is coating the surface with albumin protein, a bio adhesive, a non-ionic surfactant, or monoclonal antibodies, which are specific cell or tissue antibodies. There are three forms of active targeting [13].

1. Organs are the target of first order targeting.
2. Targeting cells is second order targeting.
3. Targeting inside the cells is known as third order targeting.

Since the NP engineering, the ligand conjugation chemistry, and the sorts of ligand that are accessible all influence the system's adequacy, planning actively-targeted NP medicate carriers could be a complex handle. Extra elements It has been illustrated that components just like the mode of organization or non-specific protein official amid the NP's section through the circulatory system can affect the NPs' capacity to target[14]. The so-called active targeting can indeed boost the drug's adequacy after it has gathered within the tumor zone. This is often fulfilled by enhancing the Nano carrier surfaces containing ligands that join to receptors that are overexpressed on cancerous cells. By utilizing this strategy, the sedate entrance will be expanded and the Nano carriers' affinities for the cancer cell surface will be progressed. The most punctual sign of this marvel was put forward in 1980 when antibodies were joined onto the surface of liposomes. Other ligand sorts, such as peptides, nucleic acids, and, were at that point included [15]. In arrange to progress the specific take-up of nanoparticles into the tumor cells, focusing on methodologies have progressed. Atomic bio acknowledgment has been attached to the Nano vectors' surface in arrange to target specific markers that the cancerous cells overexpress. These strategies have been named "dynamic focusing on" since they illustrate more noteworthy adequacy and specificity in coming to the aiming objective [16].In this approach, the target gather is distinguished and connected to the receptors on the drug conveyance system's surface, empowering the medicate to be focused on. Inside the intended cells. 4 Antibodies, egg whites protein, and bio cement non-ionic surfactants are illustrations of the target gather [17].Ever since, researchers from all around the world have been attempting to discover the leading possible treatment that targets cancer particularly whereas causing minimal side impacts. Current advancements an inventive course of Nano therapeutics that will be focused on to neoplastic cells has developed within the field of cancer, advertising energizing prospects for focused on medicate conveyance and a critical advantage over conventional chemotherapeutic specialists.

Detached and dynamic focusing on are the two strategies accessible for accomplishing nanoparticle focusing on [18]. To begin with Arrange, Moment Arrange, and Third Arrange Focusing on are the three focusing on levels that make up dynamic focusing on. The medicine is managed to capillary beds of wide target destinations, such as organs or tissues, in to begin with arrange focusing on. In pleural spaces, peritoneal depression, and lymphatic tissues such target locales incorporate the brain ventricles, the depth, the eyes, and the joints. Drugs are focused on at specific areas, like tumour cells, in second-order focusing on. Pharmaceutical coordinated towards the liver's Kupffer cells is one occurrence of this [19].

2. PASSIVE TARGETING:

Today, it is widely known that the vascular endothelium becomes more permeable under certain conditions than in a healthy state (inflammation/hypoxia typical of tumors). With rapidly increasing hypoxia, it is now widely known that the vascular endothelium becomes more permeable under certain conditions than in the healthy state (tumor-type inflammation/hypoxia). In hypoxia, rapidly growing tumors can engulf existing blood vessels or attract new ones. Because of these newly formed leaky blood vessels, selectively enhanced penetration of nanosystems and macromolecules larger than 40 kDa into the tumor stroma is possible. (3) We consider the accumulation of active pharmaceutical ingredients (API) at the target, especially in leaky blood. vessels to passive targeting. Passive targeting is modified by physical properties such as size, mass, zeta potential, etc., and properties such as charge (+/-) or polarity[20]. TUMER CELL Drug delivery systems that aim to reach the systemic circulation are known as passive targeted drug delivery systems. This method of drug targeting results from the body's innate response to the physicochemical properties of the drug or drug carrier [13]. High molecular weight molecules have a longer retention time than low molecules. Using the chemical modification method, prodrugs can be prepared with passive targeting in mind. These prodrugs are inert in nature; however, enzymatic conversion makes them the active part. Prodrugs have a lower cytotoxic effect on cells that are not cancer cells[19]. Due to the phenomenon of enhanced permeability and retention (EPR), macromolecules, including nanoparticles, preferentially accumulate in neoplastic tissues during passive targeting. first explained by Matsumura and Maeda. EPR is based on two important characteristics of neoplastic tissues: impaired lymphatic drainage and leaky vasculature, and the size range of nanoparticles in nanometers. [16] When medicines are inhaled in the form of airborne droplets, they are absorbed through the thin mucous membrane lining the nasal passages. If the drug needs to work immediately, this is the recommended method. Nasal sprays can be used to deliver medications such as corticosteroids, sumatriptan and calcitonin. do For the drug to reach the lungs through the trachea when inhaled orally, the droplet size must be smaller than when administered through the nose [18]. The presence of fenestrations in the tumor's incomplete vasculature and tissues and an inadequate lymphatic system were considered to be the cause of this tumor and its primary spread. The enhanced penetration and retention effect is named after the combination of these two phenomena. Since then, the EPR effect has become the cornerstone of many researchers seeking to effectively deliver anticancer drugs to tumors, whether they used polymer conjugates, liposomes or NPs [14]. Passive targeting of nanodrug delivery systems requires the EPR effect. Drugs that penetrate into the tumor and into the interstitium also have a longer circulation than in healthy tissues, because the interstitial pressure in the tumor centers is higher than in the periphery[20], which can engulf the already existing blood vessels or attract new ones. ; such Because of these newly formed leaky vessels, selectively enhanced penetration of nanosystems and macromolecules larger than 40 kDa into the tumor stroma is possible.(3) We consider the accumulation of active pharmaceutical ingredients (API) at the destination, especially in leaky vessels. for passive targeting. Drugs that penetrate the tumor and the interstitium also have a longer circulation time than in healthy tissues because the interstitial pressure in tumor centers is higher than in the periphery.[20]]

