# Chapter 7

# Unification of biosciences and nanotechnology - properties, synthesis, application, and regulatory issues

**Tanya Tarun[1], Smita Lata[2]* and Shalini Mehta[3]**
[1]B.Tech Biotechnology, Amity University, Jharkhand, India
[2]Teaching Assistant, Department of Biotechnology, Amity University, Ranchi, Jharkhand, India
[3]Assistant professor, Department of Botany, Ranchi Women's College, Ranchi, Jharkhand, India
*Corresponding author email:- smitalata3036@gmail.com
DOI- https://10.5281/zenodo.8423845
Corresponding author: https://orcid.org/0000-0003-2922-6698
1st Co-author: https://orcid.org/0009-0008-1426-5372
2nd Co-author: https://orcid.org/0000-0002-4130-2211

***Received:-***
10th September, 2023
***Accepted:-***
7th October, 2023
***Published:-***
(online)
27th October, 2023

**ABSTRACT:-** During the last few years, nanotechnology became one of the most investigated and explored field given the fact that nano based materials proved to have interesting, challenging, and promising characteristics suitable for various biomedical applications. The field was subject to a growing public controversy and awareness in the early 2000s and in turn the beginnings of commercial applications of nanotechnology. The newly emerging field of Nano-biotechnology is the unification of nanotechnology and biotechnology and this hybrid discipline can mean making atomic-scale machines by imitating or incorporating biological systems at the molecular level or studying the natural structural properties atom by atom.This chapter illustrates the extensive application of nanotechnology in the medical field. Some nanoparticles are being used as diagnostic instrument, targeted medicinal or pharmaceutical product, tissue enginerring, biomedical implants etc.

*Citation:* Tarun, T., Lata, S., Mehta, S. (2023). Unification of biosciences and nanotechnology - properties, synthesis, application, and regulatory issues. *Advances in Bioscience: Exploring Frontiers of Discovery, Vol. 1, ISBN: 978-93-5913-645-5. pp. 63-90. https:// 10.5281/zenodo.8423845*
*Editor: Dr. Anand Kumar Thakur, Email id: fmruanand@gmail.com*

this chapter present concise summary on properties of nanoparticles, its synthesis method, application in medical field and regulatory challenges in application of nanotechnology for biomedical purposes.

**Keywords:** Nanotechnology, Nanofluid, Drug delivery, Nanocrystal, Pharmacokinetics.

## 1. INTRODUCTION

Over the past 30 to 40 years, the synthesis of novel engineered materials, particularly nanomaterials, has increased significantly. These materials have a wide range of applications in engineering, waste management, sports equipment, electronics, optics, clothing, food, and cosmetics, which cover almost all facets of daily life[1]. This special issue discusses many ways that nano- and bio-technology are combined to use innovative materials in medical field like medicine, medical eqipments etc. There are a variety of opportunities in the medical field due to the special properties of materials at the nanometer scale and the ability to manipulate and tailor their physical-chemistry at the scale where biomolecular interactions occur. These opportunities include early detection of biomarkers, precise targeting of cells and tissues, sophisticated drug delivery systems, staging and assessing disease, and treatment of degenerative conditions[2]. At least one dimension of engineered nanomaterials must be less than 100 nm[2,3]. This concept is flexible in medicine and could, for instance, refer to a nano-drug having particles that are 200 nm or larger[4]. Furthermore, the word "nanoparticle" can be used to refer to a variety of shapes that are less than 100 nm in diameter, including organic (such as lipids, biopolymers) and inorganic nanomaterials (such as metals, oxides, and carbon) that are not spherical, such as cubes, stars, needles, spheroids, or designed shapes with complex geometries. However, the synthetic method such as the physical and chemical method used for the creation of nanoparticles increases their environmental toxicity. Nanoparticle formed by physical method generates lots of heat. Chemically generated nanoparticles have drawbacks such as chemical use and self-accumulation in an aqueous solution. Another drawback was the price of creating synthetic nanoparticles. In addition, "green nanotechnology" is now being considered as an alternative tool to manufacture nano-products and processes that are capable of battling high energy consumption and rising environmental toxicity in order to give society a friendly environment. By avoiding the use of hazardous chemicals in the manufacture of nanomaterials, green nanotechnology has established a position in the idea of a sustainable environment. It is being used to provide affordable techniques for creating nanoparticles that do not harm people or the environment[3].

## 2. PROPERTIES OF NANOPARTICLES

Nanomaterials are substances with unique qualities resulting from their tiny particle size. In many cases, the latter definition restricts nanomaterials to grain sizes below 10 nm[5]. Because nanomaterials are costly, the second definition is the more realistic one. A costly substance without unique features is useless. Some nano-crystalline ceramic or nano-glass materials with particle sizes under 10 nm have remarkable physical characteristics[6]. These are the characteristics of single, isolated particles, with the exception of those that pertain to grain boundaries. In a situation where the particles contact, these unique characteristics can be lost. Nanocomposites are required because of this occurrence. Nanomaterials have structural characteristics that fall somewhere between those of atoms and those of bulk materials. The properties of materials with nanoscale dimensions are very different from those of atoms and bulk materials, even though most microstructure materials share characteristics with the equivalent bulk materials. At this nanoscale, materials act differently for two reasons: Firstly, very small particles cover more surface area than the same amount of material crushed into a larger lump (such as when sand grains cover more surface area than the same amount of sand in a stone). Larger surface areas can make materials more reactive because the surface of the particle is involved in chemical interactions. For instance, salt grains dissolve in water much more quickly than salt rocks. Some substances, which are often inactive in their bigger forms, may actually be more reactive at the nanoscale. Second, as we examine materials at the nanoscale level, the relative relevance of the various physical law's changes, and factors that we often overlook (such as quantum effects) become more important, particularly at sizes smaller than 20 nm. Nanomaterials are already recognized to have a wide range of unique properties due to their nanoscale size. Numerous uses for nanoparticles in the field of medicine have also been suggested as a result of their unique properties.

## 2.1 MECHANICAL PROPERTIES

Covalent, metallic, ionic, and other types of atom-atom bonding determine a material's mechanical properties. Thus, even the finest materials could have intrinsic weaknesses, strengths, or brittleness. In addition to these factors, lubrication, coagulation, and surface coating also influence the mechanical properties of NPs[7]. All qualities are impacted by the presence of impurities. Materials often consist of single crystals when their size is decreased to the nanoscale. Grain size and material hardness are connected,there is a linear relationship between particle size and hardness for copper in the micrometer grain size range. It grows as grain size increases. Palladium nanoparticles and microparticles exhibit similar findings a thorough understanding of the fundamentals of the mechanical properties of NPs, including their elastic modulus and hardness, movement law, friction, and interfacial adhesion, as well as their size-dependent features, is typically necessary for successful results in fields of medical science[7]. Because of this property, it has wide applications like a polymer of nano-Ag can be used as an effective fungicide, nano-Ag and nano-Cu can increase the antibacterial properties of commercial particleboard and also increases its lifespan[8].

