



Polysaccharide-Based Nano-Drug Delivery Systems: A Systematic Review

Manisha Kumari, Sabitri Pradhan*

Mata Gujri College of Pharmacy, Kishanganj, Bihar-855107, India.

*Corresponding author's E-mail: sabitripradhan934@gmail.com

Received: 08-06-2026; Revised: 23-08-2026; Accepted: 29-08-2026; Published online: 20-09-2026.

ABSTRACT

Background: Polysaccharide-based nano-drug delivery systems (PNDDS) have gained significant attention due to their biocompatibility, biodegradability, and ability to improve drug solubility, stability, and targeted delivery. This review systematically evaluates the current progress, applications, and challenges of PNDDS in pharmaceutical research.

Methods: A systematic search of scientific databases including PubMed, Scopus, Web of Science, and ScienceDirect was conducted for studies. Articles focusing on the design, synthesis, characterization, and biomedical applications of polysaccharide-based nanocarriers were included. Data were extracted, analyzed, and categorized based on polysaccharide types, formulation strategies, and therapeutic applications.

Conclusion: PNDDS offer a versatile and sustainable platform for advanced drug delivery, with significant potential for clinical translation. Future research should focus on addressing production challenges, long-term safety, and regulatory frameworks to enable their integration into routine medical practice.

Keywords: Polysaccharides, Nano-drug delivery, Biocompatibility, Targeted therapy, Biodegradable nanocarriers.

INTRODUCTION

Polysaccharide is one important type of natural biopolymers and has been widely explored as delivery vehicles to realize targeted cancer therapy with desirable biosafety. Polysaccharide-based nanosystems have attracted significant attention as delivery platforms for the treatment of various diseases¹. Compared with other biopolymers like protein and nucleic acid, polysaccharide is more widely used to construct nanomedicine owing to its relative chemistry stability, large potential for chemical modification and low cost for processing².

CLASSIFICATION

1. Natural Polysaccharide-Based Nanoparticles (NPs)

1.1 Chitosan-Based NPs: CS is a widely available, sustainable biomaterial for health care product development and tissue engineering. Polymeric NPs based on chitosan (CS) can act as excellent drug carriers because of some intrinsic beneficial properties including biocompatibility, biodegradability, non-toxicity, bioactivity, easy preparation, and targeting specificity³. CSNPs are used for developing the stimuli-responsive NPs to carry chemo drugs to deliver specifically at cancer locations without causing any toxicity to normal cells⁴. It is a diagnostic tool for various drug delivery system such as improve the pharmacokinetics and pharmacodynamics profile, Diagnosis of cancer cells/photoimaging, overcome biological barrier, across intestinal epithelial cell layer, dual-delivery system, targeting, control release⁵.

1.2 Alginate-Based NPs: Alginate, a natural anionic polysaccharide derived from brown algae, has become a widely used biomaterial in pharmaceutical research for the development of drug delivery systems⁶. The ability of

alginate to form hydrogels through ionic crosslinking with divalent cations such as Ca^{2+} makes it ideal for encapsulating bioactive molecules. It is generally derived from three main species, including *Macrocystis pyrifera*, *Laminaria digitata*, and *Laminaria saccharina*⁷. Hydrogels are valued for their polymeric nature and for meeting specific criteria, such as the capacity to retain water, inertness, biocompatibility, photostability, and sufficient permeability to biological fluids. Alginates are hydrophilic, linear anionic chains, composed of two uronic acids encompassing (1-4)-linked- β -D-mannuronate and α -L-guluronate, and usually found in marine life such as seaweed or brown algae and could be collected as sodium salt and/or calcium salt⁸.

1.3 Hyaluronic Acid-Based NPs: Hyaluronic acid, a naturally occurring glycosaminoglycan, has been utilized for the delivery of anticancer drugs. Hyaluronic acid (HA) plays a major role in aging, cellular senescence, cancer development and progression, and tissue homeostasis⁹. It exhibits high water retention and can target specific cell types due to its receptor-mediated endocytosis. It can also be synthesized using biotechnological processes and recombinant DNA technologies in bacterial expression systems such as *Lactococcus* and *Streptococcus*¹⁰.

2. Modified Polysaccharide Nanoparticles

2.1 Carboxymethylcellulose (CMC) NPs: CMC is a derivative of cellulose and is widely used in drug delivery due to its water-soluble nature and the ability to form stable nanoparticles for controlled drug release¹¹.

2.2 Dextran Nanoparticles: Dextran, a branched polysaccharide, can be modified for improved drug delivery by introducing functional groups that allow for better drug loading and controlled release¹². Its biocompatibility has



made it suitable for use in a range of applications, including cancer treatment. Dextran -based polymer prodrugs linked by ester bonds could also increase the stability and targeting of drugs ¹³.

3. Polysaccharide Micelles and Hydrogels

3.1 Polysaccharide Micelles: Amphiphilic polysaccharide derivatives (e.g., polysaccharide–PEG conjugates) can form micelles in aqueous environments that are capable of solubilizing hydrophobic drugs ¹⁴.

3.2 Polysaccharide Hydrogels: Hydrogels formed from polysaccharides such as alginate or pectin can encapsulate drugs in their 3D network, providing controlled release over time. These systems are especially useful for localized and sustained drug release ¹⁵. Hydrogels exhibit valuable properties and advantages, such as low toxicity or swelling. Over the past decade, these systems have attracted considerable attention for the development of therapeutic biomolecule delivery systems, including hormones, growth factors (GFs), gene vectors, or monoclonal antibodies ¹⁶.

PREPARATION METHODS

There are various preparation methods of polysaccharide-based nanoparticles, which include solvent evaporation, coacervation, crosslinking, and electrostatic assembly.

1. Solvent Evaporation Method: This is one of the most common methods for preparing polysaccharide-based nanoparticles. In this technique, polysaccharide solutions containing drugs are emulsified in organic solvents, followed by evaporation of the solvent, leading to the formation of nanoparticles ¹⁷. This method is often used for encapsulating hydrophobic drugs ¹⁸.

2. Coacervation/Phase Separation: Coacervation is a technique based on the separation of liquid phases, where a polysaccharide solution undergoes phase separation to form drug-loaded nanoparticles ¹⁹. The applications of different HPCCs based on these three basic proteins are discussed, including the encapsulation of bioactive molecules, emulsion stabilization, protein separation and extraction, nanogel formation, and the development of formulas for infants. This method is especially useful for forming stable, spherical nanoparticles ²⁰.

