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Nanoparticles in Drug Delivery Systems: A Comprehensive Review

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ABSTRACT: The rapid advancements made in the past four decades with the production of Nanotechnology with an explosive growth throughout all industries from Science to Medicine. Nanotechnology products created from Nanotechnology based on Nanosciences are now playing a role in many aspects of our everyday lives, most notably in the Food Industry as Nanoparticles provide for new methods of Packaging, Preserve Shelf Life, Improve Preservation. Nanoparticles used in Medicinal Applications offer beneficial properties like Large Surface Areas, Modified Surfaces and Reactivity; thus, they provide for Enhanced Cellular Uptake of Water Soluble Drugs and Provide Increased Targeted Delivery of Chemotherapy Agent within Cancer Patients. These developments continue to enhance the styling of our everyday lives around the world while increasing our Economies, Technology and Global Competitiveness.

This review aims to critically consider characteristic properties of nanoparticles that make them either effective or toxic in biological systems, with a focus on their differences in biochemical interactions with cell membranes, proteins, and organelles compared with their bulk counterparts. This review also discusses various successful applications of nanoparticles in biological and biomedical fields, including applications in imaging, biosensors, regenerative medicine, genome delivery, and novel drug delivery systems. Particular emphasis will also be placed upon their use in theranostics, where various nanoparticles are now being used in formulations of drugs FDA-approved in the USA, which reflects a growing maturation of this branch of nanotechnologies worldwide. Despite major advances in nanotechnology, there are still worries about potential toxicity and other hazards from chronic exposure to these particles. The rising use of nanomaterials within consumer products and manufacturing operations adds to concern that toxic characteristics of nanoparticles may create safety issues as well. Potentially hazardous characteristics identified include cytotoxicity (cell death), oxidative stress (damage to cells due to excessive free radicals), and bioaccumulation (building up over time). All these (including) possibilities require a need for constant vigilance when using nanoparticles. This review, in this manner, also describes various approaches in developing strategies for safer use of nanoparticles with their increasing usage, including safer design in nanoparticles, enhanced regulatory policies, comprehensive toxicological profiling, and a lifecycle assessment of various nanotechnologybased products. This review, in critically summarizing latest understanding of nanoparticles with their properties, their use in various realms, their potential in theranostics, and their toxicity, would provide a comprehensive understanding of their dual natures in quickly expanding nanotechnologies.

KEYWORDS: Nanoparticle, Drug delivery system, Nanotechnology, Nanomedicine.

I. INTRODUCTION

Nanotechnology and the development of systems using nanoparticles have changed the way drugs are delivered. Traditional drug delivery methods often have problems, such as low absorption, lack of precision in targeting, quick removal from the body, and harmful side effects. These issues can make treatments less effective and affect how patients follow their treatment plans. Nanoparticles, which are usually between 1 and 1000 nanometers in size, offer a flexible solution to these challenges. They allow for controlled release of drugs, improve the mixing of drugs that don't mix well with water, keep drugs in the body longer, and deliver them more precisely to affected areas, all while reducing unwanted effects. Nanoparticles take advantage of special features like a large surface area, the ability to change their surface properties, and their ability to cross through biological barriers.

These properties help drugs work better in the body and interact more effectively with their targets. Important ways they do this include the enhanced permeability and retention effect (EPR) in cancer tissues, targeting specific cells using attached molecules, and releasing drugs in response to changes in pH, temperature, or enzyme activity. Many types of nanoparticle systems, such as polymeric, lipid-based (like liposomes), inorganic, and hybrid systems, have been developed to deliver different types of drugs, including large molecules like proteins and nucleic acids, as well as smaller molecule drugs. The field has grown quickly since the first nanoparticle-based treatments, like liposomal doxorubicin (Doxil), were approved in the 1990s. Many nanoparticle formulations are currently being tested or used in clinical settings for diseases such as infections, cancer, and other conditions. Recent advancements have focused on creating biocompatible materials, using nanoparticles with multiple functions, and personalizing treatment based on individual patients. This review looks at the principles, types, ways they are made, their uses, challenges, and future possibilities in drug delivery. Background and Fundamental Concepts Nanoparticles in drug delivery are a core part of nanomedicine. They are made up of tiny particles, usually between 1 and 1000 nanometers in size, that allow for the delivery of medicines. Their small size gives them special properties that differ from larger particles made from the same material. Because of their high surface area to volume ratio, they are influenced by quantum mechanics. Besides changing how drugs behave, nanoparticles enable controlled and targeted drug release at the molecular level.

