Synthesis, Characterization, and Applications of Nanoparticles: A Review

PREETI*,TUSHAR THAKUR, MOHIT BANSAL, KANIKA KUMARI, MAMTA DEVI ,AKSHITA SHARMA

SHIVA INSTITUTE OF PHARMACY BILASPUR (HIMACHAL PRADESH)

Abstract:

Keywords: Nanoparticles, Drug Delivery Systems, Synthesis Methods, Characterization Techniques**,** Biomedicine**,** Targeted Therapy, and Nanomedicine.

1. Introduction:

Nanoparticles are super tiny particles with unique sizes and different surface properties. Nanoparticles are used in various pharmaceutical applications, especially in Drug Delivery Systems as depicted in the Fig. 1. The sizes of nanoparticles range from 1-100 nanometres in their diameter (1). As nanoparticles exhibit various characteristics and their size and surface properties them highly desirable for the Targeted Drug Delivery System. Along with these properties, nanoparticles possess a small size-surface ratio, surface chemistry, and also ability to encapsulate various active pharmaceutical agents. The preparation of nanoparticles involves various methods (2). These methods include coacervation, polymerization, ionic gelation, and also supercritical fluid technology. Each method works differently for efficacy and versatility. Several factors influence the effectiveness of the drug delivery of these nanoparticles. These include drug loading capacity, particle size, and surface properties (3).

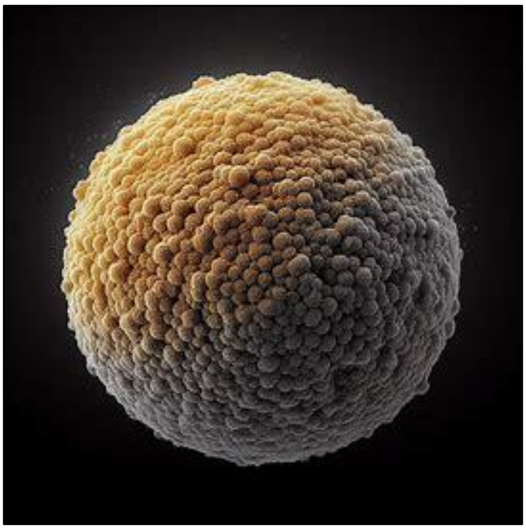

Fig. 1 Nanoparticle

The size of the nanoparticles affects the biodistribution, cellular uptake, and clearance kinetics. The smaller the nanoparticles are more the circulation time and penetration in the target tissues happen. The circulation time and the penetration into the tissue improve the efficacy of the drug (4). Several factors can alter the pharmacokinetics of the nanoparticles which can allow for specific targeting of a specific disordered cell or tissue that then enhances the therapeutic outcome of the API. The nanoparticles offer effective drug delivery that can cause a wide range of pharmaceutical applications (5).

2. Type of Nanoparticles:

Nanoparticles include a diverse range of materials with different sizes. The sizes can range from 1 to 100 nanometres. Some common types of nanoparticles include:

- **Metal Nanoparticles:** There are various types of metal nanoparticles such as copper, gold and silver. The small size of nanoparticles makes them more catalytic, electrical, and optical (6). The gold nanoparticles possess surface plasmon resonance. This makes these nanoparticles more useful in biomedical and other applications. The silver nanoparticles have anti-microbial activities. These nanoparticles can be prepared by both chemical as well as physical methods. These nanoparticles are either synthesised by constructive or destructive methods. Metal nanoparticles can be synthesized by almost all the metal. The most frequently used metals are zinc, silver, lead, iron, gold, copper, cobalt, cadmium, and aluminium (7). These nanoparticles exhibit unique attributes, including sizes ranging from 10 to 100nm, distinctive surface features such as high surface area to volume ratio, pore size, surface charge, and surface charge density as depicted in the Fig. 2. They can exist in crystalline or amorphous structures, with shapes varying from spherical to cylindrical, and exhibit diverse colours, reactivity, and sensitivity to environmental factors such as air, moisture, heat, and sunlight (8).

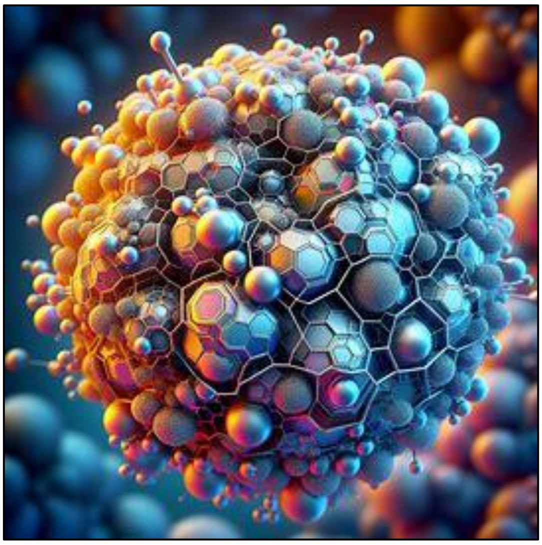

Fig 2: Metal Nanoparticle

The size, shapes, chemical characters, and applications of metal nanoparticles are listed in the table below:

Sr. No.	Nanoparticle Type	Size	Shape	Chemical Characterization	Applications	Reference
	Gold Nanoparticle	1nm-100 nm	Hexagonal, spherical, and triangular.	Highly reflective, can be made transparent or translucent	Bio-imaging and receptor detection.	(9).
	Silver Nanoparticle	1nm-100 nm	Spherical or triangular	Highly reflective, can be made transparent or translucent	For anti-microbial and anti-cancer therapy	(10).
	Iron Nanoparticle	20-40 nm	Cubes, Hexagonal, Spherical, and Rods.	Poorly conductive	Contrast agent for MRI	(11).