3. Ionic Gelation/Crosslinking: Ionic gelation is a method where polysaccharides such as chitosan are crosslinked with multivalent anions, such as tripolyphosphate, to form nanoparticles. CS-tripolyphosphate polymers: CS NPs, produced by ionic gelation with TPP are among the most intensely studied nanosystems for drug delivery ³. This method is widely used for preparing chitosan-based nanoparticles ²¹.

4. Electrostatic Assembly: This method involves the electrostatic attraction between polysaccharide-based materials and drug molecules or other polymers. The interaction leads to the self-assembly of nanoparticles, which can then be used for drug delivery ³. The basic principle of this technique involves the repulsion of equally charged molecules (induced using polyelectrolytes) as well as the attraction and adsorption of oppositely charged molecules to the initial molecule leading to form well controlled multilayer structured films after several cycles ²².

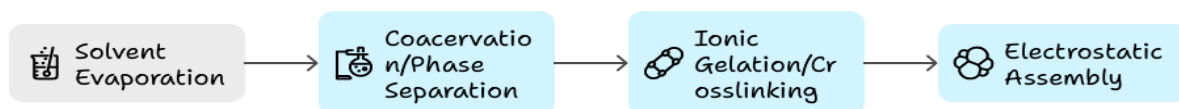


Figure 1: Preparation Methods of Polysaccharide-Based Nanoparticles

MECHANISM OF DRUG ENCAPSULATION

The encapsulation of drugs in polysaccharide-based NDDS can occur through several mechanisms, largely driven by the physicochemical properties of both the drug and the carrier. The primary mechanisms of drug encapsulation include:

1. Physical Encapsulation: Physical encapsulation refers to the entrapment of drugs within the matrix of the polysaccharide nanoparticles without significant chemical modification ²³. This process generally involves non-covalent interactions such as:

Hydrophobic Interactions: Polysaccharides, such as chitosan and dextran, can encapsulate hydrophobic drugs through hydrophobic interactions between the drug molecules and the polysaccharide matrix ²⁴. For example, chitosan-based nanoparticles have been widely studied for encapsulating hydrophobic drugs like curcumin or paclitaxel ²⁵.

Electrostatic Interactions: For polysaccharides that have charged groups (e.g., chitosan with its amine groups), drugs with opposite charges can be incorporated through ionic bonds ²⁶. This mechanism is commonly used in the preparation of nanoparticles loaded with proteins or nucleic acids (e.g., siRNA, plasmid DNA) ²⁷.

Hydrogen Bonding: Polysaccharides containing hydroxyl groups (e.g., cellulose, alginate) can interact with drugs through hydrogen bonding ²⁸. This allows for the encapsulation of both hydrophilic and hydrophobic drugs, improving their solubility and stability.

2. Chemical Cross-Linking: Cross-linking agents are often used to improve the structural integrity of polysaccharide nanoparticles, which in turn can enhance the encapsulation efficiency. Polysaccharides like alginate and chitosan are cross-linked using

divalent cations (e.g., Ca^{2+}) or other cross-linkers (e.g., glutaraldehyde), which can increase the rigidity of the nanoparticle and result in higher encapsulation efficiency²⁹. Cross-linking also aids in preventing premature drug release, making it useful for sustained release applications³⁰.

3. Solvent Evaporation or Coacervation: In the solvent evaporation method, drug-loaded polysaccharide

solutions are emulsified in an organic solvent, and the solvent is then evaporated under reduced pressure to form nanoparticles³¹. This technique is widely used for encapsulating both hydrophilic and hydrophobic drugs³⁰. The coacervation technique, where phase separation occurs upon changes in pH or temperature, can also be used to encapsulate drugs into polysaccharide nanoparticles³².

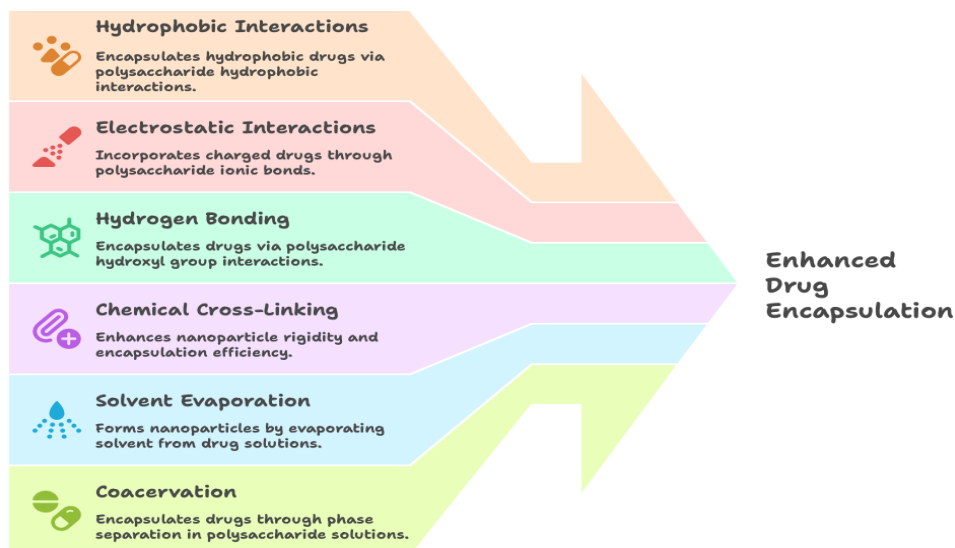


Figure 2: Mechanism of Drug Encapsulation

MECHANISM OF DRUG RELEASE

The release of drugs from polysaccharide-based NDDS can be governed by various mechanisms, often influenced by the physicochemical environment³³. The release rate is typically designed to be controlled and sustained to maximize therapeutic efficacy while minimizing side effects. The major release mechanisms include:

1. Diffusion-Controlled Release: In this mechanism, drug molecules diffuse from the nanoparticle matrix to the surrounding medium. The release rate depends on several factors, including the size of the nanoparticle, the viscosity of the drug-loaded matrix, and the solubility of the drug³⁴. Polysaccharides such as chitosan or dextran typically form matrices where the drug slowly diffuses through the polymer network.

Fickian Diffusion: In the case of Fickian diffusion, the drug release follows Fick's law of diffusion, where the release rate is governed by the concentration gradient between the inside of the nanoparticle and the external environment³⁵.

Non-Fickian Diffusion (Anomalous Diffusion): This occurs when both diffusion and polymer relaxation contribute to the release process. This is often observed in polysaccharide hydrogels.

