A PROGRESS AND FUTURE STATUS OF NANOTECHNOLOGY IN BIOMEDICAL APPLICATIONS: A MINI REVIEW

Abstract

This article introduces the fundamental ideas of nanotechnology. As it examines the dominance of nanotechnology in biomedical applications, it provides an overview of nanoscience and the importance of this field of study. A brief history of nanotechnology and biomedicines for the treatment of cancer, and other biomedical applications are addressed with reference to relevant research. It gives a comprehensive introduction to nanomaterials.

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I. INTRODUCTION

Nanotechnology and Nanoscience: Nanomaterials have evolved into an interesting class of materials widely designed for various real-world applications. Richard P. Feynman, a renowned material scientist, introduced the concept of nanotechnology in his seminal talk "There's Plenty of Room at the Bottom" at the meeting held by the American Physical Society in December 1959.[1] Ever since there have been many innovations in material science that have demonstrated Feynman's theory of atomic-scale control of material properties. Materials are considered to be nanomaterials if one or more of their dimensions fall within the range of 1 to 100 nm. Hence, the field of research known as nanoscience is concerned with the study of nanomaterials. The term "nanotechnology" refers to the regulated design, production, and evolution of molecules or atoms to build nanosized materials. Nanotechnology is an excellent illustration of technological innovations, which offer designed nanomaterials with tremendous potential for producing goods with significantly better capabilities.[2]

Fundamentally, nanotechnology entails the utilization of nanoscience.[3] Presently, nanotechnology is advancing rapidly and covering practically all areas of material science. Due to their unique physicochemical, and biological characteristics, nanomaterials like nanorods, nanosheets, nanoparticles etc. have drawn the attention of numerous researchers all over the globe.

II. NANOMATERIALS

1. **Definition of Nanomaterials:** Nanomaterials are quite small and extremely tiny. However, they might have significant effects on our everyday activities, making them fascinating and essential to be aware of. In the term "nanotechnology," the prefix "nano" refers to a "dwarf." In accordance with the metric system of measurements, the size of a nanometer corresponds to one billionth (1×10^{-9}) of a meter. Size is important but is not the only significant aspect when a material transforms into a nanomaterial. Typically, the 1-100 nm range is referred to as the nanometer scale. In theory, nanomaterials are materials with at least one dimension exhibiting a single unit size of 1–100 nm or nanoscale repetitive lengths among the single units.

2. **Classification of Nanomaterials on the Basis of Dimensions:** According to Pokropivny *et al.* classification approach, we have here categorized the nanostructured materials as depicted in **Fig. 1**. Nanomaterials have been categorized generally into four categories according to their nanosized dimensions.[4,5]

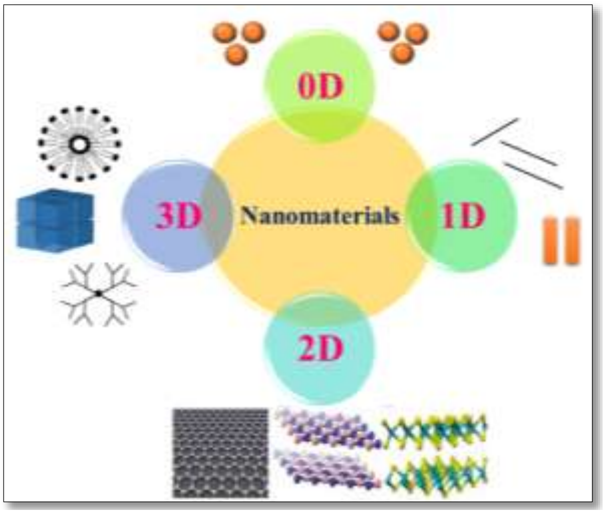

Figure 1: Categorizations of Nanomaterials Based on Nanoscale Dimensions

3. **Zero-Dimensional:** Zero-dimensional (0D) nanostructures are composed of materials with all dimensions smaller than 100 nm. In the field of nanotechnology, carbon-based nanomaterials have been extensively studied. Fullerenes and carbon dots (CDs) are types of carbon-based 0D nanostructures.[6]

4. **One-Dimensional:** One-dimensional (1D) nanostructures such as nanotubes, nanowires, quantum wires, nanobelts and nanorods have been praised by researchers as the most efficient structural elements for nanoscale devices.[7,8] Two dimensions in one-dimensional and nanomaterial are in the nanoscale range, whereas the third dimension is present in the bulk.

