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Application of Nanomaterials In Biomedicine

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ABSTRACT

Application of nanomaterials in biomedicine has an important place in research of nanomaterials. Nanomedical approaches are a major transforming factor in medical diagnosis and therapies. The great advantages of using nanomaterials in biomedical areas lies in their ability to operate on the same small scale as all the intimate biochemical functions involved in the growth, development and ageing of the human body. Achieving full potential of nanomedicine may be years of even decades away, however, potential advances in drug delivery, diagnosis, and development of nanotechnology-related drugs start to change the landscape of medicine. One of the main issues is certainly related to long-term safety of nanomaterials, both developed for in vitro and in vivo applications.

Introduction

Nanomaterials have unusual mechanical, dicine and pharmaceuticoptical, electrical and chemical behaviors, they have been widely used in meals for the sensitive detection of key biological molecules, more precise and safer imaging of diseased tissues, and novel forms of therapeutics etc. In the last two decades, a number of nanoparticle-based therapeutic and diagnostic agents have been developed for the treatment of cancer, diabetes, pain, asthma, allergy, infections, and so on. Although these nanoscale agents may provide more effective and/or more convenient routes of administration, extend the product life cycle, and ultimately reduce health-care costs, there is growing speculation about possible nanomaterial toxicity on the basis of in vitro cell-culture and in vivo animal studies. For example, carbon nanotubes can induce asbestos-like inflammation and granulomas in female mice[1]. The metabolism of CdSe Qdots leads to cadmium toxicity with adverse effects on the function, viability, and morphologic features of primary rat hepatocytes[2]. To date, there is no conclusive evidence of a known human toxic response that is specifically caused by nanomaterials. However, a study has showed that high doses of nanoparticle-based therapeutic agents led to reversible kidney toxicity,At present, people have started to pay attention to nanomaterial developments with less toxicity and more efficacy[3].

Now the applications of nanomaterials in medicine and pharmaceuticals have become a large subject area including nanomaterials that act as biological mimetics, nanomachines, nanofibers and polymeric nanoconstructs as biomaterials, and nanoscale microfabrication-based devices,In summary, the applications of nanomaterials in medicine and pharmaceuticals are very broad Considering that this field is currently expanding at a very fast speed, we cannot include all aspects of present nanomaterials in medicine and pharmaceuticals in details. In this review, we will provide an overview on nanomaterial developments with less toxicity and more efficacy in the fields of imaging and diagnosis, disease therapy, drug delivery and tissue engineering.[4].

Nanotechnology is enabling technology that deals with nano-meter sized objects. It is expected that nanotechnology will be developed at several levels: materials, devices and systems[5]. The nanomaterials level is the most advanced at present, both in scientific knowledge and in commercial applications.A decade ago, nanoparticles were studied because of their size-dependent physical and chemical properties [6].

Now they have entered a commercial exploration period[7].Living organisms are built of cells that are typically 10 µm across. However, the cell parts are much smaller and are in the sub-micron size domain. Even smaller are the proteins with a typical size of just 5 nm, which is comparable with the dimensions of smallest manmade nanoparticle [5]. This simple size comparison gives an idea of using nanoparticles as very small probes that would allow us to spy at the cellular machinery without introducing too much interference [9]. Understanding of biological processes on the nanoscale level is a strong driving force behind development of nanotechnology [10].Out of plethora of size-dependant physical properties available to someone who is interested in the practical side of nanomaterials,optical and magneticeffects are the most used for biological applications[11].

The aim of this review is firstly to give reader a historic prospective of nanomaterial application to biology and medicine, secondly to try to overview the most recent developments in this field, and finally to discuss the hard road to commercialisation. Hybrid bionanomaterials can also be applied to build novel electronic, optoelectronics and memory devices[12].

Nanomaterials have unique physicochemical properties, such as large surface area to mass ratio, ultra small size and high reactivity, which are different from bulk materials with the same composition. These properties can be used to overcome some limitations found in traditional therapeutic and diagnostic agents[13]. The application of nanomaterials in medicine and pharmaceuticals is increasing rapidly and offers excellent prospects. In this review, we will provided an overview on nanomaterial developments with less toxicity and more efficacy in the fields of imaging and diagnosis, disease therapy, drug delivery and tissue engineering. In summary, although these fields are still in their infancy, the present results have clearly demonstrated enormous potential[14].

Literature Survey

in (2000) Challa S and S. R Kumar [15] studied Nanomaterials are anticipated to revolutionize disease detection and treatment leading to the realization of a potential world market of medical

.This article provides an up to date summary of the current research investigations on Nanomaterials for medical applications. Nanomaterials have been categorized based on their shape, and within each shape they have been further categorized based on their chemical composition. Similarly, the medical applications have been categorized into four main sections:medical diagnosis, medical treatment, medical devices, and tissue engineering. Prior to the discussion of medical applications, approaches to biofunctionalization of nanomaterials are also presented as it is very important that the nanomaterials are compatible in biological environment for their application in medicine

in (2001) C. N. R. Rao and A. K. Cheetham [16] studied The science and technology of nanomaterials has created great excitement and expectations in the last few years. By its very nature, the subject is of immense academic interest, having to do with very tiny objects in the nanometer regime. There has already been much progress in the synthesis, assembly and fabrication of nanomaterials, and, equally importantly, in the potential applications of these materials in a wide variety of technologies. The next decade is likely to witness major strides in the preparation, characterization and exploitation of nanoparticles, nanotubes and other nanounits, and their assemblies. In addition, there will be progress in the discovery and commercialization of nanotechnologies and devices. These new technologies are bound to have an impact on the chemical, energy, electronics and space industries. They will also have applications in medicine and health care, drug and gene delivery being important areas. This article examines the important facets of nanomaterials research, highlighting the current trends and future directions. Since synthesis, structure, properties and simulation are important ingredients of nanoscience, materials chemists have a major role to play.