Another important concept is the enhanced permeability and retention (EPR) effect that happens in solid tumors. Because these tumors have leaky blood vessels, nanoparticles can easily enter the tumor area. Also, the high pressure inside the tumor prevents the lymphatic system from removing substances, which means nanoparticles stay in the tumor for longer. Nanoparticles can be classified into different types, such as polymeric nanoparticles (like polylactide-co-glycolic acid), lipid nanoparticles (like liposomes or solid lipid nanoparticles), inorganic nanoparticles (like silica or gold), and hybrid systems. Researchers use various techniques to include drugs inside nanoparticles, such as encapsulating them, binding them, or attaching them to the nanoparticle surface. By adding molecules that specifically target certain cells, researchers can direct drug delivery to those cells, a process known as active targeting. Alternatively, passive targeting happens through the EPR effect.

Stimuli-responsive nanoparticles are another type that releases their contents when triggered by specific signals. Internal triggers include changes in pH or the presence of reactive oxygen species, while external triggers might involve light or magnetic fields. These methods allow for more precise drug delivery with less risk of unwanted effects in the whole body.

Advantages

Drug delivery systems using nanoparticles have several major benefits compared to traditional methods.

These include:

- ***Increased solubility and bioavailability:*** Nanoparticles help drugs that don't mix well with water dissolve better, which means they are absorbed more efficiently and work better. Targeted delivery allows for higher doses where they're needed, which reduces damage to healthy tissues and side effects.
- ***Controlled and sustained release:*** Nanoparticles can keep drugs in the body for longer, maintaining their effectiveness over time.
- ***Therapeutic protection:*** Nanoparticles can protect sensitive drugs, such as proteins and siRNA, from being broken down by enzymes. They also help drugs get past physical barriers, like cell membranes or the blood-brain barrier.
- ***Multifunctionality:*** Nanoparticles can help fight drug resistance, support the use of multiple drugs at once, and even be used for both treatment and imaging (a concept called theranostics).-

--Types Of Nanoparticles

The Nanoparticles are mainly classified into organic and inorganic based on their composition. Organic nanoparticles are carbon based and biodegradable which makes them suitable for the medical application. Inorganic nanoparticles are non-carbon based (often metal or ceramic) and offer strong physical properties like magnetism or plasmonics. Lipid-based and protein-based nanoparticles are specialized subsets of organic nanoparticles, known for their excellent biocompatibility and natural origins.

1.Organic Nanoparticles(Non-Lipid, Polymeric) :

These are primarily composed of synthetic or natural polymers. (Excluding lipid and Protein). Synthesis: They are usually synthesized from the methods like Emulsion, Polymerisation, Nanoprecipitation, And Self-assembly. Properties: they have properties like the Biodegradability, High drug loading capacity, Tunable releasing profiles and Easy surface modification. Application: it has controlled drug delivery system, Gene therapy and Tissue engineering. It also has

advantages like the Low toxicity, FDA approved material and versatile function. Limitations: it has limitations like the potential immune response and different batch has different variability.

Examples: Polylactic-co-glycolic acid (PLGA), Polyethylene Glycol (PEG) Chitosan, Polylactic acid (PLA), Polymeric micelles.

2. Inorganic Nanoparticles:

These consist of metal, metals oxides or semiconductors which lacks carbon based oraganic frameworks. Synthesis: these Nanoparticles are synthesized by using the methods like the Chemical reduction, Sol-gel, Thermal decomposition and green synthesis. Properties: it has high stability , Superparamagnetism, surface plasmon resonance and photocatalytic activity. Application: these nanoparticles have various application like the catalysis, imaging, photothermal therapy, antimicrobial agent and the advantages like the high mechanical strength. Limitation: it can cause potential toxicity (heavy metal) and it is non-biodegradable.

Example:

metals- Gold(Au), Silver(Ag), Iron(Fe) ,Metal oxides- Iron oxide(FeO₄), Titanium oxide (TiO₂) silica oxide (SiO₄) ,Quantum Dots- CdSe, ZnS.

