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# Design And Evaluation Of A Nanoparticle-Based Drug Delivery System For Enhanced Therapeutic Efficacy

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## ABSTRACT:

Particle delivery systems have attracted significant research interest over recent decades as carriers for both small and large molecules in drug delivery. Among these systems, nanoparticles have shown remarkable potential to modify and enhance the pharmacokinetic and pharmacodynamic properties of various therapeutic agents. Nanoparticles, due to their unique physicochemical characteristics, offer promising avenues for targeted and controlled drug delivery.

This review explores recent advancements in nanotechnology applied to drug and gene delivery. To address the limitations of conventional delivery methods, nano-based systems with diverse compositions and biological properties have been extensively investigated. These include polymeric, metallic, ceramic, and carbon-based nanoparticles, each demonstrating specific advantages in biomedical applications.

Nanoparticles (NPs), defined as particles with dimensions ranging from 1 to 100 nanometers, exhibit distinct physical and chemical behaviors owing to their high surface-area-to-volume ratio and nanoscale size. Their optical, mechanical, and reactive properties are highly size- and shape-dependent, influencing their performance in various applications. For instance, variations in nanoparticle size affect their optical properties, producing unique colorations due to light absorption in the visible spectrum.

Given their versatility, nanoparticles are utilized in a broad spectrum of fields including medical imaging, targeted drug delivery, environmental remediation, energy research, and catalysis. However, concerns arise with heavy metal-based nanoparticles, such as those containing lead, mercury, or tin, due to their persistence in the environment and potential toxicity. These challenges highlight the need for sustainable and biocompatible nanoparticle design in future research and applications.

**Key point:** Definition, Types of Nanoparticles, Advantages, Mechanism of Drug Release, Targeting Strategies, Applications,Challenges,Recent Advances

**Introduction:** Drug delivery vehicles, commonly known as nanoparticles, are typically composed of various biodegradable materials such as metals, lipids, or natural and synthetic polymers. These particles usually measure less than 100 nanometers in at least one dimension. Due to their small size, nanoparticles are more readily absorbed by cells compared to larger molecules, making them highly effective as drug delivery and transport vehicles [2].

Nanotechnology offers several advantages in pharmaceutical applications, including:

Increased surface area

Enhanced solubility

Improved rate of dissolution

Higher oral bioavailability

Reduced dosage and dosing frequency

Protection of drugs from degradation

Faster onset of therapeutic effects

Achievement of drug targeting

Passive targeting of drugs to macrophages present in the liver and spleen (39)

**(A). Targeting Strategies in Nanotechnology (Based on Roco's Four Stages):** Dr. Mihail Roco, a key figure in the U.S. National Nanotechnology Initiative, delineated four progressive stages in nanotechnology development:

**Passive Nanostructures:**

**Function**: Designed for a single, specific purpose (e.g., coatings, nanoparticles for imaging).

**Targeting Strategy:** Passive targeting, relying on natural accumulation in certain tissues (e.g., Enhanced Permeability and Retention effect in tumors).

**2. Active Nanostructures:**

**Function**: Exhibit responsive behavior (e.g., drug delivery systems, sensors, actuators).

**Targeting Strategy:** Active targeting, using ligands (antibodies, peptides) to bind specific cellular receptors, increasing selectivity and therapeutic efficacy.

### 3. Nanosystems:

**Function**: Integration of thousands of components; capable of multitasking.

**Targeting Strategy:** Multimodal targeting, integrating multiple targeting and therapeutic functions (e.g., theranostics – therapy + diagnostics).

### 4. Integrated Nanosystems:

**Function**: Mimic complex biological systems like mammalian cells with hierarchical, dynamic interactions.

**Targeting Strategy:** Biomimetic targeting, leveraging cell-like adaptability and environmental response for highly precise targeting.

## (B). PHARMACEUTICAL NANOTECHNOLOGY-BASED SYSTEMS:

Pharmaceutical nanotechnology broadly encompasses two key categories: nanomaterials and nanodevices. These elements play a pivotal role not only in drug delivery and diagnostics but also extend their applications to areas such as orthopaedics, dentistry, and tissue engineering.