2. Swelling-Controlled Release: Some polysaccharide nanoparticles, particularly hydrogels, undergo swelling when exposed to aqueous environments. As the polymer network swells, the encapsulated drug is

gradually released. This mechanism is commonly observed in polysaccharides like alginate and pectin. The swelling is often dependent on factors like pH, ionic strength, and temperature³⁶.

pH-Sensitive Release: Certain polysaccharides (e.g., chitosan, pectin, and alginate) can be pH-sensitive. When exposed to acidic or basic environments (such as the stomach or intestines), these polysaccharides undergo structural changes, resulting in swelling or de-crosslinking, leading to drug release³⁷. For example, chitosan nanoparticles can swell and release drugs in acidic environments (e.g., gastric pH).

3. Enzyme-Responsive Release: Polysaccharides can be designed to degrade in the presence of specific enzymes, allowing for controlled drug release at targeted sites. For example, chitosan can be hydrolyzed by lysozyme, and dextran can be degraded by dextranase. This mechanism is particularly useful in targeting the delivery of drugs to specific tissues or organs, such as the gastrointestinal tract or tumor sites, where enzymes are overexpressed³⁸.

Targeted Release: Enzyme-responsive systems are used to achieve controlled release in specific tissues where certain enzymes are more abundant. This approach is increasingly being explored for cancer therapy, where tumor-associated enzymes trigger the release of therapeutic agents³⁹.

4. **Stimuli-Responsive Release:** Stimuli-responsive polysaccharide-based NDDS can release their payload in response to external or internal stimuli such as temperature, light, magnetic fields, or electrochemical changes. For example, polysaccharide-based nanoparticles can be engineered to release their drug content when exposed to near-infrared light (NIR) or changes in temperature. These stimuli can provide high spatiotemporal control over drug release ⁴⁰.

Thermo-Sensitive Release: Polysaccharide derivatives, such as thermo-sensitive copolymers (e.g., poly(N-isopropylacrylamide)-modified chitosan), exhibit a lower critical solution temperature (LCST), below which the polymer is soluble, and above which it forms a gel. This temperature-dependent transition can be used to control drug release ⁴¹.

EXAMPLES OF POLYSACCHARIDES USED IN NANO-FORMULATIONS

1. **Chitosan:** Chitosan is a deacetylated derivative of chitin and is one of the most widely studied polysaccharides in nanotechnology ⁴². Chitosan-based nanoparticles (CS-NPs) are known for their biocompatibility, biodegradability, and mucoadhesive properties, making them ideal for oral, topical, and even nasal drug delivery.

Properties: Chitosan possesses amino groups that can undergo protonation at acidic pH, leading to cationic behavior, which facilitates drug encapsulation through ionic interactions with anionic drugs or macromolecules like proteins and nucleic acids ⁴³. Its biodegradability and low toxicity are key for its use in pharmaceutical applications.

Applications: Chitosan NPs have been successfully used for delivering anticancer drugs (e.g., paclitaxel, doxorubicin), antibiotics, and vaccines. Chitosan-based systems can also deliver gene therapies, such as siRNA, due to their ability to form nanoparticles with nucleic acids ⁴².

2. **Alginate:** Alginate is a naturally occurring anionic polysaccharide derived from brown seaweed, composed of guluronic acid (G) and mannuronic acid (M) units. Its ability to form hydrogels in the presence of divalent cations (e.g., Ca^{2+}) has made it a popular choice for drug delivery and tissue engineering applications ⁴⁴.

Properties: Alginate is water-soluble, biocompatible, and capable of forming stable hydrogels. Its anionic nature allows for drug loading via ionic interactions, and its gel-forming properties can control the release of therapeutic agents ⁴⁵.

Applications: Alginate nanoparticles have been widely used for delivering anticancer agents, proteins, and even DNA vaccines. Alginate is also used in the creation of biocompatible hydrogels for wound healing, ocular drug delivery, and tissue regeneration ^{44, 45}.

3. **Hyaluronic Acid:** Hyaluronic acid (HA) is a naturally occurring glycosaminoglycan composed of alternating units of glucuronic acid and N-acetylglucosamine. It plays a crucial role in the extracellular matrix and is involved in cell signaling, making it an excellent candidate for drug delivery and tissue engineering ⁴⁶.

Properties: HA is biocompatible, biodegradable, and non-immunogenic. Its unique ability to interact with CD44 receptors, which are over expressed in many tumor cells and inflammatory tissues, makes HA an attractive choice for targeted drug delivery ⁴⁷.

Applications: HA-based nanoparticles have been extensively studied for targeted delivery of anticancer drugs, wound healing agents, and in regenerative medicine. HA nanoparticles are also being developed for gene delivery and immunotherapy ^{46, 47}.

4. **Dextran:** Dextran is a branched polysaccharide composed of glucose units. It is widely used in medical applications such as blood volume expanders, and more recently, as a carrier for drug delivery systems ⁴⁸.

Properties: Dextran is water-soluble, non-toxic, and can be easily modified by attaching various functional groups to its structure. Its flexibility and ability to form nanoparticles make it suitable for controlled drug delivery applications ⁴⁹.

Applications: Dextran-based nanoparticles are often employed for the delivery of anticancer drugs, proteins, and nucleic acids. Additionally, dextran-based systems are being developed for use in imaging and diagnostic applications due to their biocompatibility and ease of modification ^{48, 49}.

5. **Cellulose:** Cellulose, a linear polysaccharide made up of glucose units, is the most abundant natural polymer. Its use in nano-formulations is growing due to its non-toxic, biocompatible, and sustainable nature ⁵⁰.

Properties: Cellulose-based nanoparticles, including cellulose nanocrystals (CNCs) and cellulose nanofibrils (CNFs), are characterized by high mechanical strength, surface area, and functionality. Their unique structure allows for the encapsulation of both hydrophilic and hydrophobic drugs ⁵¹.

Applications: Cellulose-based nanoparticles are being developed for drug delivery, wound healing, and tissue engineering. CNCs have been particularly studied for their ability to encapsulate and release small molecule drugs, proteins, and other bioactive agents ^{50, 51}.

6. **Pullulan:** Pullulan is a water-soluble, non-toxic, and biodegradable polysaccharide produced by the fungus *Aureobasidium pullulans*. It is known for its film-forming and mucoadhesive properties ⁵².

Properties: Pullulan is non-immunogenic, highly biocompatible, and can be easily functionalized to enhance its drug encapsulation and release properties. It is especially useful for sustained release applications ⁵³.

Applications: Pullulan-based nanoparticles are being explored for controlled release of anticancer drugs, antimicrobial agents, and in gene delivery applications^{52, 53}.

