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ADVANCE IN NANOTECHNOLOGY BASED DRUG DELIVERY SYSTEM

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ABSTRACT

Nanomedicine and nano-delivery systems hold unlimited potential in the developing sciences, where nanoscale carriers are employed to efficiently deliver therapeutic drugs at specifically targeted sites in a controlled manner, imparting several advantages concerning improved efficacy and minimizing adverse drug reactions. These nano-delivery systems target-oriented delivery of drugs with precision at several site-specific, with mild toxicity, prolonged circulation time, high solubility, and long retention time in the biological system, which circumvent the problems associated with the conventional delivery approach. Recently, nanocarriers such as dendrimers, liposomes, nanotubes, and nanoparticles have been extensively investigated through structural characteristics, size manipulation, and selective diagnosis through disease imaging molecules, which are very effective and introduce a new paradigm shift in drugs. In this review, the use of nanomedicines in drug delivery has been demonstrated in treating various diseases with significant advances and applications in different fields. In addition, this review discusses the current challenges and future directions for research in these promising fields as well.

KEYWORDS: Biological system; controlled release; drug delivery system; nanocarriers; nanomedicine.

1. INTRODUCTION

Nanotechnology has rapidly changed many areas of science and industry, but its biggest impact has been in medicine and healthcare. One of the most exciting applications of nanotechnology is in drug delivery. The way medicines are delivered inside the body plays a major role in how effective they are. Traditional drug delivery methods, such as taking medicines by mouth or injecting them into the bloodstream, often have serious drawbacks. Many drugs do not dissolve well, break down too quickly inside the body, spread to unwanted areas, or fail to cross important barriers like the blood–brain barrier. Because of this, patients often need higher doses, which not only raises treatment costs but also increases the risk of harmful side effects. Nanotechnology offers new ways to solve these problems by creating tiny carriers—measured in nanometers—that can transport medicines more safely and effectively.

These nanocarriers work at a scale of 1–100 nanometers, where materials behave very differently compared to larger scales. Their special features—such as a very high surface area, the ability to be modified on the surface, and the capacity to carry many different types of drugs—make them ideal for medical use. Scientists have developed many kinds of nanocarriers, including liposomes, polymer-based nanoparticles, dendrimers, solid lipid nanoparticles, metallic nanoparticles like gold and silver, carbon-based structures such as nanotubes and graphene, and nanoemulsions. Each type has its own strengths, such as being biodegradable, biocompatible, or responsive to signals inside the body, which makes them suitable for a wide range of treatments.

One of the greatest advantages of nanotechnology in drug delivery is **targeted therapy**. Unlike conventional medicines that spread throughout the entire body, nanocarriers can be designed to release drugs directly at the diseased site. This is extremely important in conditions like cancer, where chemotherapy drugs can harm healthy tissues. Nanoparticles can target diseased areas in two ways: passively, by naturally accumulating in tumor tissues through the enhanced permeability and retention (EPR) effect, or actively, by attaching molecules such as antibodies or peptides that specifically recognize and bind to diseased cells. This targeted approach increases the effectiveness of treatment and reduces side effects, improving patient safety and comfort.

Another benefit of nanocarriers is their ability to **control the timing and rate of drug release**. Traditional medicines often need to be taken in multiple doses each day, which can be inconvenient for patients and lead to side effects. Nanotechnology makes it possible to design carriers that release medicines slowly and steadily, or in response to triggers such as changes in pH, temperature, or the presence of certain enzymes. For example, nanoparticles that respond to acidic conditions can release drugs only in tumor tissues, which are more acidic than normal tissues. This smart release system ensures that medicines work exactly where they are needed.

In recent years, researchers have also developed **theranostic nanocarriers**, which combine therapy and diagnostics in one system. These smart nanocarriers not only deliver drugs but also allow doctors to track the treatment process in real time using imaging techniques. For example, magnetic nanoparticles can deliver drugs while also being used in MRI scans to monitor how well the medicine is working. This combination marks a huge step forward in personalized medicine, where treatments can be customized for each patient and adjusted as needed.

