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Drug delivery systems based on nanotechnology: Current methods and new therapeutic possibilities for medicine

Jyoti Gupta[1*], Shilpa Mamgain[1], Sonu Sharma[2]

[1]*Galgotias College of Pharmacy, Greater Noida, U.P
[1]Galgotias College of Pharmacy, Greater Noida, U.P
[2]Galgotia College of Pharmacy, Greater Noida, U.P

ABSTRACT

The most prevalent and widely used technology that strives to raise the standard of medical treatment is nanotechnology, sometimes known as nanomedicine. Despite significant drawbacks, a lot of pharmaceutical and medical device businesses have already used medical nanotechnology. Nanotechnology has the potential to improve the safety profile of the administration of some medications with a high risk for toxicity, such as cancer chemotherapy medicines. Living cells are microscopic virtual machines that participate in all biological processes, such as cell signalling, metabolism, energy production, and nutrient transport. In light of this, it can be said that this technique is a strong contender for use in therapeutic biology and medicine. We talk about the value of nanoscience in this review as various nanotechnology platforms are applied in other areas of medicine. Additionally, we are talking about potential future opportunities for health applications of nanotechnology.

Keywords: Nanotechnology, Nanomedicine, Therapeutics, Diagnosis, Biotechnology

INTRODUCTION

By working with traditional disciplines like applied health, molecular chemistry, molecular science, pharmaceutical science, optics, and even engineering, nanoscience is the only platform to uncover the new features of matter. By developing a more efficient healthcare system, nanomedicine technologies, and therapeutic approaches in the last several decades, science and technology have frequently been well-designed to address the challenges in the field of medicinal and health sciences. Historially, Professor N. Taniguchi first used the word "nanotechnology" in 1974. Soon later, in the book "Vehicles of creation: the dawn of the nanotechnology era" published in 1986 [1], Drexler created and published the first idea (Feynman's theories) of nanotechnology. The influence of nanotechnology on humans and animals is currently opening up new avenues for research and transforming health science, making it an essential topic for consideration as a therapeutic tool. Nanotechnology is a very murky multidisciplinary field that was developed to engineer biological elements like atoms, molecules, and supramoleculars at nanoscales of approximately 1-100 nm to hold promise against current challenges by developing new devices and identifying material structures with special properties to study and comprehend lethal biological problems followed by disease diagnosis and treatment [2,3]. The most dominant and economically successful technology of these decades has emerged as nanotechnology, which is incredibly important for human life. It should be noted that living cells include incredibly important yet little machinery (nanoscale). They play a significant role in practically every biological process, including nutrition transport, energy production, metabolism, and cell signalling. As a result, nanotechnology can be seen as a key contender for developing new technologies at the level of the individual atoms in matter to deal with biology and medicine for therapeutic purposes [4]. Numerous clinically advantageous nanoscale materials are developed, and nanomedicine is quickly becoming the norm in the field of health sciences [5,6]. Numerous benefits exist for manufacturing and delivering various nanomedicine products when diseased/abnormal tissues/cells are modulated in a manner that is pathophysiologically and clinically connected. So, there may be more than one option available for tissue-specific therapeutic targeting approaches to beat the illness prognosis [7]. Nanomaterials, particularly metal nanoparticles, have drawn increased interest recently in the broad field of medical science. Nowadays, there is a lot of research being done

on how to best synthesise nanomaterials such polymers, micelles, dendrimers, liposomes, emulsions, nanocapsules, and nanoparticles.

One of the most important uses of nanotechnology today is nanomedicine, which has dedicated to producing nanoscale medical tools to create an efficient healthcare system. With the help of this method, we can better comprehend human physiology and combat various devastating diseases like cancer and cardiovascular conditions. The importance of nanomedicine is primarily used in imaging, disease diagnosis, tissue engineering, and the design of more effective, safe, and cost-effective drug delivery systems to precisely deliver drugs to target sites that can speed up treatment outcomes by reducing toxicities and off-target effects [8]. In accordance with Bebo et al. state that the US-FDA has so far approved about 51 nanomedicines. After that, 77 products are in the pre-clinical stage, with about 40% of them currently in the clinical trial stage. The majority of these authorised nanomaterials are nanocrystal and polymeric liposomal compositions. In clinical trials, the scientist plans to create more effective materials, such as micelles, protein-based nanoparticles (NPs), and a variety of inorganic and metallic particles [9].

Nanotechnology has the potential to promote revolutionary developments in the fields of medicine, communications, genetics, and robotics in human health, which could have a significant positive impact on clinical outcomes. Discussing and examining every nanotechnology application is incredibly broad and diversified.

The most important benefit of nanotechnology technologies and goods, however, may have substantial benefits for human health in global contexts[10].The importance of nanotechnology to human health is highlighted in this review, with a focus on its use in nanomedicine for imaging, screening, diagnostics, targeted drug delivery systems, and efficient treatment approaches for human diseases. Here, we also illustrated the risk connected to it and its potential for future development in the medical sciences.

NANOTECHNOLOGY (NANOMATERIALS/NANOPARTICLES) CLASSIFICATION

The dimensions, morphology, condition, and chemical makeup of nanoparticles are categorised [11]. In the field of nanotechnology, nanoparticles are a type of materials that contain chemicals in the form of particles with sizes ranging from 10 to 100 nm. These materials are generally categorised into different dimensions as 0D and 1D [12]. According to some research, these materials' sizes can affect how physiochemical compounds like gold (Au), platinum (Pt), silver (Ag), and palladium are visualised (in terms of their optical qualities) (Pd) NPs come in four distinct colours: wine red, yellowish grey, black, and deep black.

Three structural elements make up NPs. A range of tiny molecules, metal ions, surfactants, and polymers can all be used to functionalize the surface layer, which is the first layer. The second component is the shell layer, which is a chemically varied substance in contrast to the core, and the third component is the core, which is effectively the core of the NP and is typically referred to as the NP itself [13]. Drug delivery, chemical and biological sensing, gas sensing, CO2 collection, and other applications relevant to health can all be accomplished with the help of NPs in the biomedical system [14–17]. Nanoparticles are often divided into the following material-based categories, namely organic, inorganic, and carbon-based, based on their chemical properties.

NPs based on organic matter

Traditionally, the majority of these NPs' bases are organic. In order to self-assemble and create molecules that enable the conversion of organic NPs/nano-materials (NMs) into the precise desired structures, such as dendrimers, micelles, liposomes, ferritin, or polymers, nanoparticles use noncovalent interaction. Because they are biodegradable and have no harmful effects, these NPs are exceedingly specialised. Some nanoparticles (NPs), such as micelles and liposomes with hollow cores, are sensitive to thermal and electromagnetic radiation, including heat and light [18]. They are the perfect candidate for targeted medication administration in the biological system due to their remarkable appearance and characteristics.

NPs based on inorganic substances

Inorganic nanoparticles (NPs) lack a carbon backbone. Inorganic NPs are mostly created using metal ions (Al, Cd, Co, Cu, Au, Fe, Pb, Ag, and Zn) and metal oxide. Of which, metal-based NPs are made using two techniques, destructive and constructive, by nanometric size metals [19]. These NPs are distinguished by their diameters (10 nm-100 nm), high surface area to volume ratio, pore size, surface charge, and surface charge density, as well as their crystalline and amorphous structures, spherical and cylindrical geometries. The air, moisture, heat, and sunlight are one of atmospheric variables that have an impact on inorganic NPs. Contrary to metal-based inorganic NPs, metal oxide-based inorganic NPs are made by oxidising metals to produce oxides such as aluminium oxide (Al2O3), cerium oxide (CeO2), iron

oxide (Fe2O3), magnetite (Fe3O4), silicon dioxide (SiO2), titanium oxide (TiO2), and zinc oxide in the presence of oxygen (ZnO). Metal oxide NPs are created primarily because of their improved efficiency and reactivity [20]. The bioavailability of these NPs, which gives them a highly active and more focused surface area, is its unique characteristic. This surface area may be easily changed by a variety of chemical events, such as those involving a polymer chain, a coupling agent, or doping metal ions [21].

NPs with carbon base

Carbon-based NPs are special and important in many transdisciplinary domains. Carbon atoms make up the majority of these NPs. Individual chemical, physical, and mechanical characteristics of carbon-based NPs include chemical stability, conductivity, and thermal characteristics. Since they have so many applications, these NPs are drawing more attention [22]. Carbon-based NPs are divided into the following groups: graphene, fullerenes (C60), carbon nanotubes (CNT), carbon nanofibers, and carbon black. Of which, fullerenes are spherical and created through sp2 hybridization from carbon-based material.

They are mostly utilised as contrast agents in medical imaging, anti-aging cosmetics, water purification catalysts, photovoltaics, methane conversion, electronics, and composite reinforcement. An allotrope of carbon atoms is graphene. It is still in the development stage and has not yet been manufactured for use. Some authors illustrated their use in various products, such as gas separation membranes, sensors, organic LEDs, solar cells, hydrogen storage for fuel cells, electrical components with a faster electron speed than silicon, and organic LEDs as reinforcement for polymer-based composites [23]. Carbon nanotubes (CNT) are synthesised as carbon nanofiber and twisted into a cone or cup shape using graphene nano foil. They serve as composite reinforcement, scanning electron microscope tips, and field electron emission sources. Contrary to graphene nano foil, carbon atoms are twisted into hollow cylinders to create single and multilayered CNT of different lengths that self-align under the influence of van der Waals force [24]. They can be used as scaffolds for bone formation, reinforcement for composites, and tips for atomic force microscopes, among other things. The majority of carbon black is formed of amorphous carbon material and is spherical in shape. As a mechanical reinforcement, heat, UV absorber, antistatic agent, and electricity conductor, carbon black is blended with polymeric elastomers. In Fig. 1, an overview and different types of nanoparticles are shown.

