REVIEW ARTICLE

Smart Drug Delivery Systems: A New Era in Targeted Therapy

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Abstract

The world of drug delivery is undergoing a profound transformation. Nowadays, conventional drug delivery systems (DDS) are not mostly used due to their side effects and limited benefits. We have already entered the era of smart DDS (SDDS) which is an innovative wave of therapy that delivers medications precisely where and when required and always in right amounts. The heart of these systems is nanocarriers. These are microscopic transporters engineered to protect and deliver drugs with pinpoint accuracy. These tiny vehicles come in various forms such as liposomes, nanoparticles, quantum dots, dendrimers, carbon nanotubes, and superparamagnetic iron-oxide nanoparticles each offering unique advantages. This controlled delivery shines especially in areas such as cancer and gene therapy, where precision can make the difference between success and setbacks. This review focuses on the design and preparation of the nanocarriers and explore their real-world applications, from targeted tumor treatment to customized gene delivery. It helps in overcoming long-standing limitations posed by conventional drug delivery, SDDS are paving the way for treatments that are not just more effective, but also safer and more personalized. This article also gives information regarding the available marketed products of the nanocarriers along with their manufacturer's details and also the brand names. With smarter, more responsive systems, the future of disease management looks brighter than ever; bringing us closer to therapies tailored to each individual's unique needs.

Key words: Smart Drug Delivery Systems, Nanocarriers, Nanospheres, Liposomes, Quantum dots, Carbon nanotubes, dendrimers.

INTRODUCTION

Drug delivery addresses the techniques, compositions, mechanizations, and systems employed to circulate medications throughout the body, when necessary, to produce the intended therapeutic effects in a safe and effective manner.[1] Conventional drug delivery systems (DDS) frequently cause systemic side effects, mostly due to their unpredictable drug release properties and imprecise bio-distribution. To get past these drawbacks, smart DDS (SDDS) have been designed in such a way that they allow the formulation to be released at the intended locations in a controlled and coordinated manner.[2] SDDS is a type of DDS that can autonomously send signals, react, distribute the drug, and also cease the distribution of the drug.[3] The regulative signals of SDDS include external signals (light of varied wavelengths, magnetic fields, electric fields, ultrasound, etc.).[4-7] as well as certain internal signals (redox, pH, enzymatic activity, and concentration).[8-11] The primary goal of SDDS is to successfully deliver medication to the targeted location with an accurate dosage, efficiency, and specificity at the required time in a pre-determined manner, allowing patients to adhere to the treatment in a more effective way.[12] SDDS is built on the foundation of nanocarrier technology. However, not every kind of nanocarrier can be relied on to deliver medications in SDDS. A nanocarrier must fulfill a few fundamental requirements to be considered an ideal nanocarrier in SDDS, primarily smart nanocarriers should stay away from the immune system's

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cleansing procedure [Figure 1]. Second, they should only be gathered at the specified location. Third, whether stimulated internally or externally, the smart nanocarrier should release the drug at the targeted site and concentration. Last but not the least, they ought to co-deliver chemotherapeutics along with other components including genetic materials and imaging agents.[2,13-15] Certain nanocarriers, such as liposomes, nanospheres, quantum dots (QDs), dendrimers, carbon nanotubes (CNTs), and superparamagnetic iron-oxide nanoparticles, are used in SDDS.[16,17]

NANOCARRIERS USED IN SDDS

Liposomes

The most widely used and well-studied nanocarriers are liposomes, which are synthetic phospholipid vesicles that range in size from 50 to 1,000 nm and larger, and may contain a certain number of medications.[18] Liposomes are increasingly acknowledged as a possible model for "smart" delivery systems due to their advanced development. Over the past 30 years, liposomes have garnered a lot of interest as promising pharmaceutical carriers due to their advantageous qualities, which include biocompatibility, biodegradability, low toxicity, and immunogenicity.[19] Recently, "smart" liposomes have been designed to produce site-specific release of the medications. Stimuli-sensitive liposomes are a type of smart liposomes that are designed in such a way that they release the medication in response to the physicochemical stimuli such as pH or redox potential.[18] One of the limitation associated with liposomes is stability. Stability is the main concern for liposomes medication, storehouse, and the way of administration. Some of the marketed products are listed below in Table 1.