**1 Nanomaterials:** Nanomaterials are typically derived from biocompatible sources, making them suitable for medical applications such as implants and scaffolds. Surface modifications or coatings are often applied to enhance their interaction with biological tissues. Nanomaterials can be further classified into:

**2 Nanocrystalline Materials:** These materials are easy to manufacture and serve as efficient alternatives to conventional bulk materials. They are widely used in drug encapsulation, bone replacement, prosthetic devices, and implants due to their enhanced performance.

**3 Nanostructured Materials:** These are specially engineered nanomaterials with distinct structures and functionalities. Notable examples include quantum dots, dendrimers, fullerenes, and carbon nanotubes, which offer unique advantages in targeted drug delivery and imaging.

**4 Nanodevices:** Nanodevices are ultra-miniaturized systems designed to function at the nanoscale. This category includes Nano and Micro Electro-Mechanical Systems (NEMS/MEMS), microfluidic devices, and lab-on-a-chip technologies. Additionally, biosensors and nanoscale detectors are integral to modern diagnostic tools, enabling rapid and precise detection of biomarkers.

## (C). Classification of Nanoparticles:

Nanoparticles can be classified into several categories based on their morphology, size, and chemical properties. The major classes are:

**1. Carbon-based Nanoparticles:**

**Fullerenes**: Hollow carbon cages (e.g., C60) with unique structures.

Carbon Nanotubes (CNTs): Cylindrical tubes formed by rolled graphene sheets; classified as:

Single-walled (SWNTs)

Double-walled (DWNTs)

Multi-walled (MWNTs)

**Properties**: High mechanical strength, electrical conductivity.

Production Methods: Electric arc discharge, laser vaporization, chemical vapour deposition (CVD).

**2. Metal Nanoparticles:**

Composed of pure metals like copper (Cu), silver (Ag), and gold (Au).

Exhibit localized surface plasmon resonance (LSPR)—strong absorption in the visible spectrum.

Importance in optoelectronics and catalysis.

Synthesized with control over size, shape, and surface facets.

**3. Ceramic Nanoparticles:**

Inorganic, non-metallic materials.

Can be porous, hollow, dense, polycrystalline, or amorphous.

Typically formed via heat-treatment followed by cooling.

**4. Semiconductor Nanoparticles:**

Exhibit properties between metals and non-metals.

Bandgap tuning affects their optical/electronic properties.

Applications: photocatalysis, optoelectronics, solar cells, and photonics.

**5. Polymeric Nanoparticles:**

Organic nanoparticles made of natural or synthetic polymers.

**Types:**

**Nanospheres:** Solid matrix particles.

**Nanocapsules**: Reservoir-type particles with an inner core.

Surface can adsorb other molecules for targeted delivery.

**6. Lipid-based Nanoparticles:**

Composed of solid lipid cores with surrounding lipophilic matrices.

Size range: 10 to 1000 nm.

Stabilized by surfactants or emulsifiers.

Common in drug delivery and biological applications.