3. Lipid-based Nanoparticles:

These are the subset of oraganic nanoparticles composed of lipids often mimicking the cell membranes. Synthesis: the methods used for the synthesis of the are thin film hydration, extrusion, high-pressure homogenization, solvent injection. Properties: they have properties like amphiphilicity, stealth properties with PEGylation and high encapsulation for lipophilic drugs. Application: these are used in mRNA Vaccines, cancer chemotherapy, topical delivery system. It's advantages are it's good biocompatibility, low immunogenicity and efficient cellular uptake.

Limitation: it has stability issues(oxidation) which results in the limited shelf life.

Examples: solid-liquid Nanoparticles (SLNs), Nanostructured lipid carriers(NLCs), lipid polymer hybrids Liposomes.

4. Protein-based Nanoparticles:

It is also a subset from the organic nanoparticles. It's derived from the natural protien that self-assemble into cage-like or spherical structures. Synthesis: these are synthesized by the methods like the dissolution, Self-assembly, genetic engineering for recombinant protiens. Properties: It has properties like the hollow cage structure, pH-responsive disassembly, inherent targeting ability. Application: it is used in application of drug encapsulation, imaging and vaccine platform. It's advantages are that it is endogenous, has precise size control and easy biofunctionalisation. Limitations: it has potential denaturing during synthesis and limited scalability for some proteins.

II. THERAPEUTIC APPLICATIONS

Category	Biocompatibility	Biodegradability	Stability	Key Applications	Toxicity Concerns
Organic (Polymeric)	High	High	Moderate	Drug delivery, gene therapy	Low
Inorganic	Moderate	Low	High	Imaging, catalysis, therapy	Higher (accumulation)
Lipid-Based	Very High	High	Moderate	Vaccines, nucleic acid delivery	Very Low
Protein-Based	Excellent	High	High	Targeted cancer therapy, vaccines	Minimal

The Nanoparticles-based drugs delivery system has revolutionised the therapeutics by improving the drug solubility, bioavailability, controlled targeting, releasing and reducing the toxicity compared to conventional formulation. It's established applications are most prominent in cancer where nanoparticles take advantage of it's enhanced permeability and retention(EPR) effect in tumor vasculature for the passive targeting which also enables the reduced systematic side effects. In infectious diseases, it's lipid-based nanoparticles minimize the nephrotoxicity of strong and potent antifungals. In contrast application in cardiovascular diseases remain mostly investigational, with no fully approved nanoparticle drugs specifically for CVD treatment, despite it's promising preclinical data for targeted delivery to the atherosclerotic plaques or post-infection repair.

1. Cancer:-The cancer represents the dominant field for the approved nanoparticles drug delivery with many formulations which enhances the therapeutic index of the chemotherapeutics.

Examples:

1. Abraxane® (nab-paclitaxel, albumin-bound paclitaxel nanoparticles) : it is approved by the FDA in 2005 (with expansion in subsequent years) for metastatic breast cancer, non-small cell lung cancer and pancreatic cancer. It avoids the solvent related toxicity of regular paclitaxel and improves the efficiency through better tumor accumulation.
2. Doxil® (pegylated liposomal doxorubicin) : it is the first FDA approved nanomedicine in 1995 for the Kaposi's sarcoma, ovarian cancer and multiple myeloma. Pegylation extends circulation time which reduces the Cardiotoxicity and it enhances the tumor delivery.
3. Vyxeos® (liposomal daunorubicin/cytarabine combination) : it is approved in 2017 for the High-risk acute myeloid leukemia(AML). It maintains a synergistic drug ratio, prolongs exposure and improves survival over standard procedure. Other notable approval includes onivyde® (liposomal irinotecan) for pancreatic cancer. These systems primarily use the liposomes or the protein-based nanoparticles showing reduced toxicity while also maintaining or improving antitumor efficacy.

2. Infectious Diseases:-

In infectious diseases, nanoparticles have shown the safer use of highly effective but toxic agents, particularly antifungals.

