INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Article

A Review on Nanoparticles: Synthesis, Characterisation, and Applications in Pharmaceutical Sciences

Daiwashala Pawar*, Amol Ratke, Sneha Wadu, Ruchira Medankar

Department of Pharmaceutics, IVM'S Krishnarao Bhegade Institute of Pharmaceutical Education and Research, Talegaon Dabhade, Pune 410506.

ARTICLE INFO

Published: 06 July 2026
Keywords:
Nanoparticles; Drug Delivery Systems; Nanomedicine; Pharmaceutical Applications; Targeted Drug Delivery.
DOI:
10.5281/zenodo.21222368

ABSTRACT

Nanoparticles have emerged as a promising platform in pharmaceutical sciences due to their unique physicochemical properties and ability to enhance the delivery of therapeutic agents. Their nanoscale size, large surface area, and tunable surface characteristics enable improved drug solubility, bioavailability, stability, and targeted delivery. Nanoparticle-based drug delivery systems have gained significant attention for overcoming the limitations of conventional dosage forms, including poor pharmacokinetics, non-specific distribution, and undesirable side effects. Various types of nanoparticles, such as polymeric nanoparticles, lipid-based nanoparticles, metallic nanoparticles, magnetic nanoparticles, dendrimers, and mesoporous silica nanoparticles, have been extensively investigated for pharmaceutical applications. The synthesis of nanoparticles can be achieved through physical, chemical, and biological approaches, while advanced characterization techniques are essential for evaluating their size, morphology, surface charge, crystallinity, and stability. Nanoparticles have demonstrated remarkable potential in targeted drug delivery, cancer therapy, gene delivery, vaccine development, antimicrobial therapy, diagnostic imaging, and theranostic applications. Despite these advantages, challenges related to large-scale manufacturing, regulatory approval, long-term safety, and biological interactions continue to limit their widespread clinical translation. Recent advancements in artificial intelligence, personalized nanomedicine, biomimetic nanocarriers, and next-generation lipid nanoparticles are opening new avenues for the development of more effective and safer nanotherapeutics. This review provides a comprehensive overview of nanoparticle synthesis methods, characterization techniques, pharmaceutical applications, regulatory considerations, current challenges, and future perspectives. Continued progress in nanotechnology and pharmaceutical engineering is expected to accelerate the successful integration of nanoparticle-based systems into modern healthcare and precision medicine.

***Corresponding Author:** Daiwashala Pawar
Address: *IVM'S Krishnarao Bhegade Institute of Pharmaceutical Education and Research, Talegaon Dabhade, Pune*
Email : daivashalapawar9@gmail.com

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

INTRODUCTION

1.1 Definition and Fundamental Concepts

Nanoparticles are defined as particulate materials with at least one dimension in the nanoscale range of 1 to 1000 nanometers (nm). In the context of pharmaceutical sciences, nanoparticles typically refer to colloidal systems with sizes ranging from 10 to 1000 nm that can serve as carriers for therapeutic agents including small molecule drugs, proteins, peptides, nucleic acids, and imaging agents. The term "nanoparticle" encompasses a broad spectrum of carrier systems including polymeric nanoparticles, lipid nanoparticles, metallic nanoparticles, dendrimers, micelles, and hybrid systems combining multiple materials.[1] The unique properties of nanoparticles arise from their nanoscale dimensions, which confer distinct physicochemical characteristics compared to their bulk counterparts. The extremely high surface area-to-volume ratio of nanoparticles enables enhanced interaction with biological membranes and cellular components. Quantum effects become apparent at the nanoscale, particularly for metallic nanoparticles, leading to unique optical, electronic, and magnetic properties. The small size allows nanoparticles to penetrate biological barriers that are impermeable to larger particles, including the blood-brain barrier, tight junctions of the intestinal epithelium, and tumor vasculature through the enhanced permeability and retention (EPR) effect.[2]

1.2 Historical Evolution and Milestones

The concept of using colloidal particles for drug delivery dates back to the early 20th century, but the modern era of pharmaceutical nanoparticles began in the 1970s with the development of liposomes by Gregoriadis and colleagues. The first FDA-approved nanomedicine, Doxil (doxorubicin liposomes), was introduced in 1995, marking a pivotal milestone in clinical translation. Since then, the field has experienced exponential growth, with over 100 nanomedicine products receiving regulatory approval worldwide by 2025. The evolution of pharmaceutical nanoparticles can be categorized into several generations:

1. **First Generation (1970s-1990s):** Basic carrier systems including conventional liposomes, polymeric nanoparticles, and emulsions. These systems primarily focused on passive targeting through the EPR effect and simple encapsulation of hydrophobic drugs.

2. **Second Generation (1990s-2010s):** Surface-modified nanoparticles with stealth properties (PEGylation), active targeting ligands (antibodies, peptides, aptamers), and stimuli-responsive capabilities. This period also saw the development of dendrimers, solid lipid nanoparticles, and nanostructured lipid carriers.

3. **Third Generation (2010s-2020s):** Multifunctional and intelligent nanoparticles capable of simultaneous diagnosis and therapy (theranostics), gene delivery systems including lipid nanoparticles for mRNA, CRISPR-Cas9 delivery platforms, and personalized nanomedicine approaches tailored to individual patient profiles.

4. **Fourth Generation (2020s-present):** AI-designed nanoparticles, nanorobotics, 3D-printed nanoformulations, and self-assembling systems with unprecedented precision and functionality. The COVID-19 pandemic accelerated the development and regulatory approval of lipid nanoparticle-based mRNA vaccines, demonstrating the rapid clinical translation potential of nanotechnology.[3]

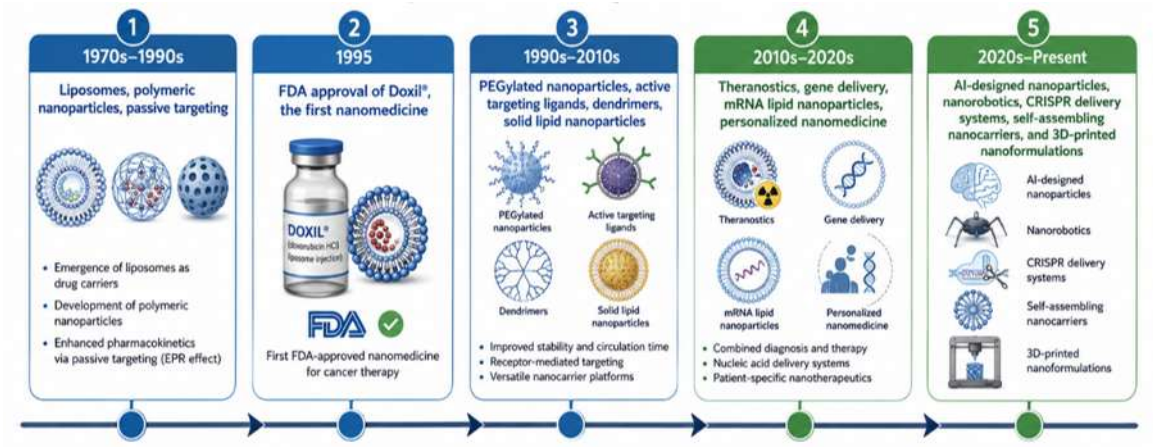

Figure 1. Historical evolution of nanoparticle-based drug delivery systems from conventional carrier systems to advanced intelligent nanomedicines.