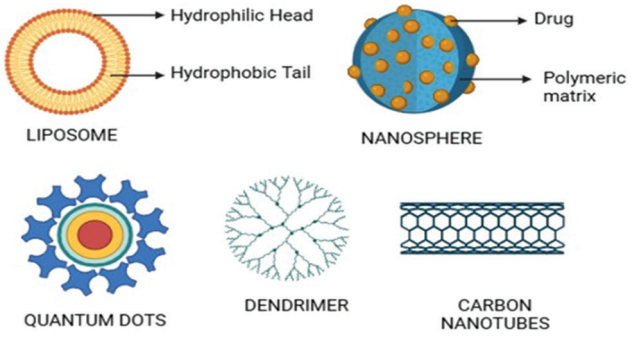

Figure 1: Various types of nanocarriers and nanoparticles used in smart drug delivery systems

pH-sensitive liposomes

These are the kinds of liposomes that react to the fluctuations in pH.[20-22] It is now commonly known that, in comparison to normal tissues, tumors, infarcts, and inflammatory areas have a mild acidity.[23] In certain situations, this characteristic can be used to alter the behavior of a medication or gene delivery system.[18]

Redox potential-sensitive liposomes

The large redox potential difference between the mop up intracellular space and oxidize extracellular space can also be applied in the fabrication of stimuli-responsive liposomes.[24] The redox sensitive liposome formulation employed in the intracellular environment are disulfide bonds ,which will get destabilized when glutathione releases its contents. Redox-responsive liposomes can also be prepared from the regular phospholipids and a little lipid with head and tail connected by a disulfide bond.[25]

Temperature-sensitive liposomes

Yatvin, *et al.* introduced the temperature-sensitive liposomes formation by implying that they could form liposomes that are stable at normal body temperature and could become leaky at higher temperature.[26] Temperature-sensitive liposomes come in different types: Liposomes are made up of temperature-sensitive lipids and liposomes that may contain temperature-sensitive lipids or may not but modified on their surfaces using temperature-sensitive polymers.[18]

Magnetically-sensitive liposomes

The term "magneto liposomes" refers to liposomes that have either magnetized polymers integrated into their lipid bilayer[27] or magnetic materials integrated into their aqueous core.[24,28] By exposing these liposomes to a magnetic field, medicinal chemicals can be directed to a particular location.[18]

Preparation of liposomes

Methods employed for the preparation of giant uni-lamellar vesicles (GUVs)

Hydration of a phospholipid film

In this method, the phospholipids are dissolved in an organic solvent either chloroform or ethanol. The prepared

Table 1: Summary of liposomal products approved by FDA and EMA

S. No.	Product name	Active pharmaceutical ingredient	Uses	References
1.	Doxil®	Doxorubicin	Ovarian, breast cancer, and Kaposi's sarcoma	[46]
2.	Arikayce®	Amikacin	Lung infections	[47]
3.	Epaxal®	Inactivated hepatitis A virus	Hepatitis A	[48]
4.	DepoDur®	Morphine Sulfate	Pain Management	[49]

solution is then deposited onto a suitable substrate, such as glass slide or Teflon surface, using techniques such as spin-coating or solvent evaporation. As the solvent evaporates, it leaves behind a thin film of phospholipids. The deposited phospholipids spontaneously organize into stacked bilayers due to their amphiphilic nature, where the hydrophilic heads face outward, and the hydrophobic tails face inward. Then, the hydration of film is done. In this process of hydration, an aqueous solution is carefully added over several days. This is not a rushed process, there is no stirring or shaking involved. Instead, everything happens slowly and gently, which is important because it keeps the delicate vesicle structures from being disrupted by harsh forces. As the water seeps in, the bilayers gradually soak it up, causing them to swell. Over time, this gentle hydration encourages the bilayers to curl up and form vesicles. Because the process is so calm and controlled, it favors the formation of GUVs. These GUVs are not only larger but also more stable than the smaller, multilamellar vesicles (MLVs) that might form if the process was rushed or agitated.[29-31]

