WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Nanoparticles: An Overview, its Challenges and Applications

Simranjeet Singh[1], Akanksha Malhotra[2], Inkashaf Alam[3], Zarque Ishan[4], Sahil Punia[5], Abhishek Gautam[6], Anchal Dhawan[7], Diksha Sharma[8]

Rayat Bahra University [1,5,6,7,8], Chandigarh University [3,4], Shoolini University[2]

ABSTRACT

Nanoparticles are microscopic particles that range from 1 to 100 nanometers (nm) in size. Recently, scientists from all around the world have become piqued by the numerous applications of nanoparticles in a variety of fields, including catalysis, gas sensing, renewable energy, electronics, medicine, diagnostics, medication delivery, cosmetics, the construction industry, and the food industry. The decisive factors that determine the properties of nanoparticles (NPs) are their sizes and shapes. It is important to form nanoparticles with appropriate size, structure, monodispersity, and morphology to achieve the aforementioned uses. In nanotechnology, new processes have been created that are environmentally friendly and can be utilized to reliably produce nanomaterials and nanoparticles. The goal of this research is to illustrate top-down and bottom-up approaches for the synthesis of nanomaterials, as well as various characterization techniques, characteristics of nanoparticles, and various uses of nanoparticles. Additionally, the reasons behind the ineffectiveness of some nanomedicines, and some important considerations in the development of nanomedicines will be discussed in brief.

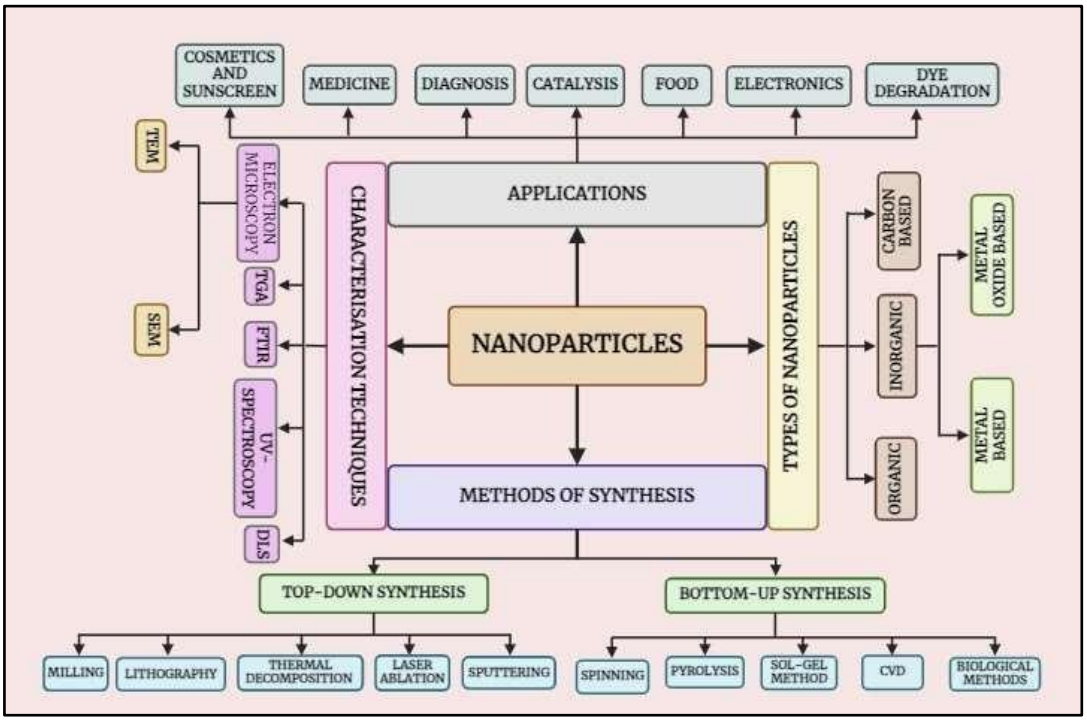

FIG 1: GRAPHICAL ABSTRACT

INTRODUCTION

Utilizing nanoparticles is the most recent and promising approach to drug delivery. A 'carrier' is used to transport the medications to various locations throughout the body. This carrier's ability to deliver the medication at a pace determined by the target tissue's requirements is crucial. The carrier should release the medication at the desired location and retain the medication until it arrives. All of this is only possible because of nanoparticles [1,2]. The medications are attached to the nanoparticle and subsequently injected into the patient. The medicine can be broken down, absorbed, or removed from the body once the nanoparticle has been released at the spot [2,3]. All of this is controlled by modifying the nanoparticle's surface characteristics and

chemical makeup. There are several benefits to using nanoparticle medication delivery over traditional injection-based drug delivery. They minimize side effects, promote drug accumulation in the target tissue, shield the drug against degradation, and improve and prolong therapeutic efficacy [4].

A growing number of drug delivery systems, including lipid-based, injectable, gene-based, and site-specific systems, are gradually moving towards nanoparticle-based delivery thanks to advancements in nanotechnology. The future of medication administration depends on this advancement [5]. A notable change in medical and healthcare therapy has been made possible by the technological advancement of controlling materials at the nanoscale. Nowadays, there is an unexpected increase in the use of variety of nanoparticles in many different fields, including physics, medicine, organic and inorganic chemistry, molecular biology, and material science [6]. Nanoparticles are becoming more and more significant in biological applications because they fill the gap between molecular structures (<1 nm) and bulk materials (1 mm). Due to their exceptional qualities such as their high surface area and small size, nanoparticles can interact with biological systems very differently from larger-scale materials [7]. Furthermore, there are several nanoparticle modifications that enable the chemical and surface aspects of the particles to be customized. These particles include metal or polymer colloids, nanospheres, and nano capsules [8]. Finally, systems for nanoparticles can be engineered to break down within the body, or they can be functionalized or tagged to target specific areas of the body using a biological system. An intriguing field for the study of nanoparticle drug delivery is created by these possible advantages over alternative molecular delivery systems that are similar in size to nanoparticles, including liposomes [9].

CATEGORIZATION OF NANOPARTICLES

Nanoparticles are generally divided into three primary categories: **organic, inorganic, and carbon-based.**

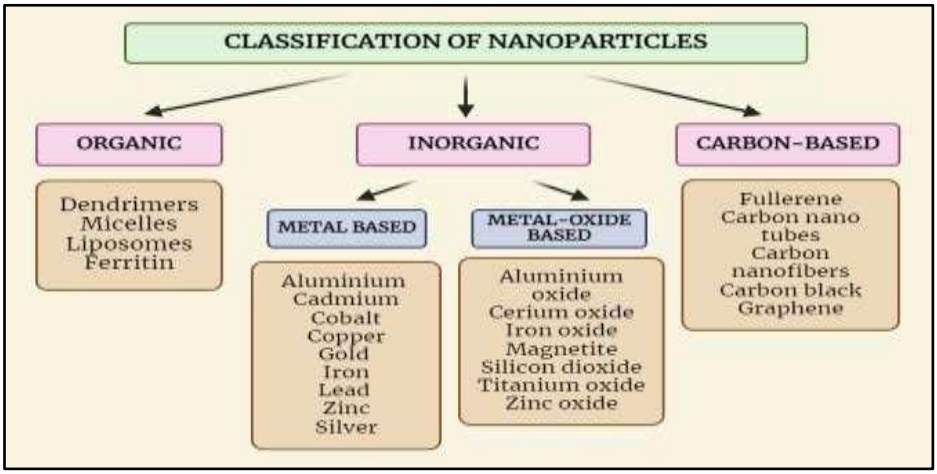

FIG 2: CATEGORIZATION OF NANOPARTICLES

Organic nanoparticles

Organic nanoparticles or polymers are broadly referred to as micelles, dendrimers, ferritin, liposomes, etc. These nanoparticles are biodegradable and non-toxic; some, such as micelles and liposomes, have void cores referred to as nanocapsules, and they react to both thermal and electromagnetic radiation, including heat and light [10]. They are ideal for delivering medications as a result of these unique characteristics. Organic nanoparticles are primarily employed in the biomedical industry for medication delivery systems since they are effective and may be injected into specific body locations, an approach known as targeted drug delivery.

Inorganic nanoparticles

Inorganic nanoparticles are also known as non-carbon-based nanoparticles. Metal-oxide-based and metal-based nanoparticles are often referred to as inorganic nanoparticles.

Metal-based nanoparticles

Metal-based nanoparticles refer to those that are produced from metals to nanometric sizes using either destructive or constructive methods. Almost any metal can be manufactured into a nanoparticle [11]. Cadmium (Cd), gold (Au), aluminium (Al), cobalt (Co), copper (Cu), silver (Ag), iron (Fe), lead (Pb), and zinc (Zn) are all metals frequently employed in the manufacturing of nanoparticles.