1.3 Significance and Advantages in Pharmaceutical Sciences

The incorporation of nanoparticles into pharmaceutical formulations offers numerous compelling advantages that address critical limitations of conventional drug delivery approaches:

- **Enhanced Solubility and Bioavailability**: Many promising therapeutic agents, particularly anticancer drugs and natural compounds, suffer from poor aqueous solubility, leading to low oral bioavailability and requiring high doses or parenteral administration. Nanoparticle encapsulation can dramatically increase the apparent solubility of hydrophobic drugs, with some systems achieving up to 100-fold improvement in dissolution rates compared to conventional formulations.

- **Targeted Drug Delivery:** Nanoparticles can be engineered to selectively accumulate in target tissues through passive targeting (EPR effect in tumors) or active targeting (ligand-receptor interactions). This targeting capability reduces systemic exposure and minimizes off-target toxicity, particularly important for cytotoxic chemotherapeutic agents.

- **Controlled and Sustained Release:** The drug release profile from nanoparticles can be precisely tuned through selection of carrier materials, particle size, surface modifications, and incorporation of stimuli-responsive elements. This enables sustained therapeutic levels over extended periods, reducing dosing frequency and improving patient compliance. Protection of Labile Drugs: Encapsulation within nanoparticles protects sensitive therapeutic agents from degradation by enzymes, pH changes, and other environmental factors during transit to the target site. This is particularly valuable for proteins, peptides, and nucleic acids that are rapidly degraded in biological fluids.

- **Crossing Biological Barriers:** The nanoscale dimensions enable nanoparticles to cross biological barriers that are impermeable to larger drug molecules. This includes the blood-brain barrier for neurological disorders, the intestinal epithelium for oral delivery of macromolecules, and the skin barrier for transdermal delivery.

- **Combination Therapy:** Nanoparticles can simultaneously encapsulate multiple therapeutic agents with different

physicochemical properties, enabling synergistic combination therapies. This approach is particularly valuable in cancer treatment where drug resistance is a major challenge.

- **Imaging and Diagnostics:** Nanoparticles can be loaded with imaging agents (contrast agents for MRI, fluorescent probes, radionuclides) to enable real-time tracking of drug distribution, monitoring of therapeutic response, and early detection of diseases.[4,5]

1.4 Classification of Pharmaceutical Nanoparticles

Pharmaceutical nanoparticles can be classified based on their composition, structure, and origin:

A. Organic Nanoparticles:

i. **Lipid-based:** Liposomes, solid lipid nanoparticles (SLN), nanostructured lipid carriers (NLC), lipid nanoparticles (LNP)

ii. **Polymeric**: Poly(lactic acid) (PLA), poly(glycolic acid) (PGA), poly(lactic-co-glycolic acid) (PLGA), poly(caprolactone) (PCL), chitosan, alginate, gelatin nanoparticles

iii. **Dendrimers**: Polyamidoamine (PAMAM), poly(propylene imine) (PPI), poly(lysine) dendrimers

iv. **Micelles:** Polymeric micelles, surfactant micelles

B. Inorganic Nanoparticles:

i. **Metallic:** Gold nanoparticles (AuNPs), silver nanoparticles (AgNPs), iron oxide nanoparticles (IONPs), copper nanoparticles

ii. **Metal oxide:** Zinc oxide (ZnO), titanium dioxide (TiO2), cerium oxide (CeO2) nanoparticles

iii. **Silica:** Mesoporous silica nanoparticles (MSN), silica nanospheres

iv. **Carbon-based:** Carbon nanotubes, graphene, fullerenes, carbon dots

C. Hybrid Nanoparticles:

i. Polymer-lipid hybrid nanoparticles

ii. Metal-polymer nanocomposites

iii. Core-shell structures

iv. Layer-by-layer assembled nanoparticles

D. Biological Nanoparticles:

i. Exosomes and extracellular vesicles

ii. Virus-like particles

iii. Protein-based nanoparticles (albumin, ferritin)

iv. Cell membrane-coated nanoparticles. [6,7]

2. SYNTHESIS OF NANOPARTICLES

2.1 Top-Down Approaches

2.1.1 Ball Milling

Ball milling is a mechanical attrition technique where bulk material is ground in a rotating cylindrical container filled with milling media (balls) under controlled conditions. The impact and shear forces generated during milling break down the material into nanoparticles. Parameters such as milling speed, duration, ball-to-powder ratio, and use of surfactants or stabilizers significantly influence the particle size and

morphology. High-energy ball milling can produce nanoparticles in the range of 10-100 nm, though the size distribution is often broad. The technique is scalable and cost-effective but may introduce contamination from the milling media and lacks precise control over particle characteristics.[8]

2.1.2 High-Pressure Homogenization

High-pressure homogenization forces a coarse suspension through a small orifice under high pressure (typically 100-2000 bar), creating intense shear, cavitation, and impact forces that reduce particle size. This technique is widely used for producing nanosuspensions of poorly water-soluble drugs. Multiple homogenization cycles are typically required to achieve the desired particle size. The method is suitable for thermolabile compounds as it operates at ambient or slightly elevated temperatures. However, the process can be energy-intensive and may require high drug concentrations.[9]

2.1.3 Media Milling (Nanocrystal Technology)

Media milling involves grinding drug particles in a liquid medium using milling beads (typically 0.2-0.5 mm) in a stirred media mill. Stabilizers such as surfactants or polymers are added to prevent agglomeration. This technique has been successfully commercialized for producing nanocrystal formulations (e.g., Rapamune, Emend). The process can achieve particle sizes below 400 nm and is scalable for industrial production. Challenges include potential contamination from milling media and the need for extensive washing steps.[10]

2.2 Bottom-Up Approaches

2.2.1 Precipitation Methods

1. **Solvent Evaporation Method**: In this widely used technique, the drug and polymer are dissolved in a volatile organic solvent (typically dichloromethane, chloroform, or ethyl acetate). The organic solution is then emulsified in an aqueous phase containing a surfactant or stabilizer using high-speed homogenization or sonication. The organic solvent is subsequently evaporated under reduced pressure or by stirring at ambient temperature, causing the polymer to precipitate around the drug and form nanoparticles. The nanoparticles are collected by centrifugation and washed to remove residual solvent and surfactant. This method is suitable for hydrophobic drugs and can achieve high encapsulation efficiency. However, the use of organic solvents raises safety concerns and requires extensive removal steps.[11]

2. **Solvent Displacement (Nanoprecipitation) Method:** Also known as the interfacial deposition method, this technique involves adding a solution of drug and polymer in a water-miscible organic solvent (such as acetone or ethanol) to an aqueous phase under moderate stirring. Rapid diffusion of the organic solvent into the aqueous phase causes precipitation of the polymer and drug, forming nanoparticles. The process is spontaneous and does not require high-energy homogenization. Hydrophobic drugs can be efficiently encapsulated, and the particle size is influenced by the solvent diffusion rate, polymer concentration, and stirring speed. The main advantages include simplicity, low energy requirements, and the ability to produce small nanoparticles (typically 100-300 nm). However, the method is limited to water-miscible solvents and may result in lower encapsulation efficiency for hydrophilic drugs.[12]

2.2.2 Emulsion-Based Methods

1. **Single Emulsion (Oil-in-Water, O/W):** This method is suitable for encapsulating hydrophobic drugs. The drug and polymer are dissolved in a volatile organic solvent (oil phase) and emulsified in an aqueous phase containing an emulsifier (surfactant or stabilizer) using high-speed homogenization or sonication. The organic solvent is then evaporated, and the polymer forms nanoparticles encapsulating the drug. Common emulsifiers include polyvinyl alcohol (PVA), poloxamers (Pluronic F68), and lecithin. The particle size depends on the homogenization intensity, emulsifier concentration, and viscosity of the phases. This method is versatile and widely used for producing polymeric nanoparticles.