CHALLENGES IN DEVELOPING POLYSACCHARIDE-BASED NANO-SYSTEMS

1. Stability and Biocompatibility Issues

Polysaccharide-based nanomaterials have garnered considerable attention in recent years due to their promising applications in drug delivery, tissue engineering, and biomedical fields. Polysaccharides, such as chitosan, alginate, dextran, and hyaluronic acid, possess a variety of advantageous properties like biocompatibility, biodegradability, non-toxicity, and the ability to undergo chemical modifications, making them ideal candidates for the fabrication of nanocarriers⁵⁴.

1.1 Stability Challenges in Polysaccharide-Based Nano-Systems

1. Degradation and Stability Under Physiological Conditions: One of the main issues associated with polysaccharide-based nanocarriers is their degradation under physiological conditions. Polysaccharides are highly susceptible to enzymatic hydrolysis by enzymes like amylase, lysozyme, and other glycosidases present in the body⁵⁵. This degradation can result in the premature release of encapsulated drugs, affecting the therapeutic efficacy and controlled release profiles of the nanocarriers.
2. Environmental Sensitivity: Many polysaccharides are highly sensitive to changes in environmental conditions, such as pH, temperature, and ionic strength. This sensitivity can result in altered physical properties (e.g., size, shape, or surface charge) of the nanoparticles, leading to instability in biological environments⁵⁶. Alginate nanoparticles may swell or disintegrate in the presence of certain cations or changes in pH, limiting their application in targeted drug delivery systems.
3. Aggregation and Size Instability: Aggregation of nanoparticles can occur during storage or after injection into the body, which can compromise the pharmacokinetics and biodistribution of the polysaccharide-based nanocarriers. Aggregation is often caused by intermolecular forces, such as van der Waals forces or hydrophobic interactions, that occur between particles, especially when the nanoparticles are exposed to biological fluids with high ionic strength⁵⁷.

1.2 Biocompatibility Issues in Polysaccharide-Based Nano-Systems

1. Immune System Response: Although polysaccharides are generally considered biocompatible, the immune response to polysaccharide-based nanoparticles can still pose a challenge⁵⁸. The body's immune system

may recognize certain polysaccharides as foreign, which could lead to inflammation, allergic reactions, or other adverse responses, especially when administered at high doses or repeatedly.

2. Cytotoxicity and Hemocompatibility: Polysaccharide-based nanoparticles may also exhibit cytotoxic effects depending on their chemical structure, charge, and size. Excessive positive charge or the presence of reactive functional groups on the surface can lead to non-specific interactions with cell membranes, potentially causing cellular damage. Polysaccharides must also be tested for their hemocompatibility- especially if used in intravenous applications- since they may cause hemolysis or blood clotting⁵⁹.
3. Slow Clearance and Long-Term Toxicity: Due to the biodegradability of polysaccharides, these nanoparticles are generally expected to be broken down over time and cleared from the body. There is still concern about the long-term accumulation of nanomaterials, which could lead to potential toxicity. Incomplete degradation or slow clearance rates might lead to the accumulation of polymeric residues in tissues, which can be toxic over time⁶⁰.

2. Scalability and Cost Constraints

The key challenges facing the widespread adoption and commercialization of the nanomaterials lies in the issues surrounding scalability and cost⁶¹.

2.1 Scalability Challenges in Developing Polysaccharide-Based Nano-Systems

1. Manufacturing Process Complexity: The fabrication of polysaccharide-based nanoparticles typically involves complex processes such as solvent evaporation, coacervation, nanoprecipitation, or spray-drying, which are scalable but often difficult to optimize at large scales. These processes require precise control over parameters such as solvent concentration, temperature, pH, and nanoparticle size distribution, which can vary when transitioning from small-scale laboratory production to industrial-scale manufacturing⁶².
2. Uniformity and Quality Control: Ensuring uniformity in the size, shape, and surface properties of polysaccharide-based nanoparticles is a significant challenge in scaling up production. In laboratory settings, small batches of nanoparticles can be closely monitored and fine-tuned, but in large-scale production, even small variations in processing conditions can lead to significant differences in the properties of the final product⁶³.
3. Solvent Removal and Drying: Polysaccharide-based nanoparticles are often synthesized using solvents, which must be removed from the final product. Scaling the solvent removal process can be challenging, as large volumes of solvent may be required, and the removal process can impact the structural integrity and



bioactivity of the nanoparticles. For example, high-temperature drying or solvent evaporation methods can alter the physicochemical properties of polysaccharide nanoparticles, leading to changes in their morphology, surface charge, and release kinetics⁶¹.

2.2 Cost Constraints in Developing Polysaccharide-Based Nano-Systems

1. **Raw Material Costs:** While polysaccharides are abundant and renewable, the cost of obtaining high-quality polysaccharides can still be significant, especially when specific, high-purity materials are required for biomedical applications. For example, chitosan, a widely used polysaccharide, is typically derived from chitin, which is extracted from crustacean shells. The extraction process is labor-intensive, and the need for purification steps to ensure pharmaceutical-grade quality can drive up costs. Other polysaccharides like hyaluronic acid are even more expensive due to the complex extraction and purification processes involved⁶⁴.
2. **Production Costs for Complex Nanoparticle Formulations:** The production of polysaccharide-based nano-systems often involves multi-step processes that require specialized equipment and reagents, further increasing the cost of manufacturing. For instance, crosslinking agents, surfactants, stabilizing agents, and encapsulation reagents may all add to the overall cost of producing high-quality nanoparticles⁶⁵.
3. **Regulatory and Quality Control Costs:** Regulatory compliance is a significant contributor to the high cost of developing polysaccharide-based nano-systems for biomedical applications. The regulatory requirements for clinical trials, manufacturing practices (GMP), and product quality assurance (QA) are stringent, which can increase both the time and cost involved in the development of polysaccharide-based nano-systems⁶⁶.
2. **Advanced Nanomaterials for Energy Applications:** The drive towards sustainable energy solutions has intensified the need for advanced materials capable of improving the efficiency of energy storage, conversion, and transmission. Nanotechnology plays a critical role in enhancing the performance of materials used in solar cells, batteries, and fuel cells. Scalability remains a significant challenge in the commercialization of nanomaterial-based energy systems⁶⁹. The cost of high-quality nanomaterials remains a bottleneck in large-scale energy applications. As manufacturing techniques improve and the demand for clean energy grows, the future of nanomaterial-based energy solutions looks promising⁷⁰.
3. **Smart and Multifunctional Materials:** Smart materials, which can respond to external stimuli such as heat, light, magnetic fields, and pH, are becoming increasingly prevalent in a wide range of applications. These materials can adapt and change their properties in real-time, offering unprecedented capabilities in fields such as sensors, robotics, and wearable devices. While the potential for smart materials is vast, challenges in material integration, energy consumption, and long-term stability need to be overcome. The fabrication of complex nanostructures for multifunctional materials at large scales still presents difficulties. Breakthroughs in nanomanufacturing techniques and the continued development of new nanomaterials will drive progress in this field⁷¹.
4. **Environmental Sustainability and Nanotechnology:** Nanotechnology has the potential to significantly impact environmental sustainability by improving waste treatment, water purification, and resource recycling⁷². Nanomaterials are being explored for reducing pollution and enabling more efficient use of resources. The potential of nanotechnology to enhance environmental sustainability, the long-term environmental impact of nanomaterials themselves is still uncertain. Researchers are focusing on developing eco-friendly, biodegradable nanomaterials and evaluating the life cycle and toxicity of nanomaterials in environmental applications⁷³.