in (2002) Ellio L. Chaikof and Joachim Kohn.et al[17]studied Most approaches currently pursued or contemplated within the framework of reparative medicine, including cell-based therapies, artificial organs, and engineered living tissues, are dependent on our ability to synthesize or otherwise generate novel materials, fabricate or assemble materials into appropriate 2-D and 3-D forms, and precisely tailor material-related physical and biological properties so as to achieve a desired clinical response. This paper summarizes the scientific and technological opportunities within the fields of biomaterials science and molecular engineering that will likely establish new enabling technologies for cellular and molecular therapies directed at the repair, replacement, or reconstruction of diseased or damaged organs and tissues.

in (2004) J.H. Choy , J.M. Oh, M. Park , K. M. Sohn and J. W. Kim [19] studied A molecular-level coding method utilizing DNA base pairs as code units has been systemized. The system consists of four steps: encoding, encrypting, decrypting and decoding (see Figure), which are realized by tailor-made nanohybrids (DNA–layered double hydroxide (LDH) and polypyrrole–maghemite). The nanohybrids give solutions to the inherent problems which hamper DNA molecular code systems; stability in encrypting and rapidity in analysis.

in (2005) Feng Wang, Wee Beng Tan .el at. [20] studied The use of labelling or staining agents has greatly assisted the study of complex biological interactions in the field of biology. In particular, fluorescent labelling of biomolecules has been demonstrated as an indispensable tool in many biological studies. Types of fluorescent labelling agents that are commonly used include conventional classes of organic fluorophores such as fluorescein and cyanine dyes, as well as newer types of inorganic nanoparticles such as QDs, and novel fluorescent latex/silica nanobeads.

The newer classes of fluorescent labels are gaining increasing popularity in place of their predecessors due to their better optical properties such as possessing an enhanced photostability and a larger Stokes shift over conventional organic fluorophores, for example. This paper gives an overview of the recent advances on these luminescent nanomaterials with emphases on their optical characteristics that are crucial in fluorescence microscopy, both advantages and limitations in their usage as well as challenges they face, and puts forward the future direction of fluorescent labels in the area of biolabelling.

in (2006) Kumar and Challa S. S. R.,[21] studied This first comprehensive yet concise overview of all important classes of biological and pharmaceutical nanomaterials presents in one volume the different kinds of natural biological compounds that form nanomaterials or that may be used to purposefully create them. This unique single source of information brings together the many articles published in specialized journals, which often remain unseen by members of other, related disciplines. Covering pharmaceutical, nucleic acid, peptide and DNA-Chitosan nanoparticles, the book focuses on those innovative materials and technologies needed for the continued growth of medicine, healthcare, pharmaceuticals and human wellness. For chemists, biochemists, cell biologists, materials scientists, biologists, and those working in the pharmaceutical and chemical industries.

in(2007) Freddy E Escorcia, Michael R McDevitt.el at.,[22] studied Nanomaterials have garnered increasing interest recently as potential therapeutic drug-delivery vehicles. Among the existing nanomaterials are the pure carbon-based particles, such as fullerenes and nanotubes, various organic dendrimers, liposomes and other polymeric compounds. These vehicles have been decorated with a wide spectrum of target-reactive ligands, such as antibodies and peptides, which interact with cell-surface tumor antigens or vascular epitopes. Once targeted, these new nanomaterials can then deliver radioisotopes or isotope generators to the cancer cells. Here, we will review some of the more common nanomaterials under investigation and their current and future applications as drug-delivery scaffolds with particular emphasis on targeted cancer radiotherapy.

in (2008) Aniruddh Solanki, John D Kim and Ki-Bum Lee.,[23] studied Although stem cells hold great potential for the treatment of many injuries and degenerative diseases, several obstacles must be overcome before their therapeutic application can be realized. These include the development of advanced techniques to understand and control functions of microenvironmental signals and novel methods to track and guide transplanted stem cells. The application of nanotechnology to stem cell biology would be able to address those challenges. This review details the current challenges in regenerative medicine, the current applications of nanoparticles in stem cell biology and further potential of nanotechnology approaches towards regenerative medicine, focusing mainly on magnetic nanoparticle- and quantum dot-based applications in stem cell research.

in (2008) Bing Xu[24] Studied This perspective focuses on the potential uses of gels as materials in biological and medical applications. It describes how molecular self-assembly can confer well-defined secondary structures (e.g., nanofibers, nanotubes, and nanospheres) in a liquid that initiates functions within biological systems. Some prospects for future development and the challenges for achieving them are discussed.

in(2010) Zoraida P. Aguilar and Ysmael Aguilar.el at.[25] studied Nanomaterials are currently being developed for various biomedical applications. Engineered nanomaterials such as quantum dots, metal and semiconductor nanoparticles, and magnetic nanoparticles are among the new materials being studied for medical applications. Nanomaterials have unique properties that include diameters from 3-50 nm, high quantum yields, resistance against photobleaching, high magnetic and electric properties, and simultaneous excitation of multiple fluorescent colors. Quantum dots have unique emission spectra even with ordinary source of light. Magnetic nanoparticles are unique because of their highly magnetic nature. Magnetic nanoparticles are used in magnetic resonance imaging and targeted drug delivery while quantum dots are increasingly being used for biomedical imaging. We report the results of our studies on the applications of nanomaterials in medicine. These include cell imaging, tissue imaging, protein detection, drug delivery, and cell targeting. Preliminary studies indicated promising applications of nanomaterials in molecular imaging and in vitro diagnostics.