## 2.2 STRUCTURAL PROPERTIES

Small clusters or nanoparticles are more than mere fragments of the larger substance. Nanomaterials can have radically distinct structures, bonds, and bond strengths. Consider silicon crystal as an example. Diamond structure forms when silicon crystallizes in large quantities. Small groups of silicon atoms can be thought of as pieces of the unit cell. However, it has been discovered that the lattice parameters may not be the same as in bulk materials, even while some nanomaterials with a slightly higher atom count (>50–60 atoms) may obtain bulk crystalline atoms. Other tiny particles exhibit up to 2.3% less lattice constant deviations than bulk crystalline materials. The crystal structure is also significantly impacted by pressure and temperature. Small ZnS particles were observed to change from their previously disorganized structure to a wurtzite (hexagonal) structure when the temperature was raised. Additionally, when the chemical capping that is frequently utilized in the creation of nanoparticles is removed; the particles have a tendency to cluster or agglomerate into larger particles. One of the most crucial methods for identifying the structural characteristics of NPs is

XRD. It provides proper information regarding the crystallinity and phase of NPs. Through the Debye-Scherer formula, it also provides a general concept of particle size[9-12]. The nanometric size makes it easy to interact with the human body's biological mechanisms that allow crossing membrane pores to access new delivery sites and interact with small proteins at different levels of DNA[13,14].

## 3. OPTICAL AND ELECTRICAL CONDUCTIVITY

Due to the importance of optical features in photocatalytic applications, photo chemists have developed a solid understanding of this method to explain how their photographic chemical reactions. These descriptions are supported by the well-known Beer-Lambert Law and fundamental lighting concepts[15]. These methods provide details on the NPs' absorption, reflectance, luminescence, and phosphorescence characteristics. It is well known that NPs in particular Metallic and semiconductor NPs are colored and have different properties. Hence, optimized for applications using photos Due to their unusual optical characteristics, which set them apart from bulk crystals significantly, nano-crystalline systems have generated a lot of interest. Important contributing elements include efficient energy and charge transmission over nanoscale distances, quantum confinement of electrical carriers within nanoparticles, and in many systems, a substantially enhanced role of surfaces. Understanding the detailed basis of nanophotonic characteristics is becoming more and more important with the advancement of these materials applications. By carefully regulating the crystal size and the chemistry of these materials surfaces, one may finely control their linear and nonlinear optical properties. As a result, the fabrication technique becomes crucial for the applications. With the help of an outside stimulus like electrons, photons, or an electric field, luminescence can be stimulated in various molecules or materials. Doped or undoped semiconductor nanoparticles show enhanced luminescence in comparison to their bulk counterparts. Because of this property, they function as transducers in biosensors, providing high electrical conductivity and optical sensitivity to a very small detection limit[16,17].

### 3.1 THERMAL PROPERTIES

Metal NPs are known to have thermal conductivities that are higher than fluids in solid form. For instance, copper has a thermal conductivity that is approximately 3000 times larger than motor oil and 700 times greater than water at ambient temperature. The thermal conductivity of even oxides, like alumina ($Al_2O_3$), is greater than that of water. Consequently, it is anticipated that the fluids containing suspended solid particles will have significantly improved thermal conductivities compared to those of traditional heat transfer fluids. The formation of nanofluids involves distributing solid particles of nanometric sizes in a liquid, such as water, ethylene glycol, or oils. The properties of nanofluids are predicted to be better than those of conventional heat transfer fluids and fluids with microscopic-sized particles. It is preferable to use particles with a large total surface area since heat transfer occurs at the surface of the particles. Nanofluid has two important characteristics required for heat transfer systems: extreme stability and ultra conductivity. Recently, nanofluid has a wide range of applications in the biomedical industry[18]. Nanofluids have been used in nano-medicine applications as iron-based NPs can be used as nanodrug delivery vehicles[19]. These fluids can also be used in cancer treatment as they can kill the cancerous cells by producing high temperatures around tumours without affecting nearby healthy cells[20].

**4. SYNTHESIS OF NANOPARTICLES**

The pharmaceutical manufacturing of nanomaterials involves two different approaches: (1) Bottom-up approaches and (2) Top-down approaches[21]. Depending on how they work, how a reaction occurs, and the protocols they use, these techniques are further divided into a number of subclasses.

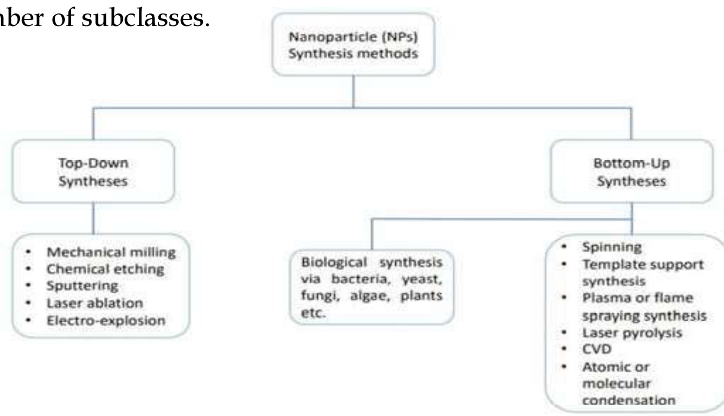


**Figure 1. Examples of common top-down and bottom-up approaches to developing NPs[40].**

## 4.1 TOP-DOWN SYNTHESIS

This methodology starts with a bigger molecule, which broke down into smaller components, these units were then transformed into appropriate NPs. Examples of this approach include grinding and milling, CVD (Chemical Vapour Deposition), PVD (Physical Vapour Deposition), and other breakdown processes[22]. This method is used to create coconut shell (CS) NPs. For this, the milling process was used, and the raw CS powders were finely ground for various lengths of time using ceramic balls and a well-known planetary mill. Through a variety of characterization approaches, they were able to demonstrate the impact of milling time on the total size of the NPs. Scherer equation calculations showed that the size of the NP crystallites diminishes as time goes on. They also noticed that the reddish color gradually faded away with each hour increment due to the NPs' decreasing size. The SEM results confirmed the X-ray pattern, which also showed that particle size decreased over time[23]. One study demonstrated the top-down destructive synthesis of spherical magnetite nanoparticles (NPs) from natural iron oxide ($Fe_2O_3$) ore with particle sizes ranging from 20 to 50 nm in the presence of organic oleic acid[24]. It was possible to create spherical particles of colloidal carbon with a controlled size using an easy top-down method. The polyoxometalates (POM) were continuously chemically adsorbed on the carbon interfacial surface as the basis for the synthesis method. Adsorption reduced the size of the carbon black aggregates into spherical particles with a high capacity for dispersion and a limited size distribution[25].

The micrographs also showed that the size of the carbon particles decreased over the course of the sonication. From their bulk crystals, a series of transition-metal dichalcogenide nanodots (TMD-NDs) were created using a mix of grinding and sonication top-down methods. Due to their limited size range, nearly all TMD-NDs with diameters smaller than 10 nm exhibit exceptional dispersion[26]. Recently, top-down laser fragmentation, which is a top-down method, was used to create highly photoactive active $CO_3O_4$ NPs. The intense laser beams create NPs with good oxygen vacancies that are uniform[27].