FUTURE PERSPECTIVE

Innovations in Nanotechnology and Material Science

1. **Nanomedicine and Drug Delivery Systems:** Nanomedicine, the application of nanotechnology for medical purposes, is poised to revolutionize healthcare by enabling targeted drug delivery, improving diagnostic imaging, and enhancing tissue regeneration.⁶⁷ The ability to design nanoscale drug delivery systems that can deliver therapeutic agents precisely to diseased tissues, such as tumors, is one of the most significant innovations in this space. Despite the immense promise, challenges remain in ensuring the biocompatibility, safety, and long-term stability of these systems. Regulatory hurdles, such as the approval process for novel nanomaterials in clinical use, also remain a significant barrier. Ongoing research into the long-term effects of nanomaterials on human health and the environment will drive the safe translation of these technologies to the clinic⁶⁸.

Integration with Modern Drug Discovery

1. **Enhancing Drug Delivery and Targeting with Nanotechnology:** One of the most promising applications of nanotechnology in drug discovery is its ability to improve drug delivery systems. Nanoparticles (NPs), such as liposomes, polymeric nanoparticles, and dendrimers, can encapsulate hydrophobic drugs, protect them from degradation, and enhance their bioavailability⁷⁴. Nanoparticles can be engineered to target specific tissues, cells, or even subcellular components, which is particularly beneficial for cancer and other diseases requiring precise therapeutic targeting. Future advancements in drug delivery will focus on developing “smart” nanocarriers that are capable of not only targeted delivery but also controlled release and monitoring of drug efficacy. Innovations in



bio-responsive materials, self-assembling nanoparticles, and multi-functional nanocarriers will improve therapeutic outcomes by enabling more personalized treatments based on an individual's disease profile ⁷⁵.

2. **Nanotechnology and High-Throughput Screening in Drug Discovery:** High-throughput screening (HTS) has been a cornerstone of modern drug discovery, enabling the screening of large libraries of chemical compounds to identify potential drug candidates. ⁷⁶ Nanotechnology has been integrated into HTS platforms to enhance the sensitivity, speed, and precision of assays. In the future, nanotechnology will enable the development of more advanced HTS technologies that combine artificial intelligence (AI) with nanomaterials. Machine learning algorithms can be used to analyze large datasets generated by nanosensor-based assays, allowing for the rapid identification of potential drug candidates with higher precision and fewer false positives ⁷⁷.
3. **Nanotechnology in Drug Development and Formulation:** Nanotechnology plays a crucial role in the development and formulation of new drugs, particularly in enhancing the solubility and stability of poorly water-soluble compounds. Many newly discovered bioactive molecules, such as small molecules and biologics, often face challenges in terms of absorption, distribution, metabolism, and excretion (ADME) ⁷⁸. Nanoparticles have the ability to increase the solubility of hydrophobic drugs, protect sensitive biologics, and enhance their half-life in circulation. The future of nanotechnology in drug formulation lies in the creation of multifunctional nanocarriers capable of delivering multiple drug payloads, targeting specific cells or tissues, and offering combination therapies. Advancements in nanotechnology-driven vaccine formulations, particularly for RNA-based and gene therapies, will be crucial for the future of personalized medicine ⁷⁹.
4. **Nanotechnology and Artificial Intelligence (AI) in Drug Discovery:** The integration of AI and machine learning with nanotechnology offers significant potential to streamline drug discovery processes. AI algorithms can analyze vast datasets to predict the pharmacokinetics, toxicity, and efficacy of drug candidates, and nanotechnology can assist in generating and testing new materials more efficiently ⁸⁰. The future will see a greater convergence of AI, nanotechnology, and high-throughput experimentation. The integration of these technologies will likely lead to the rapid design, testing, and optimization of nanomaterials for drug delivery, as well as the development of personalized treatment plans based on real-time data analysis ⁸¹.
5. **Overcoming Challenges and Regulatory Issues in Nanotechnology-Driven Drug Discovery:** Despite the exciting potential of nanotechnology in drug discovery, several challenges remain, particularly regarding the regulatory approval and safety of nanomaterials ⁸². The unique properties of nanoparticles, such as their size, shape, surface charge, and reactivity, can raise concerns

about toxicity and environmental impact ⁸³. Future efforts will focus on the development of standardized guidelines for the use of nanomaterials in drug discovery. Improved risk assessment models, better understanding of nanomaterial-biology interactions, and advancements in nanotoxicology will be crucial for overcoming these challenges and ensuring the safe integration of nanotechnology in clinical applications.

CONCLUSION

Polysaccharide-based nano-drug delivery systems offer significant advantages in enhancing drug solubility, bioavailability, targeted delivery, and patient compliance, thereby contributing to the advancement of precision medicine. There are certain issues such as structural variability of natural polysaccharides, batch-to-batch inconsistency, stability concerns, limited drug loading capacity, and potential immunogenicity remain critical obstacles. The complexity of large-scale manufacturing, stringent regulatory requirements, and high production costs further restrict their industrial application. Addressing these limitations requires innovative approaches in material modification, advanced formulation techniques, and interdisciplinary research integrating nanotechnology, pharmaceutical sciences, and biomedical engineering. With continued progress in overcoming these barriers, polysaccharide-based nano-drug delivery systems hold immense potential to revolutionize therapeutic strategies and play a pivotal role in future healthcare solutions.

Acknowledgement: Huge thanks to the entire faculty of Mata Gujri College of Pharmacy, Kishanganj, Bihar, who shared their valuable knowledge throughout this review.