in(2011) Erin Lavik and Horst von Recum.[26]studied There are a range of definitions for nanomaterials and a range of length scales that are considered nano, but one thing is consistent among fields: nanomaterials are small and special. Nanomaterials have the potential to have tremendous impact on medical treatments. In one example, nanomaterials are permitting the tracking of cells via magnetic resonance imaging (MRI) in clinical trials to assess the efficacy and safety of cellular therapies. In a second example, nanomaterials are acting as drug delivery vehicles for the targeted delivery of therapies to increase efficacy and to reduce side effects. However, there are distinct challenges that must be considered in the development and application of these materials, including careful analysis of the distribution and clearance of nanomaterials and their potential off-target effects.

in (2012) Lifeng Dong and Michael M. Craig. el at.,[27] studied Due to nanoscale effects and increased surface area, nanomaterials have been investigated as promising tools for the advancement of diagnostic biosensors, drug and gene delivery, and biomedical imaging. In comparison to their larger counterparts, nanomaterials have unique physicochemical and biological properties. Many properties of nanomaterials, such as size, shape, chemical composition, surface structure and charge, aggregation and agglomeration, and solubility, can greatly influence their interactions with biomolecules and cells. For example, nanoparticles with size-tunable light emission have been employed to produce exceptional images of tumor sites; single-walled carbon nanotubes, having diameters comparable to the width of DNA molecules, have demonstrated an impressive potential as high-efficiency delivery transporters for biomolecules into cells. Therefore, the main emphasis of this special issue focuses on the development of some nanomaterials and their applications in biology and medicine.

in (2013) Sunil K. Singh Paresh P. Kulkarni and Debabrata Dash[28] studied Within the short span of a decade, nanotechnology has evolved into a truly interdisciplinary field undergoing rapid expansion, with the promise of new developments in every traditional scientific discipline. At the nanometer scale, the self-ordering forces and properties of materials seem to be different from those at the macroscale. The application of nanotechnology in biomedical fields is one of the major thrust areas that are currently gaining momentum, as all biological systems embody the principles of nanotechnology. The nanoscience tools that are currently well understood and those that will be developed in future are likely to have an enormous impact on biology, biotechnology, and medicine.

in (2014) Natalia Barkalina, Charis Charalambous. el at.,[29] studied In the last decade, nanotechnology has been extensively introduced for biomedical applications, including biodetection, drug delivery and diagnostic imaging, particularly in the field of cancer diagnostics and treatment. However, there is a growing trend towards the expansion of nanobiotechnological tools in a number of non-cancer applications. In this review, we discuss the emerging uses of nanotechnology in reproductive medicine and reproductive biology. For the first time, we summarise the available evidence regarding the use of nanomaterials as experimental tools for the detection and treatment of malignant and benign reproductive conditions. We also present an overview of potential applications for nanomaterials in reproductive biology, discuss the benefits and concerns associated with their use in a highly delicate system of reproductive tissues and gametes, and address the feasibility of this innovative and potentially controversial approach in the clinical setting and for investigative research into the mechanisms underlying reproductive diseases.

in (2015) Samir Mitragotri, Daniel G. Anderson, .el at.,[30]studied Due to their size and tailorable physicochemical properties, nanomaterials are an emerging class of structures utilized in biomedical applications. There are now many prominent examples of nanomaterials being used to improve human health, in areas ranging from imaging and diagnostics to therapeutics and regenerative medicine. An overview of these examples reveals several common areas of synergy and future challenges. This Nano Focus discusses the current status and future potential of promising nanomaterials and their translation from the laboratory to the clinic, by highlighting a handful of successful examples.

in (2016) Amy M. Wena and Nicole F. Steinmetz.,[31] studied This review provides an overview of recent developments in “chemical virology.” Viruses, as materials, provide unique nanoscale scaffolds that have relevance in chemical biology and nanotechnology, with diverse areas of applications. Some fundamental advantages of viruses, compared to synthetically programmed materials, include the highly precise spatial arrangement of their subunits into a diverse array of shapes and sizes and many available avenues for easy and reproducible modification. Here, we will first survey the broad distribution of viruses and various methods for producing virus-based nanoparticles, as well as engineering principles used to impart new functionalities.

in (2017) Tae-Hyun Shin and Jinwoo Cheon.,[32] studied Developing innovative tools that facilitate the understanding of sophisticated biological systems has been one of the Holy Grails in the physical and biological sciences. In this Commentary, we discuss recent advances, opportunities, and challenges in the use of nanomaterials as a precision tool for biology and medicine.

in (2018) Yilong Wang , Shuyang Sun .el at.,[33] Medical science has recently advanced to the point where diagnosis and therapeutics can be carried out with high precision, even at the molecular level. A new field of “precision medicine” has consequently emerged with specific clinical implications and challenges that can be well-addressed by newly developed nanomaterials. Here, a nanoscience approach to precision medicine is provided, with a focus on cancer therapy, based on a new concept of “molecularly-defined cancers.” “Next-generation sequencing” is introduced to identify the oncogene that is responsible for a class of cancers. This new approach is fundamentally different from all conventional cancer therapies that rely on diagnosis of the anatomic origins where the tumors are found.

in (2019) Mohammad Rabiee, Navid Rabiee, Reza Salarian and Ghazal Rabiee.,[34] studied Nanomaterials generally have a specific structure, growth factor, and physical and chemical environment depending on their defined functions. In this manner, their functions about biomedical application specifically in the tissue engineering are of importance. Remodeling of tissue has a direct connection with the mechanical environment, defined function and in general, the genetic sequence as well as direct connection to the nanomaterials that replaced with any functional natural materials. In this chapter, we will focus on the introduction of the nanomaterials and their application in the genetic information of biological tissue and their development, introduction to modeling considerations along with epigenetic mechanisms and the impact of the physicochemical environment on this process. Critical effective factors such as residual stresses, morphogenesis and other physicochemical points will also be discussed.

in (2020) N'Dea S. Irvin-Choy, Katherine M. Nelson, .el at.,[35] studed Pregnancy complications are commonplace and the challenges of treatment during pregnancy with few options available pose a risk to the health of both the mother and baby. Patients suffering from conditions such as preeclampsia, placenta accreta, and intrauterine growth restriction have few treatment options apart from emergency caesarean section. Fortunately, researchers are beginning to develop nanomedicine-based therapies that could be utilized to treat conditions affecting the mother, placenta, or fetus to improve the prognosis for mothers and their unborn children.