Nanotechnology has also shown great promise in treating brain diseases, which are among the most difficult to manage. The blood–brain barrier protects the brain from harmful substances but also blocks many useful drugs. Nanocarriers can be specially designed to cross this barrier, either by attaching to receptors that transport them inside or by temporarily opening tight junctions. This makes it possible to deliver drugs for diseases such as Alzheimer's, Parkinson's, brain tumors, and epilepsy—conditions that are very hard to treat with conventional methods.

The future of nanomedicine is moving toward **personalized treatment**. By combining nanotechnology with genomics, proteomics, and even artificial intelligence, scientists are developing therapies tailored to each patient's genetic profile and disease condition. For example, nanoparticles can be designed to release drugs only in response to specific genetic mutations, providing a highly precise form of treatment. This approach has the potential to completely change the way diseases are managed, replacing the "one-size-fits-all" model with customized healthcare solutions.

Of course, there are still challenges. Manufacturing nanoparticles on a large scale, ensuring their long-term safety, reducing their cost, and passing strict regulatory approvals are major hurdles. However, rapid progress in materials science and pharmaceutical technology continues to drive this field forward. Collaboration between scientists, doctors, and policymakers will be crucial to making nanomedicine widely available.

In conclusion, nanotechnology-based drug delivery systems represent a major advancement in modern healthcare. They improve the stability, solubility, targeting, and controlled release of drugs while minimizing harmful side effects. These systems are not only useful in cancer therapy but also hold promise for neurological, cardiovascular, infectious, and metabolic diseases. As research continues, nanomedicine is expected to become a key part of future healthcare, offering safer, more effective, and highly personalized treatments for patients worldwide.

2. Characterization

The main goal of nanoparticle-based drug delivery is to make medicines work better while reducing harmful side effects. To achieve this, scientists carefully adjust the properties of nanoparticles so that they can carry and release drugs effectively.

One important factor is the **surface-to-volume ratio** of nanoparticles. Because nanoparticles are so small, they have a large surface area compared to their volume. This makes it possible to attach more ligands (special molecules that help target specific cells) to their surface. When more ligands are attached, the nanoparticles can find and bind to diseased cells more efficiently. This reduces the amount of drug and nanoparticles needed, which lowers both dosage and toxicity. In other words, patients can receive smaller or fewer doses while still getting the same treatment effect.

Another key design strategy is **surface functionalization**. This means modifying the surface of nanoparticles so they can perform extra functions, such as better drug binding, avoiding detection by the immune system, or delivering drugs only to diseased areas. Functionalization is usually done by attaching molecules (bioconjugation) or letting them stick to the nanoparticle surface naturally. By doing this, the drug is delivered more precisely to the target site, which increases its effectiveness, while the overall amount of drug circulating in the body is reduced, lowering side effects.

The **material composition** of nanoparticles is also very important. For example, **liposome-based nanoparticles**

are made from lipids (fats), which can naturally break down in the body after releasing the drug. This reduces the risk of nanoparticles building up inside tissues and causing long-term toxicity.

In some cases, **metal nanoparticles**, like gold nanoparticles, are used because they have unique optical properties. These properties make them useful for imaging techniques that are less invasive, helping doctors to see what's happening inside the body without major procedures. Gold nanoparticles can also be stimulated with light to produce heat, a process known as **photothermal therapy**. This method can directly kill tumor cells and is being explored as a treatment for certain types of cancer.

3. Platforms

Current nanoparticle drug delivery systems can be cataloged based on their platform composition into several groups: polymeric nanoparticles, inorganic nanoparticles, viral nanoparticles, lipid-based nanoparticles, and nanoparticle albumin-bound (nab) technology. Each family has its unique characteristics.

***Polymeric nanoparticles**

Polymeric nanoparticles are tiny particles made from synthetic polymers, usually ranging in size from **10 to 100 nanometers**. Some commonly used polymers for making these nanoparticles are **polyacrylamide, polyacrylate, and chitosan**. Drugs can be added to these nanoparticles in different ways—either during the polymer formation process or after the particles have already been made. Depending on the chemistry used, the drug may be:

1. Covalently bonded (chemically attached to the polymer)
2. Encapsulated inside a hydrophobic (water-repelling) core, or
3. Bound electrostatically (through charge-based interactions).