- **Metal Oxide Nanoparticles:**
  Metal oxide-based nanoparticles are the nanoparticles synthesized to alter the respective metal based counterparts as depicted in the Fig. 3.

Fig. 3: Metal Oxide Nanoparticle

For example, the iron nanoparticles freely oxidize to form iron oxide in the presence of oxygen at room temperature. This then enhance the reactivity than the nanoparticles of pure iron (12). The synthesis of these nanoparticles can primarily be determined by the reactivity and the efficacy. The commonly synthesized nanoparticles are Zinc oxide, Titanium oxide, Silicon dioxide, Magnetite, Iron oxide, Cerium oxide, and Aluminium oxide (13).

- **Carbon-based Nanoparticles:**
  These nanoparticles are composed of carbon, as these are completely carbon based. There are various types of carbon-based nanoparticles like carbon-black, carbon-nano fibers, carbon-nanotubes, fullerenes, and graphene as depicted in Fig. 4. Sometimes these are in nano size as well. Fullerenes like C60 are spherical molecules in which carbon are held together. Graphene are the two-dimensional allotrope that forms a hexagonal lattice with the thickness of around 1 nm (14).

Fig. 4: Carbon based nanoparticles

Carbon Nanotubes are the cylindrical structures that are made up of graphene. Carbon Nanofibers can be derived from graphene and are conical or cup-shaped structures. Carbon Black is an amorphous carbon material that is spherical in shape (15).

- **Polymeric Nanoparticles:**
  Polymeric nanoparticles have a diverse class of nanomaterials. These can be formed from both synthetic and natural polymers as depicted in Fig. 5. These polymers include chitosan, PEG, and PLGA. The polymeric nanoparticles are both biocompatible and biodegradable in nature (16). The PLGA nanoparticles can widely be used in various drug delivery systems as these possess the ability to encapsulate the release therapeutic agents. The PEGylated nanoparticles have the enhanced circulation time *in-vivo* (17).

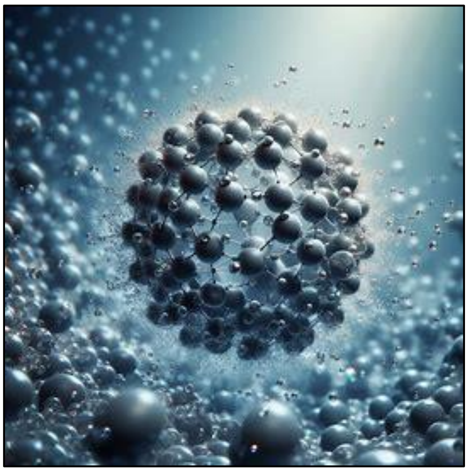

Fig. 5 Polymeric Nanoparticle

This makes them suitable for the targeted drug delivery system. The chitosan nanoparticles consist of muco-adhesive properties that enable the drug delivery to the mucosal surfaces (18). The polymeric nanoparticles can be used for various applications in fields such as agriculture, environmental science, and pharmacy (19).

- **Lipid-based Nanoparticles:**

  The lipid based nanoparticles are the nanoparticles composed of lipid or lipid like materials as depicted in Fig. 6. These include liposomes, solid lipid nanoparticles, and nano-emulsions (21). These are used in the drug delivery due to their biocompatibility, biodegradability, and the ability to encapsulate hydrophobic and hydrophilic drugs (22).

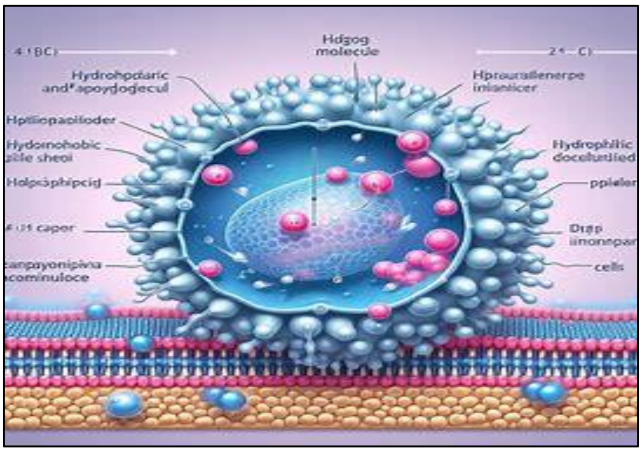

Fig. 6: Lipid based nanoparticles

These nanoparticles are the spherical vesicles that are composed of lipid bilayers. These bilayers then facilitate the drug delivery. Solid lipid nanoparticles are employed for targeted and regulated medication release since they are made of lipids in a solid form at ambient temperature (23). Colloidal dispersions of water and oil stabilised by surfactants are called nanoemulsions. They are utilised in medications, food, and cosmetics. Lipid-based nanoparticles offer effective medication delivery methods that reduce adverse effects while enhancing drug solubility, stability, and bioavailability (24).

- **Magnetic Nanoparticles:**

  At the nanoscale, magnetic nanoparticles are made of magnetic minerals like magnetite or iron oxide and have magnetic characteristics as depicted in Fig. 7. When subjected to an external magnetic field, these nanoparticles display superparamagnetism, which causes them to become magnetised and then return to a non-magnetic condition when the field is withdrawn (25).