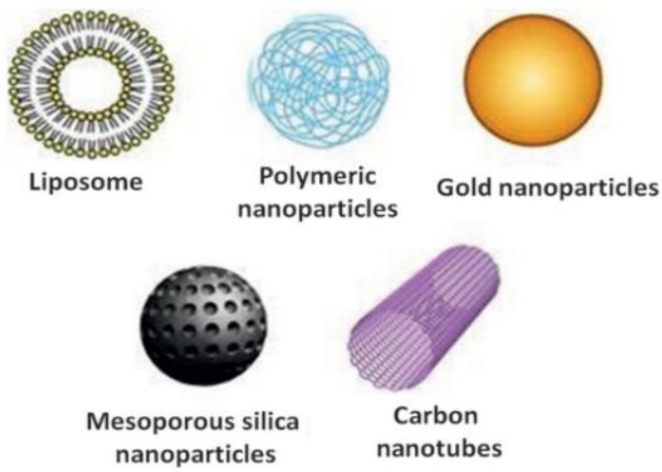
Aim of work

- Learn about the history and study of nanomaterials and the research of some scientists in the twentieth century.
- Understand the principles of nanotechnology.
- Identification of the properties of nanomaterials.
- Identification of the types of nanomaterials. -
- To identify the applications of nanomaterials at the present time and to benefit from - Its properties are in distinctive future applications.

Types of nanomaterials

Organic-based nanomaterials

As the name suggests, this class of NMs contains materials that are mainly composed of organic compounds, such as carbohydrates, lipids, or polymers that are in the range of 10 nm to 1 um. Polymeric nanoparticles have greater structural stability, integrity, and control, thus they have attracted great attention from researchers . These polymer NPs, along with several liposomes, dendrimers, and micelles, are widely implemented in drug delivery systems . These organic-based [40] nanoparticles are shown in Fig. 2. Polymer NPs form branched units

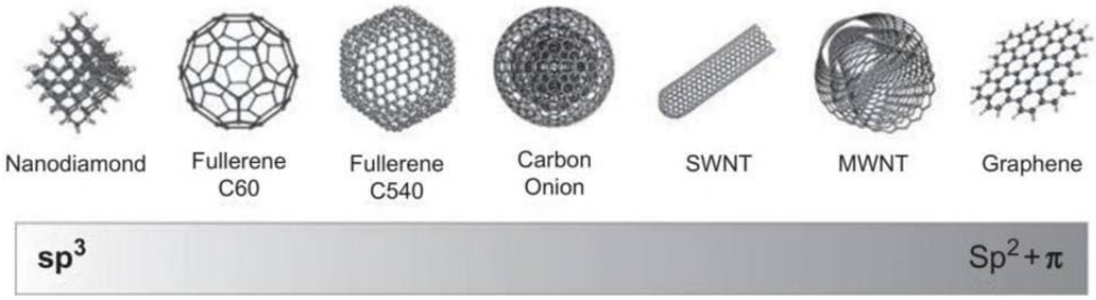


figure(2.1): Organic-based nanoparticles

and compose a nanomaterial. The dendrimer surface has chains in the end, which are tailored and used as catalysts to perform various chemical functions. The three- dimensional (3D) version of dendrimer accumulates other molecules inside its cavity, and is thus implemented in drug delivery systems

Carbon-based nanomaterials

In these nanomaterials, carbon is the main element and they exist in the form of ellipsoids, hollow spheres, and tubes. Graphite and diamond are allotropes of the most abundant element, carbon. The element carbon has a certain uniqueness and diversity in its struc- ture, with structures like 3D diamond and graphite, 2D graphite sheets, nanotubes in 1D, and fullerene in zero-dimension (Makhlouf and Barhoum, 2018). The structural config- uration and hybridization states of carbon strongly influence the electronic, physical, and chemical behavior of the nanomaterial. Carbon has six electrons and its ground state con- figuration is 1s´2s´2p". The low gap among 2s and 2p allows electron transition, thus sup- porting hybridization into sp, sp", or sp". The covalent bonding with neighbor atoms at higher levels provides energy to compensate for this configuration, which is the same for sp and sp hybridization. The unhybrid p-orbitals consider -bonding among them- selves . Thus diversity amnong the various organic compounds mainly occurs owing to the variable hybridization states. Substantial differences can be observed among configura- tions of carbon's bulk, which is presented in Fig. 3. The promising trigonometric sp configuration exists for diamond at high pressures and temperatures.[42]



Figure(2.2): Carbon-based nanomaterials and their hybridization states

in the heat formation, the planar sp configuration adds up, thus forming a single-layered sheet structure with single -bond and three sigma covalent bonding. Slight shear forces and chemical-physical separation induce weak interplanar forces among graphene sheets, and induces slip-up among them .