Source of Support: The author(s) received no financial support for the research, authorship, and/or publication of this article

Conflict of Interest: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES

1. Zeng Y, Xiang Y, Sheng R, Tomás H, Rodrigues J, Gu Z, Zhang H, Gong Q, Luo K. Polysaccharide-based nanomedicines for cancer immunotherapy: A review. *Bioactive Materials*. 2021 Oct 1;6(10):3358-82.
2. Peng P, Yang K, Tong G, Ma L. Polysaccharide nanoparticles for targeted cancer therapies. *Current Drug Metabolism*. 2018 Aug 1;19(9):781-92.
3. Mikušová V, Mikuš P. Advances in chitosan-based nanoparticles for drug delivery. *International journal of molecular sciences*. 2021 Sep 6;22(17):9652.
4. Imran H, Tang Y, Wang S, Yan X, Liu C, Guo L, Wang E, Xu C. Optimized DOX Drug Deliveries via Chitosan-Mediated Nanoparticles and Stimuli Responses in Cancer Chemotherapy: A Review. *Molecules*. 2023 Dec 20;29(1):31.
5. Herdiana Y, Wathoni N, Shamsuddin S, Muchtaridi M. Drug release study of the chitosan-based nanoparticles. *Heliyon*. 2022 Jan 1;8(1).
6. Negreanu-Pirjol BS, Negreanu-Pirjol T, Popoviciu DR, Anton RE, Prelipcean AM. Marine bioactive compounds derived from macroalgae as new potential players in drug delivery systems: a review. *Pharmaceutics*. 2022 Aug 25;14(9):1781.



7. Purcell-Meyerink D, Packer MA, Wheeler TT, Hayes M. Aquaculture production of the brown seaweeds *Laminaria digitata* and *Macrocystis pyrifera*: applications in food and pharmaceuticals. *Molecules*. 2021 Feb 28;26(5):1306.
8. Mahmoudi C, Tahraoui Douma N, Mahmoudi H, Iurciuc CE, Popa M. Hydrogels based on proteins cross-linked with carbonyl derivatives of polysaccharides, with biomedical applications. *International Journal of Molecular Sciences*. 2024 Jul 17;25(14):7839.
9. Michalczyk M, Humeniuk E, Adamczuk G, Korga-Plewko A. Hyaluronic acid as a modern approach in anticancer therapy-review. *International Journal of Molecular Sciences*. 2022 Dec 21;24(1):103.
10. Iaconisi GN, Lunetti P, Gallo N, Cappello AR, Fiermonte G, Dolce V, Capobianco L. Hyaluronic Acid: A Powerful Biomolecule with Wide-Ranging Applications—A Comprehensive Review. *International Journal of Molecular Sciences*. 2023 Jun 18;24(12):10296.
11. Rahman MS, Hasan MS, Nitai AS, Nam S, Karmakar AK, Ahsan MS, Shiddiky MJ, Ahmed MB. Recent developments of carboxymethyl cellulose. *Polymers*. 2021 Apr 20;13(8):1345.
12. Hu Q, Lu Y, Luo Y. Recent advances in dextran-based drug delivery systems: From fabrication strategies to applications. *Carbohydrate polymers*. 2021 Jul 15;264:117999.
13. Chen F, Huang G, Huang H. Preparation and application of dextran and its derivatives as carriers. *International journal of biological macromolecules*. 2020 Feb 15;145:827-34.
14. Lu A, Li S. Polysaccharides as a Hydrophilic Building Block of Amphiphilic Block Copolymers for the Conception of Nanocarriers. *Pharmaceutics*. 2024 Mar 27;16(4):467.
15. Nichifor M. Role of hydrophobic associations in self-healing hydrogels based on amphiphilic polysaccharides. *Polymers*. 2023 Feb 21;15(5):1065.
16. Rial-Hermida MI, Rey-Rico A, Blanco-Fernandez B, Carballo-Pedraes N, Byrne EM, Mano JF. Recent progress on polysaccharide-based hydrogels for controlled delivery of therapeutic biomolecules. *ACS Biomaterials Science & Engineering*. 2021 Jun 17;7(9):4102-27.
17. Di X, Liang X, Shen C, Pei Y, Wu B, He Z. Carbohydrates used in polymeric systems for drug delivery: from structures to applications. *Pharmaceutics*. 2022 Mar 29;14(4):739.
18. Plucinski A, Lyu Z, Schmidt BV. Polysaccharide nanoparticles: From fabrication to applications. *Journal of Materials Chemistry B*. 2021;9(35):7030-62.
19. Khakpour S, Hosano N, Moosavi-Nejad Z, Farajian AA, Hosano H. Advancing Tumor Therapy: Development and Utilization of Protein-Based Nanoparticles. *Pharmaceutics*. 2024 Jul;16(7):887.
20. Xie Y, Liu Q, Ge Y, Liu Y, Yang R. Formation and Applications of Typical Basic Protein-Based Heteroprotein Complex Coacervations. *Foods*. 2024 Oct 16;13(20):3281.
21. Sreekumar S, Goycoolea FM, Moerschbacher BM, Rivera-Rodriguez GR. Parameters influencing the size of chitosan-TPP nano- and microparticles. *Scientific reports*. 2018 Mar 16;8(1):4695.
22. Muto H, Yokoi A, Tan WK. Electrostatic assembly technique for novel composites fabrication. *Journal of Composites Science*. 2020 Oct 20;4(4):155-62.
23. Rehman A, Jafari SM, Tong Q, Riaz T, Assadpour E, Aadil RM, Niazi S, Khan IM, Shehzad Q, Ali A, Khan S. Drug nanodelivery systems based on natural polysaccharides against different diseases. *Advances in Colloid and Interface Science*. 2020 Oct 1;284:102251.