Metal-oxide-based nanoparticles

Metal-oxide-based nanoparticles are manufactured to improve the properties of their corresponding metal-based nanoparticles. For instance, iron (Fe) nanoparticles at room temperature rapidly oxidize to iron oxide (Fe_2O3), which increases its reactivity in comparison to iron nanoparticles. Metal-oxide nanoparticles are mainly formed due to their increased reactivity and efficiency [12]. Titanium oxide (TiO_2), aluminium oxide (Al_2O_3), iron oxide (Fe_2O_3), silicon dioxide (SiO_2), magnetite (Fe_3O_4), and zinc oxide (ZnO) are the most frequently synthesized metal-oxide-based nanoparticles.

Carbon based nanoparticles

The nanoparticles formed of carbon entirely are known as carbon-based [13]. These nanomaterials include fullerenes, graphene, carbon nanotubes (CNT), carbon nanofibers, carbon black, and activated carbon at nanoscale.

- **Fullerenes:** Fullerenes (C_{60}) are spherical carbon molecules, made up of carbon atoms bound to each other via sp^2 hybridization. The spherical structure is produced by 28–1500 carbon atoms with diameters of up to 8.2 nm for one layer and 4–36 nm for complex fullerenes.
- **Graphene:** Graphene is a carbon allotrope. Graphene is a hexagonal network of honeycomb lattices formed of carbon atoms on a 2-D plane surface. Typically, the graphene sheet is roughly 1 nm thick.
- **Carbon Nano Tubes (CNT):** Carbon Nano Tubes (CNT), a graphene nano foil with a honeycomb lattice of carbon atoms, are coiled into void cylinders to form nanotubes with diameters as low as 0.7 nm for a simple CNT and 100 nm for complex CNT, and lengths ranging from a few micrometres to several millimetres. The ends might be empty with a half fullerene molecule.
- **Carbon Nanofiber:** Carbon nanofibers are made from the same graphene nano foils as CNTs, but they are coiled into a cup or cone shape rather than cylindrical tubes.
- **Carbon black:** It is an amorphous carbon material with spherical size and shape ranging from 20-70 nm. The particles interact so strongly that they form clusters, which are approximately 500 nm in size.

CHARACTERISTICS OF NANOPARTICLES

The unique features of a nanoparticle define its potential and application. Different measurement techniques are used to carry out the nanoparticle characterization process. Various characteristics of nanoparticles are listed below:

- **Size**

Particle size is one of the most basic and crucial measures for characterisation of nanoparticles. This component influences particle size, distribution, and whether it's micro- or nanoscale. Electron microscopy is commonly used for measuring particle size and dispersion. SEM and TEM images are applied to analyse particle and cluster sizes, whereas laser diffraction is employed to evaluate solid-phase bulk materials [14]. Using centrifugation and photon correlation spectroscopy, the particles in the liquid phase are measured whereas the particles in the gaseous phase are hard and difficult to visualize, so a scanning mobility particle sizer (SMPS) is employed, which enables rapid and more precise measurements than any other method.

- **Surface area**

Another significant factor worth considering when characterizing nanoparticles is their surface area. The surface area-to-volume ratio of nanoparticles significantly affects their efficiency and characteristics. BET analysis is a widely employed method for estimating surface area [15]. Although a simple titration is adequate for estimating the surface area of particles in the liquid phase, this method can be tedious and time-consuming. Therefore, nuclear magnetic resonance spectroscopy (NMR) is used. To measure the surface area of nanoparticles in the gas phase, a differential mobility analyser (DMA) and a modified SMPS are used.

- **Composition**

The elemental composition of the nanoparticle determines its purity and functioning. Undesirable components in nanoparticles might lower its potency and cause adverse reactions and degradation. X-ray photoelectron spectroscopy (XPS) is typically employed to assess the composition of nanoparticle [16]. Gaseous phase particles are collected using filtration or electrostatics, and then analysed using spectrometric or wet chemical procedures [17].

- **Surface morphology**

Nanoparticles may be shaped and formed in many ways, allowing for optimal use of their capabilities. There are several forms, including round, flat, cylindrical, tubular, conical, and irregular. The surfaces of these forms might be crystalline, amorphous, homogeneous, or uneven. Electron microscopy imaging techniques, including SEM and TEM, are used for measuring the surface [18,19]. Gaseous phase particles are deposited on a surface for analysis, whereas liquid phase particles are captured electrostatically or through filtration for imaging with electron microscopy.

- **Surface charge**

A nanoparticle's interactions with a target depend on its surface or overall charge. Zeta potentiometers are commonly used to measure surface charges and dispersion stability in solutions [14]. A differential mobility analyser (DMA) measures the charge of nanoparticles in the gaseous phase.

- **Crystallography**

Crystallography is a scientific examination of atomic and molecular arrangements in crystals and other materials. Crystallography may determine the structure of nanoparticles by powder X-ray, electron, or neutron diffraction [20].

- **Concentration**

The concentration of nanoparticles in the gaseous phase is monitored to determine the amount of air or gas needed for the procedure. The concentration, size, and dispersion of nanoparticles in a given volume of air or gas determines its performance or efficiency. Concentration measurements are often conducted using a Condensation Particle Counter (CPC).

CHARACTERIZATION TECHNIQUES FOR NANOPARTICLES

Characterization techniques play a crucial role in understanding the properties and behaviour of nanoparticles. They provide valuable insights into nanoparticle size, shape, structure, composition, surface chemistry, and interactions, which are essential for optimizing their performance in various applications. Here are explanations of some commonly used characterization techniques:

1. **Electron Microscopy**

   A. **Transmission Electron Microscopy (TEM):** TEM produces high-resolution images of nanoparticles, allowing visualization of their composition, size, and internal structure at the nanoscale [21].

   B. **Scanning Electron Microscopy (SEM):** SEM produces detailed surface morphology images of nanoparticles, providing details on size, shape, and surface features of the particle [22].

2. **Dynamic Light Scattering (DLS)**

DLS studies the hydrodynamic size distribution of nanoparticles in solution using their Brownian motion. It provides information on nanoparticle size distribution, polydispersity, and the aggregation state in liquid environments [23].

3. **Fourier-Transform Infrared Spectroscopy (FTIR)**

FTIR is used to analyse the chemical composition and surface functional groups of nanoparticles. By measuring the absorption of infrared radiation by molecular vibrations, FTIR provides information on nanoparticle surface chemistry, ligand binding, and functionalization [24].

4. **UV-Visible Spectroscopy**

UV-Visible spectroscopy is used to characterize the optical properties of nanoparticles, such as absorption and plasmon resonance. It provides information on nanoparticle concentration, size, and optical bandgap, which are relevant for applications in sensing, imaging, and photovoltaics [25].

5. **Zeta Potential Analysis**

Zeta potential analysis investigates the electrokinetic properties of nanoparticles in solution, giving detailed information regarding their surface charge and stability. It is used to assess nanoparticle dispersion, aggregation, and colloidal stability in various environments [26].

6. **Thermogravimetric Analysis (TGA)**

TGA is used to analyse thermal stability, composition, and mass changes of nanoparticles with temperature. It provides information on the presence of organic coatings, surface modifications, and decomposition temperatures of nanoparticles [27].