To make polymeric nanoparticles, scientists use different techniques such as **microfluidic methods, electrodropping, high-pressure homogenization, and emulsion-based interfacial polymerization**. Each method has its own advantages in terms of controlling particle size, shape, and drug-loading efficiency.

A very important factor in designing these nanoparticles is **biodegradability**. When made from biodegradable polymers, the nanoparticles naturally break down inside the body through hydrolysis (reaction with water). This breakdown process produces harmless and biocompatible byproducts such as **lactic acid and glycolic acid**, which the body can easily process. This makes them safer for long-term use compared to non-degradable materials.

Polymeric nanoparticles can also be created using **self-assembly**, where polymers spontaneously arrange themselves into nanoparticle structures. Another advanced technique is called **Particle Replication in Nonwetting Templates (PRINT)**. In this method, tiny molds are used to precisely control the **composition, size, and shape** of the nanoparticles. This high level of customization allows scientists to design nanoparticles tailored for specific drugs and medical applications.

***Dendrimers**

Dendrimers are **unique, tree-like synthetic polymers** with a very precise and uniform structure. They have a **monodispersed size** (all particles are nearly the same size), a well-defined branching pattern, and a highly functionalized surface. They are usually made from building blocks such as **amino acids, nucleic acids, or carbohydrates**.

Drugs can be loaded into dendrimers in two main ways:

1. **Inside the branches (the core region)**, or
2. **On the outer surface (terminal groups)**.

This loading can happen through different types of interactions, such as **electrostatic forces, hydrophobic interactions, hydrogen bonding, chemical linkages, or covalent bonds**. One big advantage of dendrimers is that they can **increase the half-life of drugs**, meaning the drug stays active in the body for a longer period of time.

However, dendrimers also have **some limitations**. Their size is usually very small (less than 15 nm), and current synthesis methods often produce low yields, making large-scale production difficult. Additionally, **toxicity** is still a major concern, which has limited their wider use in biological systems.

A unique property of dendrimers is that as they grow to higher generations (more branches), the outer surface groups become tightly packed — a condition known as the **de Gennes dense packing limit**. This seals off the interior space from the surrounding solution. Interestingly, this property can be useful for **encapsulating hydrophobic (poorly soluble) drugs** inside the dendrimer.

Moreover, the degree of sealing can be adjusted depending on conditions such as **pH, polarity, or temperature**. By controlling these factors, scientists can fine-tune dendrimers to act as **customized drug carriers** with controlled drug release properties.

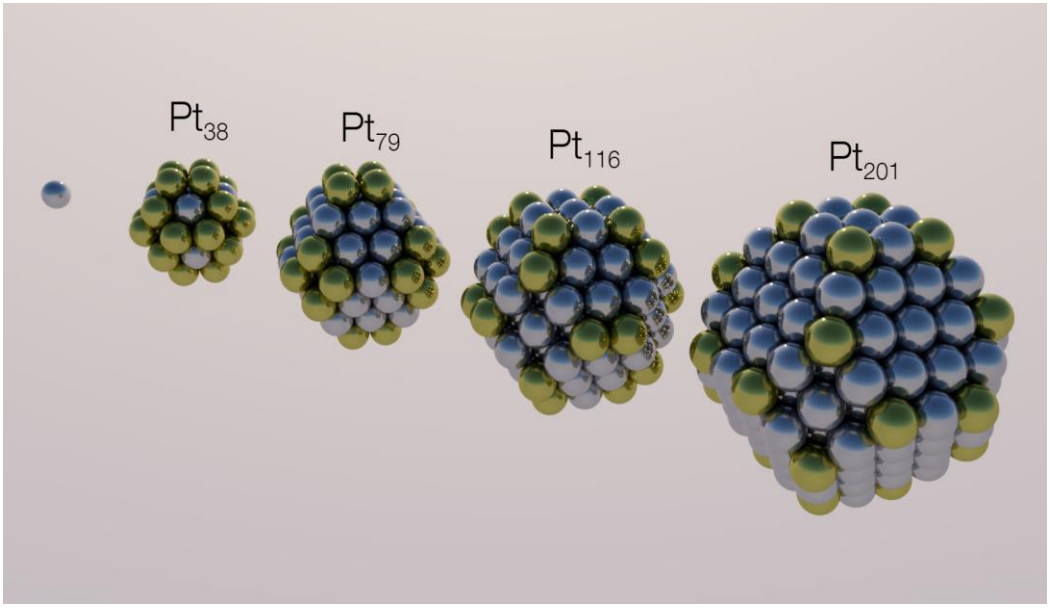
***Inorganic Nanoparticles and Nanocrystals**