1. **Dual targeting -**

When spatial and spatial methods are combined to achieve a delivery system, which is called dual focus, the spatial localization follows the drug to an organ, tissue, intracellular or subcellular compartment, and the administration is physically focused on the target. of drugs interest.[21]

2. DOUBLE TARGETING –

To have transportation systems that combine spatial and spatial methods, the goal can be said to be twofold. Spatial regulation is appropriate for drugs that target specific organs, tissues, cells, or subunits. On-time delivery refers to immediate delivery. of targeted therapies.

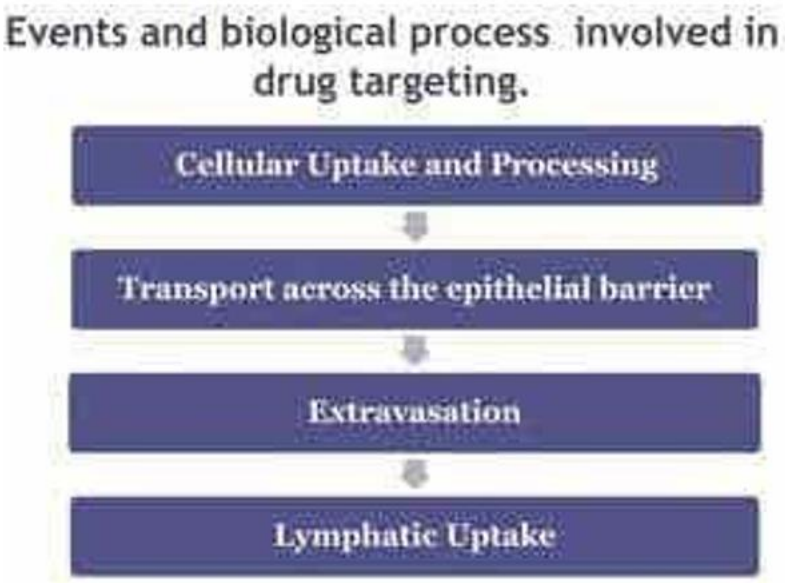
3. INVERSE TARGETING –

The purpose of retrograde absorption is to prevent free absorption of the drug delivery device by the reticuloendothelial organ. (RES). This can be done by mimicking the installation characteristics of new renewable energy sources by injecting them in large quantities. White drug delivery devices or large dextral sulfate molecules are used to fill the RES and block the identification process. Reversal of drugs in non-RES organs is very effective. Balthazar and Fung used methotrexate reversal in peritoneal tumors.The purpose of retrograde absorption is to prevent free absorption of the drug delivery device by the reticuloendothelial organ. (RES). This can be done by mimicking the installation characteristics of new renewable energy sources by injecting them in large quantities. White drug delivery devices or large dextral sulfate molecules are used to fill the RES and block the identification process. Reversal of drugs in non-RES organs is very effective. Balthazar and Fung used methotrexate reversal in peritoneal tumors.