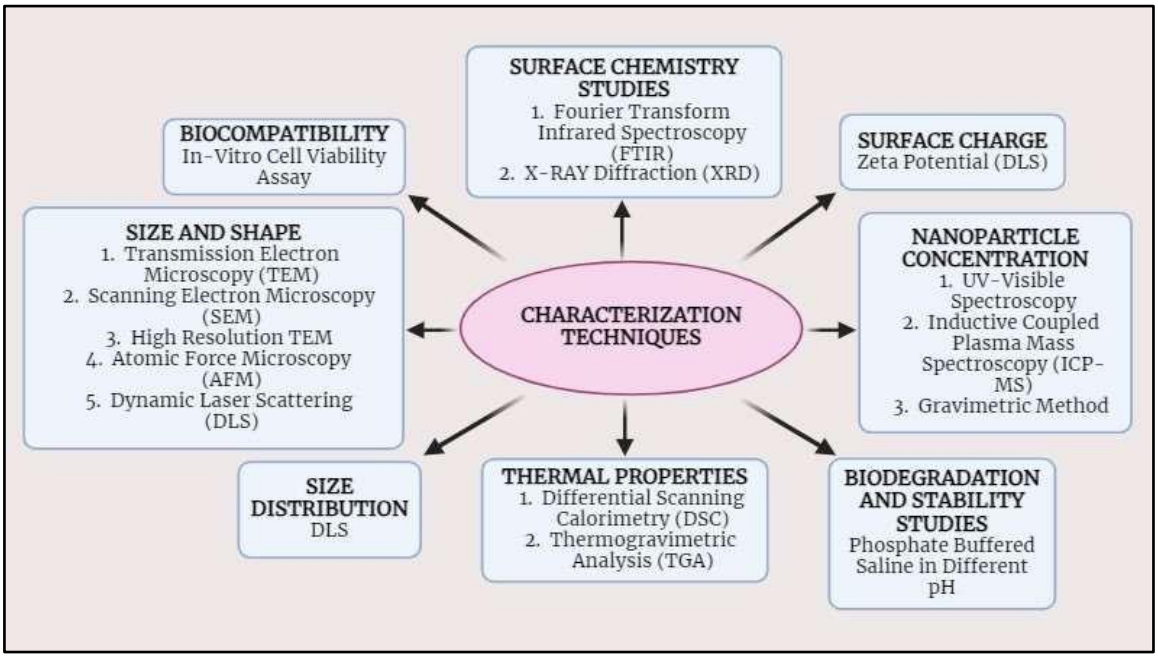

FIG 3: VARIOUS CHARACTERIZATION TECHNIQUES OF NANOPARTICLES

SYNTHESIS OF NANOPARTICLES

There are two methodologies used for the synthesis of nanoparticle: **top-down method and bottom-up method.**

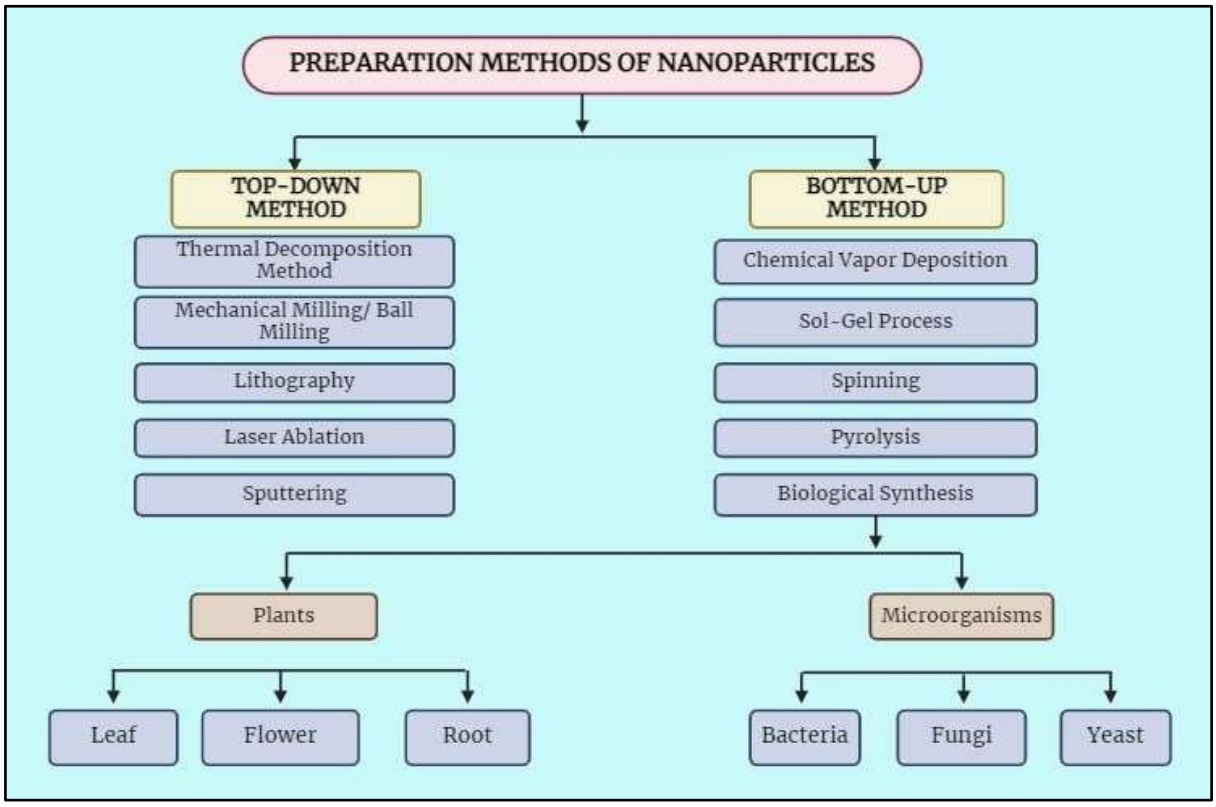

FIG 4: VARIOUS METHODS OF PREPARATION OF NANOPARTICLES

Bottom-up method

Bottom-up or self-assembly or constructive technique is the building up of material from atoms to clusters to nanoparticles. The most frequent bottom-up processes used for producing nanoparticles are sol-gel, spinning, CVD, pyrolysis, and biosynthesis.

- **Sol-gel method**

The sol is a colloidal solution that contains solid particles suspended in a liquid phase. The gel is a solid macromolecule that are immersed in a liquid. Sol-gel method is the favoured bottom-up approach due to its simplicity and ability to synthesize most nanoparticles. Such wet-chemical approach uses a chemical solution as a raw material to create an integrated system of distinct particles. Metal oxides and chlorides usually serve as raw material for this process [28]. The raw material is then dissolved in a host liquid through sonication, stirring, or shaking, resulting in a system with both a solid and liquid phase. Nanoparticles are then retrieved through phase separation using filtration, sedimentation, and centrifugation. The moisture is removed via drying [29].

- **Spinning**

A spinning disc reactor (SDR) is used to form nanoparticles. A revolving disc inside a chamber/reactor allows temperature control. To prevent chemical reactions, reactors are typically filled with inert gases such as nitrogen [12]. The disc rotates at varying speeds, allowing liquids such as precursors and water to be forced in. Spinning causes atoms or molecules to attach, which are then precipitated, collected, and dried [30].

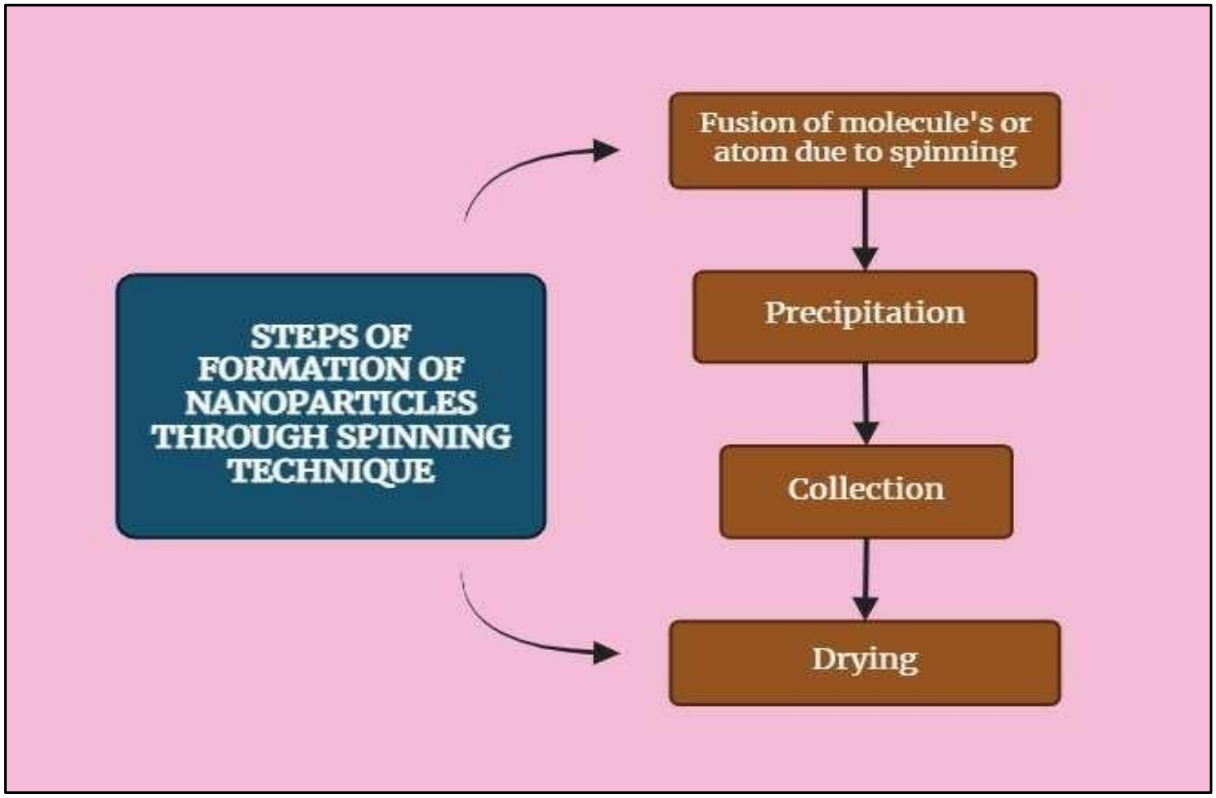

FIG 5: STEPS OF FORMATION OF NANOPARTICLES THROUGH SPINNING

- **Chemical Vapour Deposition (CVD)**

Chemical vapour deposition is a process that involves precipitating a thin layer of gaseous reactants onto a substrate. Deposition occurs in a reaction chamber at standard temperature by mixing gas molecules. A chemical reaction occurs when a heated substrate encounters the combined gas [13]. This reaction results in a thin coating of desired nanoparticle on the substrate surface, which can be recovered and used. The critical factor in CVD is the temperature of the substrate. CVD produces pure, rigid, homogeneous, and strong nanoparticles. The chemical vapor deposition (CVD) method is classified based on the energy source utilized for initiating the process, including thermally activated CVD [31], plasma-enhanced CVD [32], and photo-initiated CVD [33]. The limitations involve requirement of specific instrumentation, and the gaseous byproducts are highly hazardous [34].