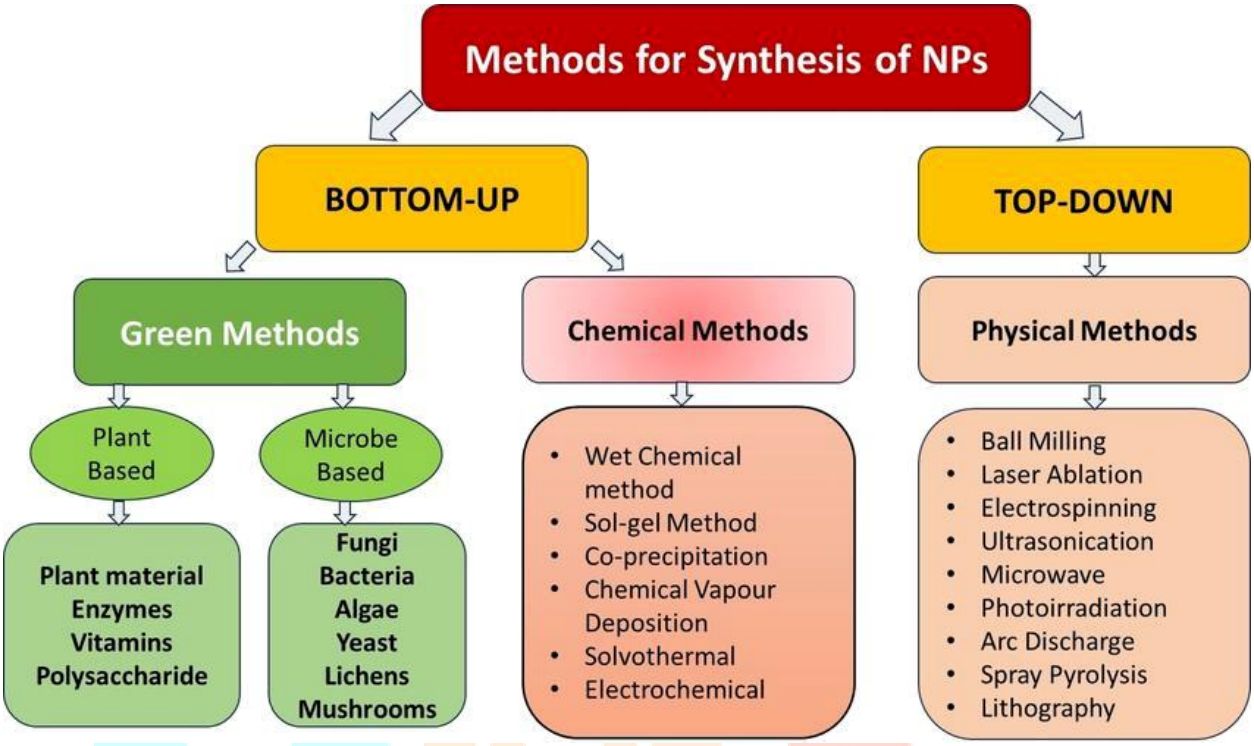
**(D). Synthesis of Nanoparticles:** Nanoparticles (NPs) can be synthesized using various methods, which are broadly categorized into two main approaches:

**1 Bottom-Up Approach:** This method involves the assembly of nanoparticles from simpler chemical units, hence it is also referred to as the "building-up" approach. Techniques such as chemical reduction, sedimentation, spinning, biological synthesis, green synthesis, and sol-gel methods fall under this category (40). Nanoparticles produced by this approach typically exhibit superior colloidal stability and uniformity.

**For example,** in the synthesis of bismuth nanoparticles, the bottom-up method involved heating bismuth acetate in ethylene glycol. This approach contrasts with the top-down method, where bismuth was first melted into a droplet and then emulsified in heated diethylene glycol. Both methods produced nanoparticles with sizes ranging from 100 nm to 500 nm (41).

**2 Top-Down Approach:** This is a "destructive" strategy where larger bulk materials are broken down into nanoparticles. Common techniques include chemical vapour deposition (CVD), physical vapour deposition (PVD), and mechanical methods such as grinding and milling.

In one study, magnetite ($Fe_3O_4$) nanoparticles were synthesized using a top-down approach by mechanically breaking down natural iron oxide ($Fe_2O_3$) ore in the presence of oleic acid. The resulting spherical nanoparticles had particle sizes ranging from approximately 20 nm to 50 nm (42).




## (E). Types of pharmaceutical nano systems:

**1. Liposomes:**

Spherical vesicles with a phospholipid bilayer.

Can encapsulate both hydrophilic and lipophilic drugs.

Biocompatible and used in cancer therapy, vaccines, etc.

**2. Niosomes:**

Similar to liposomes but made from non-ionic surfactants.

More stable and cost-effective.