Inorganic nanoparticles are increasingly used in drug delivery systems because of their **well-defined and highly customizable properties** such as size, shape, and surface chemistry. They have proven valuable in many biomedical applications, including **imaging, diagnosis, and targeted drug delivery**. Most inorganic nanoparticles are made from inert metals like **gold or titanium**, which can be shaped into nanospheres. **Iron oxide nanoparticles** are also popular, especially in imaging techniques such as magnetic resonance imaging (MRI).

Another important type of inorganic nanoparticle is the **quantum dot (QD)**, which is a tiny semiconductor nanocrystal. Quantum dots are special because of their **size-dependent optical properties**. Their diameters typically range from **2–10 nanometers**, which is close to the exciton Bohr radius, giving rise to a phenomenon called **quantum confinement**. This means their electronic and optical behavior changes depending on their size. For example, larger quantum dots emit **lower-energy (redder) light**, while smaller ones emit **higher-energy (bluer) light** when excited by fluorescence. This tunability makes QDs extremely useful for imaging and biosensing.

To make quantum dots safe and effective for biological use, **surface engineering** is essential. By adjusting the **composition, size, and structure** of the nanocrystal core, researchers can control the optical properties. Coating the core with an **organic shell** improves **biocompatibility**, reducing potential toxicity. On top of that, quantum dots can be further **functionalized with biomolecules**, such as peptides or antibodies, which allow them to specifically recognize and bind to biological targets.

This combination of features—**the strong optical properties of quantum dots and the biological functions of surface ligands**—makes them powerful tools for both **drug delivery and diagnostic applications**. Essentially, they serve as hybrid systems that bring together the best of inorganic nanomaterials and biological molecules, opening new possibilities for **targeted therapies and real-time monitoring in medicine**.



***Toxicity**

Although inorganic nanoparticles show exciting progress in materials science and have great potential in medical applications, their use inside the human body still faces serious challenges. The main concerns are **toxicity, uneven distribution within the body (biodistribution), and long-term buildup (bioaccumulation)**.

When metal-based nanoparticles break down, they release their **metal atoms** into the body. These atoms can interact with biological systems in unpredictable ways, sometimes causing harmful effects. Unlike biodegradable materials, which naturally break down into harmless byproducts, many inorganic nanoparticles may not clear easily from the body. Instead, they can **accumulate in tissues and organs over time**, leading to the risk of **metal toxicity** after repeated treatments.

Because of these issues, researchers are working to improve the **safety, clearance, and biocompatibility** of inorganic nanoparticles before they can be widely used in drug delivery and other medical applications.

***Organic Nanocrystal**

Organic nanocrystals are made almost entirely from the drug itself, with just a little bit of stabilizing material to prevent the particles from sticking together. They don't need any extra carrier system — the drug forms the nanoparticles directly.

Because these particles are extremely small (in the nanometer range), they have a **very large surface area** compared to regular drug particles. This larger surface area allows the drug to dissolve faster in body fluids, which means it gets absorbed better into the bloodstream. As a result, the **bioavailability** of the drug (the amount that actually works inside the body) increases.

This technology is already in use, and several **nanocrystal-based medicines are available on the market**, showing its practical importance in modern drug delivery.

***Liposome delivery**

Liposomes are tiny, bubble-like structures made from natural or synthetic fats called phospholipids. They form automatically in water, creating a spherical vesicle with a **water-loving core** and a **fatty (water-repelling) outer layer**. Because of this structure, liposomes can carry both **water-soluble drugs inside the core** and **fat-soluble drugs inside the membrane**, making them very versatile drug carriers.