- **Pyrolysis**
  Pyrolysis is the primary method for formation of nanoparticles on a large scale. It involves igniting a precursor with flame. The precursor is either liquid or gas that is delivered into the furnace at high pressure through a small opening and burned [35]. Nanoparticles are then recovered from combustion or by-product gases using air classification. Some of the furnaces use plasma and laser instead of flame to accomplish high temperature for simple evaporation [36]. The benefits of pyrolysis include simple, cost-effective, efficient, and continuous process with a high yield.

- **Biosynthesis**

Biosynthesis is an environmentally friendly method for producing non-toxic and biodegradable nanoparticles [37]. Biosynthesis employs plant extracts, bacteria, fungi, etc. combined with the precursors to generate nanoparticle instead of standard chemicals for bio-reduction [38].

Top-down method

Top-down or destructive technique involves breaking materials to nanometric-scale particles. Common methods for producing nanoparticles include nanolithography, sputtering, laser ablation, mechanical milling, and thermal decomposition/breakdown.

- **Mechanical milling**

Mechanical milling is the most used top-down approach for synthesising nanoparticles. It is used to mill and post-anneal nanoparticles during manufacturing, with multiple elements milled in an inert environment [39]. Mechanical milling is affected by plastic deformation, fracture, and cold-welding, all of which affects particle shape and size.

- **Nanolithography**

Nanolithography is the method of producing structures with only one dimension of 1 to 100 nm. It involves several methods, including electron-beam, nanoimprint, optical, multiphoton, and scanning probe lithography [40]. Lithography is the technique of printing a desired structure on a photo-sensitive

substance by selectively removing a piece of the material. The benefit of nanolithography is the ability to transform a single nanoparticle into a cluster of nanoparticles of appropriate size and shape. The downsides include the requirement of complicated equipments and its accompanying costs [41].

- **Laser ablation**

Laser Ablation Synthesis in Solution (LASiS) is a characteristic method for producing nanoparticles from various solvents. Irradiating a metal in a liquid solution with a laser beam creates a plasma plume, resulting in the formation of nanoparticles [42]. This top-down process is used for synthesizing metal-based nanoparticles. LASiS is a 'environmental friendly' approach since it allows steady synthesis of nanoparticles in water and organic solvents without the need of any stabilising agents.

- **Sputtering**

Sputtering is the technique of precipitating nanoparticles on a surface by ejecting particles that impact with ions [43]. Sputtering involves deposition of a thin film of nanoparticles followed by annealing. The size and shape of nanoparticles are determined by factors such as annealing temperature and duration, layer thickness, and substrate type [44].

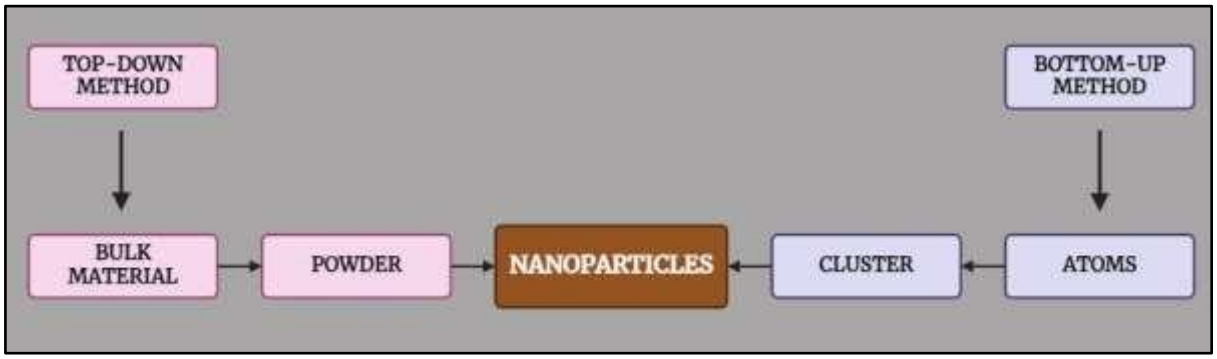

FIG 6: PROCESS OF FORMATION OF NANOPARTICLES

SIGNIFICANT CHALLENGES IN NAOPARTICLE PRODUCTION

Currently, with the growth of nanotechnology, there is a sharp increase in the amount of knowledge and study focused on nanoparticles. However, only few of them manage to advance to the point of clinical trials. The majority only get as far as the in vitro and in vivo phases. While the clinical translation of each individual nano formulation offers distinct challenges, most NPs face common barriers that can be classified into three broad groups: **biological, technological, and study-design related**.

The absence of administration routes, reducing biodistribution, NPs' disintegration, toxicity, and the channel by which they pass through biological barriers are some of the **biological obstacles** [45]. Since NPs are frequently injected intravenously (IV) into the bloodstream, it is challenging for them to stay and interact with the target site. As a result, a medication is administered at a high dosage that might not have the desired therapeutic effects [46]. However, several in vitro and in vivo studies have shown how 3D magnetic fields may be used to control the movement of NPs against blood flow, a challenge that magnetic nanoparticles can solve. Nevertheless, more investigation is required into the effects of magnetic fields on the human body, the interplay of multiple magnetic fields, and high NP concentrations.

Performance forecasts, equal optimization, and scale-up synthesis are some of the **technological problems** faced during NPs synthesis. These factors play a critical role in ensuring NPs' clinical success. Since most NPs utilized in in vitro and in vivo investigations are often manufactured in small batches, scale-up for large amounts is not always possible due to equipment and other factors. It is not a systematic or optimized process that produces the lead clinical candidates that perform well in animal models. To prevail over this, we can employ certain techniques that allow us to evaluate a large number of nano formulations and choose one optimum formulation through selected iterations [47,48,49]. Such impacts should not, however, be added straight into experiments with humans. It is difficult to predict the effectiveness and performance of nanoparticles, and it is extremely difficult to replicate the in vivo outcomes in human studies. It is possible to create theoretical or computational modelling that mimics physiological environments and tissue in conjunction with experimental data. For instance, organs-on-chips are subject of ongoing research and could improve NP predictions of efficiency and performance.

Issues with study design, such as study size, purpose, and when to administer NP treatments have a big influence on clinical trials. Most of the research uses "cell and animal models," which could not yield outcomes in human trials that are understandable. As such, it is difficult to replicate natural physiological reactions using a single model. Furthermore, given one of the important characteristics of cancer is metastasis, "models of cancer metastasis" ought to be thoroughly studied. Furthermore, if we concentrate on individualized therapy, N = 1 clinical investigation will be necessary. Numerous factors, including genetics, environment, and prior medical history, must be considered [50,51].

APPLICATIONS OF NANOPARTICLES

The important uses of nanoparticles are listed below.

A. Cosmetics and Sunscreens

Sunscreen incorporating nanoparticles, such as titanium dioxide, provides numerous benefits. The tendency to absorb and reflect UV radiation while remaining transparent to visible light, titanium oxide and zinc oxide nanoparticles have found use in sunscreens formulation. Iron oxide nanoparticles are utilized as pigment in some lipsticks [52].