   - **Nanowires:** Nanowires possess lengths of a few micrometers and diameters smaller than 20 nm with a high aspect ratio.[9] The majority of techniques for producing nanowires are adapted from methods utilized in the field of semiconductors, resulting in microchips.

   - **Nanorods:** One-dimensional nanorods with decreased boundaries of grains, defects in the surface and irregular surfaces may be beneficial with greater efficiency for charge transportation. Nanorods could be produced via a variety of methodologies, comprising thermal decomposition, hydrothermal and microwave treatment.[10]

   - **Nanotubes:** Since, Ijima's investigation of the carbon nanotube (CNT) an enormous amount of research has been put forth toward designing devices that employ 1D crystalline oxide of metal nanostructures as electrodes in lithium batteries, solar cells, catalysts, sensors and other devices.[11] Metal oxide nanotubes have unique chemical and physical characteristics, due to their small dimensions, therefore may be utilized as a platform for experimentation to conduct and fundamental research and technological advancement.

5. **Two-Dimensional Nanomaterials:** A new category of nanomaterials known as two-dimensional (2D) nanostructures have sheet-like structures with transverse dimensions greater than 100 nm and a typical thickness of less than 5 nm. They include nanodisks, nanoplates, nanoprisms and nanosheets.[12]

6. **Three Dimensional Nanomaterials:** Nanomaterials in three dimensions (3D) are those whose dimensions are not restricted to the nanoscale. Three arbitrary dimensions exceeding 100 nm are present in these materials. Several arrangements of nanosized crystals in various orientations make up bulk nanomaterials.[13]

7. **Classification of Nanomaterials Based on Morphology and Structure**

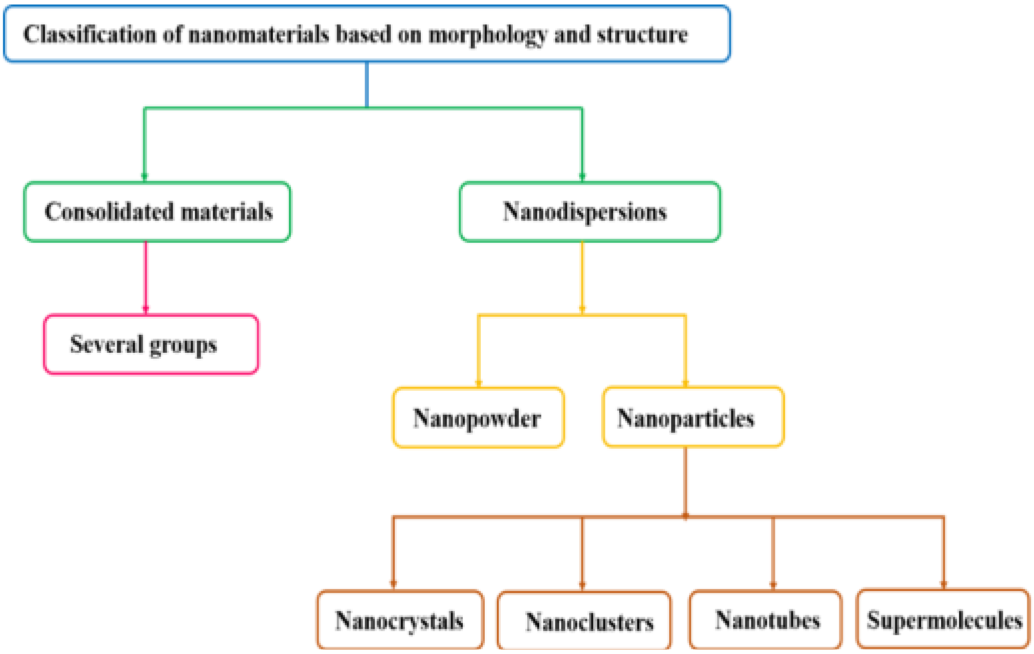

Figure 2: Classifications of Nanomaterials Based on Morphology and Structure

Nanomaterials are divided into two primary categories: Consolidated materials and Nanodispersions as shown in **Fig. 2**. Their classification is mostly based on their morphology and structure. Consolidated nanostructures are further divided into a number of categories. The terms “nanopowders” and “nanoparticles” refer to one-dimensional nano-dispersive systems. These other subcategories of nanoparticles include nanocrystals, nanotubes, nanoclusters, supermolecules etc.