2. **Double Emulsion (Water-in-Oil-in-Water, W/O/W):** The double emulsion method is employed for encapsulating both hydrophilic and hydrophobic drugs simultaneously or for hydrophilic drugs alone. In the first step, an aqueous solution of the hydrophilic drug is emulsified in an organic solution of the polymer using high-speed homogenization, forming a primary water-in-oil (W/O) emulsion. This primary emulsion is then added to a second aqueous phase containing an emulsifier and homogenized to form the W/O/W double emulsion. The organic solvent is evaporated, and the polymer precipitates to form nanoparticles with the hydrophilic drug encapsulated in the aqueous core and the hydrophobic drug (if present) in the polymer matrix. This method is particularly valuable for protein and peptide delivery but may result in lower encapsulation efficiency and broader size distribution compared to single emulsion.[13]

2.2.3 Supercritical Fluid Technology

1. **Supercritical Anti-Solvent (SAS) Method:** In the SAS method, the drug and polymer are dissolved in an organic solvent and sprayed into a vessel containing a supercritical fluid (typically supercritical CO2), which acts as an anti-solvent. The rapid diffusion of the organic solvent into the supercritical fluid causes supersaturation and precipitation of the solute as nanoparticles. The supercritical fluid simultaneously extracts the organic solvent, leaving dry nanoparticles. This technique produces solvent-free nanoparticles with controlled size and morphology. The process is environmentally friendly as CO2 is non-toxic and easily removed by depressurization.[14]

2. **Rapid Expansion of Supercritical Solutions (RESS):** In the RESS method, the drug is dissolved in a supercritical fluid (typically supercritical CO2) and the solution is rapidly expanded through a nozzle into a low-pressure chamber. The sudden decrease in pressure and temperature causes the solute to precipitate as nanoparticles. The particle size is controlled by the pre-expansion temperature, pressure, and nozzle design. This method is suitable for compounds with reasonable solubility in supercritical CO2 but may not be applicable to polar compounds without co-solvents.[15]

2.2.4 Coacervation and Ionic Gelation Methods

Coacervation Method: Coacervation involves the phase separation of a polymer solution into a polymer-rich phase (coacervate) and a polymer-poor phase. In simple coacervation, a non-solvent or change in temperature causes the polymer to separate from solution. In complex coacervation, two oppositely charged polymers interact to form a complex that separates as a coacervate phase. The drug is dispersed in the polymer solution, and

coacervation is induced, causing the polymer to encapsulate the drug particles. The coacervate droplets are then hardened by cross-linking, temperature change, or solvent removal. This method is particularly useful for natural polymers like gelatin, alginate, and chitosan. Ionic Gelation Method: Ionic gelation is a mild, aqueous-based method suitable for encapsulating sensitive biomolecules. In this technique, a polyelectrolyte solution (such as sodium alginate or chitosan) containing the drug is added dropwise to a solution containing multivalent counterions (such as calcium chloride for alginate or tripolyphosphate for chitosan). The electrostatic interaction between the polyelectrolyte and counterions causes gelation and formation of nanoparticles. The method is simple, does not require organic solvents or high temperatures, and is biocompatible. However, the particle size is relatively large (typically 200-1000 nm) and the drug loading may be limited.[16]

2.3 Green Synthesis Approaches (Emerging Trend 2023-2026)

2.3.1 Plant-Mediated Green Synthesis

Plant-mediated synthesis utilizes aqueous extracts of plant parts (leaves, roots, fruits, seeds, bark) as reducing and stabilizing agents for the production of metallic nanoparticles. The plant extracts contain a rich diversity of phytochemicals including polyphenols, flavonoids, terpenoids, alkaloids, and proteins that serve as both reducing agents (converting metal ions to metal nanoparticles) and capping agents (stabilizing the formed nanoparticles and preventing aggregation).

1. **Mechanism of Plant-Mediated Synthesis:** The synthesis process typically involves mixing an aqueous solution of metal salt (such as silver nitrate, chloroauric acid) with the plant extract at room temperature or mild heating. The phytochemicals in the extract donate electrons to reduce metal ions (M+) to metal atoms (M0). The metal atoms nucleate and grow into nanoparticles, while biomolecules from the plant extract adsorb onto the nanoparticle surface, acting as capping agents that prevent aggregation and provide stability. The color change of the reaction mixture (from colorless to brown for silver nanoparticles, or to ruby red for gold nanoparticles) indicates the formation of nanoparticles due to surface plasmon resonance.

   Recent studies have demonstrated the successful green synthesis of gold and silver nanoparticles using crude extracts of Aconitum violaceum, a medicinal plant from the Himalayan region. The synthesized AuNPs and AgNPs exhibited spherical and triangular morphologies with average sizes below 100 nm. The phytochemical screening revealed the presence of alkaloids, flavonoids, terpenoids, saponins, and anthraquinones in the extract, with alkaloids and flavonoids identified as the primary reducing and capping agents. The green-synthesized nanoparticles demonstrated effective antibacterial activities with minimum inhibitory concentrations (MICs) of 95 and 70 microg/mL against Lactobacillus acidophilus and 90 and 65 microg/mL against Escherichia coli for AuNPs and AgNPs, respectively. The enhanced antibacterial activity compared to the crude extract was attributed to the synergistic effect of phytochemicals and the nanoparticles themselves.