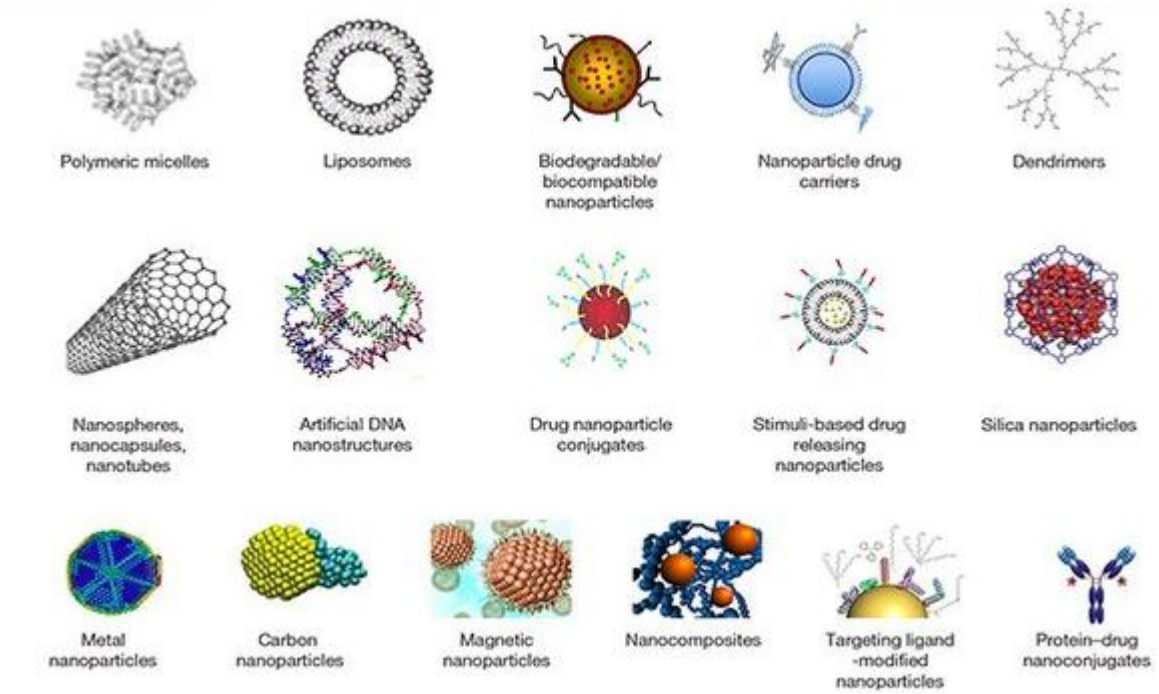

Fig. 1. Types of Nano Drug molecules.

APPLICATION IN THE FIELD OF MEDICINE

The simple fact that nanotechnology has special functional qualities and features to work in harmony with our bodies' natural systems makes it a potential area in the medical industry and healthcare system. We are aware that living cells genuinely exist at the nanoscale. Thus, it was proposed that the domain of nanotechnology is a fascinating one for

biology and medicine. Due to its focused delivery and nature, nanotechnology is now being used in medicine more and more frequently each day. Various nanoscale materials have been developed with a range of clinical applications, including the diagnosis of diseases, the delivery of drugs, and molecular medical imaging, and some products are currently undergoing clinical trials [25,26]. The field of nanotechnology offers numerous prospects for the diagnosis, prevention, treatment, and cure of diseases. To better assist patients with severe medical disorders including cancer and cardiovascular diseases, the application of nanotechnology in healthcare and medicine needs to be further investigated and developed [27]. In order to promote and create more efficient tools for bio-medical reasons, nano-medicine has become one of the most important interdisciplinary fields, bringing together biology, chemistry, medicine, and engineering. These methods are providing fresh perspectives and directions in surgical procedures, clinical practise, and the deliberate management of many diseases. Some writers claim that nanomedicine has a significant impact on implantable materials, tissue regeneration techniques, medical imaging, and diagnosis [28]. Generally speaking, there are several different types of nano-medicines, including liposomes, proteins, polymers, micelles, emulsions, nanocapsules, dendrimers, and nanoparticles. After receiving FDA approval, some nano-medical items are currently on the market. According to Bobo et al. in a recent update, 77 nanomedicines are currently in the pre-clinical or clinical stages, and 51 have received FDA approval [29]. Numerous potential uses of nanotechnology in medicine support efforts to better understand and treat the serious medical condition.

Drug delivery system

The successful application of drug molecules and therapeutic agents to their intended locations is of utmost importance in the contemporary environment for the treatment of a variety of disorders [30]. Various drug delivery methods have been used in the medical system recently. However, there are still several issues that need to be researched and addressed in order to successfully deliver medications to a targeted place. Scientists and medical experts are becoming interested in drug delivery systems that use nanotechnology. The formulation of the particular drug-targeting system is based on suitable focus, therapeutic effectiveness, and prolonged circulation time. This effective drug targeting strategy was developed by using the pathophysiological modulation that occurs with the progression of illnesses. The binding and distribution of medications to specific locations can be facilitated by this tailored delivery. The main use of nanotechnology for drug delivery has been concentrated in NPs, which are primarily suggested for the treatment of tumours [31].

When creating a target-specific drug delivery system, organic, inorganic, metallic, and polymer-based NPs including liposomes, micelles, and dendrimers are frequently taken into account. These NPs can cause the distribution of medicines with low absorption and poor solubility [32]. The effectiveness of these NPs as drug delivery systems, however, differs based on their size, shape, and other innate biophysical/chemical characteristics. The phrase NP is also known as nano constructions, nanospheres, nano vehicles, and nanocarriers. Gregory Gregoriadis created the liposome, which was the first NP for a drug delivery system [33]. Later, a number of NPs-based medication carriers emerged, and several are now being studied for a variety of disorders. There are several NP-based therapeutic drug delivery systems in use today that have been specifically formulated as polymer micelles, emulsions, and solid particles. Some nano-based medications, including Caelyx, Doxil, Transdrug, and Abraxane, are marketed for the treatment of cancer. The optimal method of medicine delivery is typically oral administration because it is noninvasive. Due to the stomach's acidic environment, peptide or protein medication administration has not yet been accomplished via the oral route [34]. To get beyond these obstacles in medicine delivery, however, nanotechnology will be used to encapsulate such medications in nanoparticles. Additionally, it improves medication site-specific targeting, preventing the delivered drug's accumulation to lessen the off-target effect. NPs-based medications are currently most frequently combined with natural products to lessen toxicological problems. drug development

The biophysical and biological characteristics and nature of the targeted medications are the primary determinants of how nanotechnology will be applied in the drug development process. Pharmacokinetic and pharmaceutical companies have been attempting to reduce the price of drug development in recent years. The pressure on the pharmaceutical manufacturing industry is coming from the rivalry among generic manufacturers, rising production costs, and elevated failure rates. Drug development may be more economically feasible with the use of nanotechnology in both lifestyle management and drug development. Drugs based on nanotechnology are especially developed to lessen toxicity and enhance health results.

Additionally, solid NPs imply significant benefits in medication development due to their biophysical stability and the potential to alter drug formulation to enable controlled drug release. A significant opportunity for product life cycle management exists due to the strong potential to manufacture NPs to achieve continual release.

Solid NPs with and without surface functionality have been created so far using a wide range of materials. The aliphatic polyesters, including poly (lactic acid), hydrophilic poly (glycolic acid), and their copolymers, may be the most commonly utilised (lactide-coglycolide). The stability of medications can be improved by NPs in the dosage maintaining their particle size during their whole self-life, which is essential for successful development.

APPLICATIONS OF NPS IN TREATMENT

Cancer therapy

The main cause of death worldwide is cancer. The most enigmatic and complex disease, cancer is thought to be a multi-stage carcinogenesis process involving many physiological cell processes, including cell signalling and death. Traditional cancer treatments like radiotherapy and chemotherapy have undergone numerous advancements, yet they still don't appear to be very effective. Because of drawbacks such chemoresistance [35–37] and serious side effects, it is hampered. For multidisciplinary research in genetics, engineering, chemistry, and medicine, nanotechnology is emerging as a new frontier. It is likely to result in major improvements in the detection, diagnosis, and treatment of cancer. By creating novel, biocompatible nanoparticles—the most important aspect of nanoparticles for drug delivery—nanomedicine has the potential to dramatically alter cancer treatment and detection. Nanoshells, nanocantilevers, nanoprobes, nanocrystals, nanopolymers, quantum dots, and dendrimers are only a few of the nanotechnologies that can be employed to treat cancer [38, 39].

Two crucial aspects of the development of nanomaterials for cancer therapy are the ability to identify tumours and reach the target tumour site without harming healthy cells. Numerous nanoparticles show promise in their capacity to recognise highly sensitive and specific cancer cells via various processes. These nanoparticles stand out from conventional cancer treatments thanks to their special qualities [40].

1. The nanoparticles themselves could be designed to carry a wide therapeutic load and possess therapeutic and investigative properties.
2. Polyvalent targeting ligands may be used to bind nanoparticles strong cell-specific specificity and affinity.
3. It is possible for nanoparticles to be made to take different pharmacological compounds that Instantaneously enable combining cancer treatment.
4. Nanoparticles can overcome the resistance to conventional drugs mechanisms

The most popular drugs are Doxil, Daunorubicin (Daunoxome), and Abraxane, are most widely used FDA-approved therapeutic nanoformulations at the currently chemotherapy for cancer is accessible. Paclitaxel is delivered by the albumin-bound nanoparticle Abraxane (Abraxis), while doxorubicin is delivered by the liposome-mediated drug delivery system Doxil. These two nanoformulations are frequently employed to treat metastatic breast cancer. It has been demonstrated that targeted liposomes containing folate receptors can overcome multidrug resistance in tumour cell lines and successfully deliver doxorubicin in vivo [38].

One of the most important aspects of tumour therapy is the interaction between chemotherapy and antiangiogenic drugs. According to Sengupta et al., tumour malfunction in the blood arteries may reduce the delivery of chemotherapeutic medications and boost the expression of drug resistance genes. Using nanoparticles with two layers, a drug delivery system was created. The first layer is a core made of poly lactic-co-glycolic acid (PLGA), which is coupled with doxorubicin and bound to a PEG and combretastatin conjugated liposome. Combretastatin is an anti-angiogenic medication, whereas doxorubicin is a cancer treatment agent. This nanoparticle was easily absorbed by the tumour when it was intravenously injected into mice with tumor-mediated (carcinoma or cell-derived melanoma) disease. They significantly slowed the growth of tumours. This nanoparticle formulation has demonstrated efficacy in mice models of lung cancer and melanoma, and similar performance is anticipated in human models [41]. When Singh et al. tested native pharmaceuticals with nanoparticles, they discovered that the dual-drug-loaded magnetic nanoparticles had greater cell penetration and synergistic effects. Her-2 was used as a target for breast cancer therapy, and it was created by encapsulating hydrophilic and hydrophobic anticancer medicines as a double-drug delivery strategy [42].