1. COMBINATION TARGETING –

Web-based scaffold systems for the targeted delivery of proteins and peptides are available as scaffolds, polymers, and molecularly specific scaffolds. For example, modification of proteins and peptides with natural polymers, polysaccharides, or synthetic polymers can change their physical properties, which is important for organ or tissue-specific targeting..[3]

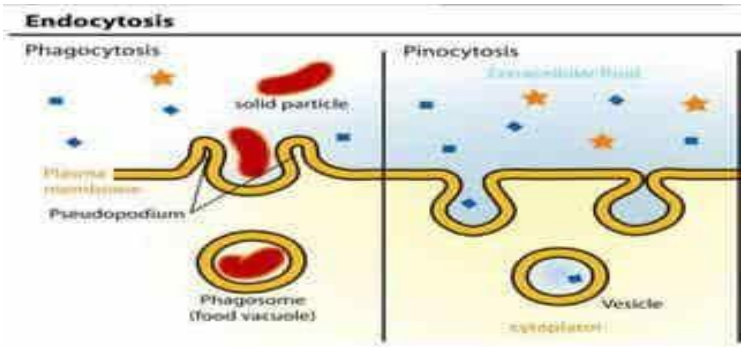
BIOLOGICAL PROCESS INVOLVED IN DRUG TARGETING



A.) cellular uptake and processing –

Therefore, macromolecular aggregates cannot enter by this simple process, so they adopt this process called endocytosis. Collecting and processing cells is a two-step process.

- Integration of the plasma membrane;
- Occurs simultaneously with the removal of external material. Pinocytosis is a more common phenomenon compared to phagocytosis. Liquid pinocytosis. Capture molecules are very slow and precise in phagocytosis. It's like concentration. [22]



A.) Transport across the epithelial barriers –

This is the removal of secondary cells, which require molecules to cross the body's epithelial barrier. Most of this layer is found in cavities such as the sinuses, mouth, throat, rectum, and nasal cavity. Biologically, there are three layers: the epithelial layer, the lamina propria, and the basal lamina. While molecules of low mass enter epithelial cells through diffusion mechanisms, larger molecules, drug carriers or macromolecules are transported by endocytosis. -The properties of the different molecules affect their transport through the epithelial barrier.

- The polar nature of the molecule makes it easier to cross the epithelial barrier through tight junctions than non-polar molecules. Epithelial cells.

- Positively charged molecules can cross the epithelial barrier more often than molecules that diffuse. epithelial cells [11].

2.) c.) Extravasation –

Many diseases stem from cellular failure outside the cardiovascular system, so drugs must pass through the central circulation to be therapeutically effective. The exchange in the blood vessels is called extravasation, which is determined by the walls of the blood capillaries. [23].

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4.) D.) Lymphatic absorption

As part of targeted therapy.

Use to develop or improve treatment methods; also to improve mucosal immunity or oral absorption macromolecular drugs[24].

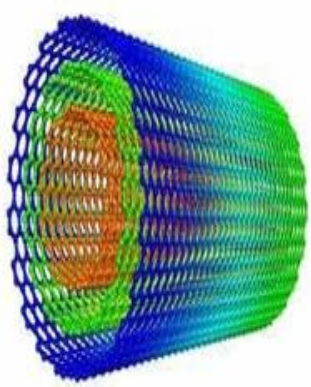
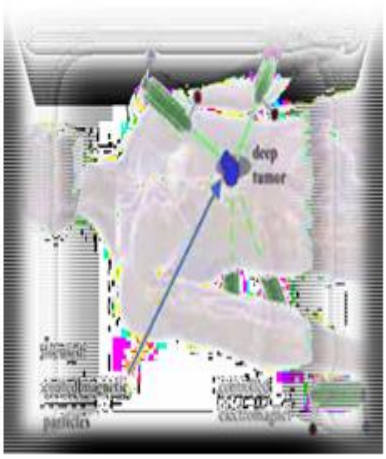
5.) Quantum dots:-