Usually, liposomes are made with natural phospholipids like **phosphatidylcholine**, and often **cholesterol** is added to make the membrane stronger and more stable. Drugs can be loaded into liposomes in different ways, such as mixing during vesicle formation, using solvent exchange, or applying pH gradients.

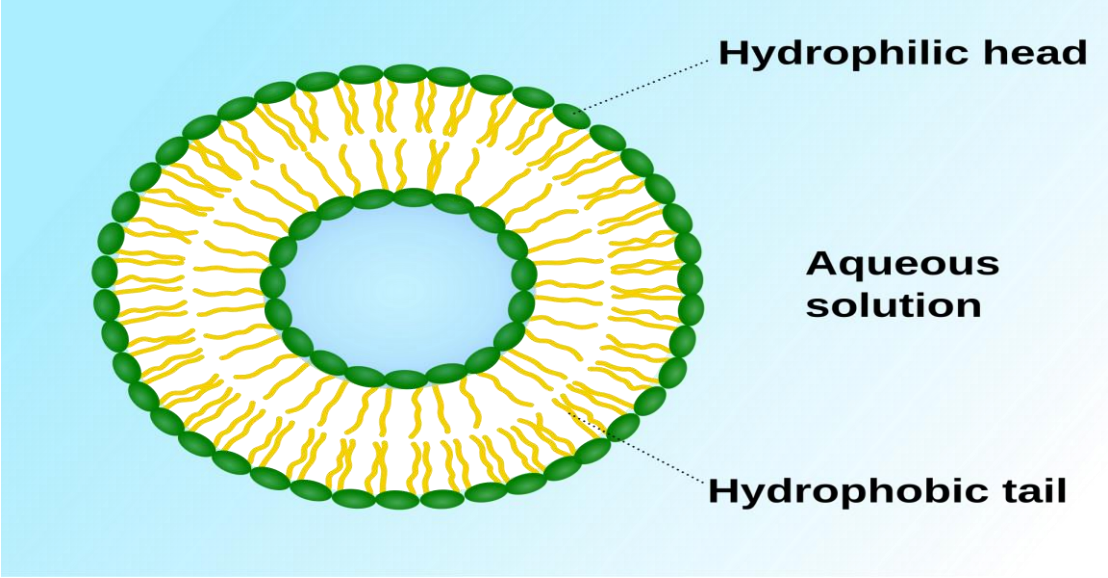
Liposomes can also be modified on their surface. For example, attaching **polyethylene glycol (PEG)** makes them less likely to be recognized and removed by immune cells, allowing them to circulate longer in the body. Their **size, charge, and flexibility** can also be tuned to control how they behave in the bloodstream.

Once in the body, liposomes can reach the target site and release their drug in different ways:
By **fusing directly** with cell membranes (since both are made of phospholipids).
By being taken up through **phagocytosis** or other active transport processes.

Advantages of Liposomes

Improve drug solubility and stability.
Enhance drug uptake by cells.
Can be decorated with ligands (like peptides or polymers) to target specific cells).
Reduce side effects by keeping the drug protected until it reaches the right site.

Several **FDA-approved liposomal drugs** already exist. For example, **doxorubicin (an anticancer drug)** is delivered in phospholipid–cholesterol liposomes to treat Kaposi's sarcoma (linked to AIDS) and multiple myeloma, with **high effectiveness and lower toxicity**. Many other liposomal formulations are in clinical trials, and liposome-based drug delivery is an **active area of research**, with promising applications in **cancer therapy, brain-targeted delivery, and nucleic acid-based treatments**.



***viral-like particles, and biological nanocarriers**

Viruses are naturally very good at delivering genetic material into cells, which is why they are widely used in **gene therapy** and **genetic engineering**. Common viral vectors include **adenoviruses, retroviruses, and bacteriophages**. Scientists can even modify the virus surface by attaching **targeting molecules (ligands)** so that the virus delivers its cargo specifically to the desired cells.