Theranostics is a biomedical technique in development that combines diagnosis and treatment in a single step. Through the aid of the key stages of medical treatment, including diagnosis and therapy will be assembled to speed up, simplify, and improve treatment. Efficient. Currently, biocompatible nanoparticles are being created as agents that will enable non-invasive and efficient cancer screening treatment for cancer. Shim and colleagues have developed an overall diagnosis and cancer-treatment methods (theranostics). Small gold nanoparticles were utilised. In order to explore the potential for combined stimulus-responsive optical imaging and stimulation-enhanced gene silencing, Si RNA was encapsulated [43].

Applications for Ocular drug delivery

One of the main issues with topical ophthalmic medication administration is poor eye absorption, which makes it challenging to maintain an appropriate concentration of the drug in the precorneal region. In comparison to conventional pharmaceuticals, which have a shorter half-life (t1/2) in tear fluids (up to 1-3 min), nanoparticles exhibit enhanced durability and a longer half-life (t1/2) in tear fluids (up to 20 min). Drug delivery methods using nanoparticles have the potential to increase the bioavailability of therapeutic drugs, reduce side effects, and maintain intraocular dose levels [44].

Pignatello et al. have employed commercially available Eudragit ® polymers to inject non-steroidal and anti-inflammatory medications into rabbits' eyes. Poly(ethyl acrylate), poly(methyl methacrylate), and poly(ethylene glycol) make up Eudragit ® RS and RL (chlorotrimethyl-aminoethyl-methacrylate). The ethanol-dissolved drug and polymer mixtures were then emulsified to create drug-injected nanoparticles that are about 100 nm in size. The conjunctivitis sac of the rabbit's eyes contained these nanoparticles, which were suspended there. Flurbiprofen and ibuprofen-filled nanoparticles effectively stopped the inflammatory reactions brought on by trauma after surgery. In addition, compared to conventional eye drop devices, the nanoparticle device produced larger concentrations of medicines in vitreous humour [45].

The retina, choroid, iris, and adjacent tissues may suffer irreparable harm as a result of CMV infection. Merodio et al. employed nanoparticles made of bovine serum albumin (BSA), which contain the medication ganciclovir, which is used to treat CMV infection. This medication was incubated in an aqueous solution containing BSA, then ethanol was added as part of the emulsification process to create droplets. The resultant nanoparticles were roughly 280 nm in diameter. These nanoparticles were redissolved in saline and given intravenously. The thin layer of the retina's thin layer continued to contain nanoparticles up to two weeks following injection, according to research. In comparison to normal eye controls, the histological analysis revealed no inflammatory responses or improvements in tissue morphology [46].

Silva and colleagues created and evaluated the effectiveness of a 0.75% w/w isotonic hydroxypropyl methylcellulose (HPMC) solution containing ceftazidime and the antibiotics chitosan, sodium tripolyphosphate, and hyaluronic acid for eye therapy. These nanoparticles also induced mucoadhesion, which led to effective interaction with the ocular mucosa and the release of antibiotics over an extended period of time. Nanoparticles may thereby lengthen the duration of the medication in the eyes. These nanoparticles were also capable of maintaining an antibacterial effect, which made them the perfect drug delivery mechanism for ocular medications with enhanced mucoadhesive qualities [47]. Dendrimers can also be utilised to deliver medications to the eyes.

Application in heart disease

A category of illnesses known collectively as cardiovascular diseases (CVDs) includes atherosclerosis, myocardial infarction, stroke, hypertension, and heart failure. All across the world, these illnesses are the main cause of fatalities for people. For cardiovascular illnesses to be prevented and effectively treated, early detection is essential. Some of the commonly utilised techniques to detect CVDs are plain X-rays, electrocardiography (ECG), computed tomography (CT), and magnetic resonance imaging (MRI). However, due to their poor specificity and sensitivity, these approaches are insufficient. To get around these challenges, innovative methods including cardiac immunoassays and molecular imaging have been developed.

Although it offers a number of advantages over the approaches mentioned above, it is still difficult to diagnose CVDs in their early stages because of their complex pathophysiology.

Over traditional diagnostic procedures, nanotechnology has many advantages. To detect early-stage CVDs, a combination of cardiac immunoassay and nanotechnology can be used. Specific biomarkers of CVDs may be found early on by using nanotechnology in immunoassays including Electrochemiluminescence (ECL) Immunoassay, Fluorescence Immunoassay, and Enzyme-Linked Immunosorbent Assay (ELISA). Nanotechnologies may have a reduced amount of non-specific binding sites, strong binding to cardiac targets, a good bioavailability, considerable signal amplification, and a variety of other uses. These characteristics of nanoparticles enable them to move through low-restriction human bodies, generate useful imaging vehicles, and significantly enhance the quality of diagnostics. When injected into the body or consumed, visible MOI-functionalized nanoparticles will disperse throughout the body and target various RNAs for diagnostics [49].

Fluorescent materials are frequently used to conjugate nanoparticles. For atherosclerotic plaque imaging, fluorescence-labelled quantum dots (QDs) produce good results. Additionally, when a PET/CT scan is employed, radio-labeled nanoparticles are crucial for atherosclerotic plaques. The fibrous caps, necrotic base, macrophage material, intraplaque

haemorrhage, and plaque neovascularization are among the plaque and thrombus compositions that the MRI may identify. Iron oxide nanoparticles, for example, are superparamagnetic nanoparticles that may increase the MRI's sensitivity by enhancing the signal with dark contrast [51,52]. Cross-linked iron oxide fluorescent nanoparticles were utilised by Aikawa et al. to quickly trap macrophages in order to measure the inflammatory response of atherosclerotic plaques [53]. For the goal of diagnosing CVDs, radionuclides such as 18F, 124I, 64Cu, 86Y, and 68Ga are conjugated with QDs, UCNPs, AuNPs, and NCs [54].

The most common kind of CVD that results in a heart attack is atherosclerosis. The arterial wall thickening is a defining feature of it which developed plaque, causing swelling. an approach based on nanotechnology methods for combating atherosclerosis include controlling lipoprotein levels, lowering of the inflammatory response, preventing coagulation, and blocking neovascularization inflammatory monocytes and macrophages trigger the rupture of atherosclerotic plaques and atherogenesis. Nakashiro Pioglitazone (an inhibitor of inflammatory reactions) was administered to circulating monocytes using bioabsorbable nanoparticles by et al. to stop the rupture of atherosclerotic plaque [55]. Hirulog (a naturally occurring hirudin-derived thrombin inhibitor) and micellar nanoparticles were used to block. After thrombosis-induced coronary artery blockage, fibrin clots developed due to the rupture and degradation of plaque [56].

Because of their distinct magnetic properties and desirable biocompatibility, iron oxide super magnetic nanoparticles can be employed to regulate and track the therapeutic effects of stem cells on myocardial infarction [57]. Chitosan alginate nanoparticles containing a placental growth factor (PlGF) were employed by Binsalamah et al. to enhance heart function at the location of myocardial infarction. PlGF is continuously released by nanoparticles, which also improves the positive effects of growth factors on acute myocardial ischemia [58]. To prevent cardiac ischemia-reperfusion injury, Nakano and colleagues recommended combining PLGA nanoparticles and irbesartan (angiotensin II receptor blockers) [59].

The most popular methods for treating hypertension are nanoemulsion, liposomes, polymeric nanoparticles, solid lipid nanoparticles (SLNs), and nanostructured lipid carriers. Angiotensin II-AT1 receptor inhibitor olmesartan medoxomil, a medication used to decrease blood pressure, has poor oral bio-absorption and accessibility since it is not water soluble and has low permeability. The plasma concentration of active olmesartan in rats exhibited a 2.8-fold increase when combined with nanoemulsion and given orally as opposed to the normal dosage. Additionally, it has been demonstrated that the drug's antihypertension benefit increases and strengthens with a threefold reduction in the usual dosage [60]. Shah et al. have shown that poly-(lactic-co-glycolic) acid (PLGA) nanoparticles charged with phelodipine can regulate blood pressure and change the electrocardiogram (ECG) for a longer amount of time while avoiding pro-phase metabolism and offering a continuous release of medications [61]. As a novel antihypertensive medication with high stability, nanowire can be utilised because of its strong encapsulation capability [62]. Antihypertensive medications like lercanidipine hydrochloride have been released in a sustained form via nanostructured lipid carriers for a longer period of time than conventional medications, according to pharmacodynamic investigations [63].

Patients with heart failure can only be treated by a heart transplant. However, due to the lack of cardiac donors and the serious issue of immunological rejection, only few patients are fortunate enough to get transplantation therapy. A promising research area to address this is tissue engineering and cell-based therapy, although there are significant downsides as well.

Tissue engineering using synthetic biology offers a potential answer to these issues. A 50:50 mixture of PLGA and carbon nanofibers improved cardiac muscle function by replicating the tensile strength and conductivity of cardiac tissue and by enhancing the adsorption of proteins thought to support cardiac muscle function, according to one study [64]. Another study found that carbon nanofibers added to PLGA made cardiac muscle growth more resilient.

Application in respiratory disease

Respiratory disorders have seen comparatively little application of nanoparticle-based medication delivery methods. Patients with allergic diseases (like asthma) are known to have lower levels of interferon- (IFN-) in their bodies, which makes them more prone to airway irritation and hyperresponsiveness. Chitosan/interferon-pDNA nanoparticles, a polymer-drug combination, have been shown by Kumar et al. to reduce allergic inflammation of the airways. The strategy was to treat IFN-deficiency by administering polymer-drug conjugate intravenously. The therapy's effects included enhanced IFN- expression by epithelial cells and a 3-6 h reduction in inflammation and lung shape in mice exposed to allergens [65].