2. **Advantages of Plant-Mediated Synthesis:** Environmentally friendly and sustainable, utilizing renewable plant resources; Elimination of toxic chemical reducing agents (such as sodium borohydride, hydrazine);

Cost-effective and easily scalable; Biocompatibility due to natural capping by biomolecules; One-pot synthesis under mild conditions (ambient temperature, atmospheric pressure); Reduced energy requirements compared to physical methods.[17,18]

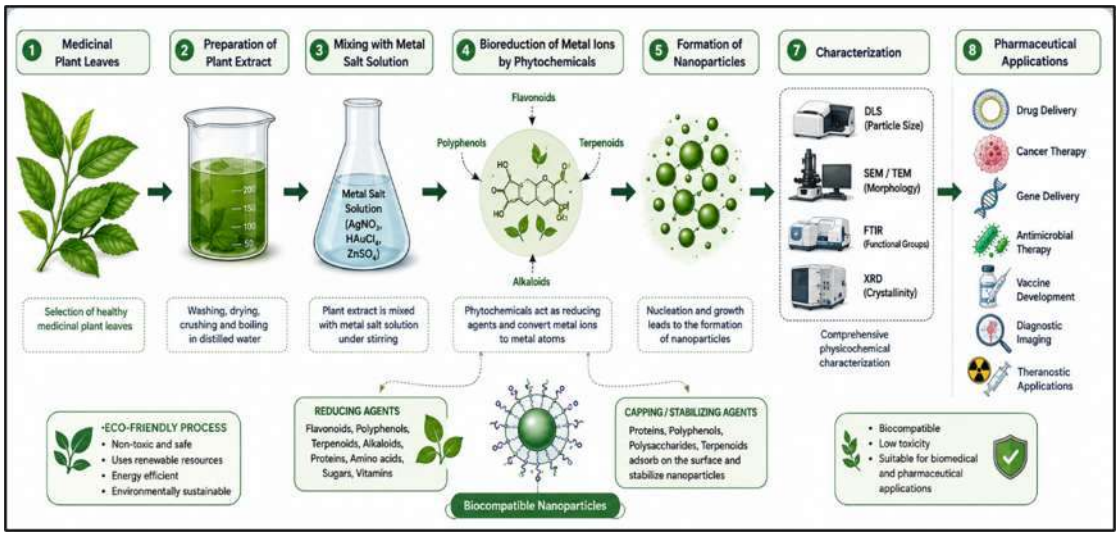

Figure 2. Green Synthesis of Nanoparticles Using Plant Extracts

2.3.2 Microbial-Mediated Green Synthesis

Microorganisms including bacteria, fungi, actinomycetes, and algae have been exploited for the biosynthesis of nanoparticles. The mechanism involves enzymatic reduction of metal ions by microbial cellular components or secreted biomolecules. Intracellular synthesis occurs within the microbial cell, while extracellular synthesis utilizes enzymes or metabolites secreted into the culture medium.

1. Bacterial Synthesis:

Bacteria such as *Pseudomonas*, *Bacillus*, and *Escherichia coli* can synthesize nanoparticles through enzymatic reduction of metal ions. This method offers rapid growth, easy cultivation, and scalability, although purification is required to remove endotoxins.

2. Fungal Synthesis:

Fungi including *Aspergillus*, *Fusarium*, and *Penicillium* species are widely used for nanoparticle synthesis due to their high enzyme production and metal tolerance. Fungal synthesis often provides higher yields and facilitates easier downstream processing.

3. Algal Synthesis:

Marine and freshwater algae can produce nanoparticles using naturally occurring polysaccharides, proteins, and pigments as reducing agents. This eco-friendly approach generates biocompatible nanoparticles suitable for pharmaceutical and biomedical applications.

2.3.3 Biopolymer-Mediated Synthesis

Biopolymers such as chitosan, alginate, starch, and cellulose derivatives can serve as both reducing and stabilizing agents for nanoparticle synthesis. Chitosan, a cationic polysaccharide derived from chitin, has been extensively studied for silver and gold nanoparticle synthesis due to its biocompatibility, antimicrobial properties, and ability to form complexes with metal ions. The amino and hydroxyl groups of chitosan participate in the reduction of metal ions and stabilization of

nanoparticles through coordination and electrostatic interactions.[19,20]

2.4 Comparison of Synthesis Methods

The selection of an appropriate synthesis method depends on various factors including the nature of the drug, desired particle characteristics, scale of production, regulatory requirements, and cost considerations. Table 1 presents a comprehensive comparison of the major synthesis methods for pharmaceutical nanoparticles.[21]

Table No. 1: Comparison of all Synthesis Methods

Method	Particle Size Range	Advantages	Limitations
Ball Milling	10-1000 nm	Scalable, cost-effective	Broad size distribution, contamination
High-Pressure Homogenization	100-1000 nm	Suitable for thermolabile compounds	Energy-intensive, high drug concentration needed
Media Milling (Nanocrystal)	<400 nm	Commercially proven (Rapamune)	Media contamination, extensive washing
Solvent Evaporation	100-1000 nm	Versatile, high encapsulation	Organic solvent residue, complex process
Nanoprecipitation	100-300 nm	Simple, low energy, small particles	Limited to water-miscible solvents
Single Emulsion (O/W)	100-1000 nm	Versatile, widely used	Organic solvents, limited to hydrophobic drugs
Double Emulsion (W/O/W)	200-1000 nm	Both hydrophilic and hydrophobic drugs	Lower efficiency, broader size distribution
Supercritical Fluid Technology	100-500 nm	Solvent-free, environmentally friendly	High equipment cost, limited solubility
Coacervation	200-1000 nm	Mild conditions, natural polymers	Complex process control
Ionic Gelation	200-1000 nm	Simple, aqueous, biocompatible	Large particles, limited loading
Green Synthesis (Plant/Microbial)	10-100 nm	Sustainable, biocompatible, cost-effective	Batch variability, limited mechanistic understanding

2.5 Recent Advances in Synthesis (2023-2026)

2.5.1 Microfluidic Synthesis

Microfluidic technology has emerged as a powerful platform for controlled nanoparticle synthesis, offering precise control over mixing, reaction conditions, and residence time. The laminar flow regime in microchannels enables rapid and uniform mixing of reagents, leading to narrow particle size distributions. Microfluidic devices can be designed with various geometries (T-junction, Y-junction, flow-focusing) to control the mixing pattern and nanoparticle formation. This technology is particularly valuable for the production of lipid nanoparticles for mRNA delivery, where precise control over lipid composition and particle size is critical for vaccine efficacy. Recent advances include the development of 3D-printed microfluidic devices and continuous flow systems for scalable production.

2.5.2 3D Printing of Nanoparticles

Three-dimensional printing technologies have been adapted for nanoparticle fabrication, enabling the creation of complex nanostructures with

precise spatial control. Techniques such as two-photon polymerization and direct laser writing can produce nanoparticles and nanostructures with resolutions below 100 nm. 3D printing allows for the fabrication of personalized nanoparticle-based drug delivery systems with tailored release profiles and geometries optimized for specific administration routes.

2.5.3 AI-Driven Nanoparticle Design

Artificial intelligence and machine learning algorithms are being increasingly applied to predict and optimize nanoparticle properties. Machine learning models trained on large datasets of nanoparticle formulations can predict the optimal synthesis parameters for desired particle characteristics, significantly reducing the time and cost of formulation development. AI-driven design is particularly promising for lipid nanoparticles, where the vast chemical space of lipid combinations makes experimental screening impractical.[22,23]

3. CHARACTERIZATION OF NANOPARTICLES

Characterization is a crucial step in the development of nanoparticle-based drug delivery systems because the physicochemical properties of nanoparticles directly influence their biological performance, therapeutic efficacy, stability, and safety. Comprehensive characterization helps in understanding particle size, morphology, surface charge, crystallinity, chemical composition, thermal behavior, drug loading capacity, and release characteristics. Regulatory agencies also require detailed characterization data to ensure product quality, reproducibility, and clinical safety.