Used for controlled drug delivery.

**3. Solid Lipid Nanoparticles (SLNs):**

Lipid-based particles solid at room and body temperature.

Improve stability and bioavailability.

Suitable for both hydrophilic and lipophilic drugs.

**4. Nanostructured Lipid Carriers (NLCs):**

Second-generation SLNs with improved loading capacity.

Better stability and controlled release.

**5. Polymeric Nanoparticles:**

Made from natural or synthetic polymers (e.g., PLGA, chitosan).

Can be nanospheres or nanocapsules.

Used for sustained and targeted drug delivery.

**6. Dendrimers:**

Branched, tree-like synthetic macromolecules.

High drug-loading capacity with controlled release.

**7. Metallic Nanoparticles:**

Typically gold or silver nanoparticles.

Used in imaging, diagnostics, and targeted drug delivery.

**8. Carbon Nanotubes (CNTs):**

Cylindrical carbon structures.

High surface area; can carry drugs or genes.

**9. Nanoemulsions:**

Fine oil-in-water or water-in-oil emulsions.

Enhanced solubility and absorption of poorly soluble drugs.

**10. Micelles:**

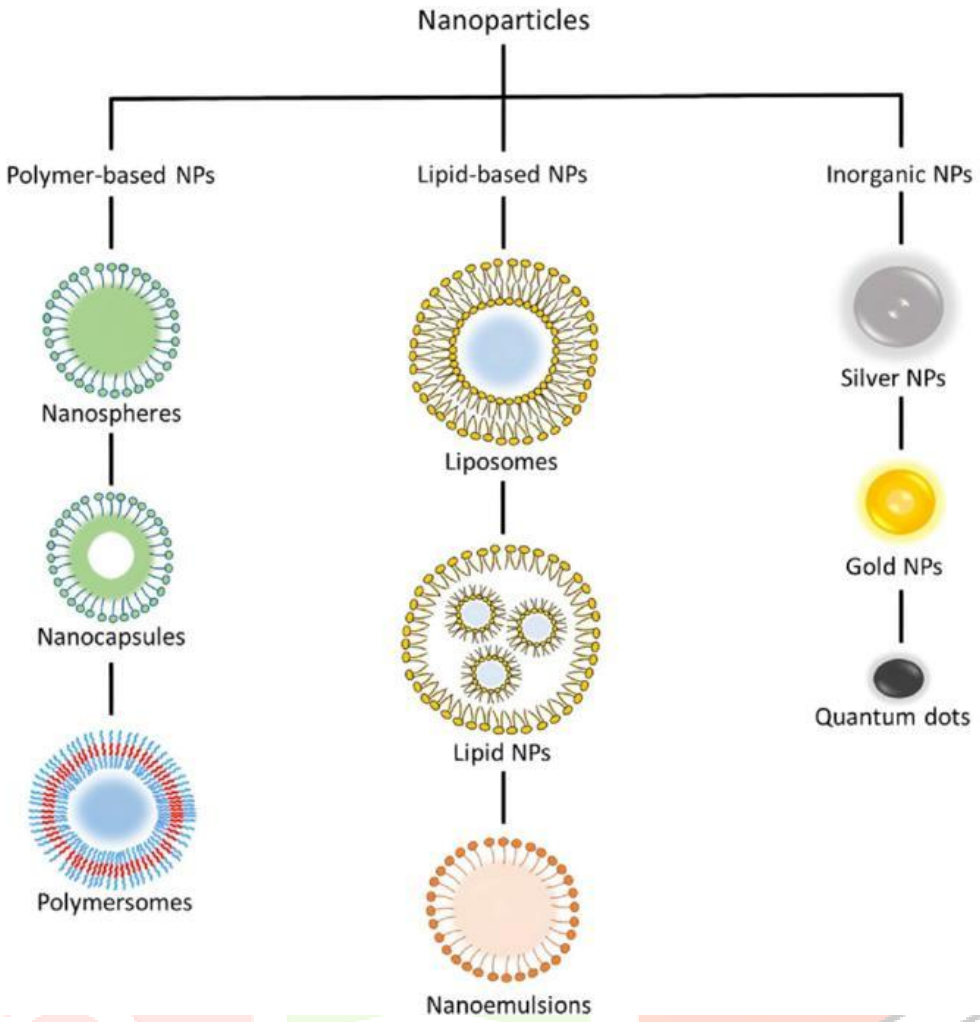
Amphiphilic molecules that form core-shell structures.