In the murine allergic asthma model, John et al. described employing a liposome-based nanoparticle medication delivery method to decrease inflammation. By reducing contacts between endothelial cells and leukocytes, the

technique involved blocking P-selectin receptors on circulating endothelium activated cells, which lessens the development of peribronchial inflammation. Fucose and sulphate ester groups were added to the liposomes' surface to achieve this goal, simulating the physiological P-selectin super ligand (PSGL-1). Selectins on activated endothelium cells are favoured when these liposomal nanoparticles have been given to animals in lung inflammation and airway hyperreactivity. In comparison to controls, it exhibits a considerable reduction in peribronchial inflammation and airway hyperreactivity [66].

The main area of study was the application of nanotechnologies to the treatment of tuberculosis. In multiple studies, Pandey and colleagues discussed the efficiency of direct nanoparticle delivery of anti-tuberculosis medications. They included vacuum-dried and multi-emulsion antituberculosis medications. Direct inhalation of the produced formulation into the guinea pigs' lungs. The medicine was administered, and its bioavailability was better than that of oral administration or injection. The drug remained high in the bloodstream for 6–8 days, and it had a half-life of up to 11 days. In this study, poly (DL, lactide-co-glycolide) (PLG) is applied to the medication inhalation carrier at intervals of 10 days, causing guinea pigs to become free of TB bacilli. The same result was still possible after 46 oral administrations [66].

In several in vitro and in vivo parameters, Bhardwaj et al. developed a ligand linked to a dry powder inhaler (DPI) and utilised it to treat TB successfully [67]. The first vaccine candidate recently introduced in clinical trials for the novel coronavirus (SARS-CoV-2) is the mRNA vaccine delivered by lipid nanoparticles, which has previously undergone phase II and phase III clinical studies [68,69]. The use of gene therapy to treat lung cancer has been the subject of recent study. It has been shown that using nanotechnology, it is possible to carefully target and deliver in situ medications to destroy cancer cells, avoiding exposure of healthy organs and tissues as well as side effects. For the treatment of cancer, researchers are currently integrating nanotechnology with gene therapy. Gopalan et al. [70] employed the DOTAP/cholesterol non-viral nanoparticle carrier to deliver tumour suppression genes with a controlled release programme to the tumour location. Prabha et al. employed P53 anti-proliferative genes and PLGA nanoparticles in a related analysis for the treatment of breast cancer [71].

Application in dermatology

Due to the nature of the epidermis, the skin serves as the primary barrier to drug penetration in dermatology. The medicine must first be absorbed via the skin and pass through successive layers of the epidermis to reach the dermis before it can enter the bloodstream and start acting [72]. Some of the drug delivery components utilised to transport active chemicals in topical administration include liposomes, cyclodextrins, microparticles like microspheres and microcapsules, and nanoparticles. Due to their excellent physicochemical stability, lack of scientific limitations, and versatility in formulations, all nanoparticles are the most efficient system [73]. Currently, allergens are captured or transformed into skin diseases using emulsions with active substances. Tolerance, such as atopic eczema, is the mechanism of the skin's protective barrier against irritants [74]. The skin is currently shielded from doxorubicin excretion through sweat glands by the use of nanoparticles as an antioxidant carrier. Similar to how high lipid content moisturisers are less effective in preventing water loss from the skin and reducing the risk of contact dermatitis in the hands, nanoparticle barrier creams frequently exhibit stronger occlusive effects and antioxidant action [75].

The main use of nanotechnology in dermatology is aseptic formulations. One of the formulations of nanoparticles containing chlorhexidine gluconate (Nanochlorex ®) exhibits an instant antibacterial impact due to its faster absorption through the capsule wall. The ongoing release from the particle nucleus is what gives it a lasting effect [76, 77]. After absorbing ultraviolet light, other nanoparticles, like TiO2, have strong antibacterial characteristics. After being exposed to UV light, bare TiO2 functions as a photocatalyst to encourage the peroxidation of the PUFA phospholipid component of the bacterial lipid membrane [78]. The most potent and widely accessible antibacterial nanomaterial to yet is nanosilver, which is also used as a room spray and a water disinfectant in addition to treating wounds and burns. By interacting with internal membrane protein thiol groups and producing mitochondrial toxicity, it demonstrates its antibacterial activity by causing oxidative stress [79].

Adapalene particles were combined with polymerized nanoparticles (PLA and PLGA) by Schaefer and colleagues, which has beneficial effects on drug delivery for intrafollicular drug delivery and for significantly better success in treating pilosebaceous diseases and other disorders of the sebaceous gland [80]. All-trans-retinoic acid (ATRA)-containing solid lipid nanoparticles are marginally less irritating than conventional retinoid cream, according to research by Castro and colleagues. These novel nanoparticle-based formulations hold promise as an alternative to retinoid-based topical acne therapy [81,82]. Benzoyl peroxide (BP) microsphere cream 5.5% (NeoBenz Micro ®, SkinMedica, Inc.) and BP microsphere wash 7% (NeoBenz Micro Wash Plus Pack ®) are two anti-acne products that use these nanoparticles as their foundation. Nanoparticle delivery systems have shown a key role in treating hair diseases and

serves as a reservoir for the prolonged release of the medicine within them because nanoparticles boost drug penetration in hair follicle openings. When treating hair diseases like androgenic alopecia and alopecia areata, nanoparticle formulations are thought to be more successful than traditional treatments like aqueous solutions and alcohol. When included in nanoparticles, chemicals for hair growth displayed 2.0 to 2.5 times longer durability in hair follicle regions compared to aqueous control solutions [74]. When minoxidil is enclosed in liposomes, Jain et al. found that it exhibits higher pilosebaceous unit penetration when compared to the drug's usual formulations [83]. If immunomodulation medicines are included in nanoparticles or nanoparticle delivery systems, oral medication administration may be able to substitute more targeted and effective topical therapy. In order to cure autoimmune hair follicle illnesses such alopecia areata, it is helpful [74].

Application in dentistry

Nanotechnology in dentistry has made some progress. The increased demand for cosmetic restorations has led to increased development of goods that are the same colour as teeth in recent years. Composite nanoparticle technology is one area of nanotechnology that is frequently applied in dentistry. Artificial nanocomposite teeth are more abrasion-resistant and stable than acrylic and composite microfill teeth, according to research. Nanoparticles enable the manufacturing of composite with a smooth surface after the polishing stage and give the content exceptional aesthetic properties. Nanoparticles are used in order to increase aesthetics by increasing transparency of surfaces and durability rate.

Dental diagnostics may be more effective and of higher quality thanks to nanomedicine. The identification of oral problems has received very little attention in nanotechnology research and therapeutic strategies.

The genetic and proteomic markers of oral cancer can be found using atomic force microscopy (AFM). Additionally, a high sensitivity real-time scan of a live bacterial cell was made possible by AFM cantilever (nanomechanical biosensors). AFM can interact with live cells directly and acquire images of them without changing their shape or other characteristics. AFM can characterise germs that are adhered to dental surfaces or implants because to this capability. AFM also offers trustworthy proof of the biomechanical interactions between bacterial cells and antibiotics. Vancomycin binds to the D-Ala-D-Ala terminal of bacterial cell wall peptidoglycan precursors, which may aid in the development of antibacterial therapy against drug-resistant microorganisms.

The nanoscale implant's surface is crucial for cellular responses in the tissues. Titanium implants with a calcium nanostructured surface have been inserted into rabbit tibias. Investigations into the effects on osteogenesis revealed that the nanostructured calcium layer increased the stability of the bone around the implant. Additionally, the surface shape of the nanoscale increases surface area, giving an implant with a responsive biological environment a larger surface area.

The trapping efficiency of PLGA and poly(lactic acid) nanoparticles were higher, reaching up to 63.8%. Triclosan-loaded nanoparticles were able to enter the epithelial junction thanks to their implantation in dogs. We used calcium-deficient HA nanoparticles to create a better osteoconductive tetracycline delivery system. The drug-loaded demonstrated sustained release of up to 88% over the course of five days and potent antibacterial activity. Growth factors have also been employed therapeutically in dental tissues. As a growth factor carrier, nanodiamonds, which are carbon nanoparticles with a diameter of 4-5 nm, have also been employed to augment the alveolar ridge [84–86].

Application in neurological disorders

The Blood-Brain Barrier (BBB) barrier protects the human brain, which is the body's most delicate and intricate organ. CNS illnesses pose a serious threat to human health since BBB is a significant treatment barrier. The BBB can only pass through lipophilic compounds or molecules with a molecular weight of 400–600 Da or less, leaving few alternatives for specific future medicinal and diagnostic procedures. Potentially given macromolecular medications are unable to pass through the endothelial capillaries in the brain, preventing them from reaching their CNS target. However, the BBB may be resolved by nanoparticles and polymer coverings, enabling medication transport to the CNS. Additionally, the capacity of NPs to traverse the BBB expands prospects for early CNS illness detection. Polymeric nanoparticles make up the majority of drug delivery methods used to treat neurological illnesses because they have been shown to pass through tight cell junctions, bypass BBB, enclose more drug, and can be coupled with ligands to produce site-specific drug release. The most efficient option for brain medication administration appears to be polymeric nanoparticles like (butyl cyanoacrylate) (PBCA) or poly(isohexylcyanoacrylate) (PIHCA), poly(lactic acid) (PLA) or copolymer (lactide-co-glycolide) (PLGA), and human serum albumin (HSA). Nonspecific binding must also be established for nanoparticle medication delivery to the CNS to be effective. The kinetics of nanoparticles will be significantly increased by surface modification and BBB transporter conjugation of molecules such vascular endothelial

growth factor, epidermal growth factor, insulin, insulin-like growth factor, albumin, transferrin, lactoferrin, and angiopep-2. Because the BBB surface contains the Lf receptor, conjugating nanoparticles with lactoferrin (Lf) results in more BBB absorption of Lfconjugated nanoparticles than non-conjugated nanoparticles.

When coupled with transferrin, NPs containing anti-cancer medications like taxols may have increased brain endothelial cell aggregation in cases of brain cancer. One of the most efficient cancer treatments is doxorubicin, however it cannot penetrate the BBB and is not approved for the treatment of brain tumours. However, when doxorubicin was loaded onto NPs coated with a polysorbate-80 surfactant, it was discovered in the brain.