Electro-formation method

In this process, first phospholipids are mixed with an organic solvent to make a phospholipid solution. The formed phospholipid solution is applied on both the electrodes and is allowed to dry. After it is dried, it forms a thin film of phospholipids on each electrode. Now, the electrodes with the phospholipid film are placed in an aqueous solution, and an electric field is applied. The hydration process lasts a few hours, during which the electric field facilitates the formation of vesicles.[32] Both alternating current (AC) and direct current (DC) can be used for the preparation of GUVs. However, the AC fields are generally more preferred as the DC fields cause electrolysis of water, which can lead to gas bubble formation.[32,33] The application of AC fields causes the swelling of the phospholipid film eventually leading to the formation of vesicles. The gentle nature of the process, combined with the electric field, helps to ensure that a significant fraction of the resulting vesicles is unilamellar and free from defects.[34]

Coalescence of small vesicles to form GUVs

Coalescence is an alternative method for producing GUVs by allowing small unilamellar vesicles or large unilamellar vesicles (LUVs) to merge overtime. First, in this method, the small vesicles are stored in suspension for several days, allowing spontaneous coalescence to occur. In addition to spontaneous coalescence, several methods can be employed to induce the fusion of LUVs, leading to the formation of GUVs. The various methods include, freeze-thaw cycles (disrupts lipid bilayer membranes, promoting fusion on thawing),[35] oppositely charged phospholipids (encourages fusion through electrostatic attraction),[36] polyethylene glycol (PEG) (a fusogen that promotes membrane merging),[36] fusogenic peptides (peptides that destabilize membranes to induce fusion),[37] and divalent cations (neutralize negative charges on lipids, reducing repulsion).[38]

Methods employed for the preparation of MLVs

Hydration of a phospholipid film under hydrodynamic flow

The hydration of a phospholipid film under hydrodynamic flow is a method used to produce MLVs from a dry phospholipid film of stacked bilayers. This technique leverages the application of strong hydrodynamic forces to facilitate the rehydration process for several hours,[39] resulting in the formation of vesicles with varying sizes and lamellarity.[31]

Solvent spherule method for the formation of MLVs

The solvent spherule method is an innovative technique for creating MLVs. It all begins with phospholipids, which are dissolved in an organic solvent. This solution is then mixed vigorously with water, forming a milky oil-in-water emulsion. From there, the solvent is gently allowed to evaporate. As it fades away, the tiny droplets are formed which start to come together and organize themselves into MLVs. These vesicles are made up of several layers of lipid bilayers which are stacked upon each other. One of the biggest benefits of this method is that it produces MLVs with a very consistent size. That uniformity really matters, it helps ensure the vesicles behave predictably inside the body, which is crucial for applications like drug delivery. Finally this method leads to the formation of a batch of stable lipid based carriers which not only protects the therapeutic agent inside it , but also guides it precisely to the required target place.[40,41]

Hydration of proliposomes

Proliposomes are a smart and efficient way to make sure drugs are delivered safely and effectively. They start out as tiny, dry, free-flowing granules, almost like a fine powder. Inside each little granule is a blended mix of phospholipids and the drug that needs to be delivered. The real magic happens when these proliposomes meets water. As soon as they are mixed into an aqueous environment, they spring to life forming MLVs, with layers of lipid bilayers ready to carry the drug to its target.

To make proliposomes, the phospholipids and drug are first dissolved together in an organic solvent. This solution is then dried using techniques such as rotary vacuum evaporation,[42] fluidized bed drying,[43] or spray drying.[44,45] The end result is a tiny, stable particle with the drug at the center, wrapped in a protective shell of phospholipids.

These drying methods are crucial as they help keep the phospholipids in a stable form that's ready to go when needed. Hence, when it is time for the proliposomes to do their job, all it takes is a little water to trigger the formation of vesicles. It is a clever, reliable way to ensure therapeutic agents reach exactly where they are needed, safely, and efficiently.[31]

Nanoparticles

Nanospheres

Nanospheres are incredibly tiny, ball-shaped particles made from polymers. They typically range from 10 to 200 nm in size.[43] These nanospheres are gaining a lot of attention in the world of drug delivery because they can carry medication evenly throughout their solid structure, acting like miniature delivery vehicles. This unique design helps the drug dissolve more efficiently, maintains stability for longer durations, and avoids breakdown too quickly by the body's enzymes or chemicals.[44,45]

There are two main kinds of nanospheres, they are; biodegradable and non-biodegradable nanospheres. The biodegradable ones are made from natural materials such as gelatin or albumin and are especially useful because they safely breakdown inside the body. As they degrade, they gradually release the drug in a controlled, steady way, all while ensuring the carrier itself does not stick around and cause problems.[46,47]