B. Electronics

The demand for huge and high-brightness screens in computer, monitors and televisions has led to increased adoption of nanoparticle display technologies. Nanocrystalline lead telluride, cadmium sulphide, zinc selenide and sulphide are employed in light emitting diodes (LEDs) of modern screens [53]. The rise of transportable consumer devices, like mobile phones and laptop computers, has created a tremendous demand for compact, lightweight, and high-capacity batteries. Nanoparticles are ideal for separator plates in batteries. The foam-like (aerogel) structure allows for significantly more energy storage compared to ordinary batteries. Nanocrystalline nickel and metal hydride batteries have a larger surface area and require less recharging, leading to longer battery life [54]. Nanoparticles can detect gases such as NO_2 and NH_3 due to their increased electrical conductivity [55]. The charge transfer from nanoparticles to NO_2 increases their pores, making them more effective gas sensors.

C. Catalysis

Nanoparticles have a large surface area, which provides greater catalytic activity. Nanoparticles' high surface-to-volume ratio makes them an effective catalyst for chemical synthesis [56]. Platinum nanoparticles can dramatically reduce the quantity of platinum needed in vehicle catalytic converters due to their high surface area, resulting in cost savings and improved performance. Some chemical reactions, such as the reduction of nickel oxide to metal nickel (Ni), use nanoparticles.

D. Medicine

Nanotechnology has helped the medical field in medicine administration. Nanoparticles provide targeted medicine delivery to particular cells [58]. Administering the medicine in the correct place and amount considerably reduces overall intake and negative effects. This procedure saves money and has fewer adverse effects. Tissue engineering involves the replication and repair of damaged tissue can be done with the aid of nanotechnology. Tissue engineering can replace conventional procedures like organ transplants and artificial implants. One of the examples is bone development using carbon nanotube scaffolds [59]. The utilization of gold in medicine is not unique. Ayurveda, an Indian medical tradition, uses gold in many ways. One typical prescription is the use of gold to improve memory. Some paediatric medicines contain gold to improve a baby's mental health [60].

E. Food

By using nanotechnology, food production, processing, preservation, and packaging all are improved. Nanocomposite coatings in food packaging may deliver anti-microbial chemicals directly onto the film coated surface [61]. In canola oil manufacturing, nanodrops are utilized as a vitamin and mineral additives.

F. Diagnosis

Several nanoparticles are employed in the detection and treatment of certain cancers. Such nanoparticles can be used accurately for imaging tumours or to distribute drugs (theragnostic approach) with minimum adverse effects. Nanodevices synthesized for oncology applications include quantum dots (QDs), carbon nanotubes (CNTs), paramagnetic nanoparticles (NPs), liposomes, gold nanoparticles (GNPs), MRI contrast agents for intraoperative imaging, and cutting-edge NP-based methods for highly specific DNA and protein detection [62,63,64,65].

G. Dye Degradation

Wastewater treatment and prospective future uses necessitate the removal of water pollutants found in bodies of water, including azo, cationic, and acid dyes, as well as other contaminants of a similar kind. These contaminants have a harmful impact on aquatic life and contribute to water pollution. NPs act as a catalyst or absorb pollutants [55]. They have a large surface area but a modest size. It has been demonstrated that both Ag and AuNPs can produce catalytic activity sufficient for the elimination of organic dyes. These nanoparticles increase the rate of reaction while decreasing the time required to remove the dyes [66,67].

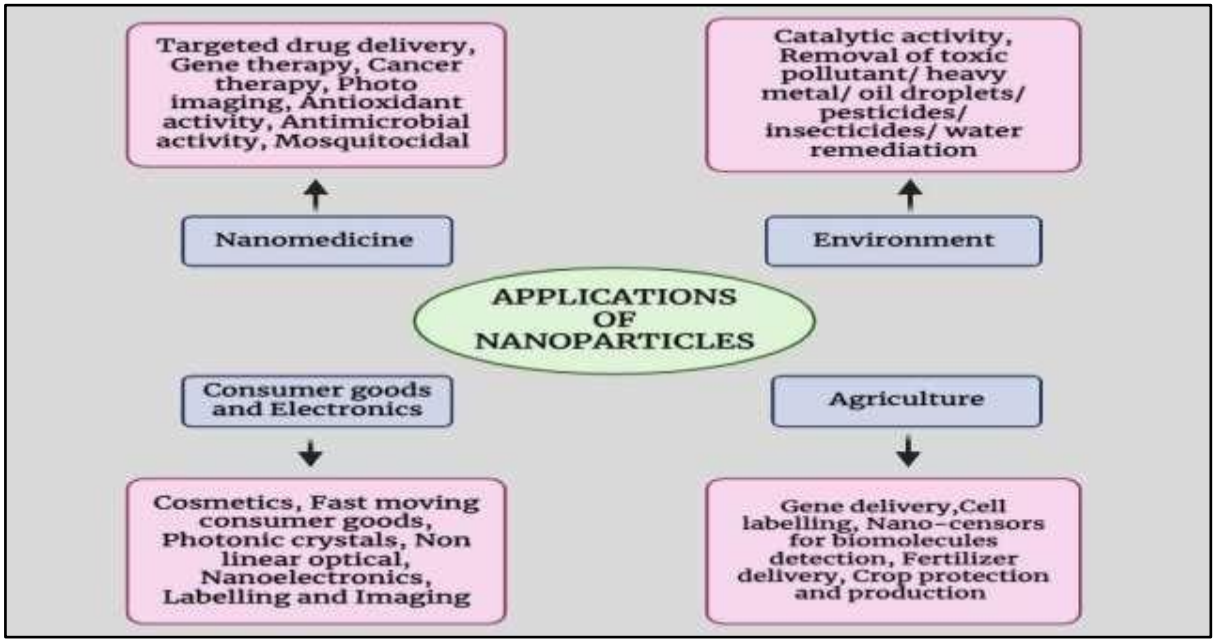

FIG 7: MAJOR APPLICATIONS OF NANOTECHNOLOGY

FUTURE DIRECTIONS IN NANOPARTICLES RESEARCH

Advanced Synthesis Techniques: Emerging trends in nanoparticle synthesis focus on developing novel synthesis techniques that offer improved control over nanoparticle size, shape, composition, and functionality. The major synthesis techniques include bottom-up approaches such as atomic layer deposition, molecular self-assembly, and biologically inspired synthesis methods, as well as top-down approaches such as nanolithography and laser-assisted synthesis techniques [68].

Multifunctional Nanoparticles: The development and creation of multifunctional nanoparticles with tailored characteristics for specific purposes is gaining momentum. Future research directions involve integrating multiple functionalities into nanoparticles, such as therapeutic agents, imaging probes, targeting ligands, and stimuli-responsive components, to enable synergistic effects and enhanced performance in biomedical, environmental, and energy applications [69].

Precision Medicine: Nanoparticles hold great potential for advancing precision medicine approaches by enabling personalized diagnosis and treatment strategies. Future directions in nanoparticle-based therapeutics include the development of targeted drug delivery systems, theragnostic nanoparticles for simultaneous imaging and therapy, and precision nanomedicine platforms tailored to individual patient characteristics, disease profiles, and treatment responses [70].

Nanomaterials for Sustainable Technologies: Nanoparticles play a crucial role in advancing sustainable technologies for environmental remediation, renewable energy, and resource conservation. Future research directions include developing nanoparticle-based materials and devices for water purification, air pollution control, energy storage and conversion, and sustainable agriculture, with an emphasis on efficiency, cost-effectiveness, and environmental compatibility [71].

Nanotoxicology and Safety Assessment: As the use of nanoparticles expands across various industries, addressing nanotoxicology and safety assessment challenges becomes increasingly important. Future research directions involve advancing nanotoxicology studies to understand the mechanisms of nanoparticle toxicity, developing predictive models for assessing nanoparticle safety, and establishing guidelines for risk assessment and regulatory decision-making [72].

APPROVED MARKETED FORMULATIONS OF NANOPARTICLES

NAME OF DRUG	TRADE NAME	TYPE OF NANOPARTICLE	YEAR OF APPROVAL	APPLICATIONS	REFERENCE
Iron Sucrose	Venofer	Inorganic/Metallic NPs	2000	Chronic renal failure with anaemia	[73,74]
Iron dextran (low MW)	INFeD	Inorganic/Metallic NPs	1974	Chronic renal failure with anaemia	[73,74]

Ferumoxytol	Feraheme	Inorganic/Metallic NPs	2009	Chronic renal failure with anaemia	[73,74]
Sodium ferric gluconate	Ferrlecit	Inorganic/Metallic NPs	1999	Chronic renal failure with anaemia	[73,74]
Lanreotide acetate	Somatuline depot	Inorganic/Metallic NPs	2007	Acromegaly	[76]
Ferric carboxymaltose	Injectafer	Inorganic/Metallic NPs	2013	Chronic renal failure with anaemia	[75]

TABLE:1 Approved marketed formulations loaded with non-polymeric nanoparticles.