Apolipoproteins B and E on the surface of NPs are absorbent by polysorbate. The outcomes demonstrated that receptor-mediated brain capillary endothelial cells were responsible for the transfer to endocytosis. According to one study, magnetic nanoparticles (MNPs) can effectively carry anticancer medications to tumour locations. When cytotoxic drugs were bound to a magnetic carrier and a magnetic field was applied to absorb the drugs at the tumour site, the drugs were released from the carrier by an enzymatic process or by changes in physiological conditions, improving the drug's absorption by the tumour cells at the target sites [87–89].

Doxorubicin (DOX) Multi-functional Micro Bubbles (MBs) paired with MNPs were developed by Fan et al. for enhanced magnetic targeting and drug delivery. For precise tissue targeting during MRI, nanoparticles, primarily iron oxide, have been employed as super magnetic particles. In one study, blood was given an intravenous injection of iron oxide nanoparticles, which were then collected using RES. Iron oxide nanoparticles, such as macrophages, can be observed by MRI once they have entered these cells. This has the potential to be very useful in determining the composition of the BBB and monitoring macrophage activity in a variety of disorders that are characterized by inflammation [90]. A dextran-coated iron oxide nanoparticle called Ferumoxtran-10, which functions as a stable imaging marker to remove brain tumours during surgery, remains in the brain well enough for postoperative MRI even after surgical manipulation [91].

The presence of beta-amyloid peptides (Ab) with 40 or 42 amino acids (Ab40 or Ab42) in the walls of the brain and the cerebral blood vessels can be used to diagnose Alzheimer's disease (AD). Ab1-42 peptide, polyethene glycol, and magnetic nanoparticles were chemically mixed by Wadghiri et al. to identify the deposition of amyloid plaques (for improvement of brain permeability). The MRI calculation demonstrated a significant imaging capability compared to wild-type animals when an advanced contrast agent was intravenously delivered into AD transgenic mice.

Parkinson's disease is characterised by the death of dopaminergic neurons in the substantia nigra and the buildup of a-synuclein in the brain stem (PD). Using photoelectrochemical immunosensors, nanotube arrays with gold and titanium dioxide detect a-synuclein. Additionally, when combined with anti-a-synuclein, polybutyl cyanoacrylate nanoparticles aided in the clearance of synuclein in neurons [92].

Gene expression is altered in neurological disorders, particularly in degenerative illnesses like Alzheimer's and Parkinson's disease, as a result of gene transfer. This often increases the capacity of neuronal cells to regenerate and live on their own. In the process of gene transfer, nanoparticles can be employed instead of viral vectors. They are more efficient, simpler to produce, and they elicit a lesser immunological reaction. As gene expression vectors and protein expression vectors, organically modified silica nanoparticles and nanoparticles coupled with chitosan and green fluorescent protein (pGFP) are both useful [88]. The CNS is difficult to heal, much like the peripheral nervous system. Seil and Webster employed ZnO nanoparticles as a tissue rejuvenation for CNS neurons because they can carry out and endure an electrical charge, which has been demonstrated to control and drive neural development; this particular form of nanoparticles has proved beneficial [93].

Application in gastroenterology

The digestive system (GI) is a desired target system for the use of nanotechnology. It is where medications are absorbed. Under some circumstances, such as when the pH, travel duration, heat, and the bacterial content nanoparticles action may be controlled throughout the transit of the digestive tract. According to Bergin et al., with sizes GI cells absorb nanoparticles at sizes smaller than 100 nm which is much higher than that of units with a micrometer-scale [94].

Disruptive natural barriers, such as low gastric pH and enzymatic digestion of intestinal excrements, must be overcome for nano-vehicles to approach the target area. In addition to the bacterial enzymes found in the local flora, intestinal motility-related mechanical forces in the colon also contribute to the degradation of nanocarriers. 5-FU is a well-known chemotherapy drug for gastrointestinal tumours since it is a confirmed DNA inhibitor. Zhang et al. created 5-FU-containing chitosan poly aspartic acid nanoparticles by ionic gelation and showed that they released 5-FU more slowly

in vitro and in vivo, maintained drug concentration for longer periods of time, and inhibited tumour growth at a faster rate than the control group.

Nanotechnology can only offer promise for improved treatment of colorectal cancer in the future as it is a frequent cancer that has spread over the globe. For the purpose of preventing colorectal cancer, a number of active targeted strategies have been suggested. In tumour cells, transferrin receptors are typically overexpressed. Transferrin-coated liposomes demonstrated increased antitumor effectiveness. Gold nanoparticles having carboxy-terminal phospholipids were combined with a single-chain antibody by Kirui et al (scFv). The A33 antigen is overexpressed on the surface of colorectal cancer cells, causing the nanoparticles to be specifically immobilised on the cancer cell surfaces. The cancer cells subsequently take up residence in the nanoparticles preferentially. With 808 nm light absorption, the cancer tissue was specifically destroyed, proving that this method is suitable for cancer detection and treatment.

IBD, or inflammatory bowel disease, includes ulcerative colitis and Crohn's disease. Due to severe side effects, there are presently no effective and targeted treatments for this chronically painful inflammatory condition. The only available treatments at this time are immunosuppressants or anti-inflammatory medications (5-aminosalicylic acid, steroids). Despite the strength of these pharmaceuticals, their immune system effects, which can have negative short- and long-term adverse effects, have restricted their usage. On the premise that immune-related cells are the target for selective oral medication administration in IBD, preliminary experiments have successfully addressed swollen tissue in an experimental model of colitis. Mice with colitis caused by the DSS have been treated with dexamethasone-filled poly-DL-lactic acid microparticles.

The abnormal production of Reactive Oxygen Species (ROS) at areas of intestinal inflammation plays a crucial role in the pathophysiology of IBD.

A novel class of nanoparticles that degrades in the presence of reactive oxygen species was developed by Wilson et al (ROS). The TNF gene has been found to play a significant influence in ROS [95]. Additionally, these nanoparticles targeted the areas of intestinal swelling, reduced TNF- -mRNA in swollen intestinal tissues, and decreased intestinal inflammation when they were conjugated with TNF- -siRNA and given orally [96-98].

Globally, the burden of liver disease on the public health system has increased significantly. Liver disease ranks as the 14th most common cause of mortality worldwide. Hepatic fibrosis, viral infections, and hepatocellular cancer are the main causes of liver disease. New drug delivery opportunities are made possible by nanotechnology for the treatment of liver disease.

Liver fibrosis has a number of probable causes, and many conditions might exist in one person. Hepatic fibrosis can develop as a result of chronic liver injury, heavy drinking, hepatitis B and C virus infections, genetic abnormalities, and other factors. In contrast to other normal tissue, fibrotic tissue has different cell types that are activated. These cells, such as activated hepatic stellate cells and myofibroblasts, promote the secretion of various matrix metalloproteinases, which alters the normal matrix and replaces it with fibrillar collagen structure.

On hepatic cells, the insulin-like growth factor 2 receptor is overexpressed. Mannose 6-phosphate stellate cells linked to a nanoparticle immediately loaded with medication, hits the receptor, and releases the substance for its actions. Collagen type VI (a matrix protein involved in cell adhesion), Integrins are widely expressed by hepatic stellate cells. Targeting is done using the RGD (Arginine-Glycine-Aspartate) sequence. the hepatic stellate cells and collagen VI in the fibrotic liver. Liposomes when combined with RGD, directly integrated with interferon (IFN)a-1b demonstrates anti-fibrotic action by targeting the integrins. Added research demonstrates the use of gold particles coated with silymarin in the treatment of liver fibrosis. The hepatic stellate cells are downregulated by gold particles.Following treatment using silymarin-coated gold nanoparticles, there is a reduction in a number of inflammatory indicators in animal models, which are predicted to be the main markers for fibrosis induction. Alpha-smooth actin muscle (-SMA) level reductions precisely result in decreased fibrogenesis and liver fibrosis. Dexamethasone (corticosteroid)-loaded liposomes are manufactured to exhibit anti-inflammatory activity and are therefore used to treat liver fibrosis.

The liver's hepatic stellate cells are the target of Berberine BSA nanoparticles, which were created by conjugating Berberine with bovine serum albumin. By suppressing the activation of hepatic stellate cells, these particles stop future fibrogenesis.

Hepatocellular carcinoma, which affects adults, is the most typical primary liver cancer (HCC). Related to the prevalence of hepatitis B virus infection, alcohol consumption, and other causes of hepatic cirrhosis, it ranks as the third

most prevalent cause of mortality globally. HCC's chemoresistance to many antitumor medications is one of the main reasons chemotherapy failed to treat it. Nanotherapeutics may increase the drug's absorption into liver tissue, reduce its availability elsewhere, and increase the therapy's efficacy.

The doxorubicin-loaded poly (isohexyl cyanoacrylate), nanoparticle formulation known as doxorubicin transdrug (DT) has shown considerable anti-tumor activity in vivo against multidrug-resistant protein overexpression in hepatocellular carcinoma.

According to one study, folic acid may be used to target radiation-induced liver cancer using silver/silica nanoparticles. When indocyanine green was combined with silver/silica nanoparticles, silver and indocyanine green, which has potential anti-folic acid capabilities, were produced. This could help prevent liver cancer.

During pre-treatment by intravenous injection, the diagnosis of HCC by liver imaging has been greatly aided by superparamagnetic iron oxide nanoparticles (SPIONs). Although the liver's Kupffer cells quickly sequester SPIONs with a mean particle width of 150 nm, this procedure improves the comparison between the liver and tumour because the tumour lacks Kupffer cells. Both Ferumoxide (Dextran-coated SPION, Endorem, Ferridex) and Ferucarbotran (Carboxydextran-coated SPION, Resovist) are SPIONS that have been approved by science for the imaging of liver cancer [98–100]. In Fig. 2, a detailed application of nanoparticles in medicine is shown.