24. Visan AI, Cristescu R. Polysaccharide-based coatings as drug delivery systems. *Pharmaceutics*. 2023 Aug 29;15(9):2227.
25. Kurczewska J. Chitosan-based nanoparticles with optimized parameters for targeted delivery of a specific anticancer drug—a comprehensive review. *Pharmaceutics*. 2023 Feb;15(2):503.
26. Lu X, Chen J, Guo Z, Zheng Y, Rea MC, Su H, Zheng X, Zheng B, Miao S. Using polysaccharides for the enhancement of functionality of foods: A review. *Trends in Food Science & Technology*. 2019 Apr 1;86:311-27.
27. Mendes BB, Connot J, Avital A, Yao D, Jiang X, Zhou X, Sharf-Pauker N, Xiao Y, Adir O, Liang H, Shi J. Nanodelivery of nucleic acids. *Nature reviews Methods primers*. 2022 Apr 14;2(1):24.
28. Hou L, Wu P. Exploring the hydrogen-bond structures in sodium alginate through two-dimensional correlation infrared spectroscopy. *Carbohydrate polymers*. 2019 Feb 1;205:420-6.
29. Zhu Y, Liu Y, Jin K, Pang Z. Polysaccharide nanoparticles for cancer drug targeting. In *Polysaccharide carriers for drug delivery* 2019 Jan 1 (pp. 365-396). Woodhead Publishing.
30. Grabska-Zielińska S. Cross-linking agents in three-component materials dedicated to biomedical applications: a review. *Polymers*. 2024 Sep 23;16(18):2679.
31. Rostamabadi H, Falsafi SR, Rostamabadi MM, Assadpour E, Jafari SM. Electrospraying as a novel process for the synthesis of particles/nanoparticles loaded with poorly water-soluble bioactive molecules. *Advances in colloid and interface science*. 2021 Apr 1;290:102384.
32. Devi N, Sarmah M, Khatun B, Maji TK. Encapsulation of active ingredients in polysaccharide–protein complex coacervates. *Advances in colloid and interface science*. 2017 Jan 1;239:136-45.
33. Wang J, Wu X, Chen J, Gao T, Zhang Y, Yu N. Traditional Chinese medicine polysaccharide in nano-drug delivery systems: Current progress and future perspectives. *Biomedicine & Pharmacotherapy*. 2024 Apr 1;173:116330.
34. Kashkooli FM, Soltani M, Souri M. Controlled anti-cancer drug release through advanced nano-drug delivery systems: Static and dynamic targeting strategies. *Journal of controlled release*. 2020 Nov 10;327:316-49.
35. Bayer IS. Controlled drug release from nanoengineered polysaccharides. *Pharmaceutics*. 2023 Apr 28;15(5):1364.
36. Farasati Far B, Naimi-Jamal MR, Safaei M, Zarei K, Moradi M, Yazdani Nezhad H. A review on biomedical application of polysaccharide-based hydrogels with a focus on drug delivery systems. *Polymers*. 2022 Dec 12;14(24):5432.
37. Alkhalidi HM, Alahmadi AA, Rizg WY, Yahya EB, HPS AK, Mushtaq RY, Badr MY, Safhi AY, Hosny KM. Revolutionizing cancer treatment: biopolymer-based aerogels as smart platforms for targeted drug delivery. *Macromolecular Rapid Communications*. 2024 May;45(9):2300687.
38. Minehan RL, Del Borgo MP. Controlled release of therapeutics from enzyme-responsive biomaterials. *Frontiers in Biomaterials Science*. 2022 Jun 27;1:916985.
39. Cook AB, Decuzzi P. Harnessing endogenous stimuli for responsive materials in theranostics. *ACS nano*. 2021 Feb 8;15(2):2068-98.
40. Song M, Aipire A, Dilxat E, Li J, Xia G, Jiang Z, Fan Z, Li J. Research progress of polysaccharide-gold nanocomplexes in drug delivery. *Pharmaceutics*. 2024 Jan 9;16(1):88.
41. Marsili L, Dal Bo M, Berti F, Toffoli G. Chitosan-based biocompatible copolymers for thermoresponsive drug delivery systems: on the development of a standardization system. *Pharmaceutics*. 2021 Nov 5;13(11):1876.
42. Jin T, Liu T, Lam E, Moores A. Chitin and chitosan on the nanoscale. *Nanoscale Horizons*. 2021;6(7):505-42.
43. Herdiana Y, Wathoni N, Shamsuddin S, Muchtaridi M. Drug release study of the chitosan-based nanoparticles. *Heliyon*. 2022 Jan 1;8(1).
44. Abka-Khajouei R, Tounsi L, Shahabi N, Patel AK, Abdelkafi S, Michaud P. Structures, properties and applications of alginates. *Marine drugs*. 2022 May 29;20(6):364.
45. Kothale D, Verma U, Dewangan N, Jana P, Jain A, Jain D. Alginate as promising natural polymer for pharmaceutical, food, and biomedical applications. *Current drug delivery*. 2020 Oct 1;17(9):755-75.
46. Juncan AM, Moisă DG, Santini A, Morgovan C, Rus LL, Vonica-Țincu AL, Loghin F. Advantages of hyaluronic acid and its combination with other bioactive ingredients in cosmeceuticals. *Molecules*. 2021 Jul 22;26(15):4429.
47. Matalqah S, Lafi Z, Asha SY. Hyaluronic acid in nanopharmaceuticals: an overview. *Current Issues in Molecular Biology*. 2024 Sep 20;46(9):10444-61.
48. Banerjee A, Bandopadhyay R. Use of dextran nanoparticle: A paradigm shift in bacterial exopolysaccharide based biomedical applications.