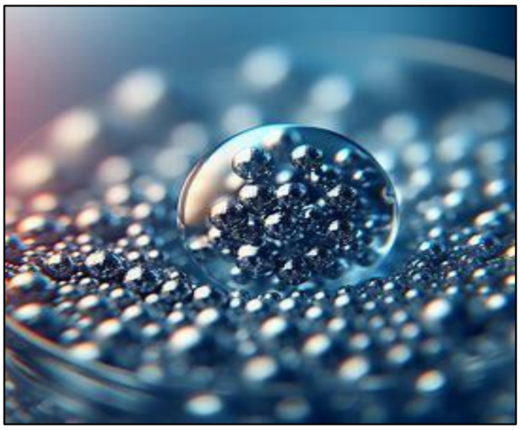

Fig. 7: Magnetic Nanoparticles

Magnetic nanoparticles find use in targeted drug administration, magnetic separation of biological molecules, magnetic resonance imaging, and magnetic hyperthermia therapy for the treatment of cancer (26).

3. Synthesis Methods and Characterization Techniques of Nanoparticles:

Different techniques can be employed to synthesise nanoparticles in order to achieve desired surface characteristics, size, shape, and composition (27). Furthermore, it is crucial to characterise nanoparticles in order to comprehend their physicochemical characteristics and to maximise their performance in various applications. Numerous techniques may be used to create nanoparticles (28).

Below is a list of all the methods:

- **Chemical Precipitation Method:**

  Nanoparticle formation can be achieved by chemical precipitation. To create a smooth combination, the ingredients are first allowed to dissolve in a liquid. To initiate a reaction, another chemical is then introduced (29). Temperature and acidity are two examples of variables that may be changed to alter the course of the reaction. By stabilising and drying them, they may be enlarged, cleaned up, and kept from adhering together. Ultimately, the nanoparticles are examined using a variety of assays. This approach is popular, scalable, and economical for producing nanoparticles for a range of applications, including chemical reaction support and drug delivery (30).

- **Sol-Gel Method:**

  A flexible way for creating thin films and nanoparticles is the sol-gel process. It includes the hydrolysis and condensation processes of precursor chemicals in a liquid media to generate a sol, a colloidal suspension of nanoparticles (31). After the sol is gelled, a three-dimensional network structure is created that may be further treated to create thin films or nanoparticles. With its ability to precisely regulate nanoparticle size, content, and shape, this technique is well-suited for a wide range of applications, including electronics, biomedical devices, and optics (32).

- **Microemulsion Method:**

  A specialised technique for creating nanoparticles with precise size and shape is the microemulsion method. It entails dissolving the precursor chemicals in stable microemulsions, which are usually made of water, oil, surfactant, and co-surfactant. Nanoparticles are created via a sequence of chemical events that take place inside the microemulsion's restricted nanodomains (33). Particle size, shape, and homogeneity can all be precisely controlled using this approach, which makes it very helpful for applications like medication delivery, catalysis, and nanocomposite materials. Its adaptability also makes it possible to synthesise many kinds of nanoparticles, such as semiconductor, oxide, and metallic nanoparticles (34).

- **Green Synthesis:**

  Green synthesis is the sustainable process of creating nanoparticles with eco-friendly ingredients and techniques. In the creation of nanoparticles, it usually entails the utilisation of natural sources as reducing agents or stabilisers, such as plant extracts, microbes, or biomolecules (35). This approach is more environmentally friendly since it uses less or no dangerous chemicals and doesn't require as many energy-intensive steps as previous synthesis methods. Green synthesis is appropriate for use in biomedicine, agriculture, and environmental remediation since it not only has a lower environmental effect but also has special benefits including biocompatibility and ease of scaling (36).

- **Hydrothermal/ Solvothermal Synthesis:**
  The processes of hydrothermal and solvothermal synthesis are used to create nanoparticles and nanostructured materials in an aqueous or organic solvent environment, respectively, at high temperatures and high pressures. These procedures include dissolving the precursor chemicals in the solvent and conducting the reaction at high temperatures in a sealed container (37). Specific sized, shaped, and crystalline nanoparticles are formed as a result of the regulated circumstances that facilitate nucleation and growth. Whereas solvothermal synthesis uses organic solvents, hydrothermal synthesis usually uses water as the solvent. These techniques are adaptable and may be used to create a broad variety of nanoparticles, such as metal oxides, semiconductors, and carbon-based materials (38). They are useful in a variety of industries, including energy storage, nanoelectronics, and catalysis (39).

4. Characterization Techniques:

Method/Technique	**Purpose**	**Examples**	
Transmission Electron Microscopy	Visualize morphology of nanoparticles	High resolution imaging of the particle size	(40).
X-ray Diffraction	Measure the particle size distribution	Assess the variations in the colloidal suspension	(41).
Dynamic Light Scattering	Determine the size of the crystal	Identification of crystalline phases in nanoparticles	(42).
Atomic Force Microscopy	Surface topography probing	Investigation of particle interaction and the roughness	(43).
Fourier Transform Infrared Spectroscopy	Chemical bond analysis	Identification of functional group in the surface of the nanoparticles	(44).

- **Transmission Electron Microscopy:**
  When examining nanoparticles at the nanoscale, Transmission Electron Microscopy is a powerful instrument that may provide remarkably accurate information on their shape, size, and distribution. Through the use of electron transmission through the material, TEM generates high-resolution pictures that reveal minute aspects of the shape and structure of nanoparticles

(45). This capacity helps scientists to identify finer details, which makes thorough characterization easier and is essential for a variety of applications in materials science, nanotechnology, and healthcare. Thus, TEM continues to be essential for deciphering the mysteries of the nanoworld, expanding our knowledge, and spurring creativity across a wide range of industries (46).