3.1 Particle Size Analysis

Particle size is one of the most important parameters influencing nanoparticle behavior. It affects cellular uptake, biodistribution, circulation time, drug release kinetics, and targeting efficiency. Nanoparticles with smaller particle sizes generally exhibit improved cellular internalization and enhanced permeability through biological barriers.

Particle size distribution is commonly expressed in terms of mean particle diameter and polydispersity index (PDI). A narrow size distribution is desirable because it ensures formulation uniformity and reproducibility.

i. Dynamic Light Scattering (DLS)

Dynamic Light Scattering is the most widely used technique for measuring nanoparticle size in suspension. The method is based on the analysis of fluctuations in scattered light caused by the Brownian motion of particles. The diffusion coefficient obtained from these fluctuations is used to calculate the hydrodynamic diameter of nanoparticles.

Advantages:

- Rapid and non-destructive analysis
- Suitable for colloidal systems
- Provides particle size and PDI simultaneously.[24]

3.2 Polydispersity Index (PDI)

PDI is a measure of particle size distribution uniformity. It indicates the degree of heterogeneity within a nanoparticle formulation.Lower PDI values indicate better formulation quality and stability.[25]

Table no.2: Polydispersity Index (PDI)

PDI Value	Interpretation
< 0.1	Highly monodisperse system
0.1-0.3	Acceptable size distribution
> 0.3	Broad size distribution
> 0.7	Highly polydisperse system

3.3 Zeta Potential Analysis

Zeta potential is a measure of the electrical charge present on the nanoparticle surface. It is an important indicator of colloidal stability because surface charges generate electrostatic repulsion between particles, preventing aggregation.The zeta potential also influences interactions with biological membranes, protein adsorption, cellular uptake, and biodistribution.[26]

Table no.3: Polydispersity Index (PDI)

Zeta Potential (mV)	Stability
Above +30	Highly stable
Between +20 and +30	Moderately stable
Between -20 and +20	Limited stability
Below -30	Highly stable

3.4 Morphological Characterization

Morphological analysis provides information regarding nanoparticle shape, surface texture, aggregation state, and structural organization. Morphology significantly affects drug loading, release behavior, and biological interactions.

i. Scanning Electron Microscopy (SEM)

SEM uses a focused electron beam to scan the sample surface and generate high-resolution images.

Applications:

- Surface morphology analysis
- Shape determination
- Aggregation assessment
- Particle size estimation

Advantages:

- High-resolution imaging
- Large depth of field
- Excellent surface visualization

ii. Transmission Electron Microscopy (TEM)

TEM involves transmission of electrons through a thin sample to obtain highly detailed images.

Applications:

- Accurate particle size determination
- Internal structure analysis
- Core-shell nanoparticle characterization
- Crystallinity assessment

Advantages:

- Extremely high resolution
- Direct visualization of nanoparticles
- Internal structural analysis

iii. Atomic Force Microscopy (AFM)

AFM employs a nanoscale probe that scans the surface of nanoparticles to generate three-dimensional topographical images.

Applications:

- Surface roughness analysis
- Morphological characterization
- Mechanical property evaluation

Advantages:

- Three-dimensional imaging
- Minimal sample preparation
- High spatial resolution.[27]

3.5 Structural Characterization

Structural characterization determines crystalline structure, phase composition, and molecular organization of nanoparticles.

- **X-Ray Diffraction (XRD)**

XRD is used to identify crystalline phases and evaluate crystal structure. The technique measures diffraction patterns generated when X-rays interact with crystalline materials.The Debye-Scherrer equation is commonly used to estimate crystallite size from XRD peak broadening.

Applications:

- Determination of crystallinity
- Phase identification
- Crystal size estimation
- Evaluation of drug encapsulation effects

Advantages:

- Non-destructive analysis
- High accuracy
- Quantitative assessment of crystallinity.[27]

3.6 Chemical Characterization

Chemical characterization identifies functional groups, molecular interactions, and surface chemistry.

1. **Fourier Transform Infrared Spectroscopy (FTIR)**

FTIR detects absorption of infrared radiation by molecular bonds, generating characteristic spectra for specific functional groups.

Applications:

- Drug-polymer compatibility studies
- Surface functionalization analysis
- Confirmation of nanoparticle formation
- Identification of chemical interactions

Advantages:

- Rapid analysis
- Minimal sample preparation
- High sensitivity

2. **Raman Spectroscopy**

Raman spectroscopy provides molecular information based on inelastic scattering of light.

Applications:

- Molecular fingerprinting
- Structural characterization
- Surface chemistry analysis
- Detection of molecular interactions

Advantages:

- Non-destructive technique
- High specificity
- Suitable for aqueous samples.[28]

3.7 Surface Area Analysis

Surface area is a critical parameter influencing drug loading, dissolution rate, and adsorption capacity.

- **Brunauer-Emmett-Teller (BET) Analysis**

BET analysis determines specific surface area by measuring gas adsorption onto the nanoparticle surface. Higher surface area generally results in improved drug loading capacity and enhanced dissolution.

Applications:

- Surface area determination
- Porosity assessment
- Evaluation of mesoporous nanoparticles.[29]

4. PHARMACEUTICAL APPLICATIONS OF NANOPARTICLES

Nanoparticles have revolutionized modern pharmaceutical sciences by providing innovative solutions to challenges associated with conventional drug delivery systems. Their unique physicochemical properties, including small particle size, large surface area-to-volume ratio, tunable surface characteristics, and ability to encapsulate a wide range of therapeutic agents, make them highly effective carriers for pharmaceutical applications. Nanoparticles can improve drug solubility, enhance bioavailability, prolong circulation time, facilitate controlled release, and enable site-specific drug delivery. As a result, nanoparticle-based systems have found widespread applications in drug delivery, cancer therapy, gene therapy, vaccine development, antimicrobial treatment, diagnostic imaging, and theranostics.[30]

4.1 Targeted Drug Delivery

Targeted drug delivery is a major application of nanoparticles that improves therapeutic efficacy while reducing systemic toxicity. Drug-loaded nanoparticles circulate in the bloodstream and accumulate at diseased tissues or tumors through passive or active targeting mechanisms. After binding to target cells, they are internalized by endocytosis and release the drug in a controlled manner, resulting in enhanced treatment outcomes and reduced damage to healthy tissues.

i. Passive Targeting

Passive targeting relies on the Enhanced Permeability and Retention (EPR) effect observed in tumor tissues and inflamed sites. Tumors possess abnormal blood vessels with large fenestrations and poor lymphatic drainage, allowing nanoparticles to preferentially accumulate within tumor tissues.

Advantages of passive targeting include:

- Increased drug concentration at the disease site.
- Reduced exposure of healthy tissues.
- Improved therapeutic index.

ii. Active Targeting

Active targeting involves surface modification of nanoparticles with ligands such as antibodies, peptides, folic acid, aptamers, or transferrin. These ligands specifically recognize receptors overexpressed on target cells, facilitating receptor-mediated uptake.

Examples include:

- Folate receptor-targeted nanoparticles for ovarian cancer.