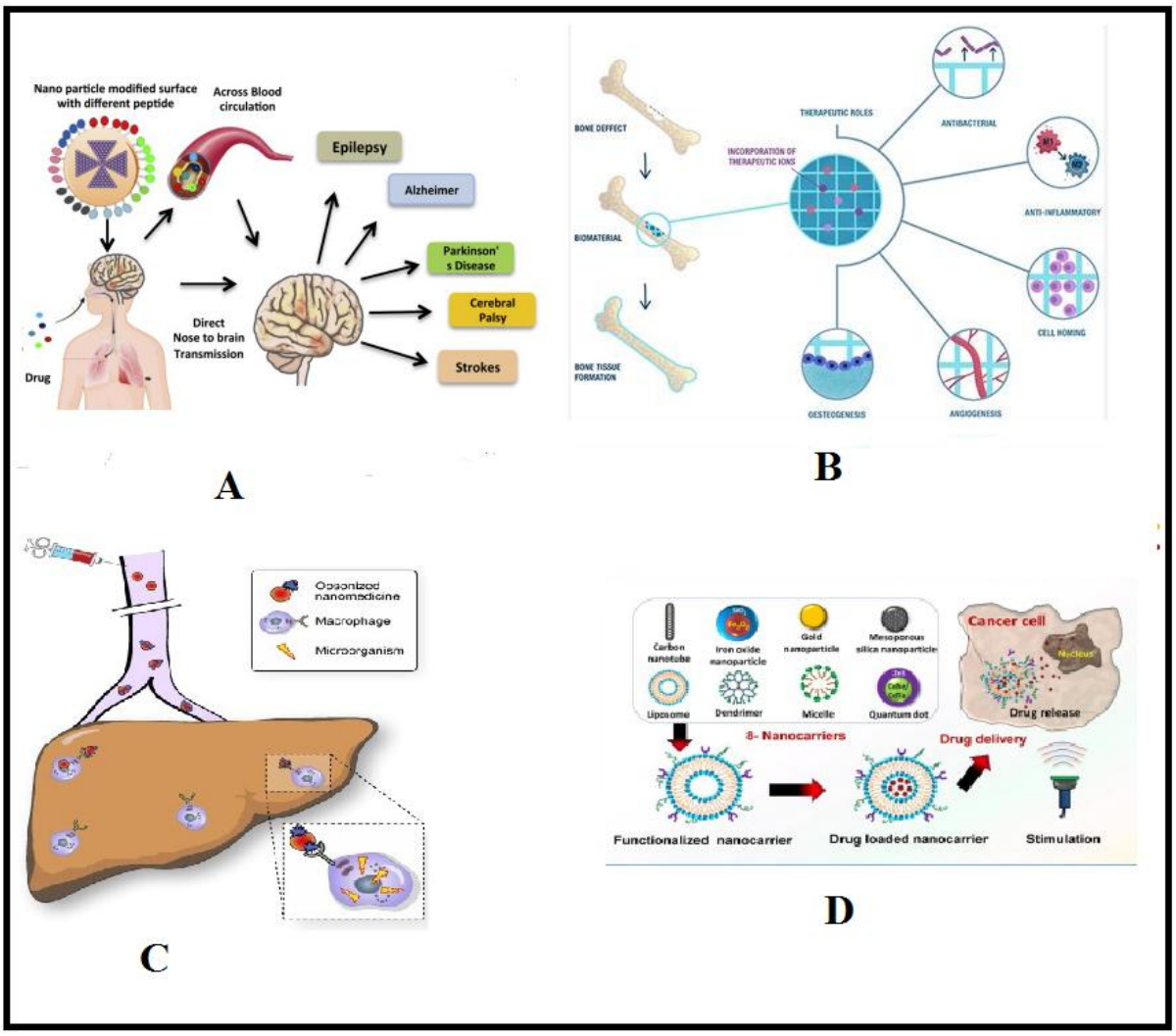

Fig. 2. Different applications of nanoparticles in medicine.

A. Nanoparticle with a various surface peptide is inhaled through the nose and travels directly to the brain to help treat or prevent a variety of neurological disorders. B nanoparticles are used directly as drug carriers to promote the

induction of mesenchyme stem cells, bone cell rejuvenation, stem cell formation, and bone tissue engineering. C nanoparticles are injected into the bloodstream and travel directly to the liver and kill microorganisms. D nanoparticles are used as decreased tumour size with various cancer therapies.

APPLICATION IN BIOMEDICAL ENGINEERING

Surgical equipments

Surgical blades

The use of catheters had influenced the advancement of minimally invasive surgery. MWCNTs had been integrated as a filter in nylon-12 (matrix bed), which leads to the fabrication of a nanotube-based polymerreinforcement catheter. This device had been tested *in-vitro* and *in vivo* both, which results in improvement with significant mechanical property and reduction in thrombogenicity, shows maximum resistance to fracture, improves electrostatic property [103]. Optical tweezers: Optical tweezers are other surgical tools with a single gradient optical trap used for non-invasive manipulation of nano-sized or micron sized objects such as viruses, DNA, etc. However, instead of using forces and tweezers, light is being used to check the dynamics of partials. Be sides, this technique is often said to be non-intrusive. It has been found that in nematodes(*c.elegance*), optical tweezers can generate stress due to continues-waves of infrared light [104]. Due to plasma polishing, which results in a reduction in coating thickness of roughly 5–25–0.5 m and a corresponding decrease in surface roughness of 20–40 nm, these blades are thin and sharp. These nano-layered blades are employed in the fields of ophthalmology and neurosurgery [102].

Invasive surgery

The development of minimally invasive surgery had been influenced by the use of catheters. A nanotube-based polymer-reinforcement catheter was made possible by the integration of MWCNTs as a filter in nylon-12 (matrix bed). The results of this device's in vitro and in vivo testing show significant improvements in mechanical properties, a decrease in thrombogenicity, maximum fracture resistance, and improved electrostatic properties [103]. Optical tweezers are other surgical instruments with a single gradient optical trap that are used for non-invasive manipulation of nano or micronsized objects like viruses, DNA, and other biological materials.However, light is being used to examine the dynamics of partials rather than forces and tweezers. Besides, this method is frequently referred to as non-intrusive. It has been found that in nematodes(c.elegance), optical tweezers can generate stress due to continues waves of infrared light [104].

Tissue engineering

Tissue functionality has been enhanced by tissue engineering. This technique provided an alternative to missing body tissue and injured or damaged tissues [105]. Tissue engineering became a boon to medical science because of its application which has given them hope to humankind for survival. Tissues engineering have been occupied as the central core of science in term of organ transplantation, bone replacement, skin grafting, nerve tissue repair, etc. In this section, the advancement of tissue engineering was discussed in brief.

Bone tissue engineering

Because collagen is present, bones may regenerate or mend. 3D porous scaffolds with similar compositions to bone and bio-ceramics scaffolds are employed for their compatibility in cases of significant bone defects or skeletal deformities [106]. These osteoconductive scaffolds use biomolecule progenitor cells and signalling for the development of new bone. Additionally, nanoparticles are created in vitro for the release of osteogenic factors to promote the production of new bone and retain the three-dimensional structure [107].

Nerve tissue engineering

Regeneration and repair in brain tissue engineering have a direct impact on human existence. It has given neurological treatment a fresh outlook. Nerve cells can typically fill gaps up to 6 mm wide. Beyond these bigger gaps, it's difficult medically to fill them. The most encouraging tissue engineering results so far have been with nanofibers because of their resemblance to the Scaffold [108]. Nanofibers have a fibrous, three-dimensional structure and are smaller than one millimetre. In tissue engineering, nanofibers with a large surface area to volume ratio are more compatible and encourage the proliferation of inner cells.Electrospinning, the most effective method for creating polymeric nanofiber, has been used to create PPLA nanofibrous scaffolds that enable neural stem cell adhesion, differentiation, and outgrowth [109].

Antibody

Nanoparticles with an antibody conjugation: While antibodies are often known to target the body's targeted antigens, nanoparticles exhibit excellent binding effectiveness due to their greater surface area to volume ratio. The significance

of antibody linked nanoparticles in biomedical engineering has been shown. Together, they provide improved central intracellular stability and the capacity for specific and selective antigen recognition [110].

Photodynamic therapy

Human cell anti-carcinoembryonic antibodies were used to attach LoVo to a TiO2 nanoparticle. A pair of photoinduced electrons and holes are created when an excited electron in TiO2's valance bond is exposed to UV light irradiation in the conduction band [111]. When exposed to UV radiation, the production of reactive oxygen species causes the presence of holes and photoinduced electrons to have redox (reduction, oxidation) reaction characteristics, which causes the demise of malignant cells [112]. These antibodies are used to label with (FITC) Fluorescein isothiocyanate and then evaluated in confocal laser microscopy to increase optical detection.To hasten the incorporation of conjugated nanoparticles in cancer cells, the electroporation approach is used. The in-vitro investigation demonstrates that the greatest amount of cancerous cells were photo-killed in just 90 minutes. Using gold-coated silica nanoparticles, photodynamic treatment is also applied to external tumours existing in the body. This causes irreversible heat damage to malignant cells present in the human breast when exposed to NMR rays in vitro [113].

Neuro therapy

Due to two physiological obstacles present in the brain, numerous efforts to treating illnesses of the central nervous system have been unsuccessful in neuroscience. Endothelial cells form a single layer that forms the blood-brain barrier (BBB). This barrier prevents any therapeutic medicine from entering the brain from the periphery. Blood cerebrospinal fluid, the other barrier, prevents the mixing of blood and cerebro spinal fluid. Low resistance is evident, and the smaller particle can diffuse through it [114]. While specifically targeting the BBB with long-circular nanoparticles demonstrates encouraging outcomes for enhancing non-invasive medications into the brain. Due to a number of characteristics, including size and large surface area, nanoparticles have demonstrated adequate adaptability when it comes to penetrating the blood-brain barrier.According to a paper, when a nanoparticle smaller than 100 nm crosses the BBB, no appreciable alterations are seen [115]. The surface of nanoparticles is covered with several active substances, such as poloxamer-188, which improves numerous drug delivery procedures. This method is connected to the brain's capillary endothelial cells' receptor-mediated process [116]. The several influx transport methods carried out by the cerebral endothelium, such as receptor-mediated endocytosis (RME) and absorptive-mediated endocytosis (AME), can be recognised by an antibody. According to the study, DOX capsules were used to cure intracranial U-87 MG brain tumours found in naked mice.Long-circulating nanoparticles that have been bound to the monoclonal antibody 2C5 show promise as a treatment to shrink tumours and lengthen patient survival [117].