and its types :

a- Graphene c- Nanotubes

b- Fullerenes d- Nanodiamond

Inorganic-based nanomaterials

Metals and metal oxide-based NMs, along with ceramic-based NMs, are part of the class of inorganic-based NMs, and exhibit unique electronic and optical features on the nano- scale. Clay is a natural inorganic NM that has evolved from the Earth's crust due to variant chemical circumstances. Similarly, cement, pigments, and fumed silica are obtained from volcanic eruptions. On the other hand, metal and metal oxide-based NMs are engineered nanoparticles, which have attracted significant attention. Inorganic quantum dots are usually semiconductors in the range of 2-10 nm and exhibit unique features like bright- ness and photo stability, which are widely implemented in diagnostics and therapeutic gears [43].

and its types :

a- Metallic nanostructures

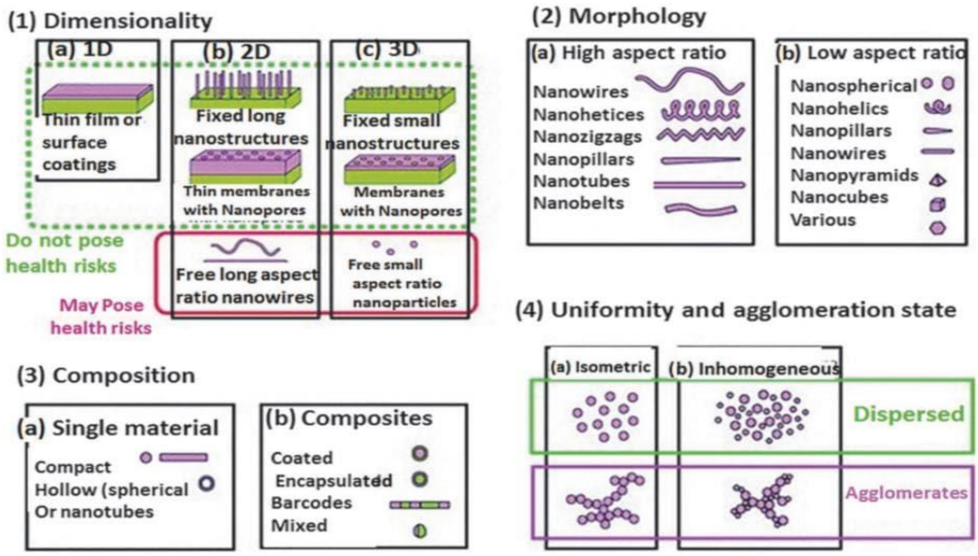
b- Metal oxides

c- **Composite-based nanomaterials**

The next class of nanomaterials is composite nanoparticles, which are made by the com- bination of two or more different materials, mixed together in order to merge their best properties. This fusion of features leads to overcome the detriments of individual mate- rials and increase the benefits of the fused compound fornmed. This nanocomposite is a solid material, which may have many phases, but one dimension of any of the phases must be in the nanoscale. Such as a many nanoparticles made of multiple materials combine in order to form a composite nanomaterial with unique features.These composite-based nanomaterials are either the comnbination of organic-organic NMs, inorganic-inorganic NMs, or organic-inorganic NMs, also known as hybrid NMs. The organic component or network of mainly organic polymers fuse together with the inorganic parts, like metal oxides or metal oxo polymers at the nano- scopic level, coupled via covalent or noncovalent bonding . Many natural nanocomposites like eggshell, abalone shell, and bones exist. Many kinds of nano- composites like metal-metal, ceramic-metal, ceramic-ceramic, polymer/nonpolymer- based, polymer-ceramic, carbon-metal, and carbon-polymer nanocomposites, have been formed with improved physio-chemical, mechanical, and biological characteristics, with extraordinary flexibility. Recently, the most popular nanocomposites have been of poly- mer, layered silica, and metal-organic rameworks [44].

2.3 Classification of nanomaterials

Materials having size equal to 100nm or less are said to be nanomaterials. There are a variety of materials, either naturally occurring or synthesized by different methods, cur- rently known, and it is expected that more will be discovered. The concept of calcifica- tion of nanomaterials was first propOsed by Gleiter in 1995. This classification of NMs is done on the basis of crystalline form as well as chemical compo- sition. The classification scheme of Gleiter was not fully complete because it did not include the dimensionality of nanostructures. In 2007, a new classification scheme of NMs was introduced by Pokropivny and Skorokhod, which includes dimensional clas- sification (0D, 1D, 2D, and 3D) as well as components. NMs can exist in any form such as single, cluster, spherical, fused, and irregular, fibers, tubes, etc. Classifications of NMs according to their composition, dimension, morphology, uniformity, and agglomeration state are given in Fig. 3. Nanomaterials have different characteristics compared to normal materials and are used in a variety of fields, such as nanotechnology , air purification [45].



Figure(2.3): Classification of nanomaterials

, water purification, medical devices, reactive membrane , etc.

Types of nanomaterials according to dimension

According to dimensions, nanomaterials are divided into four types:

- zero-dimensional (0D)
- one-dimensional (1D)
- two-dimensional (2D)
- three-dimensional (3D)

Zero-dimensional nanomaterials

Materials in which electron motion is confined along all directions within the system are said to be 0D NMs. The simplest example of 0D nanomaterials is nanoparticles. Other than nanoparticles, atomic clusters, filaments, etc. are also OD NMs . It contains materials that have all their properties within size less than 100 nm and in these materials length and width both are equal [46].