- HER2-targeted nanoparticles for breast cancer.
- Transferrin-modified nanoparticles for brain targeting.[31]

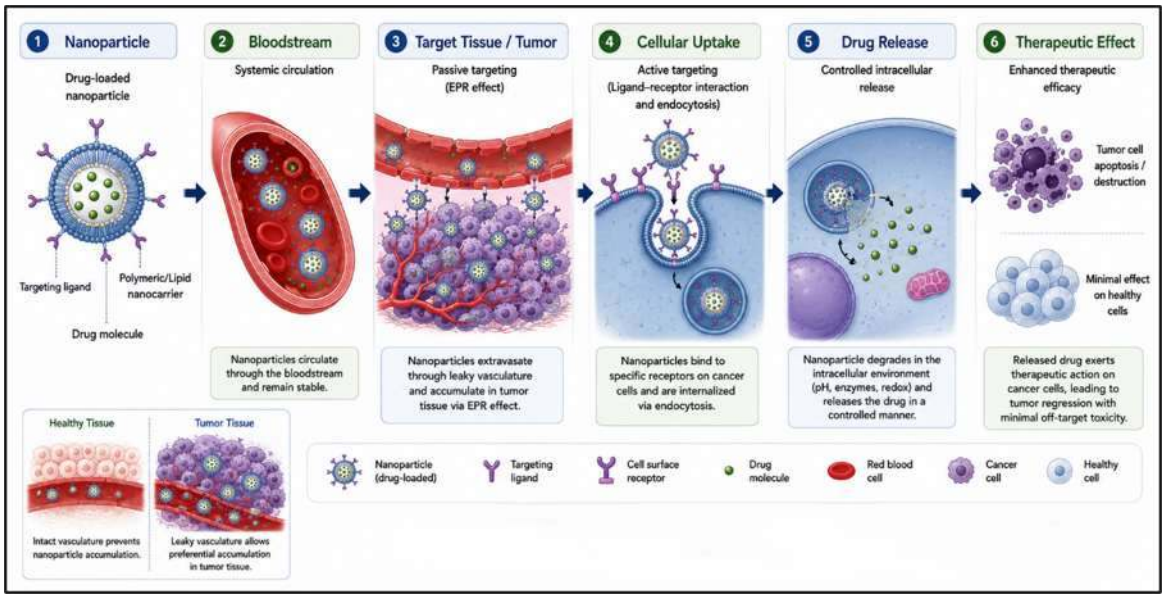

Figure 3. Schematic of Nanoparticle-Mediated Targeted Drug Delivery.

4.2 Cancer Therapy

Cancer remains one of the leading causes of mortality worldwide. Conventional chemotherapy is often associated with severe adverse effects due to non-specific distribution of anticancer drugs. Nanoparticle-based drug delivery systems have emerged as effective strategies for improving cancer treatment.

Nanoparticles can encapsulate chemotherapeutic agents and deliver them selectively to tumor tissues. This approach improves drug accumulation at the tumor site while reducing systemic exposure.

i. Polymeric Nanoparticles in Cancer Therapy

Polymeric nanoparticles composed of PLGA, PLA, and chitosan have been extensively investigated for delivering anticancer drugs such as doxorubicin, paclitaxel, and docetaxel.

Benefits include:

- Sustained drug release.
- Enhanced tumor penetration.
- Improved pharmacokinetics.

ii. Lipid-Based Nanocarriers

Liposomes and lipid nanoparticles have demonstrated considerable success in cancer treatment.

Examples:

- Liposomal doxorubicin.
- Liposomal daunorubicin.
- Lipid nanoparticle formulations for nucleic acid delivery.[32,33,34]

4.3 Gene Delivery

Gene therapy involves the delivery of genetic material to modify or regulate gene expression for therapeutic purposes. Efficient gene delivery

remains a major challenge because nucleic acids are susceptible to enzymatic degradation and exhibit poor cellular uptake. Nanoparticles serve as non-viral vectors capable of protecting genetic material and facilitating intracellular delivery.

Therapeutic agents delivered include:

- Plasmid DNA
- Messenger RNA (mRNA)
- Small interfering RNA (siRNA)
- MicroRNA (miRNA)

Advantages of nanoparticle-mediated gene delivery include:

- Reduced immunogenicity.
- Improved safety compared to viral vectors.
- Enhanced transfection efficiency.
- Protection from nuclease degradation.[35]

4.4 Vaccine Delivery

Nanoparticles have transformed vaccine development by enhancing antigen stability, immune response, and targeted delivery to immune cells. Traditional vaccines often require adjuvants to stimulate adequate immune responses. Nanoparticles can function as both carriers and adjuvants, improving vaccine efficacy.The recent success of mRNA vaccines against COVID-19 demonstrated the tremendous potential of lipid nanoparticles in vaccine delivery.

Advantages of nanoparticle-based vaccines include:

- Enhanced antigen protection.
- Improved cellular uptake.
- Sustained antigen release.
- Increased immunogenicity.

Types of nanoparticle vaccine carriers include:

- Lipid nanoparticles
- Polymeric nanoparticles
- Virus-like nanoparticles
- Inorganic nanoparticles.[36,37]

4.5 Antimicrobial Applications

The increasing prevalence of antimicrobial resistance has created an urgent need for novel therapeutic approaches. Nanoparticles possess intrinsic antimicrobial activity and can enhance the effectiveness of existing antimicrobial agents.

i. Silver Nanoparticles

Silver nanoparticles are among the most extensively studied antimicrobial nanomaterials.

Mechanisms of action include:

- Disruption of microbial cell membranes.
- Generation of reactive oxygen species.
- Inhibition of DNA replication.
- Interference with protein synthesis.

Silver nanoparticles exhibit activity against:

- Gram-positive bacteria.
- Gram-negative bacteria.
- Fungi.
- Certain viruses.

ii. Nanoparticle-Based Antibiotic Delivery

Nanoparticles can improve antibiotic therapy by:

- Enhancing drug penetration.
- Sustaining drug release.
- Reducing bacterial resistance.
- Improving intracellular drug delivery.[38,39]

5. REGULATORY ASPECTS AND SAFETY CONSIDERATIONS

The rapid growth of nanotechnology has led to the development of numerous nanoparticle-based pharmaceutical products. Despite their therapeutic advantages, nanoparticles pose unique regulatory and safety challenges due to their small size, high surface reactivity, and complex biological interactions.[40] Therefore, thorough evaluation of quality, safety, efficacy, and manufacturing consistency is essential before clinical use. Regulatory agencies such as the FDA and EMA assess nanomedicines under existing drug and biologic regulations using a case-by-case approach. Comprehensive characterization, including particle size, surface charge, morphology, drug loading, and stability, is required to ensure product quality and reproducibility. Manufacturing processes must also comply with Good Manufacturing Practices (GMP). Safety assessment is a critical aspect of nanoparticle development. Extensive preclinical studies are conducted to evaluate cytotoxicity, genotoxicity, immunotoxicity, biodistribution, and long-term safety. Since nanoparticles may accumulate in organs such as the liver, spleen, lungs, and kidneys, their potential to induce oxidative stress, inflammation, or tissue damage must be carefully examined.[41]