One of the biggest advantages of nanospheres is their versatility. They can be delivered in different ways such as by pill, injection, or even targeted delivery to specific organs or tissues. That means the drug can be sent exactly where it's needed, helping it work more effectively while reducing side effects in other parts of the body.[48] Nanospheres also open the doors to improving existing medications. By reformulating a drug inside these tiny carriers, pharmaceutical companies can extend the drug's usefulness, refresh its patent, and develop more innovative treatment options. This benefits patients by offering better, and more personalized therapies. In a nutshell, nanospheres are one of the cutting edge tools in modern medicine, making treatments safer, smarter, and more efficient than ever before.[49] This system has certain disadvantages like their huge surface region per unit mass may lead to an expanded natural reactivity that upgrades any inborn poison quality. Nanoparticles of TiO2 have been appeared to actuate a much more pulmonary reaction than bigger particles of the same chemical substance at proportionate mass measurements.

Preparation of nanospheres

Polymerization method

This process begins by making an emulsion, a mixture where tiny droplets of monomers, like methyl methacrylate, are evenly scattered throughout water. To keep these little droplets from clumping together, surfactants are added. These help in maintain the stability of emulsion. Once the emulsion is stable, polymerization begins. This is the step where the monomers inside each droplet start linking up to form solid particle, or nanospheres. This chain reaction can be triggered in a few ways; by heating, using ultraviolet light, or adding special chemicals called initiators. After the nanospheres have formed, it is time to load them with drug. This can be done in a couple of ways; either by letting the drug attach to the surface (a process called adsorption), or by dissolving the drug in water so it gets drawn inside the nanospheres. Further the formed nanospheres are carefully purified to remove any leftover materials, and then freeze-dried to create a fine, stable powder. This powder is easy to store, transport, and use later when it's time to deliver the medicine.[50]

Desolvation technique

A polymeric solution is prepared using a natural polymer, such as albumin, and a solvent like PEG. The drug intended for encapsulation is dissolved in an organic solvent, typically ethanol. Then, the organic phase is added dropwise to the polymeric solution under continuous magnetic stirring. After this, a cross-linking agent is introduced to the mixture, it continues for about 12 h, allowing sufficient time for the cross-linking reaction to occur and nanospheres to stabilize. Then, the formed and stabilized nanospheres are subjected to centrifugation and lyophilization.[51,52]

Solvent evaporation method

This process begins with the dissolution of a polymer such as polymethyl methacrylate or other suitable organic solvent like dichloromethane, or acetone. The polymer solution is then sonicated for about 2 min. Further, the drug is dispersed in the polymer solution. This can be done by adding the drug directly to the solution and sonicating again for another 2 min. Then, the drug-polymer mixture is emulsified using a suitable emulsifying agent. The formed emulsion is further subjected to solvent evaporation leading to the formation of nanospheres, which are then purified and lyophilized.[46,53]

Salting out method

In this method, firstly, the polymer is dissolved in the organic phase. Moreover, the aqueous phase is then prepared that contains a suitable emulsifier. Further, the organic phase is added to the aqueous phase under mechanical shear which leads to the formation of droplets of the organic phase dispersed in the aqueous phase. Then, pure water is gradually added to the emulsion under mild stirring, this leads to the precipitation of polymers causing the formation of nanospheres. Further, the former nanospheres are purified and subjected to lyophilization to form stable powder.[53]

Ionic gelation method

This method is also known as coacervation method. It is a widely used technique for the preparation of polymeric nanospheres, particularly utilizing natural polymers such as sodium alginate and gelatin. This method is advantageous for drug delivery applications due to its ability to encapsulate therapeutic agents effectively while maintaining biocompatibility.[54,55]

QDs

QDs are nanoscale semiconductor particles that exhibit unique optical properties due to their size and quantum effects, making them highly suitable for various biomedical applications, particularly in drug delivery and cellular imaging.[56] These are tiny, glowing particles made from elements typically found in group II and VI of the periodic table, such as cadmium sulfide, cadmium telluride, and zinc sulfide (ZnS).[56,57] At their core, these nanoparticles usually have a small semiconductor center such as cadmium selenide ranging from just 2–10 nm in size. This core is then surrounded by a shell made of another semiconductor, like ZnS, and wrapped in a protective outer layer made of various materials to keep them stable and functional.[57]