Example:

1. AmBisome® (liposomal amphotericin B) : it is a key example approved for the empirical therapy in febrile neutropenia, treatment of invasive fungal infections, cryptococcal meningitis in HIV patients and visceral leishmaniasis. The liposomal encapsulation significantly reduces nephrotoxicity and infusion reaction compared to conventional amphotericin B deoxycholate enabling higher doses and broad use in immunity compromised patients. The Lipid Nanoparticles have also supported for mRNA vaccines (e.g. COVID-19), though these are preventive rather than therapeutic for established infection.

3. cardiovascular diseases:-As of early 2026, none of the nanoparticle delivery systems being investigated through preclinical studies has had an FDA or EMA approved specifically for use in treating cardiac disease. This is primarily due to the varying nature of the diseases themselves, the ever-changing environment of the vascular system, and the challenges presented when bringing these products to market. Present-day treatment options for cardiovascular disease continue to be based upon traditional medications such as statins and antiplatelet drugs; however, there are signs that nanoparticles will prove useful in reducing inflammation and helping to heal the vascular wall, as demonstrated by numerous successful studies done using animal models.

Product	Nanoparticle Type	Active Agent(s)	Primary Indication(s)	Approval Year (FDA)	Key Benefit
Doxil®	Pegylated liposomes	Doxorubicin	Ovarian cancer, Kaposi's sarcoma, multiple myeloma	1995	Reduced cardiotoxicity
Abraxane®	Albumin-bound nanoparticles	Paclitaxel	Breast, lung, pancreatic cancer	2005	Solvent-free, improved tolerability
Vyxeos®	Liposomes	Daunorubicin + Cytarabine	Acute myeloid leukemia	2017	Synergistic ratio maintenance
AmBisome®	Liposomes	Amphotericin B	Invasive fungal infections, leishmaniasis	1997	Reduced nephrotoxicity
Onpattro®	Lipid nanoparticles	Patisiran (siRNA)	Hereditary transthyretin amyloidosis	2018	First RNAi therapeutic

III. MECHANISM

1] Preparation Methods:

acid1. Poly (Methyl Methacrylate) Nanoparticles (Radical Emulsion Polymerization) : - Mechanism: Standard free-radical polymerization starts with γ -irradiation or chemical initiators like potassium peroxodisulfate. Key controlling factors : Particle size increases with more monomer concentration. Particle size decreases with higher initiator concentration and higher temperature.

- Example: At 65°C and 10 mmol of methyl methacrylate, size ranges from 85 to 256 nm, depending on the initiator level. General characteristics: Often made without emulsifiers, which leads to a broader size distribution. Adding macromolecular colloids like proteins or casein improves uniformity. Applications: They work well as vaccine adjuvants.

2. Poly (Alkyl cyanoacrylate) Nanoparticles (Anionic Emulsion Polymerization): Mechanism: Anionic polymerization begins with OH^- from water dissociation or bases. It does not need an external initiator or heat and starts at room temperature when stirred. Distinct features: - Polymerization happens very quickly, resulting in low molecular weight polymers. - H^+ ions are involved in termination, which makes it sensitive to pH; the best performance is below pH 3.5.

- High biodegradability allows for clearance from the body in days.

- Key controlling factors:

- Particle size decreases with lower pH, higher monomer concentration (up to ~2%), and appropriate stabilizers.

- Stabilizer effect : - Dextran 70 (0.05–2.5% w/v): size changes from 212 to 126 nm (optimal around 1%). -

- Poloxamer/polysorbate series: sizes range from 71 to 254 nm. - β -Cyclodextrin: creates larger sizes (up to 3400 nm). -

- Stirring speed surprisingly increases size slightly (126 nm at 600 rpm to 161 nm at 3000 rpm) due to kinetic energy fostering coalescence and variability.

- Temperature has minimal impact on size. - Ultrasonication raises the variability in size.

- Example: Poly(butylcyanoacrylate) with 0.5% dextran at pH 2 results in a minimal size of about 130 nm.

3. Acrylic Copolymer Nanoparticles: - Made through chemical or γ -irradiation initiation of various monomer mixtures, including methyl methacrylate, 2-hydroxyethyl methacrylate, and methacrylic acid. - Selected compositions and sizes:

- 66.6% MMA + 33.3% HEMA \rightarrow 360 nm

- 50% MMA + 50% HEMA \rightarrow 200 nm

- 53% MMA + 30% HEMA + 10% MAA + 7% EGDMA \rightarrow 40 nm

- Various ternary and quaternary mixtures \rightarrow 60–150 nm - Note: Their lack of biodegradability limits their use in parenteral applications, but they are suitable as immune sorbents.