However, one big challenge is that viruses have a **natural tendency (tropism)** to infect certain cells, which can sometimes cause **off-target effects**. To overcome this, researchers often replace the viral surface proteins responsible for cell binding with **engineered (chimeric) proteins** that make the virus safer and more precise.

An alternative to using whole viruses is **virus-like particles (VLPs)**. These are made from the **protein shell (capsid)** of viruses but **don't contain any viral genetic material**, so they cannot replicate or cause infection. VLPs have several advantages:
They are **easier and safer to manufacture** than live viruses.
They have a **uniform and stable structure**, making large-scale production reliable.

Their surfaces are **easy to modify**, allowing scientists to add ligands for targeted delivery.
There are different ways to load drugs into VLPs:
Adjusting the **pH** to open small pores in the capsid, so the drug can enter and then get trapped inside.
Using molecules like **leucine zippers** or **polymer-DNA amphiphiles** to trigger capsid formation around the drug.
Chemically attaching drugs directly onto the capsid surface, often by forming amide bonds.

Delivery and release mechanisms
An ideal drug delivery system should do two main things:
1. Deliver the drug exactly where it is needed (targeting).
2. Release the drug in a controlled way (controlled release).

Targeting Strategies
There are two primary strategies used for targeting drugs to diseased tissues
Passive Targeting
This approach takes advantage of the way **tumor blood vessels are structured**.
Tumor vessels are usually leaky and have poor lymphatic drainage, which allows **large molecules and nanoparticles** to accumulate in the tumor more easily than in normal tissues.
This phenomenon is called the **Enhanced Permeability and Retention (EPR) effect**.
Because of EPR, drug-loaded nanoparticles naturally build up in tumor tissue, improving drug delivery without needing active guidance.

Active Targeting
This is a more **precise approach**.
Nanoparticles are modified with **specific ligands** (such as antibodies, peptides, or small molecules) that can recognize and bind to receptors present on diseased cells.
Once the nanoparticle binds to the target cell, the drug can be released directly where it is needed.
This method reduces damage to healthy tissues and increases therapeutic effectiveness.

Controlled Drug Release
In addition to targeting, an effective drug delivery system should control **when and how much drug is released**.
There are different strategies to achieve this:
1. Rate-Programmed Release
Here, the release is carefully adjusted based on the **diffusion rate** of the drug across the nanoparticle membrane or matrix.
This ensures a steady and predictable release over time.

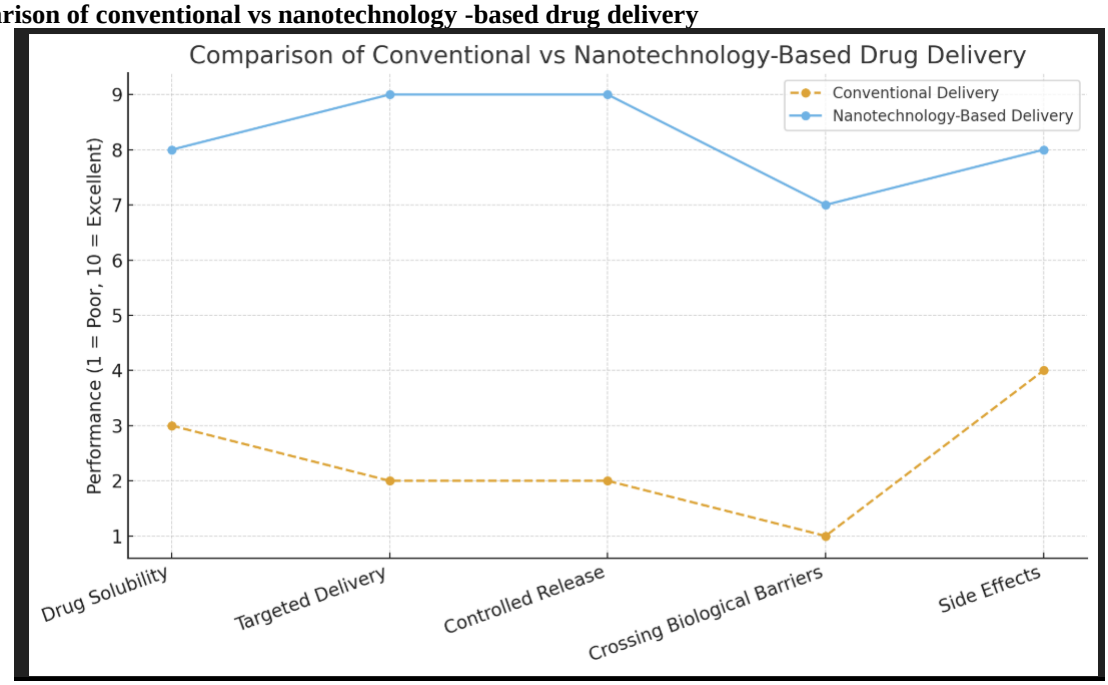
2. Activation-Modulated Release
In this case, drug release is **triggered by specific stimuli**.
These triggers can be:
External stimuli – such as light, heat, ultrasound, magnetic fields, or chemical activators introduced from outside the body.