- International journal of biological macromolecules. 2016 Jun 1;87:295-301.
49. Yusuf A, Almotairy AR, Henidi H, Alshehri OY, Aldughaim MS. Nanoparticles as drug delivery systems: a review of the implication of nanoparticles' physicochemical properties on responses in biological systems. *Polymers*. 2023 Mar 23;15(7):1596.
 50. Kumar R, Kumar N, Rajput VD, Mandzhieva S, Minkina T, Saharan BS, Kumar D, Sath PK, Duhan JS. Advances in biopolymeric nanopesticides: A new eco-friendly/eco-protective perspective in precision agriculture. *Nanomaterials*. 2022 Nov 10;12(22):3964.
 51. Antony Jose S, Cowan N, Davidson M, Godina G, Smith I, Xin J, Menezes PL. A comprehensive review on cellulose Nanofibers, nanomaterials, and composites: Manufacturing, properties, and applications. *Nanomaterials*. 2025 Feb 25;15(5):356.
 52. Rai M, Wypij M, Ingle AP, Trzcińska-Wencel J, Golińska P. Emerging trends in pullulan-based antimicrobial systems for various applications. *International journal of molecular sciences*. 2021 Dec 18;22(24):13596.
 53. Ahmed Omar N, Amédée J, Letourneur D, Fricain JC, Fenelon M. Recent advances of pullulan and/or dextran-based materials for bone tissue engineering strategies in preclinical studies: a systematic review. *Frontiers in Bioengineering and Biotechnology*. 2022 Jun 30;10:889481.
 54. Shahbaz A, Hussain N, Basra MA, Bilal M. Polysaccharides-based nano-Hybrid biomaterial platforms for tissue engineering, drug delivery, and food packaging applications. *Starch-Stärke*. 2022 Jul;74(7-8):2200023.
 55. Kotenkova E, Kotov A, Nikitin M. Polysaccharide-Based Nanocarriers for Natural Antimicrobials: A Review. *Polymers*. 2025 Jun 24;17(13):1750.
 56. Krystyan M, Khachatryan G, Khachatryan K, Krzan M, Ciesielski W, Żarska S, Szczepankowska J. Polysaccharides composite materials as carbon nanoparticles carrier. *Polymers*. 2022 Feb 26;14(5):948.
 57. Młynek M, Trzciński JW, Ciach T. Recent advances in the Polish research on polysaccharide-based nanoparticles in the context of various administration routes. *Biomedicines*. 2023 Apr 28;11(5):1307.
 58. Song M, Aipire A, Dilxat E, Li J, Xia G, Jiang Z, Fan Z, Li J. Research progress of polysaccharide-gold nanocomplexes in drug delivery. *Pharmaceutics*. 2024 Jan 9;16(1):88.
 59. Alfinaikh RS, Alamry KA, Hussein MA. Sustainable and biocompatible hybrid materials-based sulfated polysaccharides for biomedical applications: a review. *RSC advances*. 2025;15(6):4708-67.
 60. Kučuk N, Primožič M, Knez Ž, Leitgeb M. Sustainable biodegradable biopolymer-based nanoparticles for healthcare applications. *International journal of molecular sciences*. 2023 Feb 6;24(4):3188.
 61. Plucinski A, Lyu Z, Schmidt BV. Polysaccharide nanoparticles: from fabrication to applications. *Journal of Materials Chemistry B*. 2021;9(35):7030-62.
 62. Bianchera A, Bettini R. Polysaccharide nanoparticles for oral controlled drug delivery: The role of drug-polymer and interpolymer interactions. *Expert Opinion on Drug Delivery*. 2020 Oct 2;17(10):1345-59.
 63. Rosales TK, Fabi JP. Valorization of polyphenolic compounds from food industry by-products for application in polysaccharide-based nanoparticles. *Frontiers in nutrition*. 2023 May 24;10:1144677.
 64. Benalaya I, Alves G, Lopes J, Silva LR. A review of natural polysaccharides: sources, characteristics, properties, food, and pharmaceutical applications. *International Journal of Molecular Sciences*. 2024 Jan 22;25(2):1322.
 65. Fabozzi A, Della Sala F, di Gennaro M, Barretta M, Longobardo G, Solimando N, Pagliuca M, Borzacchiello A. Design of functional nanoparticles by microfluidic platforms as advanced drug delivery systems for cancer therapy. *Lab on a Chip*. 2023;23(5):1389-409.
 66. Stevanović M, Filipović N. A review of recent developments in biopolymer nano-based drug delivery systems with antioxidative properties: Insights into the last five years. *Pharmaceutics*. 2024 May 16;16(5):670.
 67. Malik S, Muhammad K, Waheed Y. Emerging applications of nanotechnology in healthcare and medicine. *Molecules*. 2023 Jan;28(18):6624.
 68. Kardani SL. Nanocarrier-based formulations: regulatory challenges, ethical and safety considerations in pharmaceuticals. *Asian Journal of Pharmaceutics (AJP)*. 2024 Jun 15;18(02).
 69. Ong WJ, Zheng N, Antonietti M. Advanced nanomaterials for energy conversion and storage: current status and future opportunities. *Nanoscale*. 2021;13(22):9904-7.
 70. Chakrabartty I, Hakeem KR, Mohanta YK, Varma RS. Greener nanomaterials and their diverse applications in the energy sector. *Clean Technologies and Environmental Policy*. 2022 Dec;24(10):3237-52.
 71. Aflori M. Smart nanomaterials for biomedical applications—a review. *Nanomaterials*. 2021 Feb 4;11(2):396.
 72. Abdel-Fatah MA, Ewies EF. Green Nanotechnology for Sustainable Ecosystems: Innovations in Pollution Remediation and Resource Recovery. *Egyptian Journal of Chemistry*. 2025 Oct 1;68(10):621-33.
 73. Jain K, Patel AS, Pardhi VP, Flora SJ. Nanotechnology in wastewater management: a new paradigm towards wastewater treatment. *Molecules*. 2021 Mar 23;26(6):1797.
 74. Emeihe EV, Nwankwo EI, Ajegbile MD, Olaboye JA, Maha CC. Revolutionizing drug delivery systems: Nanotechnology-based approaches for targeted therapy. *Int J Life Sci Res Arch*. 2024 Aug;7(1):40-58.
 75. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. *Nature reviews drug discovery*. 2021 Feb;20(2):101-24.
 76. Aldewachi H, Al-Zidan RN, Conner MT, Salman MM. High-throughput screening platforms in the discovery of novel drugs for neurodegenerative diseases. *Bioengineering*. 2021 Feb 23;8(2):30.
 77. Leong YX, Tan EX, Leong SX, Lin Koh CS, Thanh Nguyen LB, Ting Chen JR, Xia K, Ling XY. Where nanosensors meet machine learning: Prospects and challenges in detecting Disease X. *ACS nano*. 2022 Sep 6;16(9):13279-93.
 78. Liu Y, Liang Y, Yuhong J, Xin P, Han JL, Du Y, Yu X, Zhu R, Zhang M, Chen W, Ma Y. Advances in nanotechnology for enhancing the solubility and bioavailability of poorly soluble drugs. *Drug design, development and therapy*. 2024 Dec 31:1469-95.
 79. Ishaque PI. Convergence at the Nanoscale: Transformative Advances in Drug Delivery, Vaccinology, and Biomedical Diagnostics. *Sch Acad J Pharm*. 2025 Aug;6:128-62.
 80. Agrahari V, Choonara YE, Mosharraf M, Patel SK, Zhang F. The Role of Artificial Intelligence and Machine Learning in Accelerating the Discovery and Development of Nanomedicine. *Pharmaceutical Research*. 2024 Dec;41(12):2289-97.
 81. Das KP. Nanoparticles and convergence of artificial intelligence for targeted drug delivery for cancer therapy: Current progress and challenges. *Frontiers in Medical Technology*. 2023 Jan 6;4:1067144.
 82. Kardani SL. Nanocarrier-based formulations: regulatory challenges, ethical and safety considerations in pharmaceuticals. *Asian Journal of Pharmaceutics (AJP)*. 2024 Jun 15;18(02).
 83. Saha S. How nanoinformatics could pave the way to safer design of engineered nanomaterials?. *Frontiers in Nanotechnology*. 2025 Mar 5;7:1559053.

For any questions related to this article, please reach us at: globalresearchonline@rediffmail.com

New manuscripts for publication can be submitted at: submit@globalresearchonline.net and submit_ijpsrr@rediffmail.com