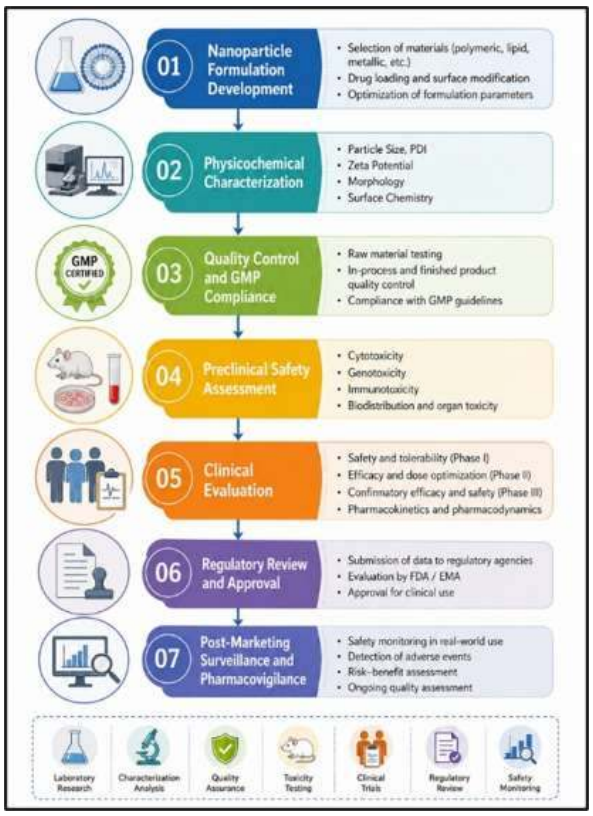

Figure 4. Regulatory and Safety Assessment Framework for Nanoparticle-Based Drug Delivery Systems

Clinical studies further assess pharmacokinetics, therapeutic efficacy, and adverse effects, while post-marketing surveillance monitors long-term safety. Although several nanomedicines have gained regulatory approval, challenges related to standardization, toxicity evaluation, and regulatory harmonization remain. Continued collaboration among researchers, industry, and regulatory authorities is essential for the safe and effective advancement of nanoparticle-based therapeutics.[42]

6. CHALLENGES AND FUTURE PERSPECTIVES

➢ Challenges

- **Manufacturing Scale-Up** - Lab-scale synthesis often fails at industrial production due to inconsistent particle size, batch variability, and drug loading issues.

Microfluidic platforms offer scalable solutions.

- **Regulatory Barriers** - Lack of standardized characterization methods and nanomedicine-specific guidelines creates submission uncertainty. High trial costs and unpredictable human pharmacokinetics from animal models hinder translation.

- **Safety Concerns** - Limited long-term data on chronic accumulation, genotoxicity, and immunogenicity necessitate standardized nanotoxicity protocols.

- **Targeting Efficiency** - Despite EPR effect, tumor accumulation remains low (<5% injected dose), with most nanoparticles cleared by RES.[43,44,45]

➢ **Future Directions**

- **AI-Driven Design** - ML algorithms predict optimal composition, synthesis parameters, and toxicity. Self-driving labs accelerate discovery through automated high-throughput screening.

- **Personalized Nanomedicine** - Patient-specific targeting based on genetic profiles, receptor expression, and pharmacogenomics. 3D bioprinting enables tailored geometries and release profiles.

- **Active Nanoparticles** - Self-propelled nanorobots using magnetic fields, ultrasound, or chemical fuels for active navigation beyond passive targeting limitations.

- **Biomimetic Systems** - Cell membrane-coated nanoparticles inheriting immune evasion and homing properties from source cells (e.g., RBC membranes for prolonged circulation).

- **Green Synthesis** -2 Plant extracts, microbial cultures, and biodegradable materials reduce environmental impact following cradle-to-cradle design principles.

- **Advanced Manufacturing** - Microfluidics for precise, continuous production; 3D printing for personalized devices; electrospinning for nanofiber-based wound dressings and implants.[46,47]

7. CONCLUSION

Nanoparticles have emerged as a transformative platform in pharmaceutical sciences, offering significant advantages over conventional drug delivery systems through improved solubility, bioavailability, stability, controlled release, and targeted delivery. A wide range of synthesis approaches, including physical, chemical, and green synthesis methods, enable the development of nanoparticles with tailored physicochemical properties for specific therapeutic applications. Comprehensive characterization techniques are essential for ensuring product quality, safety, and reproducibility. The application of nanoparticles in targeted drug delivery, cancer therapy, gene delivery, vaccine development, antimicrobial treatment, diagnostic imaging, and theranostic systems highlights their immense potential in modern healthcare. Recent advances in lipid nanoparticles, particularly for nucleic acid delivery, have further accelerated the clinical translation of nanomedicine and demonstrated the versatility of nanoparticle-based platforms. Green synthesis approaches have also gained considerable attention due to their sustainability, cost-effectiveness, and improved biocompatibility. Despite these promising developments, challenges related to large-scale manufacturing, regulatory approval, long-term safety, and targeting efficiency continue to limit broader clinical implementation. Addressing these

limitations through improved characterization methods, standardized regulatory frameworks, and advanced manufacturing technologies will be crucial for future success. Emerging innovations such as artificial intelligence-driven nanoparticle design, personalized nanomedicine, biomimetic nanocarriers, and nanoparticle-mediated gene editing are expected to further expand the scope of nanotechnology in healthcare. Overall, nanoparticles represent a rapidly evolving field with substantial potential to advance precision medicine and improve therapeutic outcomes across a wide range of diseases.