The 0D NMs can be ofany form, such as given below:

- crystalline or polycrystalline
- amorphous or crystalline
- single or multichemical elements
- contains many shapes and forms .

and its types :

a- Quantum dots

One-dimensional nanomaterials Nanomaterials

such as nanofibers (Choi et al., 2003), nanowires , and nanotubes are 1D NMs. In these, the electrons are confined in two dimensions (x&y or y&z or z&x) with undefined surface boundaries and allowed to move only in 1D. They are used in various fields such as thin films in electronic engineering, reflectors and computer chips, etc. These NMs contain all properties greater than 100nm, and in this, length is much greater than width. Deposition of thin film of 1D nanomaterials is done in a controlled manner; this deposited layer is known as a monolayer. For synthesizing 1D NMs, different techniques are used, such as vapor deposition, electro deposition, etc. Different materials such as nanowhiskers, nanocables, and nanofibers are also included in one-dimensional NMs. However, each material has different diam- eter ranges; for example, whiskers and fibers range from several nm to a hundred microns . ZnO nanowires are an example of a 1D nanomaterial [47].

and its types :

a- Nanotubes

b- Nanowires

Two-dimensional nanomaterials

The materials such as nanosheets, nanoribbons, graphene, nanofilms, nanolyers, and nanocoating are included in 2D NMs .In two dimensional nanomaterials, the electrons are confined in one dimension only and cannot move freely in this direction. They also have large aspect ratio (length and width relation). These materials possess high mechanical flexibility as well as optical transparency. The two-dimensional NMs are synthesized by using different synthesis techniques such as bottom-up and top-down lithography. These materials have gained attention due to their applications in a variety of fields such as electronics, biomedicines, sensors, photodetectors, battery electrodes, topological insulators, etc. . Due to their size characteristics and specific geometry, 2D NMs can be utiUzed in a variety of nanode vices [48].

It is an example : Graphene and hexagonal boron nitride

Three-dimensional nanomaterials

The nanomaterials in which electrons are not confined to any dimension—tenned as delocalized electrons—are said to be 3D NMs. Three dimensional NMs are also known as bulk materials and contain arbitrary direcdons beyond lOOnm. The materials containing equiaxed nm-sized grains are included in the 3D NMs category . These materials have high absorption capability and large surface area, due to which they are taken into account in research fields and applications. Due to these properties, they are used for transportation of molecules or drugs. 3D NMs can be found in various structural fonns such as nanocoils, nanoflowers, nanoballs, nanocones, nanopillars, etc [49] .

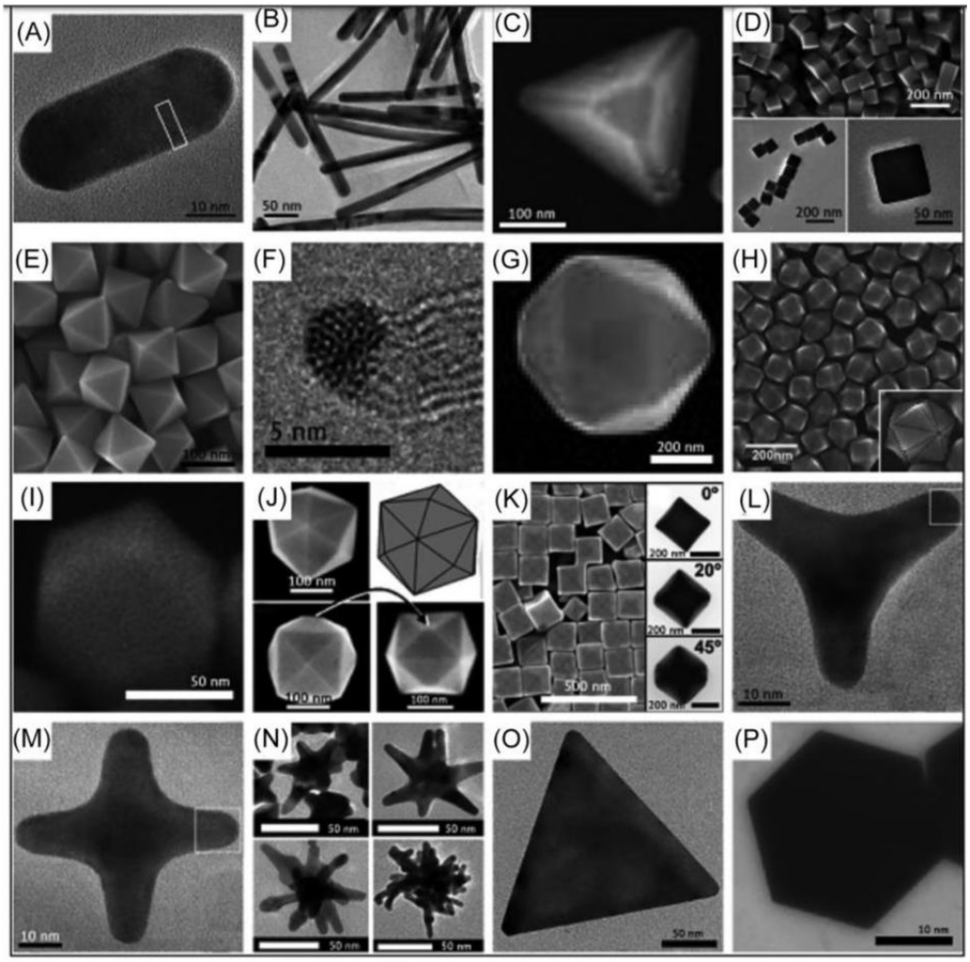
It is an example : Dendrimers

High aspect ratio nanoparticles

On the basis of morphological characterization nanoparticles can be divided into,