4. Transmission Electron Micrograph: - Poly (isobutyl cyanoacrylate) nanoparticles display distinct shell-like wall structures, showing core-shell morphology with diameters around 100–200 nm, confirmed by the scale bar.

5. Other Emulsion-Based Methods Mentioned Briefly: - Interfacial polymerization/deposition (e.g., poly (alkyl cyanoacrylate), poly lactic acid). - Albumin nanoparticles made through oil emulsion denaturation. - Carbohydrate nanoparticles created by acryloylating polysaccharides. - Solvent evaporation process for poly (lactic) and poly(hydroxyl butyrate).

2] Drug Loading & Release:

The nanoparticles are really useful for delivering medicine to people. They help get the medicine to the place in the body. This is especially important for medicines that are not very good at getting into the body on their own like some cancer treatments. Nanoparticles can also help control how much medicine is released and when. This makes nanoparticles very good at helping people get the medicine they need like cancer treatments that can be very bad for people if they are not used correctly. Nanoparticles are used to deliver lots of kinds of medicine including the ones that are not very good, at getting into the body.

In drug loading, basically putting the medicine into or, on these tiny things called NPs. The important things to measure with drug loading include: Drug Loading Content (DLC): Percentage of drug mass relative to total NP mass (often 10–50% in advanced systems, up to >50% in prodrug-based designs).

The Encapsulation Efficiency or EE for short is very important. It is the percentage of the drug that is to be encapsulate successfully. As it is required to be as high as possible more, than 80 to 90 percent of the initial drug. This means that the Encapsulation Efficiency is a measure of how we can get the drug inside the thing that is supposed to hold it. A good Encapsulation Efficiency is necessary for the drug to work properly. The Encapsulation Efficiency is a part of making sure that the drug is effective.

Methods of loading:

Physical encapsulation (adsorption into pores or matrix). Chemical conjugation (covalent linking for stability). Ionic/hydrophobic interactions. Factors influencing loading: Drug-polymer compatibility (e.g., hydrophobic interactions in polymeric NPs). The composition of something, like a nanoparticle is really important. For example: mesoporous silica it is great because it has lots of space inside and can control the size of the pores. This means can put a lot of stuff inside the nanoparticle composition like an amount of a certain substance because the pores can be adjusted to fit.

Making tiny particles is really good for some kinds of medicine that do not mix with water. For example the nano precipitation method is great, for hydrophobic drugs because it helps them work well. Drug properties (solubility, charge; loading is highest near isoelectric point for proteins). Drug Release Nanoparticles or NPs usually release things in two parts. First there is a release of the drug that is stuck to the surface of the NPs. Then the NPs release the rest of the drug slowly over time. The ways that NPs do this include: Diffusion is when a drug moves through the matrix or pores of a nanoparticle. This usually happens with nanoparticles that are made of polymers or lipids. The drug diffuses through the nanoparticle matrix or pores.

Erosion or degradation of a material is when it breaks down. This can happen to polymers. For example something called hydrolysis can break down PLGA NPs. When this happens it releases the drug that's inside the PLGA NPs. This is how the drug is set free, from the polymer. The polymer breakdown is what makes the drug come out. When a solvent gets into the matrix it makes the matrix swell up. This swelling of the matrix enables the solvent to move around and spread out which is called diffusion. The swelling of the matrix is important because it helps the solvent to penetrate into the matrix. The matrix swells up because the solvent gets into the spaces, in the matrix. This makes it easier for the solvent to diffuse through the matrix. Stimuli-responsive: Triggered by pH (acidic tumor environment), temperature, enzymes, or light for controlled release. Factors affecting release: NP size, porosity, and surface charge. Environmental conditions (pH, temperature). Drug-matrix interactions (stronger bonds slow release).