Size is a key property of nanomaterials. Nanomaterials are usually classified based on the extent to which their dimensions lie between the nanoscale ranges. The term “nanoparticle” refers to a nanomaterial whose three dimensions are all nanoscale and there is essentially no variation among the most lengthy and shortest axes. Nanofibres are materials that have two dimensions at the nanoscale. Nanotubes are solid nanofibers that are hollow, while nanorods are solid nanofibers that are hollow. Nanoplates are materials having only one dimension at the nanoscale. Nanoribbons are nanoplates with two distinct longer dimensions.

8. Classification of Nanomaterials Based on Phases of Matter

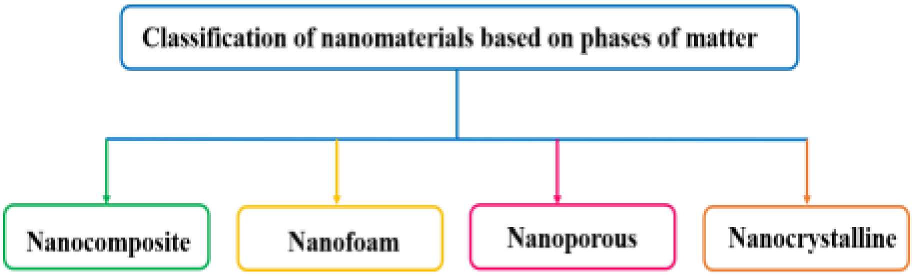

Figure 3: Classification of Nanomaterials Based on Phases of Matter

Nanomaterials can be and classed as nanocomposite, nanoporous, nanofoam and nanocrystalline depending on the phases of matter they include as depicted in **Fig. 3**. Nanocomposites are solid materials having at least one chemically or physically distinctive region in addition to at least one region possessing nanoscale dimensions. Among, the two phases of a nanofoam, which can be either liquid or solid, has been filled with a gaseous state. Nanoporous materials are solids that have nanopores or cavities that have nanoscale dimensions. Nanoscale crystal grains are present in nanocrystalline materials.

9. Classification of Nanomaterials Based on Composition: Dendrimers, nanocomposites, carbon-based materials, and materials based on metals are the four primary categories of specifically produced nanomaterials as illustrated in **Fig.4**.

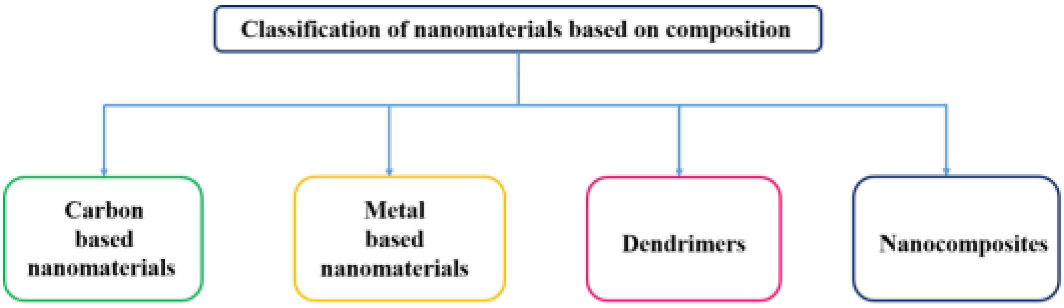

Figure 4: Classification of Nanomaterials Based on Phases of Composition

- **Carbon-Based Nanomaterials:** Fullerenes are synthetically produced carbon-based nanostructures. These include buckyballs and carbon nanotubes. Carbon-assisted vapor deposition is a common method to produce carbon nanotubes.[14,15] despite the one exception of carbon black, the main methods of production for these carbon-based substances include chemical vapor deposition (CVD), bend release and laser removal. These nanostructures have extraordinary physical and chemical characteristics that make them among the most desirable potential alternatives for various applications like biomedical, sensing, energy storage, catalysis, etc.[16,17]

- **Metal-Based Nanomaterials:** Quantum dots and gold nanoparticles are examples of metal-based nanomaterials.[18,19] there are various ways to produce quantum dots. One technique entail making small particles of two distinct substances at extremely high temperatures. The dimensions of the nanometer-scale nanocrystals may be precisely monitored by altering temperature and other factors. The fluorescent color is determined by the size. Tiny semiconductors known as quantum dots, are suspended in a solution.