Useful for delivering poorly water-soluble drugs.

**11. Quantum Dots:**

Semiconductor nanoparticles used in imaging and diagnostics.

Can also be linked with drugs for targeted delivery.




## (F). Effect of Characteristics of Nanoparticles on Drug Delivery:

**Particle Size** Particle size and its distribution are critical characteristics of nanoparticle systems. These parameters significantly influence various aspects of drug delivery and therapeutic outcomes, including:

- **In vivo distribution:** Determines how nanoparticles travel and accumulate in different tissues and organs.
- **Biological fate:** Affects interactions with biological systems, such as cellular uptake, metabolism, and elimination.
- **Toxicity:** Influences the potential for adverse effects.
- **Targeting ability:** Impacts the precision of drug delivery to specific sites.
- **Drug loading:** Determines the amount of drug that can be encapsulated.
- **Drug release:** Affects the rate and extent of drug release from the nanoparticles.
- **Stability:** Plays a key role in the long-term stability of the formulation.

Due to their small size and enhanced mobility, nanoparticles can access a broader range of biological targets compared to microparticles. They typically exhibit higher intracellular uptake. For example, a study by Desai et al. using Caco-2 cell lines demonstrated that 100 nm nanoparticles showed a 2.5-fold higher uptake than 1 µm particles and a 6-fold higher uptake than 10 µm particles[^14].

**Impact on Drug Release:**

**Smaller particles** have a higher surface area-to-volume ratio, which often leads to a greater amount of drug being located at or near the surface, resulting in **faster drug release**.

**Surface properties of nanoparticles:** The surface properties of nanoparticles play a crucial role in determining their physical, chemical, and biological behavior. Here are the key surface properties:

**1. Surface Area:** Nanoparticles have a very high surface area-to-volume ratio.

This enhances reactivity and interaction with biological systems or other chemicals.

**2. Surface Charge (Zeta Potential):** Indicates the electrical potential at the particle surface.

Affects stability, aggregation, and interaction with cells and biomolecules.

Positive or negative charge can influence cellular uptake and biodistribution.

**3. Surface Energy:** High surface energy leads to a tendency to agglomerate.

Surface modifications (e.g., with surfactants or polymers) help stabilize nanoparticles.

**4. Hydrophilicity/Hydrophobicity:** Determines the solubility and dispersion in aqueous or organic media.

Hydrophilic surfaces improve circulation time in biological systems.

**5. Surface Functional Groups:** Presence of –OH, –COOH, $–NH_2$, etc., allows chemical modification or drug attachment.

Enables targeting and enhances biocompat

**Drug loading:** It's refers to the amount of active pharmaceutical ingredient (API) that is incorporated into a drug delivery system (like nanoparticles, microspheres, or hydrogels) relative to the total weight of the carrier or formulation.

It is usually expressed as:

Drug Loading (%) = (Weight of drug in the formulation / Total weight of formulation) × 100

This value is important because it indicates how efficiently a drug has been incorporated into the carrier system and influences the dosage, release profile, and therapeutic effectiveness of the formulation.

**7. Applications of Pharmaceutical Nanotechnology:** Miniaturization has revolutionized pharmaceutical technology. Although it has introduced increased complexity, it has also provided numerous advantages in drug delivery, diagnostics, and therapeutic applications. Nanotechnology is now an integral part of various pharmaceutical and biochemical domains.