Biological stimuli – such as **pH, temperature, enzyme levels, or osmotic pressure**, which naturally vary in different parts of the body (e.g., tumors are more acidic than normal tissues)

Polymeric nanoparticles
Polymeric nanoparticles can be designed to **respond to changes in their environment**, which makes them very useful for **controlled drug delivery**. Researchers often use **special polymers that naturally react to stimuli** such as changes in **temperature or pH**. These changes allow the nanoparticles to alter their structure and release drugs only under certain conditions.

One of the most widely studied polymers for this purpose is **poly(N-isopropylacrylamide) (PNIPAm)**. This polymer has a unique property:
At **room temperature**, it dissolves easily in water.
When the temperature rises above a certain point (called the **Lower Critical Solution Temperature, LCST**), it changes its structure, going from an **extended chain** to a **collapsed chain**.
This transition makes the polymer less water-loving (**hydrophilic → hydrophobic**), which can be used to control when drugs are released.
Researchers are also working on **dual stimuli-responsive systems**, which respond to **more than one trigger**. For example:
A specially designed **triblock copolymer** made of PEG-b-PAPMA-b-PNIPAm can form **micelles** (tiny spherical structures with a core–shell–corona design) when heated above the LCST.
This system is also **sensitive to pH change**
Because of this dual responsiveness, the drug release can be tuned either by **adjusting the temperature** or by **changing the pH** of the environment.
This type of "smart" design means that drugs can be released **more precisely**, for example, in the acidic environment of a tumor or in response to body temperature changes, impr:oving treatment efficiency and reducing side effects.

Comparison of conventional vs nanotechnology -based drug delivery



CONCLUSION

Nanotechnology has changed the way we think about drug delivery. Traditional methods often struggle with problems like poor solubility, instability, or harmful side effects. Nanocarriers help solve these issues by protecting drugs, improving how well they dissolve, releasing them in a controlled way, and making sure they reach the exact place in the body where they are needed. Different types of nanocarriers—such as polymeric nanoparticles, dendrimers, liposomes, inorganic particles, virus-like particles, and nanocrystals—each bring their own strengths, giving doctors and researchers many options to improve treatment.

A key advantage of nanotechnology is **targeted therapy**. These systems can either naturally accumulate in diseased tissues (passive targeting) or be guided more precisely using special molecules that bind to diseased cells (active targeting). Some nanocarriers are also designed to release drugs only when triggered by changes in temperature, pH, or light. Even more exciting is the rise of **theranostics**, where one system can both deliver medicine and help doctors track how the disease is responding. Importantly, some nanocarriers can even cross the blood–brain barrier, opening new doors for treating brain diseases that were once very hard to manage.

Of course, challenges remain. Making these systems on a large scale, ensuring long-term safety, avoiding unwanted immune reactions, and meeting strict regulatory standards are still hurdles that need to be cleared. But with continuous progress in science and technology, these problems are gradually being solved.

In short, nanotechnology-based drug delivery is a major step forward for modern medicine. It offers safer, more effective, and personalized treatments that could greatly improve patients' lives. With ongoing research and collaboration between scientists, doctors, and regulators, nanomedicine is expected to play a central role in the future of healthcare worldwide.

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