## 4.2 BOTTOM-UP SYNTHESIS

This method is used in reverse to top-down method since NPs are created from relatively simpler materials; for this reason, it is also known as the building-up method. Techniques like sedimentation and reduction serve as examples in this situation. It involves spinning, biological synthesis, green synthesis, and general chemical synthesis[28]. For the photocatalytic degradation of methylene blue, they synthesized the photoactive composite using alizarin and titanium isopropoxide as precursors. Alizarin was chosen because of its potent ability to attach to $TiO_2$ via its axial hydroxyl terminal groups. The XRD pattern verified the anatase form. SEM reveals that as the temperature rises, NP size also does so[29]. Using a laser irradiation top-down approach, well-uniform monocrystalline spherical Au nanospheres have been created. By adjusting the laser treatment time and other reaction parameters, Liu *et al*. selectively convert the octahedra morphology to a spherical shape[30,31]. Recently, the solvent-exchange approach has been employed to produce limit-sized low-density lipoprotein (LDL) NPs with the aim of delivering cancer drugs to patients. Nucleation is the bottom technique in this procedure, and growth is the up approach. The LDL NPs were created without the use of phospholipids and had a high level of hydrophobicity, which is crucial for applications involving drug delivery[32]. While bismuth was transformed into molten form and then the molten drop was emulsified within the cooked diethylene glycol to make the NPs in the top-down approach, bismuth acetate was boiled within ethylene glycol in the bottom-up method. The NPs produced by both procedures ranged in size from 100 nm to 500 nm[33].

The bottom-up synthesis that is green and biogenic is becoming increasingly popular among researchers due to its viability and less hazardous nature. These technologies, which accomplish NP synthesis through biological systems like using plant extracts, are economical and environmentally beneficial. The manufacture of NPs involves the utilization of bacteria, yeast, fungi, Aloe Vera, tamarind, and even human cells. Au NPs have been created using the biomass of wheat and oats as well as plant and microbial extracts as reducing agents[34,35]. An environmentally friendly technique to create nanoparticles is by using the biological method, which is provided as an alternative to chemical and physical methods. Additionally, none of the expensive, hazardous, or toxic ingredients is needed for this procedure[36]. Bacteria are obvious targets in the manufacture of nanoparticles due to their rapid development, affordable cost of culture, and ease of control and manipulation of the growing environment. In addition, it is well known that several bacteria species have unique ability to suppress the toxicity of metals or heavy metals. For these reasons, bacteria are favored since they can produce nanoparticles both in- and ex-situ. Metal ions can be reduced and precipitated to create nanoparticles by using reducing agents found in bacteria, such as proteins and enzymes, and biochemical pathways[37,38]. Algae are eukaryotic aquatic photo sites that use pigments, proteins, carbohydrates, lipids, nucleic acids, and secondary metabolites to break down metallic ions into nanoparticles. The synthesis of nanoparticles that may have antimicrobial properties without generating any toxic by-products is accomplished by adding metal solutions of the appropriate pH and concentration to the algae extract that already exists in an aqueous medium at a specific temperature[39,40]. Plants are a promising, quick, and cost-effective way to remove metal-borne contaminants since they have a high capacity for detoxification, reduction, and accumulation of metals. Metallic nanoparticles with varied morphological traits can be created both inside and outside of cells. Extracts from plant parts including leaves, roots, and fruits are added to a solution of metal ions to start the synthetic process. The plant extract, which contains components including sugar, flavonoids, proteins, enzymes, polymers, and organic acids, acts as a reducing agent and is responsible for the bioinduction of metal ions into nanoparticles[39-42].

## 5. BIOLOGICAL APPLICATIONS OF NANOPARTICLES

Target-specific drug delivery, molecular imaging, and other clinical uses of nanobiotechnology are all currently being systematically researched. These advanced bioscience applications will surely change the fundamentals of diagnosis, therapy, water purification, environmental impact, and illness prevention. Below are some of these uses discussed[43,44].

### 5.1 DIAGNOSTIC DETECTION:

Most diseases are currently diagnosed through visual symptoms appearing first, which allows medical experts to identify the patient's illnesses. However, the probability of a successful response to treatment may have decreased by the time those symptoms have shown. Therefore, the probability of finding a cure increases with earlier disease detection. By detecting the binding of a particular antibody to the illness-related

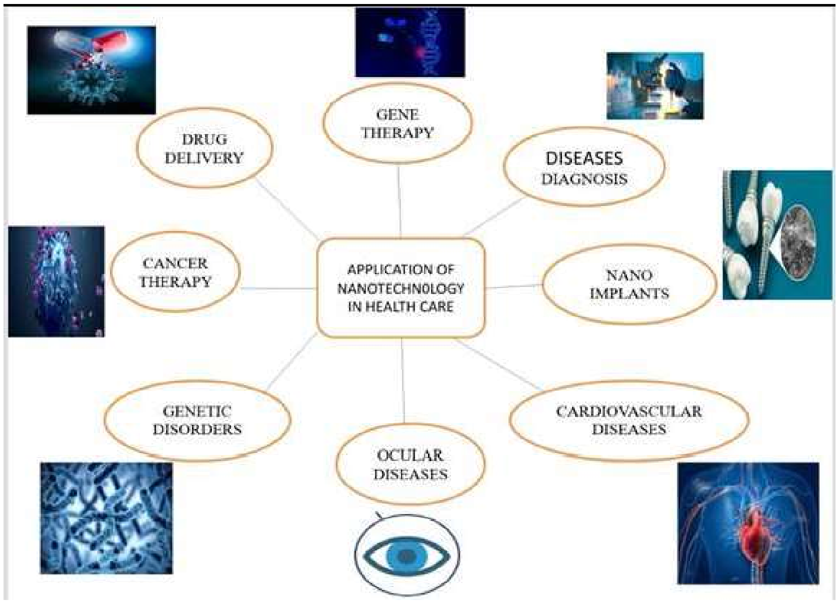


**Figure 2: Application of nanotechnology in health care[43].**

target, many presently used/conventional clinical tests can identify the presence of a molecule or an organism that causes a disease. Such tests are often carried out by conjugating the antibodies with inorganic/ organic dyes and observing the signals inside the samples using electronic or fluorescence microscopy. The specificity and viability of the detection methods are frequently constrained by dyes, though. Utilizing semiconductor nanocrystals (also known as "quantum dots"), nanobiotechnology provides an option. Compared to normal organic molecules, which more easily degrade, these tiny probes can resist a substantial number of cycles of excitations and light emissions[45]. In gold, both light scattering and absorption are particularly effective. The possibility of gold nanoparticles to diagnose cancer quickly and simply is now being explored by researchers[46]. The epidermal growth factor receptor (EGFR), a protein found on the surface of many cancer cells, is absent from healthy cells. Researchers successfully delivered and attached gold nanoparticles to cancer cells by fusing EFGR antibodies to the nanoparticles[47]. The cancer cells were found by using a field dark microscopy apparatus as bright spots. These nanoparticles are unable to stick to healthy cells. This makes the healthy cells look darker than the cancerous cells. This technology for cancer diagnosis is quicker and less expensive than other traditional methods. According to this study, these nanoparticles can connect to tumor cells with a strength that is hundreds of times greater than that of ordinary healthy cells. It is possible to analyze various molecules using multiple probes at once since each nanoparticle absorbs and scatters light differently depending on its shape and size. The appealing feature of this technology is that it can be used with just a basic optical microscope and does not require any expensive equipment, such as sophisticated microscopes[48].