3] Surface Modification:

The functionalization of nanoparticles through surface modification is a crucial step in adjusting their properties to fit various applications including drug delivery, biomedical imaging, catalysis, composites, and environmental applications. This fundamentally deals with problems of aggregation, instability in biological fluids, toxicity, and the lacking of targeting ability. Surface Modification is Essential Nanoparticles that are not coated or functionalized (especially those inorganic ones such as metals, metal oxides, quantum dots) have the tendency to: -Form agglomerates due to their high surface energy -Experience rapid oxidation or degradation -Interact non-specifically with proteins (opsonization) which makes the immune system clear them rapidly. -Have high toxicity or low biocompatibility -Not have any specificity for targeting Surface modification allows enhanced colloidal stability, biocompatibility, stealth properties (longer circulation), targeting ability and also permits payload conjugation (drugs, genes, imaging agents). Main Strategies for Surface Modification, Surface modification could be done by two broad methods:

1. Non-covalent interactions: These are mainly electrostatic attraction, hydrophobic interactions, hydrogen bonding, van der Waals forces.

Examples: Surfactant adsorption, polymer physisorption

-Advantages: Simple, reversible

-Disadvantages: Less stable under harsh conditions

2. Covalent conjugation: Strong chemical bonds (e.g., thiolmetal, silaneoxide, amide bonds)

- Popular chemistries:

- Thiol chemistry (Au, Ag, QDs very strong MS bonds) - Silanization (oxides like SiO₂, FeO SiOM bonds) - EDC/NHS coupling (carboxylamine) - Click chemistry (CuAAC, strain, promoted azidealkyne) - Maleimide-thiol coupling.

Method	Typical Nanoparticles	Key Agents/Ligands	Main Benefits	Applications
PEGylation	Au, Ag, Fe ₃ O ₄ , QDs, liposomes	PEG-SH, PEG-NH ₂ , PEG-COOH	Stealth effect, ↓ protein adsorption, ↑ circulation time	Drug delivery, imaging
Silanization	SiO ₂ , Fe ₃ O ₄ , TiO ₂ , BaTiO ₃	APTES, MPTMS, OTES, DTES	Stable in aqueous/organic media, tunable charge	Composites, nanofluids, EOR
Polymer coating	Most types	Chitosan, PVA, PEI, polyoxazolines	Enhanced stability, pH/muco-adhesion	Gene/drug delivery, mucoadhesive systems
Ligand exchange	Au, Ag, QDs	Thiols → PEG-thiols, peptides	Phase transfer (organic → aqueous)	Biosensing, theranostics
Click chemistry & bioconjugation	All types	Azides/alkynes, aptamers, antibodies, peptides	Precise, bio-orthogonal targeting	Active targeting, cancer therapy
Surfactant adsorption	Various	CTAB, SDS, oleic acid	Quick stabilization, tunable charge	Initial synthesis protection

4) Targeting Strategies:

Targeting

methodologies of nanoparticles in drug delivery are vital (especially in cancer therapy) to raise the therapeutic effectiveness, lessen the side effects, and boost the accumulation of the drugs at the site of the tumor.

1. Passive Targeting: This method exploits the inherent physiological traits of the target tissue (e.g., cancerous) without the involvement of specific ligands. The main process is that of Enhanced Permeability and Retention (EPR) effect: - Tumor vasculature is leaky (because of swift angiogenesis) with holes 100-600 nm in size. - Due to the deficiency of lymphatic drainage, nanoparticles (usually 10-200 nm) get trapped in the tumor interstitium. - After systemic administration, nanoparticles (e.g., liposomes, polymeric NPs) preferentially localize to tumors. - Advantages: No surface modification is required, simple.

- Disadvantages: Tumors in humans are heterogeneous (EPR effect is quite consistent in animal models), penetration is limited in thick stroma.

2. Active Targeting: In this case, nanoparticles are decorated with ligands that specifically bind to receptors on the surface of target cells (e.g., tumor cells) thus enabling receptor-mediated endocytosis for increased cellular uptake.

Typical ligands are: - Antibodies (e.g., anti-HER2, anti-EGFR) - Peptides (e.g., iRGD, folate) - Aptamers and Small Molecules (e.g., transferrin) - Active targeting usually serves as a complement to passive targeting by enhancing the specificity and cellular internalization of the nanomedicines following EPR, mediated extravasation.