- **Scanning Electron Microscopy:**
  A potent imaging method for high-resolution analysis of the surface topography and morphology of materials, including nanoparticles, is scanning electron microscopy. SEM scans the surface with a concentrated electron beam, producing secondary electrons, backscattered electrons, and other signals, unlike TEM, which transmits electrons through the material (47). The surface characteristics of the sample are revealed by these signals, which enable an in-depth visualisation of the size, shape, and distribution of nanoparticles. SEM is a very useful instrument for characterising nanoparticles and comprehending their characteristics for a range of applications in materials science, nanotechnology, and other fields because of its adaptability in sample preparation and imaging modalities (48).

- **X-ray Diffraction:**
  An essential method for examining the phase composition and crystal structure of materials, including nanoparticles, is X-ray diffraction, or XRD. When X-rays are applied to a sample, the atoms in the material scatter the X-rays, creating patterns of constructive interference (49). The crystal lattice structure of the material may be inferred from the angles and intensities of these diffraction peaks, which include lattice spacing, orientation, and phase purity. When it comes to recognising crystalline phases, figuring out crystallographic characteristics, and evaluating the strain and size of nanoparticles, XRD is quite helpful (50). Understanding the physical characteristics and behaviour of nanoparticles is crucial for a wide range of research and practical applications, including materials engineering, electronics, and catalysis (51).

- **Dynamic Light Scattering:**
  A non-invasive method for determining the size distribution of colloidal and nanoparticle particles in solution is dynamic light scattering. DLS determines the hydrodynamic diameter of suspended particles by examining the variations in scattered light intensity brought on by Brownian motion (52). This method is especially helpful for tracking changes in particle size brought on by aggregation or dissolution, as well as for figuring out the size distribution and polydispersity of nanoparticles in solution. DLS is often used to characterise nanoparticle suspensions and comprehend their stability and behaviour in solution in domains including medicines, biotechnology, and materials research (53).

- **UV-Visible Spectroscopy:**
  A popular method for examining how chemicals, including nanoparticles, absorb ultraviolet and visible light is UV-Visible Spectroscopy. It provides details on the electrical structure and composition of a sample by calculating the quantity of light absorbed as a function of wavelength (54). UV-visible spectroscopy is used in nanoparticle research to characterise the

optical characteristics of the particles, including bandgap energy and absorption spectra. It is very helpful for monitoring the production and stability of nanoparticles as well as their size, shape, and concentration in solution. UV-visible spectroscopy is used to research the optical characteristics and behaviour of nanomaterials in a variety of domains, such as chemistry, materials science, and nanotechnology (55).

5. Applications of Nanoparticles:

- **Biomedicine and Healthcare:**
  Targeted drug delivery: Using nanoparticles as carriers allows for controlled release, improved therapeutic efficacy, and less systemic adverse effects (56).
  Imaging: By acting as contrast agents in different imaging modalities including computed tomography, magnetic resonance imaging, and fluorescence imaging, nanoparticles help to diagnose diseases early and track how well a treatment is working (57).
  Therapeutics: By using photothermal treatment, photodynamic therapy, and gene therapy, nanoparticles provide novel ways to treat infections, cancer, and genetic abnormalities (58).

- **Catalysis and Chemical Engineering:**
  Catalysis: By providing more catalytic activity, selectivity, and stability than bulk materials, nanoparticles operate as catalysts in a variety of chemical reactions, resulting in more environmentally friendly and long-lasting chemical processes (59).
  Sensors: High sensitivity, specificity, and quick reaction times are achieved by using nanoparticles in sensor systems to identify and measure analytes such gases, biomolecules, and contaminants (60).

- **Environmental Remediation:**
  Water Purification: To remove organic contaminants, heavy metals, and pollutants from water, water treatment technologies use nanoparticles. This helps to produce practical and affordable solutions for clean water supply (61).
  Air Filtration: To improve indoor air quality and reduce respiratory health concerns, nanoparticles are included into air filtration systems to capture particulate matter, allergens, and airborne pathogens (62).

- **Nanomedicine and Personal Care:**
  Diagnostics: To enable early diagnosis and personalised therapy, nanoparticles are used in diagnostic assays and biosensors to detect infections, illnesses, and biomarkers with high sensitivity and specificity (63).
  Cosmetics: By adding nanoparticles to skincare and makeup products, manufacturers may increase the performance and safety of their innovative formulas while also increasing the efficacy of sunscreens, hydrating the skin, and having anti-aging benefit (64)

6. Applications of Nanoparticles in Medicine and Healthcare:

As they provide cutting-edge approaches to medication distribution, imaging, diagnostics, and therapy, nanoparticles have completely transformed the medical and healthcare industries. (65)

Their distinct physicochemical characteristics, such as their compact size, high surface area-to-volume ratio, and adjustable surface chemistry, allow for exact regulation of drug release, specificity of targeting, and effectiveness of treatment.

- **Imaging and Diagnostics:**
  In several imaging modalities, such as magnetic resonance imaging, computed tomography, positron emission tomography, and optical imaging, nanoparticles act as adaptable contrast agents. (66) Their adjustable characteristics and compact size allow for selective accumulation at disease sites, resulting in better sensitivity and contrast for early illness detection and surveillance. Because of their high magnetic susceptibility and biocompatibility, magnetic nanoparticles like iron oxide nanoparticles—are frequently utilised as contrast agents in magnetic resonance imaging. These nanoparticles provide very sensitive and spatially resolved non-invasive imaging of inflammation, tumours, and cardiovascular disorders (66). Nanoparticles are used in diagnostic tests and biosensors for the high-sensitivity and specificity detection of infections, disease-associated chemicals, and biomarkers, in addition to imaging applications (67).