**5.1 INDIVIDUAL TARGET PROBES**:

The medical community will continue to favor optical and colorimetric detections regardless of the benefits of magnetic detections. One of the companies that created methods that enable medical professionals to optically detect the genetic material of biological specimens is Nanosphere. The foundation of the simple-to-read test for the presence of any certain genetic sequence consists of nanogold particles studded with brief DNA segments. In the event that the sequence of interest is present in the samples, it connects to complementary DNA tentacles on numerous nanospheres to create a visual web of gold balls. With far higher sensitivity than currently available tests, this technique allows for or simplifies the detection of harmful organisms and has demonstrated encouraging results in the detection of anthrax[49].

**5.3 PROTEIN CHIPS: - NUTRITIONAL SNACKS**

The biological phenotype of organisms in both healthy and pathological states is mostly determined by proteins, which are a better indicator of functionality. Proteomics is crucial for the development of pharmaceuticals that can change signaling pathways and for the diagnosis of disease. Protein chips can be treated with chemical groups or tiny protein modules that can bind only to proteins with a certain structural or biochemical pattern[50]. Agilent, Inc. and Nano Ink, Inc. are two companies that are active in this application field at present. Agilent prints oligos and entire cDNAs at the nanoscale onto glass slides to create microarrays using a non-contact ink-jet technology. Dip-pen nanolithography (DPN) technology is used by Nano Ink to construct structures at the nanoscale[51].

**5.4 SPARSE CELL DETECTION: -**

For example, cancer cells, lymphocytes, fetal cells, and HIV-infected T cells are examples of sparse cells that are rare and physiologically different from their surrounding cells in normal physiological conditions. However, it is difficult to identify and then isolate these sparse cells. Nanobiotechnology presents new opportunities for advancement in this field. Scientists have created nanosystems that are capable of identifying and isolating these sparse cells. This method utilizes or benefits from the special qualities of sparse cells, which can be seen in variations in deformation, surface charges, and affinity for particular receptors and/or ligands. For instance, cells can be precisely sorted according to surface charge by introducing electrodes into microchannels. Additionally, they can be sorted utilizing biocompatible surfaces that have precisely sized nanopores. Currently, the Cornell University Nano-Biotechnology Center (NBTC) is utilizing these technologies to create potent diagnostic tools for the isolation and identification of numerous diseases[52].

**5.5 APPLICATIONS IN DRUGS DELIVERY: -**

The development of novel nanodevices that can be used in a wide range of physical, biological, biomedical, and pharmaceutical applications, as well as nano-sized inorganic particles of either simple or complex nature is becoming increasingly important[53,54]. Therapeutic nanoparticles can be administered to specific places, even those that are difficult for conventional medications to access. If a treatment can, for instance, be chemically linked to a nanoparticle, it can then be directed to the site of the disease or infection by radio or magnetic signals. These nanodrugs may also be programmed to "release" only in the presence of particular molecules or in response to outside signals (such as infrared heat). Based on their optical characteristics, NPs are chosen to produce effective contrast for biological and cell imaging applications as well as for photothermal therapeutic applications. Many medications, whose poor bioavailability prevents oral administration, will now be able to be used in treatment utilizing nanotechnology[55,56]. Agents that undergo degradation or denaturation when exposed to high pH are protected by nano-formulations, which also extend half-life via increasing retention of the effects of a medication bio-adhesion-based synthesis[57]. The transfer of antigens for immunization is another widespread application of nanotechnology[58,59]. Recent developments in encapsulation and the creation of appropriate animal models have shown that microparticles and nanoparticles can improve immunization[60]. The advantages of the nanostructures in drug delivery include the following: (a) drug distribution that can be achieved by various physical damages to tissues[61]. (b) By concentrating the drug dose in the target area with the help of nanomaterials, ordinary drug losses will be reduced[62] (c) Nanosystem efficiency in agitated tissues is enhanced by improved microvascular permeability in tumors, leading to improved retention and transport Enhanced permeability and retention-like extravasation of nanoparticles from the vasculature into tuberculosis granulomas in zebrafish and mouse models[63]. (d) Nanosystems are capable of suppressing tumors and inflammatory tissues preferentially[64]. Formulation and characterization of nano liposomal 5-fluorouracil for cancer nano therapy. (e) Nanomaterials are able to cross the blood-brain barrier, demonstrating their potential for use in the treatment of brain cancer[65]. (f) Drug-loaded nanoparticles alter cellular transport in biological engineering and science, enhancing the efficacy of drug delivery while reducing the risk of adverse consequences[66]. Advances in oral nano-delivery systems for colon targeted drug delivery in inflammatory bowel disease: selective targeting to diseased vs healthy tissue. Nanodiamonds may be used as fluorescent biomarkers for the detection of many diseases, including Alzheimer's disease[67]. Functionalization of stable fluorescent nanodiamonds toward reliable detection of biomarkers for Alzheimer's disease

**5.7 BIOMOLECULAR ENGINEERING APPLICATION: -**

The supply of bioactive molecules is constrained by the cost and time associated with traditional biomolecule design. Techniques for nanoscale assembly and synthesis offer an alternative to conventional approaches. Due to the ability to conduct chemical and biological reactions on solid substrates as opposed to conventional solution-based procedures, improvements can be made. Utilizing a solid substrate typically results in less waste and far more exact biomolecule manipulation. Engines, a company based in Waltham, Massachusetts, invented the field of biomolecular engineering. The company created engineered genomic operating systems that produce programmable biomolecular machines using organic and inorganic building blocks. These biomolecule machines have a wide range of commercial applications, including those for biosensors, chemical synthesis and processing, bioelectronic devices and materials, nanotechnology, functional genomics, and drug discovery.

**5.8 NANOTECHNOLOGY IN DENTAL CARE:**

One of the most widespread oral disease-related conditions in the world, dental caries is highly expensive[68]. Dental-related solutions derived from nanotechnology aim to reduce or even completely eradicate the clinical impact of caries by improving the remineralization process and managing biofilm growth[68]. Antibacterial resins may be used in restorative and orthodontic dentistry in clinical settings[69]. These resins could be employed as bracket or branked bonding materials in orthodontics and as filling or denture base materials in restorative dentistry[69]. Therefore, a technique for adding AgNPs to acrylic resin denture-base materials was devised to enhance their physico-mechanical properties and antibacterial effects[70]. Dental materials and implants are more susceptible to contamination and subsequent colonization processes because the mouth cavity is an active ecosystem that is typically populated by a variety of pathogenic bacteria[71]. The inclusion of silver-based nano systems inside adhesive resins[72,73], orthodontic cements[74,75], and dental composite have shown promise in terms of better antibacterial activity.

**The following is a list of the different benefits of nanotechnology in biological applications:**

- Nanoparticles employed in biotherapeutics can be utilized in blood-brain barrier (BBB) medicine delivery, brain tissue engineering, and cellular and molecular imaging[76].
- Nanoparticles can easily change their shape and size to adapt to drug absorption[77].
- The pharmacokinetic strategies of drug molecules, such as bio distribution and bioavailability, have been shown to be particularly useful in nanoscale drug delivery processes. Rugs are released in a precise and effective manner, including tissue-specific drug delivery with a reduction in adverse effects[78].
- Enhancing drug absorption, increasing water solubility and dissolving, and avoiding enzymatic degradation are all benefits

of nano-carrier-based oral pharmaceutical delivery[79].