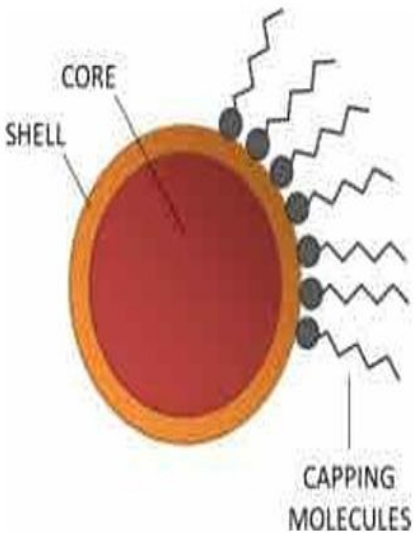
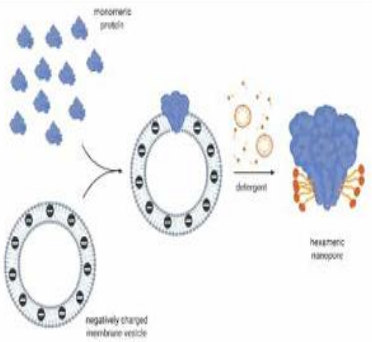
Quantum dots are semiconductor nanostructures that confine the movement of conduction band electrons, valence band holes, or abstraction (pairs of bonded electrons and valence band holes) in three spatial directions. Adhesion can occur due to electrical effects, the possible interface between different semiconductors (e.g., core-shell nanocrystal systems), the presence of a semiconductor surface (e.g., nanocrystals), or a combination of these. Quantum dots are of particular interest in optical applications due to their high theoretical performance. The size of genomes can be miniaturized for many applications, making them one of the most promising candidates for computational synthesis and analysis, drug delivery, and tissue engineering. , catalysis, analysis and fiber technology..[25]

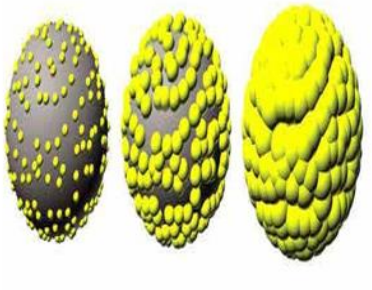
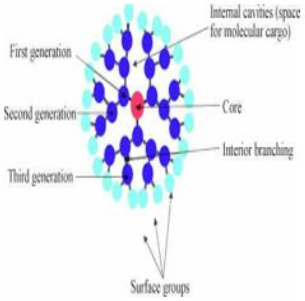
6.) GOLD NANO PARTICLES:-

Gold has been utilized for restorative purposes since antiquated times, particularly in India and China, where it was related with life span and richness. It is still utilized in a few Ayurvedic arrangements in India. Gold nanoparticles comprise of a gold-containing center encompassed by a defensive external layer of natural ligands. Between metal nanoparticles have been appeared to be secure and less harmful operators and have especially great optical, plasmonic and attractive properties and huge surface range Gold has been utilized for restorative purposes since antiquated times, particularly in India and China, where it was related with life span and richness. It is still utilized in a few Ayurvedic arrangements in India. Gold nanoparticles comprise of a gold-containing center encompassed by a defensive external layer of natural ligands. Between metal nanoparticles have been appeared to be secure and less harmful operators and have especially great optical, plasmonic and attractive properties and huge surface range.[26]

Table 1 :- Nanoparticles and their Applications

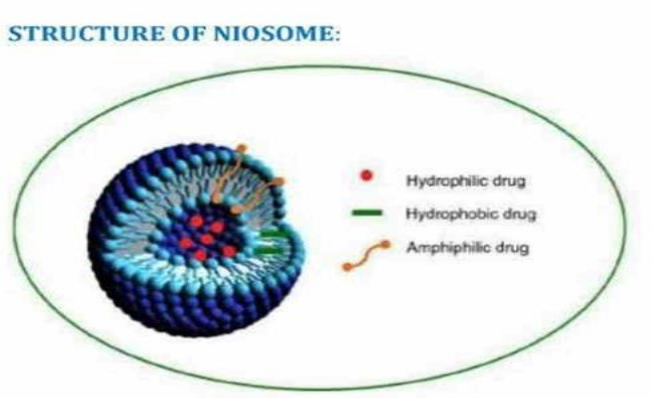
S.no	Nanocarriers	Description	Image structure	Appliction
1.	**Nanotubes**	Nano tubes are carbon molecules within the shape of empty barrels that can be filled and fixed to hold conceivable drugs delivery.		Cellular scale neddle for connecting sedate atom to cancer cells.As an cathode in thermo cells .
2.	**Nanowires**	These tiny devices can identify tumours and other abnormalities in the brain, localise the source of seizures, and pinpoint damage from stroke and injury.		Procedure has potential as a treatment for parkinson`s and comparative diseases.
3.	**Nanoshell`s**	Gold-coated empty silica circles are known as nanoshells. By including antibodies to their surfaces, researchers can make the shells particularly target		Technique has potential for targeting cancerous drug.