NAME OF DRUG	TRADE NAME	TYPE OF NANOPARTICLE	YEAR OF APPROVAL	APPLICATIONS	REFERENCE
Megestrol acetate	Megace ES	Nanocrystals	2005	Anorexia	[73,74]
Fenofibrate	Tricor	Nanocrystals	2004	Hyperlipidaemia	[73,74]
Aprepitant	Emend	Nanocrystals	2003	Vomiting agent	[73,74]
Methylphenidate HCl	Ritalin LA	Nanocrystals	1955	Mental stimulant	[73,74]
Sirolimus	Rapamune	Nanocrystals	2000	Immunosuppressant	[73,74]
Paliperidone palmitate	Invega Sustenna	Nanocrystals	2009,2014	Schizoaffective disorder	[77]
Tizanidine HCl	Zanaflex	Nanocrystals	2002	Muscle relaxant	[73,74]
Griseofulvin	Gris-Peg	Nanocrystals	1982	Fungal infection	[79]
Brinzolamide	Azopt	Nanocrystals	1998	Glaucoma	[79]
Theophylline	Elixophyllin Nostrum Labs Inc	Nanocrystals	1979	Bronchial dilation	[79]
Naproxen sodium	Naprelan	Nanocrystals	1996	Anti-inflammation	[79]
Nabilone	Cesamet	Nanocrystals	1995	Anti-emetic	[79]
Olanzapine	Zyprexa	Nanocrystals	1996	Schizophrenia	[73,74]
Dantrolene sodium	Ryanodex	Nanocrystals	2014	Malignant benign hypothermia	[78]

TABLE:2 Approved marketed formulations loaded with crystalline nanoparticles.

NAME OF DRUG	TRADE NAME	TYPE OF NANOPARTICLE	YEAR OF APPROVAL	APPLICATIONS	REFERENCE
Irinotecan	Onivyde	Liposomal irinotecan	2015	Pancreatic cancer	[81]
Cytarabine	DepoCyt	Liposomal cytarabine	1999	Lymphoma	[73,74]
Doxorubicin	Doxil	Liposomal doxorubicin	1995	Kaposi sarcoma, ovarian cancer, multiple myeloma	[73,74]
Octocog alfa	Advate	Liposome	2004	Haemophilia A	[83]
Mifamurtide	Mepact	Liposomes	2004	Myosarcoma	[84]
Daunorubicin	DaunoXome	Liposomal daunorubicin	1996	Kaposi sarcoma	[73,74]
Amphotericin B	AmBisome	Liposomal amphotericin B	1997	Fungal infection	[73,74]

Perflutren	Definity	Perflutren lipid microspheres	2001	Ultrasound contrast agent	[82]
Vincristine	Marqibo	Liposomal vincristine	2012	Acute lymphocytic blood clot	[80]
Moderna	Moderna	Liposomal nanoparticles	2020 (EUAs)	Covid-19	[85,86]
Pfizer-BioNTech	Pfizer-BioNTech	Liposomal nanoparticles	2020 (EUAs)	Covid-19	[85,86]
Cytarabine: daunorubicin	VYXEOS	Liposomes	2017	Acute myeloid leukaemia	[82]
Propofol	Diprivan	Liposomes	1989	Anaesthesia	[82]

TABLE:3 Approved marketed formulations loaded with lipid-based nanoparticles.

NAME OF DRUG	**TRADE NAME**	**TYPE OF NANOPARTICLE**	**YEAR OF APPROVAL**	**APPLICATIONS**	**REFERENCE**
Ibritumomab tiuxetan	Zevalin	Suspension	2002	Lymphoma	[73,74]
Verapamil HCl	Verelan PM	PLGA nanoparticles	1998	Hypertension, angina, and rhythm disorders	[79]
Denileukin diftitox	Ontak	Protein NP	1999	T-cell lymphoma	[73,74]
Docetaxel	Taxotere	Micelles	1996	Anti-neoplastic	[76]
Pegvisomant	Somavert	PEGylated HGH receptor antagonist	2003	Acromegaly	[73,74]
Pegaspargase	Oncaspar	Polymer-protein conjugate	1994	Acute lymphocytic blood clot	[73,74]
Pegloticase	Krystexxa	Polymer-protein conjugate	2010	Chronic gout	[73,74]
PEGylated factor VIII	Adynovate	Polymer-protein conjugate	2015	Haemophilia	[73,74]
Factor IX	Rebinyn	Glyco-pegylated coagulation factor IX	FDA 2017	Haemophilia	[88]
Triamcinolone acetonide	Zilretta	PLGA hydrogel	2017	Osteoarthritis	[88]
Trastuzumab	Kadcyla	Maytansine derivative, DM1	2013	Breast cancer	[87]
Paclitaxel	Abraxane	Protein NP	2005	Breast cancer	[82]
Pegfligrastim	Neulasta	PEGylated GCSF protein	2002	Leukopenia by chemotherapy	[73,74]
Peginterferon alfa-2A	Pegasys	PEGylated IFN alpha-2a protein	2002	Hepatitis Band C	[73,74]

TABLE:4 Approved marketed formulations loaded with polymer-based nanoparticles.

CONCLUSION

In conclusion, nanoparticles represent a groundbreaking field of science with vast potential for transformative applications across various industries. Their unique properties have led to significant advancements in medicine, electronics, energy, environmental science, cosmetics, food, textiles, automotive, and aerospace sectors, and among others. However, alongside these opportunities come various challenges.

One major challenge is the potential environmental and health impacts of nanoparticles, which require careful assessment and regulation to ensure their safe use. Additionally, the scalability of nanoparticle production and the cost-effectiveness of large-scale manufacturing remain areas of concern. Furthermore, ethical considerations surrounding the use of nanoparticles in areas such as medicine and food require ongoing attention.

Despite these challenges, the opportunities presented by nanoparticles are immense. Continued research and innovation in nanotechnology promise to revolutionize industries, enhance human health and well-being, and address pressing global challenges such as climate change and resource scarcity. By navigating these challenges effectively, stakeholders can harness the full potential of nanoparticles to drive sustainable development and create a brighter future for society.

REFERENCES

[1] Blanco E, Shen H, Ferrari M. Principles of nanoparticle design for overcoming biological barriers to drug delivery. Nat Biotechnol. 2015;33(9):941-51.

[2] Jokerst JV, Lobovkina T, Zare RN, Gambhir SS. Nanoparticle PEGylation for imaging and therapy. Nanomedicine (Lond). 2011;6(4):715-28.

[3] Davis ME, Chen ZG, Shin DM. Nanoparticle therapeutics: an emerging treatment modality for cancer. Nat Rev Drug Discov. 2008 Sep;7(9):771-82.

[4] Alexis F, Pridgen E, Molnar LK, Farokhzad OC. Factors affecting the clearance and biodistribution of polymeric nanoparticles. Mol Pharm. 2008;5(4):505-15.

[5] Hua S, Wu SY. The use of lipid-based nanocarriers for targeted pain therapies. Front Pharmacol. 2013; 4:143.

[6] O.V. Salata, Applications of nanoparticles in biology and medicine. J. Nanobiotechnology. 2, 1–6 (2004)

[7] Mahmoudi M, Lynch I, Ejtehadi MR, Monopoli MP, Bombelli FB, Laurent S. Protein−nanoparticle interactions: opportunities and challenges. Chem Rev. 2011 Jun 8;111(9):5610-37.

[8] Dreaden EC, Alkilany AM, Huang X, Murphy CJ, El-Sayed MA. The golden age: gold nanoparticles for biomedicine. Chem Soc Rev. 2012 Jan 7;41(7):2740-79.

[9] Zhang L, Gu FX, Chan JM, Wang AZ, Langer RS, Farokhzad OC. Nanoparticles in medicine: therapeutic applications and developments. Clin Pharmacol Ther. 2008 Jul;83(5):761-9.

[10] Tiwari DK, Behari J, Prasenjit Sen PS. Application of nanoparticles in waste water treatment.

[11] Salavati-Niasari M, Davar F, Mir N. Synthesis, and characterization of metallic copper nanoparticles via thermal decomposition. Polyhedron. 2008 Nov 25;27(17):3514-8.

[12] Tai CY, Tai CT, Chang MH, Liu HS. Synthesis of magnesium hydroxide and oxide nanoparticles using a spinning disk reactor. Industrial & engineering chemistry research. 2007 Aug 15;46(17):5536-41.

[13] Bhaviripudi S, Mile E, Steiner SA, Zare AT, Dresselhaus MS, Belcher AM, Kong J. CVD synthesis of single-walled carbon nanotubes from gold nanoparticle catalysts. Journal of the American Chemical Society. 2007 Feb 14;129(6):1516-7.

[14] Marsalek R. Particle size and zeta potential of ZnO. APCBEE procedia. 2014 Jan 1; 9:13-7.