Encapsulation

Encapsulating monoclonal antibodies allows for the avoidance of issues like shorter in-vitro half-life and decreased physiochemical stability. Medications can be enclosed in nanoparticles without the coupling reaction changing, increasing the amount of drugs that can be loaded into them [118]. The ability to use nanoparticles that contain antibodies as biosensors is their principal benefit. Nanoparticles can be used to encapsulate antigens for immunisation because they increase the solubility in the blood stream. Cationic nanoparticles are used in the nasal delivery system with recombinant proteins such Hbs-Ag and -galactosidase, which cause an in-vivo humoral, mucosal, and cellular response due to their electrostatic attraction to the mucosal layer's negative charge [119].

Visualisation

Quantum dots imaging

Covalent conjugation of a quantum dot loaded with mercapto-acetic acid to transferrin protein was used to apply quantum dots in vivo for cell surface antigen labelling. Cancerous cells undergo endocytosis while clinging to their vivid fluorescent [120]. It is possible to investigate this method further in order to label intracellular cells. Using the cdsc/ZnS quantum dots coated with polyethene glycol and inserted into Xenopus laevis embryos, the small amount of work has already been investigated. Furthermore, microscopic fluorescence imaging analysis revealed that their differentiation and cell lineage showed normal embryo development, and no evidence of toxicity was discovered even after several injections of quantum dots particles [121].

Tumour targeting imaging

Using quantum dots to target a therapeutic human cancer cell in vivo, this method was first demonstrated in naked mice. It's interesting that a subdermal tumour just needs a tiny depth of penetration for imaging. Polyethene glycol coupled with quantum dots and functionalized with an anti-membrane antigen was injected into naked mice (prostate-specific). Antigen antibody binding, the retention effect, and the permeability of vascular tumours were the initial causes of conjugation. The inherent vascular permeability of cancer tissue lacking lymphatic drainage protects against this impact. Non-conjugated with antibody, poly ethelynglycol-containing quantum dots were used to study the

influence and permeability on a mouse model of tumour induction.It has been discovered, nonetheless, that this approach is less effective than active targeting of probes [122]. Fig. 3 shows the developments in nanoparticle development for biomedical engineering.

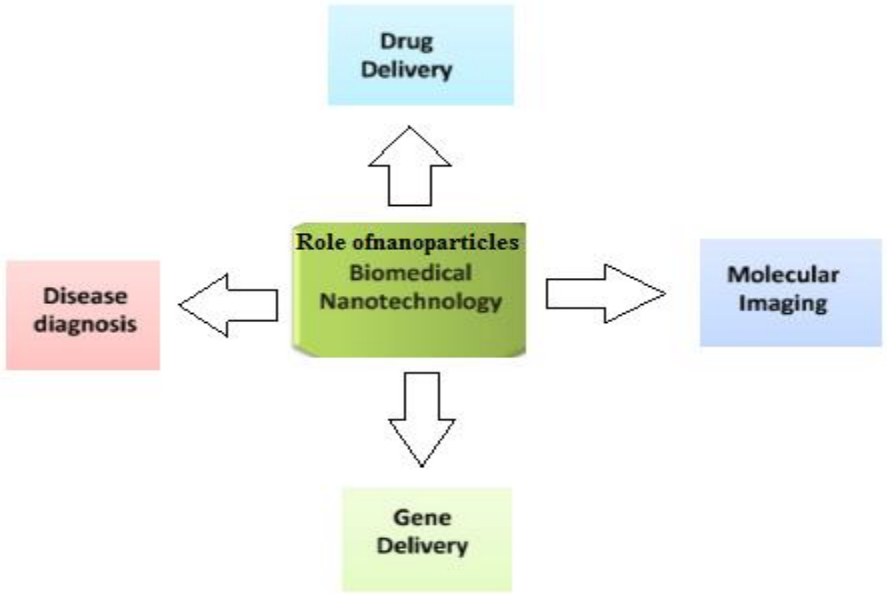

Fig. 3.Recent developments in the biomedical engineering of nanoparticles.

THE RISK ASSOCIATED WITH NANOTECHNOLOGY

A developing area of study, nanotechnology has a wide range of uses in fields such as medicine, health care, and human welfare. Along with these uses, worries about the potentially harmful effects of these nanoparticles caught the attention of many researchers, and various studies were conducted to determine their toxicity. According to the findings of these studies, nanoparticles' subsequent qualities may cause them to have dangerous effects.

Reduced size of nanoparticles

These nanoparticles are decreased to their most attractive forms in order to maximise efficiency, but at this small diameter, it is very hard to process them further; as a result, if these nanoparticles infiltrate undesirable cells or tissues, their accumulation may have hazardous effects..

Different shape may lead to toxic impacts

Nanoparticles can have varying shapes, and these variations in shape can have dangerous effects on the same target. For example, rod-shaped ZnO nanoparticles seem to be more hazardous to the lungs' epithelium than spherical ZnO nanoparticles.

Rate of movement

According to the relationship between size and mobility, any particle's mobility is inversely correlated with its size. Because nanoparticles have such a high mobility rate, they can invade many internal tissues or cells, where their accumulation or aggregation can have toxic effects and block many useful pathways.

Property of aggregation

The ability of nanoparticles to aggregate into clusters in order to achieve stability can occasionally result in aberrant physiological processes. High conductivity, magnetic properties, and changed thermal properties are a few more characteristics that could cause slight anomalies in cells [123]. Numerous pathways exist for these tiny particles to enter people, animals, and plants, including the nasal passages and epidermal pores.

RISK ASSOCIATED WITH HUMAN HEALTH

Lungs damage

Absorption of nanoparticles in any form results in their passage to a variety of organs, including the lungs, brain, liver, and spleen, as well as their accumulation in the mucosal layers of the epidermis. This invasion causes toxic effects on

physiology, for instance, TiO2 nanoparticle exposure to rats in a model system implied that the nanoforms of these compounds are relatively more toxic than that of the bulk material and cause pulmonary inflammations [124].

Skin damage

The pores on the skin are another potential entry point for these nanoparticles, and the use of sunscreen is the best illustration of the toxic effects of nanoparticle invasion through the skin. Although new technologies have provided an opportunity to use nanoparticles in sunscreen to do is provide effective protection against excessive UV exposure, excessive or prolonged use of these sunscreens has resulted in adverse effects on the skin, including patching, sunburn, and a number of other skin disorders.

Immunosuppressant

However, studies have shown that these nanoparticles first interact with phagocytic cells (macrophages) of the immune system, and if the encounter is not successful enough, this event can trigger an inflammatory response or autoimmune disorders [126]. Nanoparticles have important applications in the field of immunological research; they have been demonstrated to be a powerful substance to deal with numerous drug targeting and delivering issues.

Cancer therapy

In the case of cancer patients, where clarity in tumour imaging is a crucial step of treatment and patients are given nanoparticles for clear visualization and analysis, quantum dots have played a prominent part in improving the bio-imaging process. However, in many cases, it has been observed that all these nanoparticles invade the tumour and cause cytotoxicity.

LIMITATION OF NANOMEDICINE

There is virtually little research on the entirely new field of nanomedicine. To be on the safe side, we still want to see the practical application of nanomedicine; we should note that it is always in the experimental stage. We are unable to state with certainty what the health dangers of nanotechnology are due to a lack of knowledge regarding the drawbacks of nanomedicine. Nevertheless, we can accept the truth that nanoparticles can enter our bodies in a variety of ways, which may cause considerable worry.

Even while nanomedicine has many uses and benefits, it cannot be said to be flawless. This conclusion is supported by the fact that the size variation is drastically limited when they move from micro to nanosized particles.

The mononuclear phagocytic system in the organs traps nanoparticles (MPS). For nanostructures developed for pharmacological activity in another portion of the body, the same characteristic might have proven problematic. The chemical reactivity of nanoparticles increases with their surface area, creating important instability in their behaviour under various conditions and their capacity to pass the biological membranes and enter cells. Reactive oxygen species (ROS) are created when the chemical reactivity of nanoparticles is increased. ROS can directly result in undesirable consequences by causing oxidative stress, inflammation, and damage to DNA, proteins, and membranes.The fundamental disadvantage of nanomedicine is that apart from their size, nanoparticles do not share any characteristics. Therefore, each particle needs to be evaluated separately.

In addition, distinct chemical and physical compounds that are semi at 100 nm may change in shape and structure to become harmful at 1 nanometer or the opposite. Another drawback of such molecules is their reliance on ambient particles, which might collect or disintegrate and cause toxicity. These particles may interact in unexpected ways inside the body, which could result in unexpected outcomes.

When nanoparticles are injected into the body, they pass through cell membranes, enter capillaries, travel from the site of injection to other areas of the body, and then strangely enter the BBB. Effects that were not seen with traditional treatment could be brought on by nanoparticles. such as harm to different cellular components, like the mitochondria or nucleus. Additionally, they might trigger blood clotting processes and improve platelet aggregation. Despite being designed to decrease systemic adverse drug effects, carrier systems can be hazardous in and of themselves. Future prospects for nanomedicine are bright, particularly for conditions like cancer. Nanomedicine is expected to increase the therapeutic index by enhancing the efficiency of drug delivery in targeted cells and controlling drug release at a particular site.As a result, in order to gain the support of the community, the ethical, social, and legal issues of nanomaterials must be appropriately addressed. There is confusion regarding the danger aspects that individuals could be exposed to it while utilising nanomedicine, despite efforts to raise awareness of its usage in humans. More nanomedicine-based medical trials are required for unmistakable validation. Risk management, communication, and

assessment are significant ethical challenges in clinical investigations. It is crucial to educate people about the benefits and challenges of nanomedicine in order to prevent potential public backlash.

FUTURE PERSPECTIVE

At a compound annual growth rate (CAGR) of 13.5%, the size of the worldwide nanomedicine market is expected to rise from an estimated $53 billion in 2009 to greater than $100 billion in 2014. The potential for developing a system that is more effective for the creation of nanoproducts is constrained. It is essential to comprehend how nanomaterials are distributed within the body. This is related to a second limitation that calls for imaging techniques to track the biodistribution of nanomedicine over time.