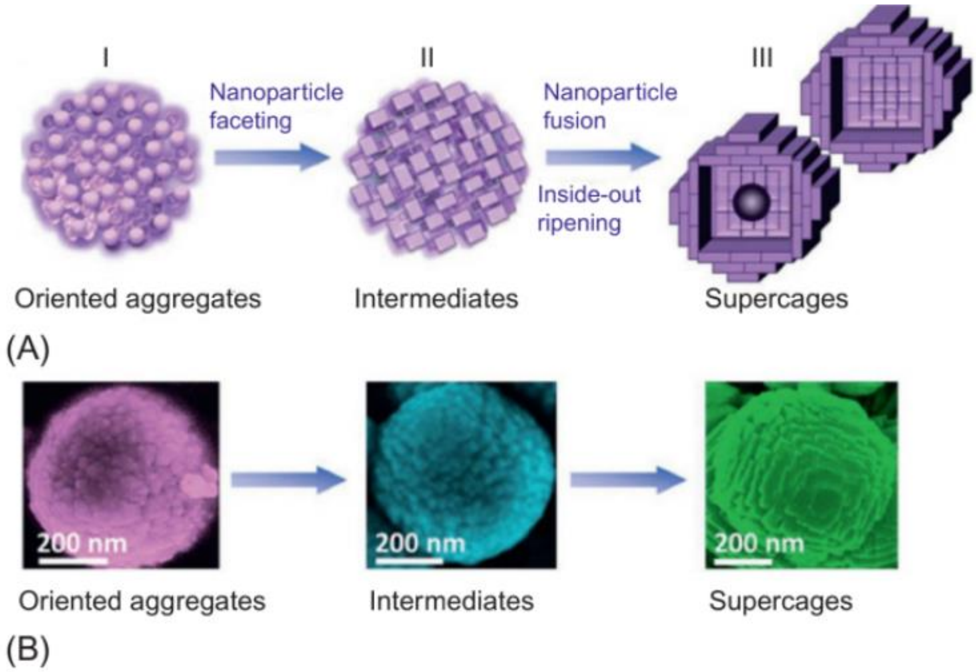
- nanorods
- nanohooks
- nanohelices
- nanostars
- nanospnng
- nanoplates

Some of the above examples are shown in Fig. 4.



Figure(2.3.2): SEM/TEM images of different types of nanoparticles. (A) Au octagonal single-crystal rod, (B) Au pentagonally twinned rods, (C) Au tetrahedron NP, (D) Pd hexahedron (i.e., cube) NPs, (E) Au octahedron NPs, (F) decahedron, (G) Au icosahedron NP, (H) Au trisoctahedron NPS, 0) Au rhombic dodecahedron NP, () Pt tetrahexahedron NPs, (K) Au concave hexahedron NPs, (L) Au tripod NP, (M) Au tetrapod NP, (N) Au star NPS, (0) Au triangular plate/prism NP, and (P) Au hexagonal plate/ prism NP[50].

As discussed earlier, on the basis of morphology, nanoparticles can also classified basedon aspect ratio. High or long aspect ratio nanoparticles include carbon and palladium nanotubes or silicon nanowires and silver nanowires.Complex morphologies such as core-shell and spherical core-shell are also possible; these include CdSe-CdS and Pd-Cu core-shell nanoparticles[51].

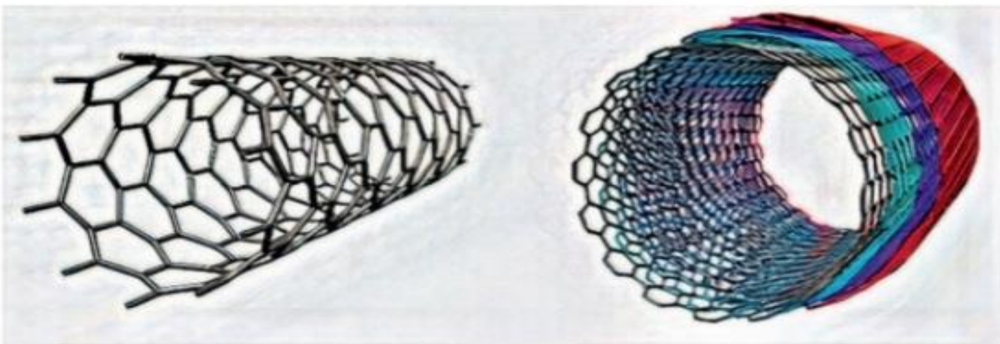


Figure(2.3) :(A) Schematic sketch of the development process of BaTiO3 supercages and (B) SEM images showing the morphology transition process .

Figure(2.3) explains the complex morphologies of barium titanate nanoparticles. There is a large body of data available on the subject of nanomaterials or nanoparticles due to the colossal importance it holds in fields like physics, chemistry, and the medical industry.

Nanotubes

In nanotechnology, nanotubes are mostly referred to as carbon nanotubes. Nanotubes have been the most discussed morphology of nanoparticles for a long time because of their intriguing applications. Nanotubes can be made from boron nitride in the case of inorganic nanoparticles and from peptide proteins in the case of organic nanoparticlesCarbon nanotubes, however, have the most interesting applications and properties. Carbon nanotubes are shown in [12]. Figure(2.3):



Figure(2.3): an image of carbon nanotubes.

Nanomaterials Applications

Nanomaterials in medicine and pharmaceuticals: nanoscale materials developed with less toxicity and more efficacy

The application of nanomaterials in imaging and diagnosis

In recent years, it was found that nanomaterials possessed many advantages in bioimaging field. For example, non-invasive and deep tissue penetration by the near-infrared (NIR) excitation, sharp visible emission lines, long fluorescence lifetime, superior photo-stability, and the high signal-to-background ratio etc. This indicates that some nanomaterials may be a new generation of probes for bioimaging and have great potential utility in early-stage diagnosis of diseases. Some imaging modalities including optical imaging (OI), magnetic resonance imaging (MRI), ultrasound imaging (UI), and radionuclide imaging (RI), have been developed today [55].