- **Therapeutics and Therapy:**
  Therapeutic applications involving nanoparticles include the treatment of infectious diseases, cancer, and regenerative medicine. When compared to traditional treatment approaches, nanoparticle-based therapies offer targeted delivery, controlled release, and better therapeutic effectiveness (68).

- **Nanoparticle-mediated cancer therapy:**
  Chemotherapy, photothermal treatment, photodynamic therapy, and immunotherapy are some of the methods used in nanoparticle-mediated cancer therapy. Through active targeting or passive targeting, nanoparticles can preferentially concentrate in tumour tissues, resulting in localised drug delivery and less systemic toxicity (69).

- **Gold nanomaterials:**
  Because gold nanoparticles have special photothermal characteristics, they are being researched intensively for cancer treatment. Gold nanoparticles produce heat when exposed to near-infrared light, which causes tumour cells to undergo thermal ablation and become hyperthermic while leaving the surrounding healthy tissues unaffected (70) To increase the effectiveness of treatment, gold nanoparticles can also be used as carriers to carry nucleic acids or chemotherapeutic medications to tumours (71).

- **Nanoparticle-based vaccines:**
  A potential method for avoiding infectious illnesses and stimulating the immune system against pathogens is the use of vaccinations based on nanoparticles (72). Targeting antigen-presenting cells, nanoparticles can encapsulate adjuvants, nucleic acids, or antigens. This promotes antigen absorption, processing, and presentation, resulting in strong immune activation and long-lasting immunity (73).

- **Gene therapy using nanoparticle carriers:**
  Utilising nanoparticle carriers, gene therapy delivers nucleic acids, such as DNA, RNA, or gene-editing tools, to target cells in an attempt to cure genetic abnormalities, cancer, and infectious illnesses (74). Nanoparticles provide precise regulation of gene expression and improved therapeutic results by preventing nucleic acids from degrading, promoting intracellular transport, and facilitating cellular absorption (75).

- **Targeted Therapy and Precision Medicine:**
  Approaches that specifically deliver therapeutic chemicals to sick tissues or cells while protecting healthy tissues are made possible by nanoparticles. In order to improve nanoparticle uptake and treatment effectiveness, active targeting techniques functionalize nanoparticles with ligands, antibodies, or peptides that identify certain biomarkers overexpressed on sick cells (76). Utilising drug delivery methods based on nanoparticles, precision medicine techniques customise therapies for each patient according on their genetic composition, illness phenotype, and response to therapy. Precision medicine based on nanoparticles delivers treatments to certain molecular targets or patient groups, allowing for tailored and optimised therapeutic interventions with better results and fewer side effects (77).

- **Regenerative Medicine and Tissue Engineering:**
  Nanoparticles are essential for cell treatment, medication transport, and scaffold design in regenerative medicine and tissue engineering. Scaffolds coated with nanoparticles enable the controlled release of growth factors, cytokines, or medications in specific areas to facilitate tissue regeneration, repair, and functional restoration. Bioactively functionalized nanoparticles promote tissue regeneration by facilitating cell adhesion, proliferation, and differentiation (78). This improves the integration of implanted scaffolds with host tissues. Furthermore, therapeutic cells, stem cells, or gene-editing instruments can be delivered to target tissues using nanoparticles for regenerative treatment applications (79).

Abbreviations:

1. **API:** Active Pharmaceutical Ingredient.
2. **PEG:** Polyethylene Glycol.
3. **PLGA:** Poly(lactic-co-glycolic acid).
4. **MRI:** Magnetic Resonance Imaging.
5. **SEM:** Scanning Electron Microscopy.
6. **TEM:** Transmission Electron Microscopy.
7. **CT:** Computed Tomography.
8. **PET:** Positron Emission Tomography.
9. **NIR:** Near-Infrared.

References:

1. Bhatia S, Bhatia S. Nanoparticles types, classification, characterization, fabrication methods and drug delivery applications. Natural polymer drug delivery systems: Nanoparticles, plants, and algae. 2016:33-93.
2. Panda MK, Panda SK, Singh YD, Jit BP, Behara RK, Dhal NK. Role of nanoparticles and nanomaterials in drug delivery: an overview. Advances in pharmaceutical biotechnology: recent progress and future applications. 2020:247-65.
3. Bala I, Hariharan S, Kumar MR. PLGA nanoparticles in drug delivery: the state of the art. Critical Reviews™ in Therapeutic Drug Carrier Systems. 2004;21(5).
4. Wei Y, Quan L, Zhou C, Zhan Q. Factors relating to the biodistribution & clearance of nanoparticles & their effects on in vivo application. Nanomedicine. 2018 Jun;13(12):1495-512.
5. Kamaly N, Xiao Z, Valencia PM, Radovic-Moreno AF, Farokhzad OC. Targeted polymeric therapeutic nanoparticles: design, development and clinical translation. Chemical Society Reviews. 2012;41(7):2971-3010.
6. Slepička P, Slepičková Kasálková N, Siegel J, Kolská Z, Švorčík V. Methods of gold and silver nanoparticles preparation. Materials. 2019 Dec 18;13(1):1.
7. Yaqoob SB, Adnan R, Rameez Khan RM, Rashid M. Gold, silver, and palladium nanoparticles: a chemical tool for biomedical applications. Frontiers in Chemistry. 2020 Jun 3;8:376.
8. Albanese A, Tang PS, Chan WC. The effect of nanoparticle size, shape, and surface chemistry on biological systems. Annual review of biomedical engineering. 2012 Aug 15;14:1-6.
9. Lee L. AFRL-AFOSR-JP-TR-2018-0043.
10. Gumel AM, Surayya MM, Yaro MN, Waziri IZ, Amina AA. Biogenic synthesis of silver nanoparticles and its synergistic antimicrobial potency: An overview. J. Appl. Biotechnol. Bioeng. 2019;6(1):22-8.
11. Myrovali E. Magnetic nanoparticle arrays: features, properties, applications. Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης (ΑΠΘ). Σχολή Θετικών Επιστημών. Τμήμα. 2020 Mar.
12. Voinov MA, Pagán JO, Morrison E, Smirnova TI, Smirnov AI. Surface-mediated production of hydroxyl radicals as a mechanism of iron oxide nanoparticle biotoxicity. Journal of the American Chemical Society. 2011 Jan 12;133(1):35-41.
13. Nikolova MP, Chavali MS. Metal oxide nanoparticles as biomedical materials. Biomimetics. 2020 Jun 8;5(2):27.
14. Dizaj SM, Mennati A, Jafari S, Khezri K, Adibkia K. Antimicrobial activity of carbon-based nanoparticles. Advanced pharmaceutical bulletin. 2015 Mar;5(1):19.
15. Thakur A, Thakur P, Baccar S. Structural Properties of Nanoparticles. InIntegrated Nanomaterials and their Applications 2023 Dec 7 (pp. 57-80). Singapore: Springer Nature Singapore.
16. Jarai BM, Kolewe EL, Stillman ZS, Raman N, Fromen CA. Polymeric nanoparticles. InNanoparticles for biomedical applications 2020 Jan 1 (pp. 303-324). Elsevier.
17. Rafiei P, Haddadi A. Docetaxel-loaded PLGA and PLGA-PEG nanoparticles for intravenous application: pharmacokinetics and biodistribution profile. International journal of nanomedicine. 2017 Jan 27:935-47.

18. Ariful Islam M, Park TE, Reesor E, Cherukula K, Hasan A, Firdous J, Singh B, Kang SK, Choi YJ, Park IK, Cho CS. Mucoadhesive chitosan derivatives as novel drug carriers. Current pharmaceutical design. 2015 Sep 1;21(29):4285-309.

19. Shakiba S, Astete CE, Paudel S, Sabliov CM, Rodrigues DF, Louie SM. Emerging investigator series: polymeric nanocarriers for agricultural applications: synthesis, characterization, and environmental and biological interactions. Environmental Science: Nano. 2020;7(1):37-67.

20. Amoabediny G, Haghiralsadat F, Naderinezhad S, Helder MN, Akhoundi Kharanaghi E, Mohammadnejad Arough J, Zandieh-Doulabi B. Overview of preparation methods of polymeric and lipid-based (niosome, solid lipid, liposome) nanoparticles: A comprehensive review. International Journal of Polymeric Materials and Polymeric Biomaterials. 2018 Apr 13;67(6):383-400.

21. Srivastava A, Yadav T, Sharma S, Nayak A, Kumari AA, Mishra N. Polymers in drug delivery. Journal of Biosciences and Medicines. 2015 Dec 25;4(1):69-84.

22. Duan Y, Dhar A, Patel C, Khimani M, Neogi S, Sharma P, Kumar NS, Vekariya RL. A brief review on solid lipid nanoparticles: Part and parcel of contemporary drug delivery systems. RSC advances. 2020;10(45):26777-91.

23. McClements DJ. Nanoemulsions versus microemulsions: terminology, differences, and similarities. Soft matter. 2012;8(6):1719-29.

24. Ajinkya N, Yu X, Kaithal P, Luo H, Somani P, Ramakrishna S. Magnetic iron oxide nanoparticle (IONP) synthesis to applications: present and future. Materials. 2020 Oct 18;13(20):4644.

25. Wu M, Huang S. Magnetic nanoparticles in cancer diagnosis, drug delivery and treatment. Molecular and clinical oncology. 2017 Nov 1;7(5):738-46.

26. Cuenya BR. Synthesis and catalytic properties of metal nanoparticles: Size, shape, support, composition, and oxidation state effects. Thin Solid Films. 2010 Apr 2;518(12):3127-50.

27. Joudeh N, Linke D. Nanoparticle classification, physicochemical properties, characterization, and applications: a comprehensive review for biologists. Journal of Nanobiotechnology. 2022 Jun 7;20(1):262.

28. Thorat AA, Dalvi SV. Liquid antisolvent precipitation and stabilization of nanoparticles of poorly water soluble drugs in aqueous suspensions: Recent developments and future perspective. Chemical Engineering Journal. 2012 Feb 1;181:1-34.

29. Reed MH. Calculation of multicomponent chemical equilibria and reaction processes in systems involving minerals, gases and an aqueous phase. Geochimica et Cosmochimica Acta. 1982 Apr 1;46(4):513-28.

30. Schmidt H. Considerations about the sol-gel process: From the classical sol-gel route to advanced chemical nanotechnologies. Journal of sol-gel science and technology. 2006 Dec;40:115-30.