**7.1 Nanomaterials for Tissue Engineering:** Nanomaterials play a pivotal role in tissue engineering due to their unique physical and chemical properties. Their applications include:

Tissue regeneration

Implant coatings

Bone reconstruction

Development of structural implant materials

Tissue repair

Bioresorbable materials

In addition to tissue engineering, nanotechnology is also employed in:

Surgical instruments

Operating instruments

Implantable devices (e.g., retinal implants, sensory aids)

Smart instruments

These innovations contribute to improved biocompatibility, precision, and functionality in both diagnostics and therapeutics.

**7.2 Drug Carrier Systems:** Nanomaterial-enabled drug delivery systems exhibit improved physical, chemical, and biological properties, making them valuable tools for administering bioactive agents. Examples of these nano-based carrier systems include:

Polymeric nanoparticles

Liposomes

Dendrimers

Polymeric micelles

Polymer-drug conjugates

Antibody-drug conjugates

These systems can be classified into several categories based on their structure, composition, and mechanism of action:

**1. Nanoparticle-Based Systems:** These include polymeric and metallic nanoparticles that encapsulate drugs to enhance solubility, stability, and bioavailability.

Polymeric nanoparticles (e.g., PLGA, chitosan) are biodegradable and can provide sustained drug release.

Metallic nanoparticles (e.g., gold or silver) are often used for targeted delivery and diagnostic applications.

**2. Vesicular Systems:** These carriers form bilayer or multilayer structures suitable for both hydrophilic and lipophilic drugs.

Liposomes are spherical vesicles made of phospholipid bilayers, widely used for targeted and sustained drug delivery.

Niosomes are non-ionic surfactant-based vesicles with enhanced chemical stability compared to liposomes.

**3. Polymeric Micelle Systems:** These are self-assembling systems formed from amphiphilic block copolymers. The hydrophobic core carries poorly water-soluble drugs, while the hydrophilic shell provides stability in biological fluids.

**4. Dendrimer-Based Systems:** Dendrimers are highly branched, tree-like polymers with functional end groups. They offer high drug-loading capacity, low toxicity, and precise targeting through surface modifications.

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**5. Conjugate Systems:** Polymer-drug conjugates involve covalent attachment of drug molecules to polymer chains, allowing controlled release.

Antibody-drug conjugates (ADCs) combine the specificity of monoclonal antibodies with potent cytotoxic drugs for targeted therapy, especially in oncology.

**6. Stimuli-Responsive Systems:** These smart systems release the drug in response to specific stimuli such as pH, temperature, enzymes, or redox potential, enabling site-specific and controlled drug delivery.

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# The Carrier Systems are widely Used in the given Regions

**7.2.1 Cancer Treatment:** Nanotechnology has revolutionized the landscape of cancer diagnosis and therapy. Conventional treatments—such as radiation therapy, immunotherapy, chemotherapy, and surgery—can be significantly enhanced through the integration of nanotechnology-based tools.

**Key Nano carriers in Cancer Therapy:**

Carbon Nanotubes: Used in DNA mutation detection and for identifying disease protein biomarkers.

Dendrimers: Employed for controlled drug delivery and as image contrast agents.

**Major Challenges in Cancer Treatment:** Localized Delivery: Ensuring the therapeutic agent reaches the tumor site effectively.

Targeted Therapy: Minimizing off-target effects by selectively targeting cancer cells, thus reducing harm to healthy tissues.

Nanotechnology addresses these challenges by exploiting unique tumor pathophysiology, such as the leaky vasculature commonly found in cancerous tissues. Nanocarriers can significantly modify the pharmacokinetics and biodistribution of anticancer drugs, enhancing both efficacy and safety.

**Therapeutic Applications of Nanotools:**

Thermotherapy

**Photothermal Therapy:** Utilizes silica nanoparticles and carbon nanotubes.

**Magnetic Field-Induced Hyperthermia:** Employs magnetic nanoparticles.

**Photodynamic Therapy:** Uses quantum dots.

**Chemotherapy:** Involves nanostructured polymer nanoparticles, dendrimers, and nan shells.

**Radiotherapy:** Uses carbon nanotubes and dendrimers.

## Mechanisms of Action:

Targeting Biomarkers: Nanotools identify and bind to specific molecules on cancer cell surfaces.