REFERENCES

1. Gawai AY, Hatwar PR, Bakal RL, Nehar KN, Bhujade PR. Stimuli-Responsive Nanocarriers for Site-Specific Drug Delivery System. Asian J Pharm Res Dev. 2025;13(2):100-6.
2. Fatima M, Almalki WH, Khan T, Sahebkar A, Kesharwani P. Harnessing the Power of Stimuli-Responsive Nanoparticles as an Effective Therapeutic Drug Delivery System. Adv Mater. 2024;36(24).
3. Hajebi S, Chamanara M, et al. Advances in stimuli-responsive gold nanorods for drug-delivery and targeted therapy systems. Biomed Pharmacother. 2024;180:117493.
4. Tiwari H, Rai N, Singh S, Gupta P, Verma A, Singh AK, et al. Recent Advances in Nanomaterials-Based Targeted Drug Delivery for Preclinical Cancer Diagnosis and Therapeutics. Bioengineering. 2023;10(7):760.
5. Tressa A, Singh A, Pal R, Kumar N. Novel Nanocarriers Microencapsulation: Current, Patents and Clinical Trials Comprehensive Review. J Drug Deliv Ther. 2025;15(4):188-20.
6. Ghazi R, Ibrahim TK, Nasir JA, Gai S, Ali G, Boukhris I, Rehman Z. Iron oxide based magnetic nanoparticles for hyperthermia, MRI and drug delivery applications: a review. RSC Adv. 2025;15:11587-616.
7. Wang T, Wu C, Hu Y, Zhang Y, Ma J. Stimuli-responsive nanocarrier delivery systems for Pt-based antitumor complexes: a review. RSC Adv. 2023;13:16488-511.
8. Khadam VKR, Singh RP, Prajapati D, Yunus M, Prajapat B, Rai SK, et al. An updated comprehensive review on novel drug delivery systems in pharmaceuticals. J Drug Deliv Sci Technol. 2024;85:104789.
9. Pathak U, Vashistha V, Arora S. Novel drug delivery systems: advances and challenges. Pharmaceutics. 2025;17(2):315-29.
10. Mitchell MJ, Billingsley MM, Haley RM, Wechsler ME, Peppas NA, Langer R. Engineering precision nanoparticles for drug delivery. Nat Rev Drug Discov. 2020;20(2):101-24.
11. Jose A, Anju SS, Cinu TA, Aleykutty NA, Thomas S. In vivo pharmacokinetics and biodistribution of resveratrol-loaded solid lipid nanoparticles for brain delivery. Int J Pharm. 2014;474(1-2):6-13.
12. Ahmad S, et al. Green synthesis of gold and silver nanoparticles using crude extract of Aconitum violaceum and evaluation of their antibacterial, antioxidant and photocatalytic activities. Front Plant Sci. 2024;15:1359077.
13. Kaushik A, Singh RK, Tyagi PK. Green synthesized nanoparticle based drug delivery: Recent trends and future prospects. Precision Nanomedicine. 2023;6(4):1109-31.
14. Kar S, Sanderson H, Roy K, Benfenati E, Leszczynski J. Green chemistry in the synthesis of pharmaceuticals. Chem Rev. 2022;122(3):3637-710.
15. European Pharmaceutical Review. Key trends and technologies in drug delivery for 2025 and beyond. 2025 May 5.
16. IIP Series. Nanomaterial Characterization Techniques. Futuristic Trends in Chemical, Material Sciences & Nano Technology. 2024;3(13):125-34.
17. PMC12707129. Key Clinical Frontiers of mRNA Loaded Lipid Nanoparticles in Cancer Vaccines. 2025.
18. PMC10807692. Green synthesis of gold and silver nanoparticles using crude extract of Aconitum violaceum. 2024.

19. Weissig V, Pettinger T, Murdock N. Nanopharmaceuticals (part 1): products on the market. Int J Nanomedicine. 2014;9:4357-73.
20. Bobo D, Robinson KJ, Islam J, Thurecht KJ, Corrie SR. Nanoparticle-based medicines: a review of FDA-approved materials and clinical trials to date. Pharm Res. 2016;33(10):2373-87.
21. Barenholz Y. Doxil -- the first FDA-approved nano-drug: lessons learned. J Control Release. 2012;160(2):117-34.
22. Desai N. Challenges in development of nanoparticle-based therapeutics. AAPS J. 2012;14(2):282-95.
23. Park K. Facing the truth about nanotechnology in drug delivery. ACS Nano. 2013;7(9):7442-7.
24. Wilhelm S, Tavares AJ, Dai Q, Ohta S, Audet J, Dvorak HF, Chan WC. Analysis of nanoparticle delivery to tumours. Nat Rev Mater. 2016;1(5):16014.
25. Maeda H, Nakamura H, Fang J. The EPR effect for macromolecular drug delivery to solid tumors: improvement of tumor uptake, lowering of systemic toxicity, and distinct tumor imaging in vivo. Adv Drug Deliv Rev. 2013;65(1):71-9.
26. Allen TM, Cullis PR. Liposomal drug delivery systems: from concept to clinical applications. Adv Drug Deliv Rev. 2013;65(1):36-48.
27. Torchilin VP. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. Nat Rev Drug Discov. 2014;13(11):813-27.
28. Shi J, Kantoff PW, Wooster R, Farokhzad OC. Cancer nanomedicine: progress, challenges and opportunities. Nat Rev Cancer. 2017;17(1):20-37.
29. Peer D, Karp JM, Hong S, Farokhzad OC, Margalit R, Langer R. Nanocarriers as an emerging platform for cancer therapy. Nat Nanotechnol. 2007;2(12):751-60.
30. Pardi N, Hogan MJ, Porter FW, Weissman D. mRNA vaccines -- a new era in vaccinology. Nat Rev Drug Discov. 2018;17(4):261-79.
31. Schoenmaker L, Witzigmann D, Kulkarni JA, Verbeke R, Kersten G, Jiskoot W, Crommelin DJA. mRNA-lipid nanoparticle COVID-19 vaccines: structure and stability. Int J Pharm. 2021;601:120586.
32. Kulkarni JA, Witzigmann D, Thomson SB, Chen S, Leavitt BR, Cullis PR, van der Meel R. The current landscape of nucleic acid therapeutics. Nat Nanotechnol. 2021;16(6):630-43.
33. Doshi N, Mitragotri S. Macrophages recognize size and shape of their targets. PLoS One. 2010;5(3):e10051.
34. Alexis F, Pridgen E, Molnar LK, Farokhzad OC. Factors affecting the clearance and biodistribution of polymeric nanoparticles. Mol Pharm. 2008;5(4):505-15.
35. Oberdorster G, Oberdorster E, Oberdorster J. Nanotoxicology: an emerging discipline evolving from studies of ultrafine particles. Environ Health Perspect. 2005;113(7):823-39.
36. Nel AE, Madler L, Velegol D, Xia T, Hoek EM, Somasundaran P, et al. Understanding biophysicochemical interactions at the nano-bio interface. Nat Mater. 2009;8(7):543-57.
37. Dobrovolskaia MA, McNeil SE. Immunological properties of engineered nanomaterials. Nat Nanotechnol. 2007;2(8):469-78.
38. FDA. Guidance for Industry: Considering Whether an FDA-Regulated Product Involves the Application of Nanotechnology. 2014.
39. EMA. Reflection paper on the data requirements for intravenous liposomal products developed with reference to an innovator liposomal product. 2013.
40. ICH Q8(R2). Pharmaceutical Development. 2009.
41. Muller RH, Radtke M, Wissing SA. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. Adv Drug Deliv Rev. 2002;54(Suppl 1):S131-55.
42. Puri A, Loomis K, Smith B, Lee JH, Yavlovich A, Heldman E, Blumenthal R. Lipid-based nanoparticles as pharmaceutical drug carriers: from concepts to clinic. Crit Rev Ther Drug Carrier Syst. 2009;26(6):523-80.

43. Moghimi SM, Hunter AC, Murray JC. Long-circulating and target-specific nanoparticles: theory to practice. Pharmacol Rev. 2001;53(2):283-318.
44. Gref R, Minamitake Y, Peracchia MT, Trubetskoy V, Torchilin V, Langer R. Biodegradable long-circulating polymeric nanospheres. Science. 1994;263(5153):1600-3.
45. Langer R. Drug delivery and targeting. Nature. 1998;392(6679):5-10.
46. Langer R, Peppas NA. Advances in biomaterials, drug delivery, and bionanotechnology. AIChE J. 2003;49(12):2990-3006.
47. Farokhzad OC, Langer R. Impact of nanotechnology on drug delivery. ACS Nano. 2009;3(1):16-20.

HOW TO CITE: Daiwashala Pawar, Amol Ratke, Sneha Wadu, Ruchira Medankar, A Review on Nanoparticles: Synthesis, Characterisation, and Applications in Pharmaceutical Sciences, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 7, 1184-1203. https://doi.org/10.5281/zenodo.21222368