		other shells, like cancer cells.		
4.	**Quantum dots**	Small semiconductor particles called quantum dots can act as markers for specific kinds of molecules or cells throughout the body.		Technique has potential for targeting cancerous drug.
5.	**Nano pores**	These are microscopic holes that are engineered into particles, letting DNA molecules to pass through them one strand at a time. This allows for incredibly accurateand effective DNA s equencing.		Potential in hereditary building and biotechnology..

6.	**Goldnano particles**	exceedingly delicate location procedure for DNA and protein markers connected to a assortment of cancer sorts, counting breast and prostate cancer, has been created by researchers utilizing gold nanoparticles.		In cancer treatment and hereditary engineering..
7.	**Dendrimers**	Dendrimers are finely characterized, manufactured nanoparticles with a breadth of approximately 510 nm. They comprise of polymer layers encompassing a control center. There are various areas on the dendrimer surface where medicines		In quality transfection, therapeutic imaging
		may be connected.		

1.) NIOSOMES:

Niosomes and drugs are formed in the endoplasmic reticulum. Vesicles are a bilayer structure consisting of an amphiphilic phase connected by a belt and an anhydrous nonionic surfactant phase, hence the name niosome. Niosomes are very small and small in size. Niosomes contain nonionic compounds, a moisturizing environment, and lipids, including cholesterol. The strength of the belt system depends entirely on its components. It is also important to understand the basic components of niosomes before working with them because there is an overview of the construction of niosomes and encapsulated drugs.[27,28]



1.) LIPOSOMES :

Liposomes are drug delivery systems composed of phospholipids and lipids. A two-layer membrane forms in the water system. It is widely used as a drug delivery system to improve solubility, hydrophilic or hydrophobic properties. Medicines contained in liposomes are protected. Enzymatic digestion, the chemical promotes recovery by weakening the immune response and rapid emptying of plasma. Our work is expanding. Because the drug is contained in a liposome, it is small. Living in healthy tissues has few negative side effects.[29,30]

THERAPEUTIC APPLICATION:

1.) **CANCER TREATMENT**

Targeted drug delivery is extensively utilised in oncology to specifically target cancer cells, minimizing the damage to healthy tissue.[31]

2.) Neurological disorders

Targeted delivery to the central nervous system (CNS) aids in treating condition like Alzheimer's and Parkinson's diseases.[32]

3.) INFLAMMATORY DISEASES

Targeted delivery help manage inflammatory conditions such as rheumatoid arthritis and inflammatory bowel diseases[33]

4.) CARDIOVASCULAR DISORDER

The targeted drug delivery system can be used to treat cardiovascular diseases, including atherosclerosis [34]

CONCLUSION

Finally, advances in drug delivery systems have greatly improved the accuracy of drug administration. These innovations offer great ways to reduce side effects, increase drug effectiveness, and improve patient outcomes. From nanotechnology to bio-responsive materials, the growing landscape of drug delivery is playing an important role in changing therapeutic approaches in various medical domains. As research continues to uncover new opportunities, the incorporation of these technologies into clinical practice will usher in a new era of personalized and effective medicine. Medical applications for targeted drug delivery span a variety of therapeutic areas, from oncology to autoimmune diseases. The ability to deliver drugs to specific cells or tissues not only improves treatment efficacy but also opens up the possibility of new treatment strategies. As the field progresses, addressing issues such as scalability and regulatory considerations will be critical to the widespread deployment of these systems. In the coming years, the intersection of technology and medicine will provide many ways to tailor treatments to the needs of individual patients, representing a paradigm shift toward more precise and targeted medical interventions.

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11. 1 Gita Chaurasia, 2 Swati kale, 3Payal Pansare 1Associate professor, Siddhant college of Pharmacy, Sudumbare, Pune, India 2,3Assistant professor, Siddhant college of Pharmacy, Sudumbare, Pune, IndiaA REVIEW ON EMERGING TRENDS IN TARGETED DRUG DELIVERY SYSTEMS: EVENTS, APPROACHES AND SPECIFIC DRUG TARGETING© 2022 JETIR August 2022, Volume 9, Issue 8 (ISSN-2349-5162)
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