Detecting Mutations: They assist in recognizing genetic alterations in cancer cells.

**7.2.2 Implantable Delivery Systems:** Implantable drug delivery systems, particularly those utilizing nanoparticles, offer numerous advantages due to their small size and ability to provide controlled, near-zero-order release kinetics. This sustained and predictable drug release minimizes fluctuations in plasma concentration, thereby reducing the risk of toxic peak levels and associated adverse effects.

Examples of implantable drug carriers include:

Ecosphere's: Extracellular vesicles naturally secreted by cells that can serve as biocompatible delivery vehicles.

**Transfersomes:** Ultra-flexible liposomes capable of deforming and traversing narrow intercellular spaces for enhanced tissue penetration.

Stealth Liposomes: Liposomes modified, often with polyethylene glycol (PEG), to evade detection and clearance by the immune system.

**Advantages of these systems include:**

Reduced risk of adverse drug reactions

Lower and more stable plasma drug concentrations

Extended and more predictable drug action

Decreased need for frequent dosing

Enhanced patient compliance and acceptance (25)

**7.2.3 Gene Therapy:** Gene therapy is a technique that involves the introduction, removal, or alteration of genetic material within a patient's cells to treat or prevent disease. It aims to correct defective genes responsible for disease development by:

**1**. Replacing a mutated gene that causes disease with a healthy copy.

**2**. Inactivating or silencing a malfunctioning gene that is functioning improperly.

**3**. Introducing a new gene into the body to help fight a disease.

## Types of Gene Therapy:

**Somatic Gene Therapy:** Targets non-reproductive cells; changes are not inherited by future generations.

**Germline Gene Therapy:** Targets reproductive cells (sperm or egg); changes can be passed to offspring (currently not approved for human use in many countries due to ethical concerns).

**Delivery Methods:** Viral Vectors: Modified viruses like adenoviruses or retroviruses deliver therapeutic genes into cells.

Non-viral Methods: Include liposomes, nanoparticles, or direct injection of genetic material (like plasmid DNA).

## Applications of Gene Therapy:

Treatment of genetic disorders (e.g., cystic fibrosis, hemophilia, sickle cell anemia).

Certain cancers (e.g., CAR-T cell therapy in leukemia).

Some viral infections (e.g., HIV research).

Challenges and Considerations:

Immune response to vectors.

Ensuring targeted and regulated gene expression.

Long-term effects and safety.

Ethical and social implications'.

## 7.3 Biosensors and Bio-labels:

**Biosensors:** Biosensors are analytical devices that combine a biological recognition element with a transducer to detect specific biological analytes. They are widely used in diagnostics, environmental monitoring, food safety, and pharmaceutical research.

**Components of a Biosensor:**

**1. Bio receptor –** A biological molecule (e.g., enzyme, antibody, nucleic acid) that specifically interacts with the analyte.

**2. Transducer –** Converts the biorecognition event into a measurable signal (electrical, optical, thermal, etc.).

**3. Signal Processor –** Amplifies and processes the signal for display and interpretation.

## Types of Biosensors:

Electrochemical (e.g., glucose sensors)

Optical (e.g., surface plasmon resonance)

Piezoelectric (e.g., quartz crystal microbalance)

Thermal (e.g., calorimetric sensors)

## Applications:

Medical diagnostics (e.g., blood glucose monitoring)

Detection of pathogens and toxins

Drug discovery

Environmental pollutant detection

**Bio-labels:** Bio-labels are markers used to tag biological molecules for identification, tracking, or quantification in assays and imaging.