What really makes QDs stand out is their bright and stable fluorescence. They can emit light in the near-infrared (NIR) range (above 650 nm), which is especially useful for biological imaging since this type of light can penetrate deeper into tissues. Even better, their optical properties such as color and brightness can be precisely adjusted by tweaking their size or composition. This makes them far more versatile and reliable than traditional organic dyes used in imaging. In biomedical applications, QDs can be used for real-tie monitoring of drug delivery and tumor visualization; for instance, QDs labeled cells can be tracked in living organisms using techniques like multiphoton microscopy. In addition, their high sensitivity and resistance to photobleaching make QDs ideal for developing advanced biosensors for cancer imaging and diagnosis.[16,56,57]

However, the use of heavy metals (e.g., Cd and Hg) in QDs raises concerns about toxicity, which can be mitigated by functionalizing the QD surface with biocompatible molecules. Furthermore, QDs can experience nonspecific uptake by the reticuloendothelial cells, but this can be addressed through PEGylation, allowing QDs to accumulate in tumor sites through the enhanced permeability and retention effect.[58] To enhance targeting capabilities, QDs can be modified with various ligands, such as peptides, folate, and monoclonal antibodies, facilitating active targeting of tumor sites. This combination of sensing, imaging, and therapy in a single platform, known as nanotheranostics, is a growing area of interest that leverages the unique properties of QDs.[59] Certain commercially available QDs are listed below in Table 2. Overall, QDs represent a promising class of nanocarriers in the biomedical field, with ongoing research focused on addressing their toxicity and enhancing their targeting capabilities to improve safety and efficacy in clinical applications.[16]

Synthesis of QDs

Bottom-up approach

This approach involves the self-assembly processes in solution through chemical reduction.[56,57]

Top-down approach

This approach utilizes sophisticated techniques such as molecular beam epitaxy, ion implantation, electron-beam lithography, or X-ray lithography for the synthesis of QDs.[56,57]

Dendrimers

Dendrimers are truly remarkable nanoparticles, tiny, and tree-like structures built with incredible precision. They can be defined as molecular trees, with branches made of polymers radiating out from a central core. Each layer of these branches represents a new "generation," and with every generation, the structure becomes more intricate.[60,61]

Dendrimers are considered to be so special because the scientists can control their size, shape, and surface chemistry down to the finest detail. This precise control leads to highly uniform nanostructures, which is crucial for many advanced applications. One of the most exciting things about dendrimers is their versatile surface. They can be tailored to carry different chemical groups, opening up a whole world of possibilities from acting as targeting agents in medicine to serving as imaging tools or affinity ligands in diagnostic and research. In drug delivery, dendrimers have shown incredible promise, particularly in gene therapy. Their unique architecture allows them to effectively transport genetic material into cells; a crucial step in therapies that aim to correct genetic disorders. Delivering the right genetic information to the right cells can dramatically improve treatment outcomes.[62-64]

The behavior of dendrimers in solution depends on a variety of factors such as the generation (or size), the length of their connecting segments, any chemical modifications made to their surface, and environmental factors such as pH and

Table 2: List of QDs and their developers

S. No.	QD developers (company)	QD	Uses	References
1.	Nanoco™	Vivodots®	Intraoperative mapping of tumorous tissues	[84]
2.	Nanoco™	HeatWave™	Non-invasive qualification of biomolecules in human blood	[84]
3.	QD Laser™	Visirium®	Helps with visual disorders	[84]
4.	NNCrystal US corporation	NN-Labs®	Cellular imaging, *in vivo* imaging, and as probes for molecular labelling	[84]

QDs: Quantum dots

temperature.[65,66] One key feature is their surface charge, which plays a major role in how they interact with drugs. Dendrimers can increase the solubility and bioavailability of water-insoluble (hydrophobic) drugs, either by trapping them inside their internal cavities or attaching them to their surface. To understand the behavior of dendrimers in these environments, researchers often rely on techniques like small-angle scattering, which helps them analyze the structure and dynamics of these nanomaterials in solution.[66-68]

A particularly exciting area of research is the combination of dendrimers with biologically active molecules like sugars (saccharides) or peptides. These hybrid structures, that is, dendrimer conjugates are being explored for their potential to create new types of antimicrobial, antiviral, and even antiprion agents. They can also help improve solubility and stability of drugs, making treatments more effective and longer-lasting.[69]