- **Dendrimers:** Complex nanoparticles called dendrimers are made up of interconnected, branching components. An inner shell, an outer shell and a core comprise each dendrimer. Each dendrimer has branching terminals. A dendrimer's core, internal shell, external shell and branching ends can all be constructed to perform a particular chemical reason. Dendrimers can be formed via either a convergent method or a divergent one, beginning at the core and working outward.[20] Owing to the numerous molecular "hooks" found on their surfaces, dendritic molecules, that possess highly branching architectures, have been used in nanomedicine since the early 1980.[21]

- **Nanocomposites:** Nanocomposites combine nanoparticles with other nanomaterials or with bigger, bulk materials. According to their matrix, there are three different forms of nanocomposites: metal matrix nanocomposites (MMNC), polymer matrix nanocomposites (PMNC) and ceramic matrix nanocomposites (CMNC).

  CMNCs, which are often referred to as nanoclays, are frequently used in coating packaging materials. They improve the material's capacity to withstand heat and resist flame.

  Over bulk metals, MMNCs are more lightweight and more potent. MMCs can be utilized to manufacture vehicles that are light enough to be airlifted or to minimize heat in "server farms" of computers.

  Many industrial plastics contain PMNCs. Developing PMC "tissue scaffolding" is one promising field of nanomedical research. Nanostructures known as tissue scaffolds serve as supports for the growth of tissue, including skin and organs. Treatment for burn wounds and organ loss might be completely altered as a result of this.[22,23]

10. Classification of Nanoporous Materials: Nanoporous materials are categorized by the IUPAC as microporous with pore sizes of 0.2-2 nm, mesoporous with pore sizes of 2–50 nm, and macroporous with pore sizes of 50–1000 nm as revealed in **Fig. 5**.

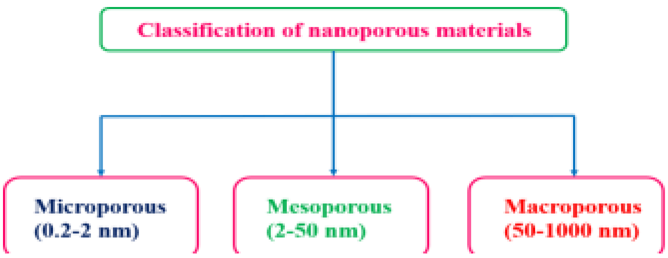

Figure 5: Classification of Nanoporous Materials

11. **Metal Oxide Nanomaterials:** The size and shape of the metal oxide nanomaterials are both related to their physicochemical characteristics.[26] Some of them exhibit chemical stability and biocompatibility.[27] According to reports, certain metal oxide nanomaterials are able to kill cancerous cells at low concentrations while being harmless to healthy cells. Recent research has broadened the potential uses of metal oxide nanomaterials in biomedicine, involving the therapy of cancer, biological sensors and retinopathy.[28,29] Many metal oxides can interact with carrier surfaces to form monolayer oxide structures for drug delivery.[30]

12. **Metal Oxide Nanocomposites:** Metal oxides often have two or more different types of metals. Oxides can be categorized as binary, ternary, quaternary and so on depending on the number of distinct metal cations they contain.[31] Chemistry researchers and material scientists are particularly interested in metal oxide because of its unique characteristics and substantial applications in a variety of sectors.[32] The characteristics and general application of composites are improved over those of single metal oxide. A nanocomposite is made up of many phases at least one of which must have a dimension smaller than 100 nm.

- **Synthesis Techniques of Metal Oxides Nanomaterials:** The top-down method for producing nanoparticles entails breaking up big particles into small fragments (as in a ball mill), whereas the bottom-up method assembles nanoparticle micelles atom by atom or molecule by molecule. The two primary steps in the bottom-up strategy are nucleation and growth. The assembly of atoms is shaped during the nucleation process, which is a significant phase alteration step. Studying nanocrystalline materials and how their size depends on their structures and features is crucial for understanding how crystals form and grow. The top-down and bottom-up categories are displayed in **Fig. 6**.