[15] Khan Y, Sadia H, Ali Shah SZ, Khan MN, Shah AA, Ullah N, Ullah MF, Bibi H, Bafakeeh OT, Khedher NB, Eldin SM. Classification, synthetic, and characterization approaches to nanoparticles, and their applications in various fields of nanotechnology: A review. Catalysts. 2022 Nov 8;12(11):1386.

[16] Sharma V, Rao LJ. An overview on chemical composition, bioactivity, and processing of leaves of Cinnamomum tamala. Critical reviews in food science and nutrition. 2014 Jan 1;54(4):433-48.

[17] Bzdek BR, Zordan CA, Luther III GW, Johnston MV. Nanoparticle chemical composition during new particle formation. Aerosol Science and Technology. 2011 Aug 1;45(8):1041-8.

[18] Hodoroaba VD, Rades S, Unger WE. Inspection of morphology and elemental imaging of single nanoparticles by high-resolution SEM/EDX in transmission mode. Surface and interface analysis. 2014 Oct;46(10-11):945-8.

[19] Radnik J, Kersting R, Hagenhoff B, Bennet F, Ciornii D, Nymark P, Grafström R, Hodoroaba VD. Reliable surface analysis data of nanomaterials in support of risk assessment based on minimum information requirements. Nanomaterials. 2021 Mar 5;11(3):639.

[20] Meng C, Das P, Shi X, Fu Q, Müllen K, Wu ZS. In situ and operando characterizations of 2D materials in electrochemical energy storage devices. Small Science. 2021 Apr;1(4):2000076.

[21] Yano F, Hiraoka A, Itoga T, Kojima H, Kanehori K, Mitsui Y. Influence of ion-implantation on native oxidation of Si in a clean-room atmosphere. Applied surface science. 1996 Jul 2; 100:138-42.

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

[23] Williams DB, Carter CB. Transmission electron microscopy: a textbook for materials science. Diffraction. II. Springer Science & Business Media; 1996.

[24] Jia Z, Li J, Gao L, Yang D, Kanaev A. Dynamic light scattering: a powerful tool for in situ nanoparticle sizing. Colloids and Interfaces. 2023 Feb 16;7(1):15.

[25] Kumari A, Yadav SK, Pakade YB, Singh B, Yadav SC. Development of biodegradable nanoparticles for delivery of quercetin. Colloids and Surfaces B: Biointerfaces. 2010 Oct 15;80(2):184-92.

[26] Kelly KL, Coronado E, Zhao LL, Schatz GC. The optical properties of metal nanoparticles: the influence of size, shape, and dielectric environment. The Journal of Physical Chemistry B. 2003 Jan 23;107(3):668-77.

[27] Honary S, Zahir F. Effect of zeta potential on the properties of nano-drug delivery systems-a review (Part 2). Tropical journal of pharmaceutical research. 2013 May 9;12(2):265-73.

[28] Yang K, Feng L, Shi X, Liu Z. Nano-graphene in biomedicine: theranostic applications. Chemical Society Reviews. 2013;42(2):530-47.

[29] Ramesh S. Sol-gel synthesis and characterization of Ag.

[30] Mann S, Burkett SL, Davis SA, Fowler CE, Mendelson NH, Sims SD, Walsh D, Whilton NT. Sol− gel synthesis of organized matter. Chemistry of materials. 1997 Nov 18;9(11):2300-10.

[31] Mohammadi S, Harvey A, Boodhoo KV. Synthesis of TiO2 nanoparticles in a spinning disc reactor. Chemical Engineering Journal. 2014 Dec 15; 258:171-84.

[32] Tyagi A, Walia RS, Murtaza Q. Tribological behavior of temperature dependent environment friendly thermal CVD diamond coating. Diamond and Related Materials. 2019 Jun 1;96:148-59.

[33] Vasudev MC, Anderson KD, Bunning TJ, Tsukruk VV, Naik RR. Exploration of plasma-enhanced chemical vapor deposition as a method for thin-film fabrication with biological applications. ACS applied materials & interfaces. 2013 May 22;5(10):3983-94.

[34] Dion CD, Tavares JR. Photo-initiated chemical vapor deposition as a scalable particle functionalization technology (a practical review). Powder technology. 2013 May 1;239:484-91.

[35] Hachem K, Ansari MJ, Saleh RO, Kzar HH, Al-Gazally ME, Altimari US, Hussein SA, Mohammed HT, Hammid AT, Kianfar E. Methods of chemical synthesis in the synthesis of nanomaterial and nanoparticles by the chemical deposition method: a review. BioNanoScience. 2022 Sep;12(3):1032-57.

[36] Kammler HK, Mädler L, Pratsinis SE. Flame synthesis of nanoparticles. Chemical Engineering & Technology: Industrial Chemistry-Plant Equipment-Process Engineering-Biotechnology. 2001 Jun;24(6):583-96.

[37] D'Amato R, Falconieri M, Gagliardi S, Popovici E, Serra E, Terranova G, Borsella E. Synthesis of ceramic nanoparticles by laser pyrolysis: From research to applications. Journal of analytical and applied pyrolysis. 2013 Nov 1; 104:461-9.

[38] Kuppusamy P, Yusoff MM, Maniam GP, Govindan N. Biosynthesis of metallic nanoparticles using plant derivatives and their new avenues in pharmacological applications–An updated report. Saudi Pharmaceutical Journal. 2016 Jul 1;24(4):473-84.

[39] Hasan S. A review on nanoparticles: their synthesis and types. Res. J. Recent Sci. 2015; 2277:2502.

[40] Yadav TP, Yadav RM, Singh DP. Mechanical milling: a top down approach for the synthesis of nanomaterials and nanocomposites. Nanoscience and Nanotechnology. 2012 Aug 31;2(3):22-48.

[41] Pimpin A, Srituravanich W. Review on micro-and nanolithography techniques and their applications. Engineering journal. 2012;16(1):37-56.

[42] Hulteen JC, Treichel DA, Smith MT, Duval ML, Jensen TR, Van Duyne RP. Nanosphere lithography: size-tunable silver nanoparticle and surface cluster arrays. The Journal of Physical Chemistry B. 1999 May 13;103(19):3854-63.

[43] Amendola V, Meneghetti M. Laser ablation synthesis in solution and size manipulation of noble metal nanoparticles. Physical chemistry chemical physics. 2009;11(20):3805-21.

[44] Shah P, Gavrin A. Synthesis of nanoparticles using high-pressure sputtering for magnetic domain imaging. Journal of magnetism and magnetic materials. 2006 Jun 1;301(1):118-23.

[45] Lugscheider E, Bärwulf S, Barimani C, Riester M, Hilgers H. Magnetron-sputtered hard material coatings on thermoplastic polymers for clean room applications. Surface and Coatings Technology. 1998 Oct 10; 108:398-402.

[46] Chua KJ, Chou SK, Ho JC (2007) An analytical study on the thermal effects of cryosurgery on selective cell destruction. J Biotech 40(1):100-116.

[47] Choi HS, Frangioni JV. Nanoparticles for biomedical imaging: fundamentals of clinical translation. Mol Imaging. 2010 Oct;9(6):291-310

[48] Xia Y, Rao L, Yao H., Wang Z, Ning P, Chen X (2020) Engineering macrophages for cancer immunotherapy and drug delivery.

[49] Dobrovolskaia MA, Aggarwal P, Hall JB, McNeil SE (2008) Preclinical studies to understand nanoparticle interaction with the immune system and its potential effects on nanoparticle biodistribution. Mol Pharm 5(4):487–495.

[50] Akinc A, Zumbuehl A, Goldberg M, Leshchiner ES, Busini V, Hossain N, Bacallado SA, Nguyen DN, Fuller J, Alvarez R, Borodovsky A, Borland T, Constien R, de Fougerolles A, Dorkin JR, Narayanannair Jayaprakash K, Jayaraman M, John M, Koteliansky V, Manoharan M, Anderson DG (2008) A combinatorial library of lipid-like materials for delivery of RNAi therapeutics. Nat Biotechnol 26(5):561–569.

[51] Love KT, Mahon KP, Levins CG, Whitehead KA, Querbes W, Dorkin JR, Qin J, Cantley W, Qin LL, Racie T, Frank-Kamenetsky M, Yip KN, Alvarez R, Sah DW, de Fougerolles A, Fitzgerald K, Koteliansky V, Akinc A, Langer R, Anderson DG (2010) Lipid-like materials for low-dose, in vivo gene silencing. Proc Natl Acad Sci USA 107(5):1864–1869.

[52] Schork NJ (2015) Personalized medicine: time for one-person trials. Nature 520(7549):609–611.