31. Caruso RA, Antonietti M. Sol− gel nanocoating: an approach to the preparation of structured materials. Chemistry of materials. 2001 Oct 15;13(10):3272-82.

32. Wani IA. Nanomaterials, novel preparation routes, and characterizations. InNanotechnology applications for improvements in energy efficiency and environmental management 2015 (pp. 1-40). IGI Global.

33. Terna AD, Elemike EE, Mbonu JI, Osafile OE, Ezeani RO. The future of semiconductors nanoparticles: Synthesis, properties and applications. Materials Science and Engineering: B. 2021 Oct 1;272:115363.

34. Shanker U, Jassal V, Rani M, Kaith BS. Towards green synthesis of nanoparticles: from bio-assisted sources to benign solvents. A review. International Journal of environmental analytical chemistry. 2016 Jul 14;96(9):801-35.

35. Samuel MS, Ravikumar M, John J A, Selvarajan E, Patel H, Chander PS, Soundarya J, Vuppala S, Balaji R, Chandrasekar N. A review on green synthesis of nanoparticles and their diverse biomedical and environmental applications. Catalysts. 2022 Apr 20;12(5):459.

36. Ahmed SF, Mofijur M, Rafa N, Chowdhury AT, Chowdhury S, Nahrin M, Islam AS, Ong HC. Green approaches in synthesising nanomaterials for environmental nanobioremediation: Technological advancements, applications, benefits and challenges. Environmental Research. 2022 Mar 1;204:111967.

37. Li J, Wu Q, Wu J. Synthesis of Nanoparticles via Solvothermal and Hydrothermal Methods 12.

38. Ndlwana L, Raleie N, Dimpe KM, Ogutu HF, Oseghe EO, Motsa MM, Msagati TA, Mamba BB. Sustainable hydrothermal and solvothermal synthesis of advanced carbon materials in multidimensional applications: A review. Materials. 2021 Sep 6;14(17):5094.

39. Astruc D. Introduction: nanoparticles in catalysis. Chemical reviews. 2020 Jan 22;120(2):461-3.

40. Mühlfeld C, Rothen-Rutishauser B, Vanhecke D, Blank F, Gehr P, Ochs M. Visualization and quantitative analysis of nanoparticles in the respiratory tract by transmission electron microscopy. Particle and fibre toxicology. 2007 Dec;4:1-7.

41. Dorofeev GA, Streletskii AN, Povstugar IV, Protasov AV, Elsukov EP. Determination of nanoparticle sizes by X-ray diffraction. Colloid Journal. 2012 Nov;74:675-85.

42. Lim J, Yeap SP, Che HX, Low SC. Characterization of magnetic nanoparticle by dynamic light scattering. Nanoscale research letters. 2013 Dec;8:1-4.

43. Rao A, Schoenenberger M, Gnecco E, Glatzel T, Meyer E, Brändlin D, Scandella L. Characterization of nanoparticles using atomic force microscopy. InJournal of Physics: Conference Series 2007 Apr 1 (Vol. 61, No. 1, p. 971). IOP Publishing.

44. Faghihzadeh F, Anaya NM, Schifman LA, Oyanedel-Craver V. Fourier transform infrared spectroscopy to assess molecular-level changes in microorganisms exposed to nanoparticles. Nanotechnology for environmental engineering. 2016 Dec;1:1-6.

45. Wang ZL. New developments in transmission electron microscopy for nanotechnology. Advanced Materials. 2003 Sep 16;15(18):1497-514.

46. Shnoudeh AJ, Hamad I, Abdo RW, Qadumii L, Jaber AY, Surchi HS, Alkelany SZ. Synthesis, characterization, and applications of metal nanoparticles. InBiomaterials and bionanotechnology 2019 Jan 1 (pp. 527-612). Academic Press.

47. Akhtar K, Khan SA, Khan SB, Asiri AM. Scanning electron microscopy: Principle and applications in nanomaterials characterization. Springer International Publishing; 2018.

48. Mayeen A, Shaji LK, Nair AK, Kalarikkal N. Morphological characterization of nanomaterials. InCharacterization of Nanomaterials 2018 Jan 1 (pp. 335-364). Woodhead Publishing.

49. Giannini C, Ladisa M, Altamura D, Siliqi D, Sibillano T, De Caro L. X-ray diffraction: a powerful technique for the multiple-length-scale structural analysis of nanomaterials. Crystals. 2016 Aug 4;6(8):87.

50. Ali A, Chiang YW, Santos RM. X-ray diffraction techniques for mineral characterization: A review for engineers of the fundamentals, applications, and research directions. Minerals. 2022 Feb 6;12(2):205.

51. Khan I, Saeed K, Khan I. Nanoparticles: Properties, applications and toxicities. Arabian journal of chemistry. 2019 Nov 1;12(7):908-31.

52. Shukla V, Niveria K, Shashidhar P, Verma AK. Dynamic light scattering (DLS) particle size analysis for biomedical nanotechnology. InAnalytical Techniques for Biomedical Nanotechnology 2023 Jul 1 (pp. 16-1). Bristol, UK: IOP Publishing.

53. Modena MM, Rühle B, Burg TP, Wuttke S. Nanoparticle characterization: what to measure?. Advanced Materials. 2019 Aug;31(32):1901556.

54. Mills GD. Ultraviolet/visible spectroscopy. ASTM International; 2012 Jan 1.

55. Zhang JZ. Optical properties and spectroscopy of nanomaterials. World Scientific; 2009 Jul 21.

56. Chenthamara D, Subramaniam S, Ramakrishnan SG, Krishnaswamy S, Essa MM, Lin FH, Qoronfleh MW. Therapeutic efficacy of nanoparticles and routes of administration. Biomaterials research. 2019 Nov 21;23(1):20.