- For the progress of biosensors in many cancer kinds, nanomaterials that have excellent thermal, mechanical, optical, & and electrical properties are on the horizon[80].
- Because they are neutral and biodegradable, protein-based nanostructures are widely used in biotherapeutics to encapsulate active chemicals.
- The efficiency of anticancer medicines is increased while side effects are decreased by targeted delivery, which involves coupling pharmaceuticals with tumor-specific receptors and antibodies or other cell surface markers[81].
- Due to the similarities between the sizes and structures of nanoparticles and those of biological components and structures, they are frequently used in in vitro biomedical research.
- In comparison to traditional medication administration, nanoscale drug delivery results in a greater drug concentration at the target site[82].

## 6. REGULATORY CHALLENGES OF APPLICATION OF NANOTECHNOLOGY FOR BIOMEDICAL PURPOSE:

### 6.1 NANOMEDICINES IN THE PHARMACEUTICAL MARKET: -

Nanomedicines have been successfully introduced into clinical practice over the last few decades, and ongoing advances in pharmaceutical research are producing more sophisticated ones that are now being tested in clinical trials. In the European Union, the nanomedicine market is composed of nanoparticles, nanocrystals, nanoemulsions, liposomes, polymeric-protein conjugates, and nano complexes[83].

### 6.2 MARKET ACCESS AND PHARMACOECONOMICS

After a nanomedicine receives marketing authorization, there is a long road ahead before it is used in clinical practice in all EU countries. This is because drug pricing and reimbursement decisions are made at the individual level in each EU member state[84]. The multidisciplinary process of Health Technology Assessment (HTA) is being developed in order to provide patients access to medicines. HTA generates information about medicine safety, effectiveness, and cost-effectiveness to assist health and political decision-makers[84].

Pharmacoeconomics studies are currently playing an important role prior to the commercialization of nanomedicines. They use indicators such as quality-adjusted life expectancy years and hospitalization to assess both the social and economic importance of the added therapeutic value. The EUnetHTA was established to harmonize and improve the introduction of new medicines into clinical practice in order to provide patients with novel medicines. The primary goal of EUnetHTA is to create decisive, relevant, and transparent information to assist HTAs in EU countries. Currently, EUnetHTA is working on Joint Action 3 until 2020, with the main goal of "defining and implementing a sustainable model for scientific and technical cooperation in health." [84].

**6.3 NANOMEDICINES AND NANOSIMILARS:**

Nanomedicine includes medical products that are both biological and non-biological. Biological nanomedicines are derived from biological sources, whereas non-biological complex drugs (NBCD) are derived from non-biological sources, with the active principle consisting of various synthetic structures[85]. Several parameters must be demonstrated in order to introduce a generic medicine into the pharmaceutical market, as described elsewhere. A more comprehensive analysis that goes beyond plasma concentration measurement is required for both biological and non-biological nanomedicines. A stepwise comparison of bioequivalence, safety, quality, and efficacy in comparison to reference medicine is required, which leads to therapeutic equivalence and, ultimately, interchangeability[86].

**7. FUTURE PROSPECT**

The promise of advanced breakthroughs in robotics, communications, genetics, and medicine served as an encouragement for the development of nanotechnology. However, this method creates many of the same challenges as any new technology, such as issues with toxicity and the effect of nanomaterials on the environment[87]. Even if there are various disagreements, this technology offers great hope for the future. By taking a significant part in a variety of biomedical applications, such as medication administration, gene therapy, molecular imaging, biomarkers, and biosensors, it may result in innovations. Target-specific medication therapy and early illness diagnosis and treatment techniques are two of these applications that are the main research goals at the moment[88]. Output, methane content, and biocomposting. In order to increase the yield of methane produced through AD procedures, it is necessary to gain more in-depth insights into the impacts of NPs on the microbial population and waste digestion process. Due to the complicated microbial population, studying commercial scale is extremely complicated. Due to their high volume ratio and potential for excessive reactivity, NPs are suitable for a variety of reactions. As a result, NP types and concentrations should be altered or adjusted according to the effects observed in commercial production. As a result, NPs in bio-composting research produce nutrient-rich compost that is stable and mature by international standards. One of the most important future technologies is nanotechnology, which has the potential to solve some of the world's most pressing problems, including shortages of water and pollution, energy shortage and demand, wellness and health maintenance, agricultural productivity, and biodiversity management. Various governmental and scientific organizations control nanotechnology, as they do with other new technologies, to maximize advantages and reduce potential hazards. Most governments provide voluntary laws, directives, or guidelines when a new technology emerges with unknown concerns, but once thorough research is finished, governmental restrictions become necessary to reduce any potential problems connected with the technology. Similar actions were taken in relation to nanotechnology before and after 2010, which marks the technology's emergence and widespread application, respectively[89].

## 8. CONCLUSION

We provided a thorough overview of Nanoparticles their synthesis, physiochemical properties, and applications in this chapter. Because of their small size and large surface area, Nanoparticles are a good choice for a variety of applications. Although there are many uses for NPs, their unrestrained use and discharge into the environment pose some health risks that should be taken into account in order to make their use more convenient and environmentally acceptable. The creation of novel drugs as well as the reformulation of current ones has been helped by the expansion of nanomedicine research. Some of the modifications that nanotechnology introduces in medications include changes in toxicity, solubility, and bioavailability profiles. At some time, these developments' consequences will be so pervasive that they will likely have an impact on almost every area of science and technology. There are numerous applications for nanobiotechnology in medicine. Drug delivery systems are just one example of an innovation that represents the beginning of something new. Nanotechnology has the potential to one day heal many diseases for which there is currently no treatment.

**9. REFERENCES**


1. Bayda, S., Adeel, M., Tuccinardi, T., Cordani, M., & Rizzolio, F. (2019a). The history of nanoscience and nanotechnology: From chemical–physical applications to nanomedicine. *Molecules*, 25(1): 112. https://doi:10.3390/molecules25010112
2. Ratner, B. D. (2019). Biomaterials: Been there, done that, and evolving into the future. *Annual Review of Biomedical Engineering*, 21(1): 171–191. https://doi:10.1146/annurev-bioeng-062117-120940
3. Razack, S. A., &Duraiarasan, S. (2020). A way to create a sustainable environment. *The ELSI Handbook of Nanotechnology*, 359–425. https://doi:10.1002/9781119592990.ch14
4. Contera, S., Bernardino de la Serna, J. and Tetley, T.D. (2020). 'Biotechnology, nanotechnology and medicine', *Emerging Topics in Life Sciences*, 4(6): 551–554. . https://doi:10.1042/etls20200350
5. Laurent, S., Forge, D., Port, M., Roch, A., Robic, C., Vander Elst, L., & Muller, R. N. (2008). Magnetic iron oxide nanoparticles: Synthesis, stabilization, vectorization, physicochemical characterizations, and biological applications. *Chemical Reviews*, 108(6): 2064–2110. https://doi:10.1021/cr068445e
6. Dreaden, E. C., Alkilany, A. M., Huang, X., Murphy, C. J., & El-Sayed, M. A. (2012). The golden age: Gold nanoparticles for Biomedicine. Chem. Soc. Rev., 41(7): 2740–2779. https://doi.org/10.1039/c1cs15237h
7. Guo, D., Xie, G., & Luo, J. (2013a). Mechanical properties of nanoparticles: Basics and applications. *Journal of Physics D: Applied Physics*, 47(1): 013001. https://doi:10.1088/0022-3727/47/1/013001
8. Taghiyari, H.R., Moradi-Malek, B., Kookandeh, M.G., Bibalan, O.F. (2014). Eûects of silver and copper nanoparticles in

particleboard to control Trametes versicolor fungus, *Int. Biodeterior. Biodegrad.* 94: 69-72. https://doi:10.1080/17480272.2020.1847186