[53] Wiechers J W and Musee N 2010 Engineered Inorganic Nanoparticles and Cosmetics: Facts, Issues, Knowledge Gaps and Challenges 6

[54] Teng W, Jeng S, Kuo C, Lin Y, Liao C and Chin W 2008 liquid crystal displays 33 1663–5

[55] Arico AS, Bruce P, Scrosati B, Tarascon JM, van Schalkwijk W. Nanostructured materials for advanced energy conversion and storage devices. Nat Mater. 2005 May;4(5):366-77.

[56] Liu X, Zhang J, Wang L, Yang T, Guo X, Wu S, Wang S. 3D hierarchically porous ZnO structures and their functionalization by Au nanoparticles for gas sensors. Journal of Materials Chemistry. 2011;21(2):349-56.

[57] Crooks R M, Zhao M, Sun L I, Chechik V and Yeung L E K 2001 Dendrimer-Encapsulated Metal Nanoparticles: Synthesis, Characterization, and Applications to Catalysis 34 181–90

[58] Bobo D, Robinson KJ, Islam J, Thurecht KJ, Corrie SR. Nanoparticle-based medicines: A review of FDA-approved materials and clinical trials to date. Pharm Res. 2016 Oct;33(10):2373-87.

[59] Mudshinge S R, Deore A B, Patil S and Bhalgat C M 2011 Nanoparticles: Emerging carriers for drug delivery Saudi Pharm. J. 19 129–41

[60] Shinde NC, Keskar NJ, Argade PD. Nanoparticles: Advances in drug delivery systems. Res. J. Pharm. Biol. Chem. Sci. 2012 Jan 1;3(1):922-9.

[61] Laad M, Jatti VK. Titanium oxide nanoparticles as additives in engine oil. Journal of King Saud University-Engineering Sciences. 2018 Apr 1;30(2):116-22.

[62] Jamieson, T.; Bakhshi, R.; Petrova, D.; Pocock, R.; Imani, M.; Seifalian, A. Biological applications of quantum dots. *Biomaterials* **2007**, *28*, 4717–4732.

[63] Abbasi, E.; Kafshdooz, T.; Bakhtiary, M.; Nikzamir, N.; Nikzamir, N.; Nikzamir, M.; Mohammadian, M.; Akbarzadeh, A. Biomedical and biological applications of quantum dots. *Artif. Cells Nanomed. Biotechnol.* **2016**, *44*, 885–891.

[64] Kircher, M.F.; Mahmood, U.; King, R.S.; Weissleder, R.; Josephson, L. A multimodal nanoparticle for preoperative magnetic resonance imaging and intraoperative optical brain tumor delineation. *Cancer Res.* **2003**, *63*, 8122–8125.

[65] Nam, J.-M.; Stoeva, S.I.; Mirkin, C.A. Bio-Bar-Code-Based DNA Detection with PCR-like Sensitivity. *J. Am. Chem. Soc.* **2004**, *126*, 5932–5933

[66] Suvith, V.; Philip, D. Catalytic degradation of methylene blue using biosynthesized gold and silver nanoparticles. *Spectrochim. Acta Part A Mol. Biomol. Spectrosc.* **2014**, *118*, 526–532.

[67] Panáček A, Prucek R, Hrbáč J, Nevečná TJ, Šteffková J, Zbořil R, Kvítek L. Polyacrylate-assisted size control of silver nanoparticles and their catalytic activity. Chemistry of materials. 2014 Feb 11;26(3):1332-9.

[68] Huang H, Ge H, Ren Z, Huang Z, Xu M, Wang X. Controllable synthesis of biocompatible fluorescent carbon dots from cellulose hydrogel for the specific detection of Hg2+. Frontiers in Bioengineering and Biotechnology. 2021 Jan 28;9:617097.

[69] Yang H, Li Y, Li T, Xu M, Chen Y, Wu C, Dang X, Liu Y. Multifunctional core/shell nanoparticles cross-linked polyetherimide-folic acid as efficient Notch-1 siRNA carrier for targeted killing of breast cancer. Scientific reports. 2014 Nov 17;4(1):7072.

[70] Swami A, Shi J, Gadde S, Votruba AR, Kolishetti N, Farokhzad OC. Nanoparticles for targeted and temporally controlled drug delivery. Multifunctional nanoparticles for drug delivery applications: imaging, targeting, and delivery. 2012:9-29.

[71] Davari MR, Bayat Kazazi S, Akbarzadeh Pivehzhani O. Nanomaterials: implications on agroecosystem. Nanotechnology: An agricultural paradigm. 2017:59-71.

[72] Fadeel, B., Bussy, C., Merino, S., Vázquez, E., Flahaut, E., Mouchet, F., ... & Kostarelos, K.2018). Safety assessment of graphene-based materials: focus on human health and the environment. ACS nano, 12(11), 10582-10620.

[73] Choi YH, Han HK. Correction to: Nanomedicines: Current status and future perspectives in aspect of drug delivery and pharmacokinetics. Journal of Pharmaceutical Investigation. 2019 Jan 15; 49:201-.

[74] Choi YH, Han HK. Nanomedicines: current status and future perspectives in aspect of drug delivery and pharmacokinetics. Journal of pharmaceutical investigation. 2018 Jan;48(1):43-60.

[75] Lyseng-Williamson KA, Keating GM. Ferric carboxymaltose: a review of its use in iron-deficiency anaemia. Drugs. 2009 Apr;69:739-56.

[76] Bajwa SZ, Munawar A, Khan WS. Nanotechnology in medicine: innovation to market. Pharmaceutical Bioprocessing. 2017 Jan 1;5(2):11-5.

[77] Kaduk JA, Dmitrienko AO, Gindhart AM, Blanton TN. Crystal structure of paliperidone palmitate (INVEGA SUSTENNA®), C39H57FN4O4. Powder Diffraction. 2017 Dec;32(4):222-7.

[78] Patra JK, Das G, Fraceto LF, Campos EV, Rodriguez-Torres MD, Acosta-Torres LS, Diaz-Torres LA, Grillo R, Swamy MK, Sharma S, Habtemariam S. Nano based drug delivery systems: recent developments and future prospects. Journal of nanobiotechnology. 2018 Dec; 16:1-33.

[79] Bhakay A, Rahman M, Dave RN, Bilgili E. Bioavailability enhancement of poorly water-soluble drugs via nanocomposites: Formulation–Processing aspects and challenges. Pharmaceutics. 2018 Jul 8;10(3):86.

[80] Silverman JA, Deitcher SR. Marqibo® (vincristine sulfate liposome injection) improves the pharmacokinetics and pharmacodynamics of vincristine. Cancer chemotherapy and pharmacology. 2013 Mar;71(3):555-64.

[81] Zhang H. Onivyde for the therapy of multiple solid tumors. OncoTargets and therapy. 2016 May 20:3001-7.

[82] Anselmo AC, Mitragotri S. Nanoparticles in the clinic: An update. Bioengineering & translational medicine. 2019 Sep;4(3): e10143.

[83] Morigi V, Tocchio A, Bellavite Pellegrini C, Sakamoto JH, Arnone M, Tasciotti E. Nanotechnology in medicine: from inception to market domination. Journal of drug delivery. 2012;2012.

[84] Venkatakrishnan K, Liu Y, Noe D, Mertz J, Bargfrede M, Marbury T, Farbakhsh K, Oliva C, Milton A. Pharmacokinetics and pharmacodynamics of liposomal mifamurtide in adult volunteers with mild or moderate renal impairment. British journal of clinical pharmacology. 2014 Jun;77(6):986-97.

[85] Bouazzaoui A, Abdellatif AA, Al-Allaf FA, Bogari NM, Al-Dehlawi S, Qari SH. Strategies for vaccination: conventional vaccine approaches versus new-generation strategies in combination with adjuvants. Pharmaceutics. 2021 Jan 22;13(2):140.

[86] Pardi N, Hogan MJ, Pelc RS, Muramatsu H, Andersen H, DeMaso CR, Dowd KA, Sutherland LL, Scearce RM, Parks R, Wagner W. Zika virus protection by a single low-dose nucleoside-modified mRNA vaccination. Nature. 2017 Mar 9;543(7644):248-51.

[87] Kim MT, Chen Y, Marhoul J, Jacobson F. Statistical modeling of the drug load distribution on trastuzumab emtansine (Kadcyla), a lysine-linked antibody drug conjugate. Bioconjugate chemistry. 2014 Jul 16;25(7):1223-32.

[88] Farjadian F, Ghasemi A, Gohari O, Roointan A, Karimi M, Hamblin MR. Nanopharmaceuticals and nanomedicines currently on the market: challenges and opportunities. Nanomedicine. 2019 Jan;14(1):93-126.