Another fascinating aspect of dendrimers is their interaction with cell membranes. Depending on their chemical composition, size, and surface charge, dendrimers can behave in various ways like; they might stick to a membrane, create pores in it, or even disrupt it entirely. These behaviors depend on a delicate balance of forces such as the electrostatic pull between charged dendrimers and membrane lipids, and the hydrophobic interactions between dendrimer arm and lipid tails. The chemical groups on the dendrimer's surface can also be customized with targeting molecules such as folic acid or antibodies. This allows scientists to direct dendrimers to specific tissues or disease sites, which is especially valuable in cancer therapy.[69-72]

All in all dendrimers are emerging as powerful tools in medicine and biotechnology. They can form complexes with nucleic acids, under physiological conditions, these complexes, known as dendriplexes, maintain a positive charge and can bind to negatively charged molecules on cell membranes. Once inside the cells, dendrimers are taken up through a process called nonspecific endocytosis and are eventually broken down by lysosomes. This process releases the targeting genes, allowing them to enter the nucleus and perform their therapeutic functions.[73,74] Some of the commercially available dendrimers are given below in Table 3.

While dendrimers hold great promises for targeted drug delivery and improving the efficacy of treatments, more research is needed to fully understand the complex relationships between their structures and functions. As scientists continue to explore the potential of dendrimers, we may see significant advancements in modern medicine, particularly in the fields of pharmaceutics and nanomedicine. Their unique structure and adaptability make them ideal carriers for drugs and genes, opening up new avenues for innovative therapies that have the potential to transform lives.[16] Dendrimers will result in non-reducible pharmacokinetic behavior that is observed in multifunctional dendrimers synthesized through the random-statistical approach that leads to a mixture of products which may be the major limitation of the system.

CNTs

CNTs are an exciting and powerful class of nanomaterials that have captivated scientists for their unique structure and impressive capabilities. Part of the fullerene family, CNTs are essentially rolled-up sheets of graphene that form tiny, tube-like cylinders, as illustrated in [Figure 1]. This needle-like shape gives them a special advantage that is they can easily enter the cells through a natural process called endocytosis, which makes the ideal for delivering drugs directly into cells.[75,76] There are two main types of CNTs. Single-walled CNTs are very slim, with diameters between 0.4 and 2 nm. Multi-walled CNTs, on the other hand, are made of multiple layers and are slightly thicker, ranging from 2 to 100 nm in diameter.[75,77]

Despite their small width, CNTs can be extremely long relative to their size. Their length-to-diameter ratio often exceeds 200, which contributes to their exceptional strength and flexibility. One of the standout features of CNTs is their large surface area, which allows them to interact efficiently with biological environments. They are also known for their excellent electrical conductivity and mechanical strength, making them useful not only in medicine but also in electronics and materials science.[75,77]

In the medical world, CNTs have shown great potential, especially in cancer treatment. They can carry drugs either by trapping them inside their hollow cores or by adsorbing them to their surfaces using certain chemical bonds such as covalent or non-covalent bonds. This makes them incredibly versatile drug carriers. Some of the key anti-cancer drugs successfully delivered using CNTs include doxorubicin, methotrexate, paclitaxel, and cisplatin; all are known for

Table 3: Some examples of commercially available dendrimers

S. No.	Dendrimers	Type of dendrimers	Applications	References
1.	Dendris	Phosphorous	Molecular diagnosis	[85]
2.	3DNA®	DNA	Drug delivery	[85]
3.	VivaGel®	Poly (amidoamine)	Condom lubricant	[85]
4.	Polyfect®	Poly (amidoamine)	Transfection reagent	[85]

their effectiveness against various types of cancers.[76,78,79] However, CNTs are not just about delivering drugs; they are also making waves in cancer diagnostics. When modified or "functionalized," CNTs can help detect cancer at very early stages. They absorb light strongly in the NIR region, which is a valuable property in a treatment called photothermal therapy. In this approach, CNTs absorb NIR light and convert it into heat, selectively targeting and destroying cancer cells without harming nearby healthy tissues.[76]

In summary, CNTs are more than just microscopic tubes; they are powerful tools in the fight against cancer. Their ability to carry drugs, assist in diagnosis, and even destroy tumors with heat gives them a unique edge in modern medicine. With ongoing research and development, CNTs are paving the way toward more targeted, efficient, and less invasive treatments for cancer and other serious diseases.[16] The researchers are still not able to completely know how these CNTs work in spite of the broad investigation. They are difficult to handle, control and are costly.