57. Hahn MA, Singh AK, Sharma P, Brown SC, Moudgil BM. Nanoparticles as contrast agents for in-vivo bioimaging: current status and future perspectives. Analytical and bioanalytical chemistry. 2011 Jan;399:3-27.

58. Hou YJ, Yang XX, Liu RQ, Zhao D, Guo CX, Zhu AC, Wen MN, Liu Z, Qu GF, Meng HX. Pathological mechanism of photodynamic therapy and photothermal therapy based on nanoparticles. International journal of nanomedicine. 2020 Sep 15:6827-38.

59. Roldan Cuenya B. Metal nanoparticle catalysts beginning to shape-up. Accounts of chemical research. 2013 Aug 20;46(8):1682-91.

60. Wang L, Ma W, Xu L, Chen W, Zhu Y, Xu C, Kotov NA. Nanoparticle-based environmental sensors. Materials Science and Engineering: R: Reports. 2010 Nov 22;70(3-6):265-74.

61. Kumar S, Ahlawat W, Bhanjana G, Heydarifard S, Nazhad MM, Dilbaghi N. Nanotechnology-based water treatment strategies. Journal of nanoscience and nanotechnology. 2014 Feb 1;14(2):1838-58.

62. Mata TM, Martins AA, Calheiros CS, Villanueva F, Alonso-Cuevilla NP, Gabriel MF, Silva GV. Indoor air quality: a review of cleaning technologies. Environments. 2022 Sep 7;9(9):118.

63. Colino CI, Millán CG, Lanao JM. Nanoparticles for signaling in biodiagnosis and treatment of infectious diseases. International journal of molecular sciences. 2018 May 31;19(6):1627.

64. Salvioni L, Morelli L, Ochoa E, Labra M, Fiandra L, Palugan L, Prosperi D, Colombo M. The emerging role of nanotechnology in skincare. Advances in colloid and interface science. 2021 Jul 1;293:102437.

65. Zahin N, Anwar R, Tewari D, Kabir MT, Sajid A, Mathew B, Uddin MS, Aleya L, Abdel-Daim MM. Nanoparticles and its biomedical applications in health and diseases: special focus on drug delivery. Environmental Science and Pollution Research. 2020 Jun;27(16):19151-68.

66. Hahn MA, Singh AK, Sharma P, Brown SC, Moudgil BM. Nanoparticles as contrast agents for in-vivo bioimaging: current status and future perspectives. Analytical and bioanalytical chemistry. 2011 Jan;399:3-27.

67. MacRitchie N, Frleta-Gilchrist M, Sugiyama A, Lawton T, McInnes IB, Maffia P. Molecular imaging of inflammation-Current and emerging technologies for diagnosis and treatment. Pharmacology & therapeutics. 2020 Jul 1;211:107550.

68. Masud MK, Na J, Younus M, Hossain MS, Bando Y, Shiddiky MJ, Yamauchi Y. Superparamagnetic nanoarchitectures for disease-specific biomarker detection. Chemical Society Reviews. 2019;48(24):5717-51.

69. Yetisgin AA, Cetinel S, Zuvin M, Kosar A, Kutlu O. Therapeutic nanoparticles and their targeted delivery applications. Molecules. 2020 May 8;25(9):2193.

70. Liu Y, Crawford BM, Vo-Dinh T. Gold nanoparticles-mediated photothermal therapy and immunotherapy. Immunotherapy. 2018 Sep;10(13):1175-88.

71. Stabile J, Najafali D, Cheema Y, Inglut CT, Liang BJ, Vaja S, Sorrin AJ, Huang HC. Engineering gold nanoparticles for photothermal therapy, surgery, and imaging. InNanoparticles for biomedical applications 2020 Jan 1 (pp. 175-193). Elsevier.

72. Siddique S, Chow JC. Gold nanoparticles for drug delivery and cancer therapy. Applied Sciences. 2020 May 31;10(11):3824.

73. Pati R, Shevtsov M, Sonawane A. Nanoparticle vaccines against infectious diseases. Frontiers in immunology. 2018 Oct 4;9:385476.

74. Storni T, Kündig TM, Senti G, Johansen P. Immunity in response to particulate antigen-delivery systems. Advanced drug delivery reviews. 2005 Jan 10;57(3):333-55.

75. Kavanagh EW, Green JJ. Toward gene transfer nanoparticles as therapeutics. Advanced Healthcare Materials. 2022 Apr;11(7):2102145.

76. Xiao Y, Shi K, Qu Y, Chu B, Qian Z. Engineering nanoparticles for targeted delivery of nucleic acid therapeutics in tumor. Molecular Therapy-Methods & Clinical Development. 2019 Mar 15;12:1-8.

77. Anarjan FS. Active targeting drug delivery nanocarriers: Ligands. Nano-Structures & Nano-Objects. 2019 Jul 1;19:100370.

78. Manzari MT, Shamay Y, Kiguchi H, Rosen N, Scaltriti M, Heller DA. Targeted drug delivery strategies for precision medicines. Nature Reviews Materials. 2021 Apr;6(4):351-70.

79. Fathi-Achachelouei M, Knopf-Marques H, Ribeiro da Silva CE, Barthès J, Bat E, Tezcaner A, Vrana NE. Use of nanoparticles in tissue engineering and regenerative medicine. Frontiers in bioengineering and biotechnology. 2019 May 24;7:113.