## Types of Bio-labels:

**Radioactive labels –** Use isotopes like $^{32}P$ or $^{125}I$ for sensitive detection.

**Fluorescent labels –** Use fluorophores (e.g., FITC, Rhodamine) for visualization under specific wavelengths.

**Enzyme labels –** Linked to antibodies in ELISA to produce a detectable colour change.

**Nanoparticle labels –** Use gold or quantum dots for enhanced sensitivity in bioimaging or biosensing.

## Applications:

Immunoassays (e.g., ELISA, Western blot)

Fluorescence microscopy

Flow cytometry

Targeted drug delivery and tracking

**7.4 Nanoparticles for Oral Delivery of Peptides and Proteins:** Oral delivery of peptides and proteins poses significant challenges due to their poor stability in the gastrointestinal (GI) tract and low permeability across the intestinal epithelium. Nanoparticle-based drug delivery systems have emerged as a promising strategy to overcome these obstacles.

## Key Advantages of Nanoparticles:

**Protection from enzymatic degradation:** Nanoparticles can shield peptides/proteins from proteolytic enzymes in the GI tract.

**Improved absorption:** By enhancing permeability across the intestinal epithelium via mechanisms like paracellular transport or receptor-mediated endocytosis.

**Controlled release:** Nanoparticles can be engineered for sustained or targeted release, improving bioavailability.

**Types of Nanoparticles Used:**

**1. Polymeric nanoparticles (e.g., PLGA, chitosan):** Biocompatible and biodegradable.

Chitosan enhances mucoadhesion and opens tight junctions.

**2. Lipid-based nanoparticles (e.g., solid lipid nanoparticles, nanostructured lipid carriers):**

High loading capacity for lipophilic peptides.

Protect proteins from degradation.

**3. Dendrimers:**

Highly branched polymers with controlled size and surface functionality.

Capable of encapsulating peptides and facilitating transport across cell membranes.

**4. Inorganic nanoparticles (e.g., silica, gold):**

Offer stability and surface modification potential, though biocompatibility must be carefully evaluated.

**Strategies to Enhance Oral Bioavailability:**

**PEGylation:** Improves stability and reduces immune recognition.

**Surface modification with targeting ligands (e.g., vitamin B12, transferrin):** Enhances uptake by receptor-mediated transport.

Use of absorption enhancers: Surfactants or bile salts can increase permeability.

Challenges and Considerations:

Toxicity and immunogenicity of nanoparticles.

Scalability of production methods.

Regulatory hurdles due to complex formulation and characterization.

**7.5 Drug Discovery:** Nanotechnology plays a vital role in modern drug discovery. Single-walled carbon nanotubes have been effectively used to identify pathogen surface proteins. Quantum dots allow for the real-time tracking of individual glycine receptors and the study of their dynamics within the neuronal membranes of living cells, with temporal resolution from milliseconds to minutes. Gold nanoparticles and nan bodies—small, intact antigen-binding fragments—are widely used in diagnostic applications. Overall, nanotechnology enhances target identification and validation by enabling precise detection of surface proteins on disease targets.

**Conclusion:** In this paper, we provided a comprehensive overview of nanoparticles (NPs), including their types, synthesis methods, characterization techniques, physicochemical properties, and diverse applications. Characterization tools such as SEM, TEM, and XRD revealed that NP sizes typically range from a few nanometres up to 500 nm. Moreover, their morphology can be controlled through various synthesis techniques. Due to their high surface area and small size, NPs are excellent candidates for a wide range of applications. Their notable optical properties at the nanoscale further emphasize their value in photocatalytic processes. Synthetic methods allow for precise control over NP size, shape, and magnetic properties, enhancing their functional potential.

Despite their vast applications, concerns remain regarding the unregulated use and environmental discharge of NPs, which pose potential health risks. Therefore, responsible development and regulation are crucial to making nanoparticle use more practical and environmentally sustainable. Pharmaceutical nanotechnology, in particular, holds promise in advancing materials, devices, and therapeutic approaches—especially in areas where conventional technologies have reached their limits. Additionally, it offers the pharmaceutical industry new opportunities through the development of patentable technologies, providing a strategic response to revenue loss from off-patent drugs.

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