9. Khan, I., Abdalla, A., & Qurashi, A. (2017). Synthesis of hierarchical WO3 and BI2O3/WO3 nanocomposite for solar-driven water splitting applications. *International Journal of Hydrogen Energy*, 42(5): 3431–3439. https://doi:10.1016/j.ijhydene.2016.11.105
10. Khan, I., Ali, S., Mansha, M., & Qurashi, A. (2017). Sonochemical assisted hydrothermal synthesis of pseudo-flower shaped bismuth vanadate (BIVO4) and their solar-driven water splitting application. *Ultrasonics Sonochemistry*, 36: 386–392. https://doi:10.1016/j.ultsonch.2016.12.014
11. Khan, I. *et al.* (2017) 'Sonochemical assisted synthesis of RGO/zno nanowire arrays for photoelectrochemical water splitting', *Ultrasonics Sonochemistry*, 37:669–675. https://doi:10.1016/j.ultsonch.2017.02.029.
12. Ullah, H., Khan, I., Yamani, Z. H., & Qurashi, A. (2017). Sonochemical-driven ultrafast facile synthesis of SNO2 nanoparticles: Growth mechanism structural electrical and hydrogen gas sensing properties. *Ultrasonics Sonochemistry*, 34: 484–490. https://doi:10.1016/j.ultsonch.2016.06.025
13. Mbunge, E., Muchemwa, B., Batani, J., (2021). Sensors and healthcare 5.0: transformative shift in virtual care through emerging digital health technologies. *Glob Health J*, 5(4):169-177. https://doi.org/10.1016/j.glohj.2021.11.008
14. Rodrigues, J.J.F., Paulovich, F.V., de Oliveira, M.C., de Oliveira, J.O.N. (2016). On the convergence of nanotechnology and big data analysis for computer-aided diagnosis. Nanomedicine, 11(8): 959-982. https://doi.org/10.2217/nnm.16.35
15. Swinehart, D. F. (1962). The beer-lambert law. *Journal of Chemical Education*, 39(7):333. https://doi:10.1021/ed039p333
16. Holzinger, M., Goff, A.L., Cosnier, S., (2014). Nanomaterials for biosensing applications: a review. *Front Chem.* 63(2):1-10 . https://doi.org/10.3389/fchem.2014.00063
17. Kwiatkowski, M., Bezverkhyy, I., Skompska, M. (2015). ZnO nanorods covered with a TiO2 layer: simple solegel preparation,

and optical, photocatalytic and photoelectrochemical properties. *J. Mater Chem A.* 3:12748–12760. https://doi.org/10.1039/C5TA01087J.

18. Haile, E., Shankar, B., (2015). A steady MHD boundary-layer flow of water-based nanofluids over a moving permeable flat plate. *Int J Math Res*, 4: 27–41. https//doi:10.18488/journal.24/2015.4.1/24.1.27.41.
19. Shawgo, R.S., Richards Grayson, A.C., Li, Y., (2002). Cima MJ. BioMEMS for drug delivery. *Curr Opin Solid State Mater Sci*. 6:329–34. http://dx.doi.org/10.1016 .
20. Jordan A, Scholz R, Wust P, Fähling H. (1999). Magnetic fluid hyperthermia (MFH): cancer treatment with AC magnetic field induced excitation of biocompatible superparamagnetic nanoparticles. *J Magn Magn Mater*. 201:413–9. http://doi.10.1016/S0304-8853(99)00088-8. org/10.1016 .
21. Wang, Y., & Xia, Y. (2004). Bottom-up and top-down approaches to the synthesis of monodispersed spherical colloids of low melting-point metals. *Nano Letters*, 4(10): 2047–2050. https://doi:10.1021/nl048689j
22. Iravani, S. (2011). Green synthesis of metal nanoparticles using plants. *Green Chemistry*, 13(10): 2638. https://doi:10.1039/c1gc15386b
23. Bello, S. A., Agunsoye, J. O., & Hassan, S. B. (2015). Synthesis of coconut shell nanoparticles via a top down approach: Assessment of milling duration on the particle sizes and morphologies of coconut shell nanoparticles. *Materials Letters*, 159: 514–519. https://doi:10.1016/j.matlet.2015.07.063
24. Priyadarshana, G., Kottegoda, N., Senaratne, A., de Alwis, A., & Karunaratne, V. (2015). Synthesis of magnetite nanoparticles by top-down approach from a high purity ore. *Journal of Nanomaterials*. 1–8. https://doi:10.1155/2015/317312
25. Garrigue, P., Delville, M.-H., Labrugère, C., Cloutet, E., Kulesza, P. J., Morand, J. P., & Kuhn, A. (2004). Top"down approach for the preparation of colloidal carbon nanoparticles. *Chemistry of Materials*, 16(16): 2984–2986. https://doi:10.1021/cm049685i
26. Zhang, X., Lai, Z., Liu, Z., Tan, C., Huang, Y., Li, B., … Zhang, H. (2015). A facile and universal top-down method for

preparation of monodisperse transition-metal dichalcogenide Nanodots. *AngewandteChemie International Edition*. 54(18): 5425–5428. https://doi:10.1002/anie.201501071

27. Zhou, Y., Dong, C.-K., Han, L., Yang, J., & Du, X.-W. (2016). Top-down preparation of active Cobalt Oxide Catalyst. *ACS Catalysis*, 6(10): 6699–6703. https://doi:10.1021/acscatal.6b02416
28. Iravani, S. (2011). Green synthesis of metal nanoparticles using plants. *Green Chemistry*, 13(10): 2638. https://doi:10.1039/c1gc15386b
29. Mogilevsky, G., Hartman, O., Emmons, E. D., Balboa, A., DeCoste, J. B., Schindler, B. J., Karwacki, C. J. (2014). Bottom-up synthesis of anatase nanoparticles with graphene domains. *ACS Applied Materials & Interfaces*, 6(13): 10638–10648. https://doi:10.1021/am502322y
30. Liu, D., Li, C., Zhou, F., Zhang, T., Zhang, H., Li, X., … Li, Y. (2015). Rapid synthesis of monodisperse au nanospheres through a laser irradiation -induced shape conversion, self-assembly and their electromagnetic coupling SERS enhancement. *Scientific Reports*, 5(1). https://doi:10.1038/srep07686
31. Liu, J., Liu, Y., Liu, N., Han, Y., Zhang, X., Huang, H., … Kang, Z. (2015). Metal-free efficient photocatalyst for stable visible water splitting via a two-electron pathway. *Science*, 347(6225): 970–974. https://doi:10.1126/science.aaa3145
32. Needham, D., Arslanagic, A., Glud, K., Hervella, P., Karimi, L., Høeilund-Carlsen, P.-F., … Walke, P. (2016). Bottom up design of nanoparticles for anti-cancer diapeutics: "put the drug in the cancer's food." *Journal of Drug Targeting*, 24(9): 836–856. https://doi:10.1080/1061186x.2016.1238092
33. Wang, Y., & Xia, Y. (2004). Bottom-up and top-down approaches to the synthesis of monodispersed spherical colloids of low melting-point metals. *Nano Letters*, 4(10): 2047–2050. https://doi:10.1021/nl048689j
34. Ahmed, S. *et al*. (2016). Biosynthesis of gold nanoparticles: A green approach', J*ournal of Photochemistry and Photobiology B:*

*Biology*, 161:141–153. https://doi:10.1016/j.jphotobiol.2016.04.034.