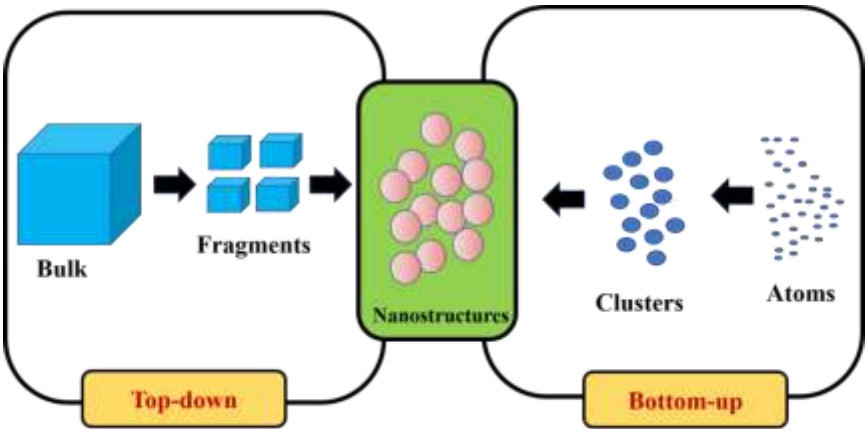

Figure 6: “Top-Down” and “Bottom-up” Synthesis Methods

- **Hydrothermal Method:** This synthesis is carried out in Teflon-lined autoclaves under controllable temperature, low pressure and aqueous solutions. A new method for the production of nanoparticles can be developed by combining this method with others. Hydrothermal-sonochemical processing and hydrothermal-microwave processing are two examples of such methods.

- **Co-precipitation Method:** The co-precipitation process entails the dissolution of salt precursors in water (or another solvent) such as chloride, acetate, oxychloride, sulfate, and nitrate. By adding a basic solution, that includes sodium hydroxide or the aqueous solution of ammonia, the relevant metal hydroxide compounds precipitate in water to produce metal oxides. The resulting solid was cleaned with acetone and distilled water to get eliminate the free salts. After filtration, the hydroxides are subsequently calcined to produce the powdered final oxides.[33, 34]

- **Sol-gel Method:** As indicated by the name, sol-gel combines two different kinds of materials: sol and gel. The general sol-gel method relies on the change of a system's phase from a liquid "sol" (usually a suspension of colloids of particles) to a gelatinous matrix "gel" phase. This method comprises two distinct reactions: first, the metal alkoxide is hydrolyzed to yield hydroxyl groups and then the hydroxyl molecules and remaining alkoxy groups are polycondensed to form a three-dimensional network. The sol-gel method produces amorphous nanoparticles that require additional heat treatment to become crystalline.[35]

- **Chemical Vapour Deposition (CVD) Method:** The CVD method is currently most likely the most popular bottom-up strategy. Today, it is employed to produce materials like nanotubes, nanowires, and nanoparticles. A variety of CVD procedures, including classical, plasma-assisted, metal-organic and photo CVD methodologies, are utilized to create nanoparticles. Although it necessitates a precise initial setup of the experimental settings, the positive aspects of this technology include producing homogenous, pure, and repeatable nanoparticles and films.[36]
- **Mechanochemical Method:** The area of solid-state chemistry known as mechanochemistry deals with the mechanical breaking of intermolecular interactions. The word "mechanochemistry" only refers to chemical reactions that occur after an external mechanical force directly breaks an intermolecular connection. The technique includes a variety of various steps, including milling steps like ball milling, jet milling, colloidal milling and manual grinding.

- **Combustion Method:** The combustion process is used to produce homogenous oxides of metal and their composite forms. An oxidizer, often precursor metal nitrates, and fuels like glycine, urea, and hydrazine after dissolving in water take part in a self-sustaining reaction throughout this synthesis. Two categories of combustion synthesis can be distinguished. Glycine, urea or hydrazine are utilized as a fuel in solution combustion synthesis (a), and citric acid is used as fuel in gel combustion synthesis (b) also known as the "pechini process."

III. APPLICATIONS OF NANOMATERIALS

The functionality of 0D, 1D, 2D and 3D nanostructured materials enhanced by the efficient, simple and fast synthesis procedures that provided fine control over the dimensions and morphology of the final products in various sectors like biomedical applications, energy storage, sensing, catalysis, etc. However, the formation of 0D, 1D, 2D and 3D-based nanomaterials will benefit the strengthening of our existing technology and deeper analysis will produce more striking results which might help both humanity and the industry.

Nanomaterials can indeed be observed in cluster centers, colloidal particles, quantum dots and nanocrystals. These nanostructures remarkable mechanical, optical, and electromagnetic features had already sparked a great deal of curiosity among researchers in the fields mentioned in **Fig. 7**.