Additional/Emerging Strategies :

- Stimuli-responsive targeting: Nanoparticles carry and release therapeutic agents at tumor site in response to various tumor micro-environmental cues such as pH, oxidation, reduction, enzymes, and temperature. Multifunctional/hybrid approaches, combining passive + active + stimuli-responsive for precision. - Biomimetic targeting: - Use of cell membrane, coating of nanoparticles for immune evasion by a NPs and enhanced tumor site homing.

5) Characterization:

Physical

Characterization Methods: These methods mainly characterize the structural, morphological, and size-related properties via non-destructive or imaging-based techniques. They give you either direct visualizations or scattering-based information.

Some common examples are: - Transmission Electron Microscopy (TEM) and High Resolution TEM (HRTEM), for size, shape, internal structure, and lattice fringes. - Scanning Electron Microscopy (SEM), for studying surface morphology and

topography.-Atomic Force Microscopy (AFM), for 3D surface imaging, roughness and the study of mechanical properties.-Dynamic Light Scattering (DLS), for hydrodynamic size distribution and the state of aggregation in suspension. - X-ray Diffraction (XRD), for determining crystallinity, phase identification, and crystallite size.-Small, Angle X, ray Scattering (SAXS), for determining the overall shape and size in solution. These techniques are termed as "physical" because they use an electron beam, light scattering, or X, rays to interact with the matter without changing the chemical composition. Chemical Characterization Methods: These methods are used to study the elemental composition, surface chemistry, the presence of functional groups, and the bonding states. Some common examples are:-Fourier, Transform Infrared Spectroscopy (FTIR), for identification of functional groups and capping agents.-UV, Visible Spectroscopy, for determining optical properties (e.g. plasmon resonance in metal nanoparticles) and concentration.- X-ray Photoelectron Spectroscopy (XPS), for determining the surface elemental composition and oxidation states.

Energy, Dispersive X, ray Spectroscopy (EDS/EDX), typically combined with TEM/SEM for elemental mapping. Inductively Coupled Plasma Mass Spectrometry (ICP, MS) for accurate measurement of element concentration (including single, particle mode to determine size/number concentration). Zeta Potential Measurement to get surface charge and colloidal stability. These allow to uncover the chemical nature, purity, and surface alterations. Biological Characterization Methods: They evaluate, for instance, toxicity, biocompatibility, cellular uptake, and bioactivity that are typical of the interactions with biological systems (very much the case for biomedical or eco, toxicology applications). These methods are mostly based on in vitro/in vivo assays.

6] Biological Interactions (Assessment methods):

Protein Corona: The protein corona happens when tiny particles, like nanoparticles pick up proteins from the fluids, in body. This changes what the nanoparticles are so they are not the same anymore. The protein corona is called as thing that forms around the nanoparticles. Isolation methods include things, like:-Centrifugation (differential or density gradient)

-Magnetic separation-Size exclusion chromatography (SEC). Flow-field-flow fractionation (F4), The ways to characterize something are:-Dynamic light scattering (DLS) and zeta potential for size/charge changes Transmission electron microscopy (TEM) for visualization, Liquid chromatography-mass spectrometry (LC-MS) for protein composition, Gel electrophoresis, FTIR, and isothermal titration calorimetry (ITC) for affinity and stoichiometry, These things helps to tell the difference, between a corona that is tightly bound and a soft corona that is loosely bound. The hard corona and the soft corona are different because of how they are bound. This is important to know about the corona.

Cellular Uptake:-The uptake of things happens mostly when cells take in stuff from outside. This process is called endocytosis. It happens in a few different ways.-Cells can use clathrin to help take in things. They can use caveolin.- Sometimes cells will just swallow up a lot of stuff at once this is called macropinocytosis. They will eat up whole cells or particles which is called phagocytosis.-So uptake happens mainly through these types of endocytosis, like clathrin-mediated endocytosis, caveolin-mediated endocytosis, macropinocytosis and phagocytosis. The ways we assess things include:-Flow cytometry (quantitative, high-throughput for fluorescent NPs), Confocal laser scanning microscopy (qualitative localization), Plate reader assays for fluorescence intensity