35. Parveen, K., Banse, V. and Ledwani, L. (2016) 'Green synthesis of nanoparticles: Their advantages and disadvantages', AIP Conference Proceedings [Preprint]. https://doi:10.1063/1.4945168.
36. Nadaroglu, H., Ince, S. and Gungor, A.A. (2016) 'Green synthesis of gold nanoparticles using quail egg yolk and investigation of potential application areas', *Green Processing and Synthesis*. 6(1):43–48. https://doi:10.1515/gps-2016-0091.
37. Hussain, I. *et al.* (2015) 'Green synthesis of nanoparticles and its potential application', *Biotechnology Letters*. 38(4):545–560. https://doi:10.1007/s10529-015-2026-7.
38. Korbekandi, H., Iravani, S. and Abbasi, S. (2009) 'Production of nanoparticles using organisms', *Critical Reviews in Biotechnology*, 29(4): 279–306. https://doi:10.3109/07388550903062462.
39. Boroumand Moghaddam, A. *et al*. (2015). 'Nanoparticles biosynthesized by fungi and yeast: A review of their preparation, properties, and medical applications', *Molecules*, 20(9): 16540–16565. https://doi:10.3390/molecules200916540.
40. Siddiqi, K.S. and Husen, A. (2016). 'Fabrication of metal and metal oxide nanoparticles by algae and their toxic effects', *Nanoscale Research Letters*, 11(1). https://doi:10.1186/s11671-016-1580-9.
41. Nadaroglu, H. *et al.* (2017). 'Green synthesis and characterisation of platinum nanoparticles using quail egg yolk', SpectrochimicaActa Part A: *Molecular and Biomolecular Spectroscopy*, 172: 43–47. https://doi:10.1016/j.saa.2016.05.023.
42. Park, S., Sung, H.K. and Kim, Y. (2016). 'Green synthesis of metal nanoparticles using sprout plants: Pros and cons', *Journal of Nanoscience and Nanotechnology*, 16(5): 4444–4449. https://doi:10.1166/jnn.2016.10970.
43. Shaffer, C. (2005). Nanomedicine transforms drug delivery', Drug Discovery Today, 10(23–24): 1581–1582. https://doi:10.1016/s1359-6446(05)03654-8.
44. Moghimi, S.M., Hunter, A.C. and Murray, J.C. (2005) 'Nanomedicine: Current status and future prospects', *The*

*FASEB Journal*, 19(3):311–330. https://doi:10.1096/fj.04-2747rev.

45. Göpel, W. (1993). 'Nanosystems: Molecular Machinery, manufacturing and computation. Byk. Eric Drexler, J. Wiley & Sons, Chichester, UK 1992, 556 pp., hardcover, £ 19.50, ISBN 0-471-57547-X', *Advanced Materials*, 5(11):865–866. https://doi:10.1002/adma.19930051119.
46. Cai, W. (2008). 'Applications of gold nanoparticles in cancer nanotechnology', *Nanotechnology, Science and Applications*. 1: 17–32. https://doi:10.2147/nsa.s3788
47. Kao, H.-W. *et al.* (2013) 'Evaluation of EGFR-targeted radioimmuno-gold-nanoparticles as a theranostic agent in a tumor animal model', *Bioorganic & Medicinal Chemistry Letters.* 23(11): 3180–3185. https://doi:10.1016/j.bmcl.2013.04.002.
48. Aliofkhazraei, M. and Ali, N. (2014). 'Recent developments in miniaturization of sensor technologies and their applications', *Comprehensive Materials Processing*. pp. 245–306. https://doi:10.1016/b978-0-08-096532-1.01309-1.
49. Dong, H., Wen, B., Melnik, R., 2014. Relative importance of grain boundaries and size effects in thermal conductivity of nanocrystalline materials. *Sci. Rep*. 4: 7037. https://doi:org/10.1038/srep07037.
50. Lee, K.-B. *et al.* (2002) 'Protein nanoarrays generated by Dip-Pen Nanolithography', *Science*. 295(5560): 1702–1705. https://doi:10.1126/science.1067172.
51. Todescato, F. *et al.* (2016). 'Engineering of semiconductor nanocrystals for Light Emitting Applications', *Materials*, 9(8): 672. https://doi:10.3390/ma9080672.
52. Weiss, J., Takhistov, P. and McClements, D.J. (2006). 'Functional materials in food nanotechnology', *Journal of Food Science*, 71(9). https://doi:10.1111/j.1750-3841.2006.00195.x.
53. Loureiro, A., Azoia, N.G., Gomes, A.C., Cavaco-Paulo, A., (2016). Albumin-based nanodevices as drug carriers. *Curr. Pharm. Des*. 22: 1371–1390. http//doi:10.2174/1381612822666160125114900

54. Loureiro, A. *et al*. (2016). 'Albumin-based nanodevices as drug carriers', *Current Pharmaceutical Design,* 22(10):1371–1390. https://doi:10.2174/1381612822666160125114900.
55. El-Shabouri, M.H. (2002). 'Positively charged nanoparticles for improving the oral bioavailability of cyclosporin-A', *International Journal of Pharmaceutics*, 249(1–2), pp. 101–108. https://doi:10.1016/s0378-5173(02)00461-1.
56. Hu, L., Tang, X. and Cui, F. (2004) 'Solid lipid nanoparticles (SLNS) to improve oral bioavailability of poorly soluble drugs', *Journal of Pharmacy and Pharmacology*, 56(12), pp. 1527–1535. https://doi:10.1211/0022357044959.
57. Arangoa, M.A. *et al*. (2001) *Pharmaceutical Research*, 18(11): 1521–1527. https://doi:10.1023/a:1013018111829.
58. Diwan, M. *et al*. (2003). 'Biodegradable nanoparticle mediated antigen delivery to human cord blood derived dendritic cells for induction of primary T cell responses', *Journal of Drug Targeting*, 11(8–10):495–507. https://doi:10.1080/10611860410001670026.
59. Köping-Höggård, M., Sánchez, A. and Alonso, M.J. (2005) 'Nanoparticles as carriers for nasal vaccine delivery', Expert Review of Vaccines, 4(2), pp. 185–196. https://doi:10.1586/14760584.4.2.185.
60. Lutsiak, M.E. *et al*. (2002) *Pharmaceutical Research*, 19(10): 1480–1487. https://doi:10.1023/a:1020452531828.
61. Hegner, M. and Arntz, Y. (2004). 'Advanced biosensing using micromechanical cantilever arrays', *Atomic Force Microscopy*, pp. 39–50. https://doi:10.1385/1-59259-647-9:39.
62. Guo, X. *et al*. (2017). 'Dimeric drug polymeric micelles with acid active tumor targeting and fret traceable drug release', *Advanced Materials*, 30(3): https://doi:10.1002/adma.201705436.
63. Fenaroli, F. *et al*. (2018). 'Enhanced permeability and retention-like extravasation of nanoparticles from the vasculature into tuberculosis granulomas in zebrafish and mouse models', *ACS Nano*. 12(8): 8646–8661. https://doi:10.1021/acsnano.8b04433.
64. ElMeshad, A.N., Mortazavi, S.M. and Mozafari, M.R. (2014). 'Formulation and characterization of nanoliposomal 5-

fluorouracil for cancer nanotherapy', *Journal of Liposome Research*. 24(1): 1–9. https://doi:10.3109/08982104.2013.810644.