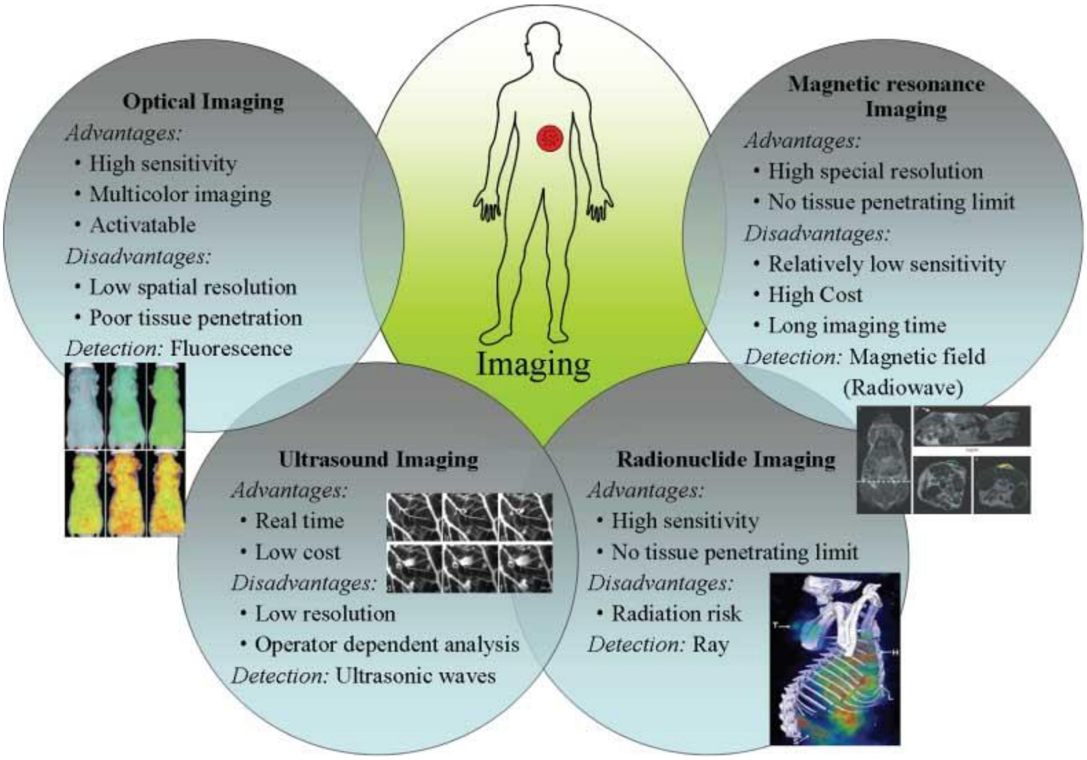


Figure (2.4) Main imaging modalities of nanomaterials used for biomedical fields.

Optical imaging (OI)

OI is an important and challenging technique in the biomedical field due to its high temporal and spatial resolutions. In living organisms, OI employs a sensitive camera to detect fluorescence emitted from fluorophores [56]. Conventional fluorophores, generally including organic fluorophores, quantum dots, fluorescent proteins and luminescent transition metal complexes, have been widely used. Among them, fluorophores with long emission at the NIR region are generally preferred in living tissue for their great properties such as the lower autofluorescence and greater penetration depth . It was reported that lanthanide (Ln)-doped upconversion nanoparticles (UCNPs) had tremendous advantages over conventional fluorophores, such as low cytotoxicity, non-photobleaching, non-photoblinking and high spatial resolution etc . Chatterjee et al. reported that UCNPs could enhance penetration depth into tissues upon NIR excitation [57]. In addition, there is a significant decrease of auto-fluorescence from surrounding tissues . Due to the low vibration energy, fluoride-based UCNPs have also been identified as one of the most efficient upconversion fluorescent nanoparticles nowadays Chatterjee et al. have further demonstrated that the luminescence from Ln-doped UCNPs could be still clearly observed upon NIR excitation when the nanoparticles were located ~10 mm beneath the skin in vivo animal imaging. In summary, Ln-doped UCNPs hold great potential as novel fluorophores in biomedical field [58]..

Magnetic resonance imaging (MRI)

MRI is a non-invasive imaging technique, which uses a strong magnet and radiofrequency waves to produce images of internal organs. Colloidal iron oxide nanoparticles (IONPs) generally produce enhanced proton relaxation rates at significantly lower doses than paramagnetic ions due to their larger magnetic moment, and provide negative contrast by enhancing T2 relaxivity of water protons. So, colloidal IONPs, such as superparamagnetic iron oxides (SPIOs) and ultra superparamagnetic iron oxides (USPIO), have been widely explored in MRI field. Several SPIO agents with a variety of surface coatings have been extensively studied for the detection and diagnosis of solid tumors It was found that SPIOs were mostly taken by macrophages in the liver and spleen and subsequently metabolized over several days after intravenous injections. Active targeting of SPIOs can lead to increased contrast enhancement of tumors over non-targeted tissues. SPIOs functionalized with antibodies have been used to image rectal carcinoma and breast cancer . Although passive targeting of iron oxide NPs to tumors can be achieved through the EPR effect, a range of molecules have been attached on their surface to improve tumor targeting for MRI applications, including proteins, antibodies, peptides, and oligosaccharides. Researchers have recently shown preferential accumulation of SPIOs functionalized with a targeting peptide overexpressed in MMP-2 glioma tumors . Folic acid, a vitamin, is another ligand, which has been extensively used as targeting agent. Iridium complexes have been loaded into magnetic NPs for dual-modal luminescent and magnetic resonance imaging[59]..

USPIO with diameters <40 nm have also been clinically investigated as contrast agents, which can accumulate at the margins of human brain tumors, improve their delineation on MRI. Researchers have compared the utility of USPIOs with Gd-chelates for brain-tumor MRI and found that USPIOs could offer prolonged delineation due to lower diffusion from tumor sites and increased internalization by tumor cells [60].

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