Superparamagnetic iron-oxide nanoparticles (SPIONs)

SPIONs are tiny particles made from iron oxides like magnetite (Fe_3O_4), and maghemite (Fe_2O_3). Recently, these nanoparticles have captured the imagination of scientists and doctors alike, especially for their potential in targeted drug delivery using magnetic forces to guide medicines exactly where they are needed.[80-82] When these nanoparticles are shrunken down to just 10–20 nm (that's thousands of times smaller than a human hair!), they become "superparamagnetic." In simple terms, this means they act like tiny magnets only when a magnetic field is present, and lose their magnetism as soon as the field is removed. This property is incredibly useful in medicine, because it allows for precise control without leaving any lingering magnetic effects in the body.[16]

Another big advantage of SPIONs is their ability to be "functionalized." Scientists can coat their surfaces with special molecules that prevent them from sticking together or rusting. Even better, these coatings can be designed to carry drugs, or attach to specific targeting molecules such as proteins, antibodies, or peptides. This not only helps the nanoparticles circulate longer in the bloodstream but also ensures they are more likely to reach diseased tissues, like tumors, while avoiding healthy ones.[80]

By applying a strong magnetic field outside the body, doctors can steer SPIONs to accumulate at a specific site, say a tumor.[80,81,83] This targeted approach is further enhanced by modifying the surface of SPIONs to allow them to bind with various proteins, antibodies, peptides, and anti-cancer drugs.[74] For example, if SPIONs are loaded with the anti-cancer drug methotrexate and modified to recognize folate receptors (which are often found on tumor cells), they can target the cancer cells and deliver the medicament right where it is needed most.[83]

However, despite their promising applications in medicine, there are some critical concerns associated with SPIONs. Some studies suggest that SPIONs might affect gene expression, disrupt the body's iron balance, cause oxidative stress, or change how cells behave. These are serious concerns that need to be carefully studied before SPIONs can become a routine part of medical treatment. In summary, SPIONs offer an exciting new way to deliver drugs with pinpoint accuracy, potentially transforming how we treat diseases like cancer. But before these "magnetic messengers" can be widely used in hospitals, researchers must continue to investigate their safety and long-term effects.[80]

CONCLUSION

The emergence and rapid advancement of SDDS are significantly reshaping the landscape of modern therapeutics, particularly in the domain of targeted treatment strategies. By harnessing the capabilities of nanoscale delivery platforms such as liposomes, polymeric and inorganic nanoparticles, QDs, dendrimers, CNTs, and SPIONs, researchers are now able to achieve drug delivery with an unprecedented level of precision and control. This progress translates into improved therapeutic efficacy, reduced systemic toxicity, and better patient outcomes.

A defining characteristic of SDDS is their responsiveness to specific stimuli, whether endogenous (e.g., Ph, temperature, redox potential, or enzymatic activity) or exogenous (e.g., magnetic fields, light, or ultrasound). This stimulus-responsiveness enables spatiotemporal control over drug release, allowing for dynamic, on-demand delivery tailored to the unique pathophysiological conditions of individual patients. Such functionality is especially beneficial in the treatment of complex diseases like cancer, where the therapeutic window is narrow and precise targeting is essential to minimize damage to healthy tissues.

Despite the remarkable progress, several challenges remain. Key areas of ongoing research include enhancing the biocompatibility and biodegradability of nanocarriers, improving the specificity of targeting ligands, overcoming biological barriers, and scaling up manufacturing for clinical translation. In addition, long-term safety assessments are critical, as some nanomaterials may include unintended biological responses, including oxidative stress, immunogenicity, or off-target effects.

Nevertheless, the trajectory of research in this field is promising. As we continue to deepen our understanding of disease biology and material science, SDDS are poised to play a central role in the future of personalized medicine. By

enabling precise, patient-specific therapeutic interventions, these systems hold the potential to transform conventional treatment paradigms, ushering in a new era of highly efficient, minimally invasive, and outcome-driven healthcare.

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