Figure 7: Outline of nanomaterials in diverse fields

IV. ROLE OF NANOTECHNOLOGY IN BIOMEDICAL APPLICATIONS

A subfield of nanotechnology known as biomedicine employs nanomaterials for the diagnosis, treatment, and prevention of diseases to boost human health.[37] It is evident that nanotechnologies have arisen for a wide range of essential applications, from the scientific method to biomedicines and aerospace.[38] The prospective usage of nanotechnology in biomedical science comprises the preliminary recognition and cure of infections. The fast-growing field of biomedical science connects biology, technology and medicine.[39] The significant innovations in biomedicine and nanosystems are most likely to be driven by an understanding of manufacturing theories, and the design of projected ways to regulate them. An effective technique for disease diagnosis and therapy with minimal adverse effects is nano-biomedicines. Recently, the targeted delivery of drugs for cancer treatment has gained more attention.[40] Clinical diagnosis, immunization, medication and even medical products have all been impacted by nanoscience and nanotechnology. Chemical conjugation, physical impregnation or adsorption could be used to couple varied biochemical substances with nanomaterials. As illustrated in **Fig. 8**, the broad field of emergent nanotechnology for biomedical applications can be divided into four groups.

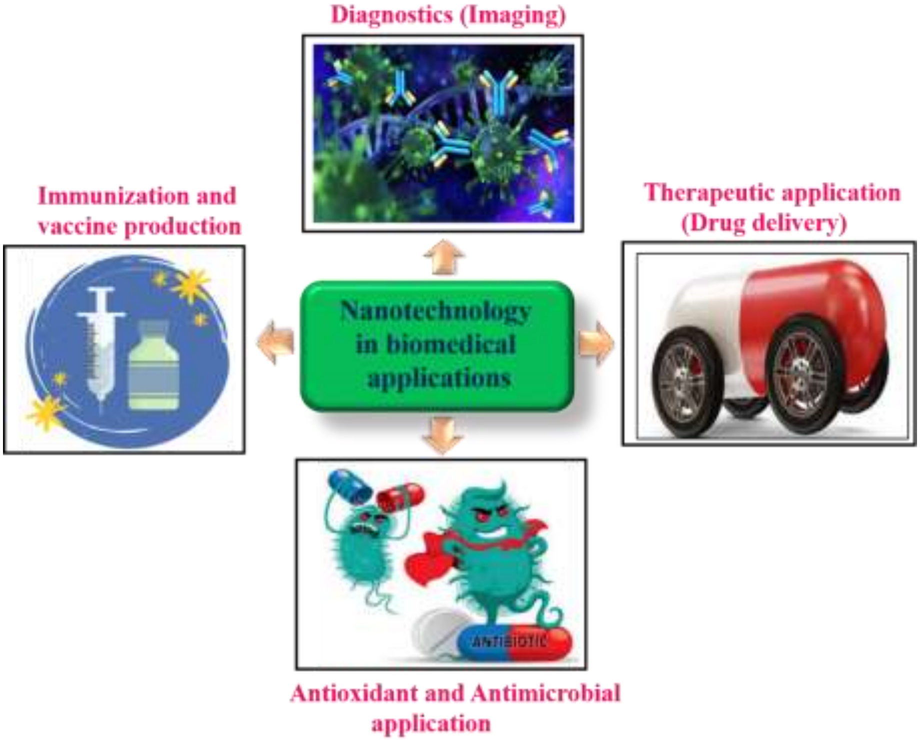

Figure 8: Biomedical applications of nanotechnology [6]

- **Biomedical applications of nanomaterials and their composite materials:** In general, the size and morphology of nanomaterials and composite including nanorods, nanosheets and nanogranular, greatly influence their physical and electrical characteristics. [41] Nanomaterials have significant potential for biomedical applications due to their tunable nanosize, biocompatibility, lack of toxicity and other properties. The dimension of nanomaterials is smaller than or equivalent to that of bio-entities such as 10–100 µm cells, 5–50 nm proteins, 10–100 nm genes and 20–450 nm viruses. The small size of nanomaterials and their composite materials is advantageous for interaction with bio-entities. To minimize their agglomeration and increase biocompatibility, surface modification of the nanomaterials is essential for application purposes by forming various compositions with metal oxides or surfactants. In order to successfully graft materials onto nanoscale objects, surface modification is necessary.

V. CONCLUSION

Nanomaterials are enchanting to the development of different technological aspects in exotics applications like antioxidant, antimicrobial, drug delivery, anticancer etc. due to their fascinating properties. Hence, with attention to the importance of nanomaterials, the present article encompasses the information of nanomaterials and innovation in biomedical applications based on nanomaterials has been discussed in detail.

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