-Transmission electron microscopy (TEM) for intracellular visualization The uptake of something depends on how big it's. Usually things that are 50 nanometers in size work the best. The shape of the thing is also important. Things that are shaped like a ball work than things that are shaped like a rod. The charge of the thing and what its surface is made of are also factors, for uptake of the thing. Uptake of the thing is affected by all these things. Barriers (e.g., mucus, blood-brain barrier - BBB) The main goal is to understand how things get through the mucus barrier. The mucus barrier penetration is a thing to study. Multiple particle tracking (MPT) or fluorescence recovery after photobleaching (FRAP), The synthetic mucus barrier arrays are like tools. These tools are also known as diffusion chambers. The synthetic mucus barrier. Diffusion chambers are used to study how things move through mucus. The synthetic mucus barrier. Diffusion chambers are very helpful, in understanding how the body works. BBB crossing uses: In vitro models (e.g., brain endothelial cell co-cultures) with trans-endothelial electrical resistance In vivo imaging or bio-distribution studies Transcytosis (receptor-mediated or adsorptive) is key; strategies include ligand functionalization (e.g., transferrin, insulin).

7] Pharmacokinetics (Assessment methods) and Toxicity & Safety(Assessment methods):Pharmacokinetics (Assessment Methods):

ADME and Bio-distribution:ADME (absorption, distribution, metabolism, excretion) and bio-distribution studies track nanoparticle fate. People usually do these things:Radiolabeling (e.g., for mass balance, tissue distribution via quantitative whole-body autoradiography)-In vivo fluorescence or PET imaging for real-time tracking-Inductively coupled plasma mass spectrometry (ICP-MS) for elemental NPs, Tissue homogenization + LC-MS or ELISA for quantification, The liver and the spleen are the parts of our body that often have the amount of something accumulated in them. When we do long term studies we want to see how our body gets rid of things like through urine or feces and where they build up in body like, in the liver and the spleen.

Toxicity & Safety (Assessment Methods):There are kinds of toxicity. Types of toxicity include:-Acute cytotoxicity, Oxidative stress, Inflammation, Genotoxicity, Immunogenicity. Organ-specific (e.g., hepatotoxicity, neurotoxicity), Things that are involved in the mechanisms include:-Reactive oxygen species (ROS) generation, Mitochondrial dysfunction, Protein corona effects. Metal ion release (for ion-shedding NPs), Signaling pathway modulation, Membrane damage, The ways we figure out how well something is working include: *n vitro*: MTT/MTS/WST-1 (viability), LDH (membrane integrity), ROS assays (e.g., DCFH-DA), comet assay (DNA damage), apoptosis/necrosis kits, cytokine profiling, *In vivo*: Histopathology, organ function tests, bio-distribution-linked toxicity, omics (transcriptomics, proteomics) for mechanistic insights Emerging: 3D models, organoids, and adverse outcome pathways (AOPs) for better prediction

IV. CONCLUSION

The nanoparticles have really helped to improve the way drugs are delivered. They make the drugs work better in human bodies. They can be targeted to specific areas. This means that the drugs are released in a controlled way and that helps to reduce the side effects. As per observation, the products that have been approved by the FDA and the EMA. Even with all these advances there is not see many nanoparticles being used to help people in a big way. The use of nanoparticles, in clinics is still very limited. The main problems with this are the ways that tiny things and living things interact like when proteins build up on the surface of tiny things or when the body's immune system reacts to them. This can also include reactions and poison. Another issue is that what happens in a lab does not always match what happens in life. It is also hard for these things to get past the body's natural barriers. Then there are problems with making a lot of these tiny things like it costs a lot of money they do not last long and the process of making them is very sensitive. The cost of all of this and the fact that the rules are not clear because there are no guidelines, for tiny medicine slows down the process of developing and approving these things.

The future of this technology looks really great. New kinds of nanoparticles that can respond to their environment and systems that can both treat and diagnose problems are going to make a difference. Artificial intelligence is also going to help in design and improve these systems. We are also learning from nature. Using ideas, like cell membranes and tiny sacs that cells release to make new systems. All of these things are going to help to make treatments that are more precise, safer and tailored to individual people especially when it comes to cancer and gene therapy. Nanoparticles and these new systems are really going to change the way we do things in the areas of oncology and gene therapy and nanoparticles will play a big role in this. Regulatory outlook: Nanoparticles are regulated under existing drug frameworks using a risk-based, case-by-case approach. Early regulatory engagement and robust characterization are critical.

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