65. Saraiva, C. *et al.* (2016). Nanoparticle-Mediated Brain Drug Delivery: Overcoming blood–brain barrier to treat neurodegenerative diseases', *Journal of Controlled Release*, 235: 34–47. https://doi:10.1016/j.jconrel.2016.05.044.
66. Hua, S. *et al.* (2015). Advances in oral nano-delivery systems for colon targeted drug delivery in inflammatory bowel disease: Selective targeting to diseased versus healthy tissue', *Nanomedicine: Nanotechnology, Biology and Medicine*, 11(5): 1117–1132. https://doi:10.1016/j.nano.2015.02.018.
67. Morales-Zavala, F. *et al.* (2018). Functionalization of stable fluorescent nanodiamonds towards reliable detection of biomarkers for alzheimer's disease', *Journal of Nanobiotechnology*. 16(1): https://doi:10.1186/s12951-018-0385-7.
68. Cheng, L. *et al.* (2015). Nanotechnology strategies for antibacterial and remineralizing composites and adhesives to tackle dental caries', *Nanomedicine*, 10(4):627–641. https://doi:10.2217/nnm.14.191.
69. Chambers, C. *et al.* (2017). 'Silver doped titanium dioxide nanoparticles as antimicrobial additives to dental polymers', *Dental Materials*, 33(3). https://doi:10.1016/j.dental.2016.11.008.
70. Mahross, H.Z. and Baroudi, K. (2015). 'Effect of silver nanoparticles incorporation on viscoelastic properties of acrylic resin denture base material', *European Journal of Dentistry*. 09(02):207–212. https://doi:10.4103/1305-7456.156821.
71. Pokrowiecki, R. *et al.* (2017) '*In vitro* studies of nanosilver-doped titanium implants for oral and maxillofacial surgery', *International Journal of Nanomedicine*. 12: 4285–4297. https://doi:10.2147/ijn.s131163.
72. Lee, S.J. *et al.* (2018). Preparation and characterization of antibacterial orthodontic resin containing silver nanoparticles', *Applied Surface Science*, 432: 317–323. https://doi:10.1016/j.apsusc.2017.04.030.
73. Ai, M. *et al.* (2017). Composite resin reinforced with silver nanoparticles–laden hydroxyapatite nanowires for dental

application', *Dental Materials*. 33(1): 12–22. https://doi:10.1016/j.dental.2016.09.038.

74. Paiva, L. *et al*. (2018). Antibacterial properties and compressive strength of new one-step preparation silver nanoparticles in glass ionomer cements (NanoAg-GIC)', *Journal of Dentistry*. 69: 102–109. https://doi:10.1016/j.jdent.2017.12.003.
75. Slane, J. *et al.* (2015). Mechanical, material, and antimicrobial properties of acrylic bone cement impregnated with silver nanoparticles', *Materials Science and Engineering: C*, 48: 188–196. https://doi:10.1016/j.msec.2014.11.068.
76. Nair, S.B., Dileep, A. and Rajanikant, G.K. (2012). Nanotechnology based diagnostic and therapeutic strategies for neuroscience with special emphasis on ischemic stroke', *Current Medicinal Chemistry*, 19(5): 744–756. https://doi:10.2174/092986712798992138.
77. Sadrieh, N. and Tyner, K.M. (2010). Nanotechnology and therapeutic delivery: a drug regulation perspective', *Therapeutic Delivery*, 1(1): 83–89. https://doi:10.4155/tde.10.6.
78. Allen, T.M. and Cullis, P.R. (2004). Drug Delivery Systems: Entering the mainstream', *Science*, 303(5665): 1818–1822. https://doi:10.1126/science.1095833.
79. Vasir, J., Reddy, M. and Labhasetwar, V. (2005). Nanosystems in drug targeting: Opportunities and challenges', *Current Nanoscience*, 1(1): 47–64. https://doi:10.2174/1573413052953110.
80. Vasir, J.K. and Labhasetwar, V. (2005). Targeted drug delivery in cancer therapy', *Technology in Cancer Research & Treatment*, 4(4): 363–374. https://doi:10.1177/153303460500400405.
81. Feng, S.-S. *et al.* (2004). Nanoparticles of biodegradable polymers for clinical administration of Paclitaxel', *Current Medicinal Chemistry*, 11(4): 413–424. https://doi:10.2174/0929867043455909.
82. Chavda, V.P. (2019). Nanotherapeutics and Nanobiotechnology. *Applications of Targeted Nano Drugs and Delivery Systems*, pp. 1–13. https://doi:10.1016/b978-0-12-814029-1.00001-6.
83. Pepic, I., Hafner, A., Lovric, J., & Perina Lakos, G. (2014). Nanotherapeutics in the EU: An overview on current state and

Future Directions. *International Journal of Nanomedicine*, 1005. https://doi:10.2147/ijn.s55359
84. Sainz, V., Conniot, J., Matos, A. I., Peres, C., ZupanÒiÒ, E., Moura, L., … Gaspar, R. S. (2015). Regulatory aspects on nanomedicines. *Biochemical and Biophysical Research Communications*, 468(3): 504–510. https://doi:10.1016/j.bbrc.2015.08.023
85. Tinkle, S., McNeil, S. E., Mühlebach, S., Bawa, R., Borchard, G., Barenholz, Y. (Chezy), … Desai, N. (2014). Nanomedicines: Addressing the scientific and regulatory gap. *Annals of the New York Academy of Sciences*, 1313(1): 35–56. https://doi:10.1111/nyas.12403
86. Astier, A. *et al.* (2017). How to select a nanosimilar', *Annals of the New York Academy of Sciences*, 1407(1): 50–62. https://doi:10.1111/nyas.13382.
87. Buzea, C., Pacheco, I. I., & Robbie, K. (2007). Nanomaterials and nanoparticles: Sources and toxicity. *Biointerphases*, 2(4). https://doi:10.1116/1.2815690
88. Sahoo, S. K., & Labhasetwar, V. (2003). Nanotech approaches to drug delivery and imaging. *Drug Discovery Today*, 8(24): 1112–1120. https://doi:10.1016/s1359-6446(03)02903-9
89. Soltani, A. M., & Pouypouy, H. (2019). Standardization and regulations of nanotechnology and recent government policies across the world on nanomaterials. *Advances in Phytonanotechnology*. 419–446. https://doi:10.1016/b978-0-12-815322-2.00020-1