The safety of nanomedicine has not yet been fully established, despite rigorous standards and ongoing identification of potential benefits. Nanotechnology is anticipated to be used in diagnostics, molecular research methods, and instruments as it advances concurrently in other domains.Although it should concentrate on resolving current concerns, such as the accessibility of medications for the underprivileged and simple and affordable diagnostic options, rather than pursuing new and profound nanotechnology uses. The majority who require primary healthcare facilities will be served by it.

In order to develop nanotechnology-based therapy options, additional research is required with a stronger emphasis on transport processes, endocytosis, cellular barriers, degradation pathways, and control over its potential harmful effects.

CONCLUDING REMARKS

Plans for "theranostics," a merger of therapy and diagnostics, are at the more futuristic end of the scale. In the realm of health and medical sciences, nanotechnology has recently undergone a revolution. It is a cutting-edge method for both medication delivery and drug discovery. Nanoparticle applications are straightforward and effective. Though, nothing is known about the toxicity of nanomaterials. One of the biggest obstacles in the realm of health and medicine is the variety of nanoparticles and the number of contraindications. Despite this, numerous crucial studies were conducted in medicine to address the radically dissimilar characteristics of nanoparticles. In this article, we've discussed the current state of several nanoparticle kinds and their diagnostic and therapeutic applications in treating a range of medical issues.

Nanotechnology is an interdisciplinary field that spans a wide range of scientific disciplines, including biology, chemistry, electrical engineering, and materials science. Additionally, it is challenging for one researcher to become an expert in all subjects. Therefore, to ensure that innovation can result in useful goods, nanotechnology developers should cooperate.

REFERENCES

[1]. S. Bayda, et al., The history of nanoscience and nanotechnology: from chemical physical applications to nanomedicine, Molecules 25 (1) (2019).
[2]. Coil embolization for intracranial aneurysms: an evidence-based analysis, Ont. Health Technol. Assess. Ser. 6 (1) (2006) 1–114.
[3]. J.A. Sichert, et al., Quantum size effect in organometal halide perovskite nanoplatelets, Nano Lett. 15 (10) (2015) 6521–6527.
[4]. C. Zandonella, Cell nanotechnology: the tiny toolkit, Nature 423 (6935) (2003) 10–12.
[5]. S.M. Moghimi, Z.S. Farhangrazi, Nanomedicine and the complement paradigm, Nanomedicine 9 (4) (2013) 458–460.
[6]. P. Zarrintaj, et al., Can regenerative medicine and nanotechnology combine to heal wounds? The search for the ideal wound dressing, Nanomedicine 12 (19) (2017) 2403–2422.
[7]. D.L. Stirland, et al., 3 - targeted drug delivery for cancer therapy, in: K. Park (Ed.), Biomaterials for Cancer Therapeutics, Woodhead Publishing, 2013, pp. 31–56.
[8]. M.A. Dobrovolskaia, Pre-clinical immunotoxicity studies of nanotechnology formulated drugs: challenges, considerations and strategy, J. Contr. Release 220 (Pt B) (2015) 571–583.
[9]. S.K. Sahoo, S. Parveen, J.J. Panda, The present and future of nanotechnology in human health care, Nanomedicine 3 (1) (2007) 20–31.
[10]. A. El-Sayed, M. Kamel, Advances in nanomedical applications: diagnostic, therapeutic, immunization, and vaccine production, Environ. Sci. Pollut. Control Ser. 27 (16) (2020) 19200–19213.

[11]. I. Khan, K. Saeed, I. Khan, Nanoparticles: properties, applications and toxicities, Arab. J. Chem. 12 (7) (2019) 908–931.
[12]. D. Chenthamara, et al., Therapeutic efficacy of nanoparticles and routes of administration, Biomater. Res. 23 (1) (2019) 20.
[13]. H. Heinz, et al., Nanoparticle decoration with surfactants: molecular interactions, assembly, and applications, Surf. Sci. Rep. 72 (1) (2017) 1–58.
[14]. S.B. Ghaffari, et al., Functionalization of ZnO nanoparticles by 3-mercaptopro pionic acid for aqueous curcumin delivery: synthesis, characterization, and anticancer assessment, Mater. Sci. Eng. C Mater. Biol. Appl. 79 (2017) 465–472.
[15]. J.E. Lee, et al., Multifunctional mesoporous silica nanocomposite nanoparticles for theranostic applications, Accounts Chem. Res. 44 (10) (2011) 893–902.
[16]. M. Mansha, et al., Synthesis, characterization and visible-light-driven photoelectrochemical hydrogen evolution reaction of carbazole-containing conjugated polymers, Int. J. Hydrogen Energy 42 (16) (2017) 10952–10961.
[17]. H. Ullah, et al., Sonochemical-driven ultrafast facile synthesis of SnO2 nanoparticles: growth mechanism structural electrical and hydrogen gas sensing properties, Ultrason. Sonochem. 34 (2017) 484–490.
[18]. Y. Xin, et al., Recent progress on nanoparticle-based drug delivery systems for cancer therapy, Canc. Biol. Med. 14 (3) (2017) 228–241.
[19]. A. Heuer-Jungemann, et al., The role of ligands in the chemical synthesis and applications of inorganic nanoparticles, Chem. Rev. 119 (8) (2019) 4819–4880.
[20]. M.P. Nikolova, M.S. Chavali, Metal oxide nanoparticles as biomedical materials, Biomimetics 5 (2) (2020) 27.
[21]. L. Das, et al., Synthesis of hybrid hydrogel nano-polymer composite using Graphene oxide, Chitosan and PVA and its application in waste water treatment, Environ. Technol. Innov. 18 (2020) 100664.
[22]. A. Kaushik, in: Akash Deep, Sandeep Kumar (Eds.), Advances in Nanosensors for Biological and Environmental Analysis: Book Review, Elsevier, 2019, ISBN 978-0- 12-817456-2, p. 101. Biosensors, 2019. 9(3).
[23]. Y. Zhu, D.K. James, J.M. Tour, New routes to graphene, graphene oxide and their related applications, Adv. Mater. 24 (36) (2012) 4924–4955.
[24]. E. Ghavaminezhad, M. Mahnama, N. Zolfaghari, The effects of van der Waals interactions on the vibrational behavior of single-walled carbon nanotubes using the hammer impact test: a molecular dynamics study, Phys. Chem. Chem. Phys. 22 (22) (2020) 12613–12623.
[25]. B. Pelaz, et al., Diverse applications of nanomedicine, ACS Nano 11 (3) (2017) 2313–2381.
[26]. S. Chen, et al., Nanomaterials in medicine and pharmaceuticals: nanoscale materials developed with less toxicity and more efficacy, Eur. J. Nanomed. 5 (2) (2013) 61.
[27]. M. Chandarana, A. Curtis, C. Hoskins, The use of nanotechnology in cardiovascular disease, Appl. Nanosci. 8 (7) (2018) 1607–1619.
[28]. M. Mozafari, Nanotechnology in wound care: one step closer to the clinic, Mol. Ther. : J. Am. Soc. Gene Ther. 26 (9) (2018) 2085–2086.
[29]. D. Bobo, et al., Nanoparticle-based medicines: a review of FDA-approved materials and clinical trials to date, Pharm. Res. (N. Y.) 33 (10) (2016) 2373–2387.
[30]. M.A. Obeid, et al., Delivering natural products and biotherapeutics to improve drug efficacy, Ther. Deliv. 8 (11) (2017) 947–956.
[31]. R. Devulapally, R. Paulmurugan, Polymer nanoparticles for drug and small silencing RNA delivery to treat cancers of different phenotypes, Wiley Interdiscipl. Rev. Nanomed. Nanobiotechnol. 6 (1) (2014) 40–60.
[32]. A.Z. Mirza, F.A. Siddiqui, Nanomedicine and drug delivery: a mini review, Int. Nano Lett. 4 (1) (2014) 94.
[33]. G. Gregoriadis, Liposomes in drug delivery: how it all happened, Pharmaceutics 8 (2) (2016) 19.
[34]. R. Bajracharya, et al., Recent advancements in non-invasive formulations for protein drug delivery, Comput. Struct. Biotechnol. J. 17 (2019) 1290–1308.
[35]. S. Russi, et al., Adapting and surviving: intra and extra-cellular remodeling in drug-resistant gastric cancer cells, Int. J. Mol. Sci. 20 (15) (2019).
[36]. H.K. Verma, et al., Micro RNA facilitated chemoresistance in gastric cancer: a novel biomarkers and potential therapeutics, Alexand. J. Med. 56 (1) (2020) 81–92.
[37]. H.K. Verma, Exosomes facilitate chemoresistance in gastric cancer: future challenges and openings, Precis. Radiat. Oncol. 3 (4) (2019) 163–164.

[38]. J. Larocque, D.J. Bharali, S.A. Mousa, Cancer detection and treatment: the role of nanomedicines, Mol. Biotechnol. 42 (3) (2009) 358–366.
[39]. J.K. Patra, et al., Nano based drug delivery systems: recent developments and future prospects, J. Nanobiotechnol. 16 (1) (2018) 1–33.
[40]. R. Misra, S. Acharya, S.K. Sahoo, Cancer nanotechnology: application of nanotechnology in cancer therapy, Drug Discov. Today 15 (19–20) (2010) 842–850.
[41]. S. Sengupta, et al., Temporal targeting of tumour cells and neovasculature with a nanoscale delivery system, Nature 436 (7050) (2005) 568–572.
[42]. A. Singh, et al., Composite polymeric magnetic nanoparticles for co-delivery of hydrophobic and hydrophilic anticancer drugs and MRI imaging for cancer therapy, ACS Appl. Mater. Interfaces 3 (3) (2011) 842–856.
[43]. M.S. Shim, et al., Combined multimodal optical imaging and targeted gene silencing using stimuli-transforming nanotheragnostics, J. Am. Chem. Soc. 132 (24) (2010) 8316–8324.
[44]. S.A.A. Rizvi, A.M. Saleh, Applications of nanoparticle systems in drug delivery technology, Saudi Pharmaceut. J. 26 (1) (2018) 64–70.
[45]. R. Pignatello, et al., Flurbiprofen-loaded acrylate polymer nanosuspensions for ophthalmic application, Biomaterials 23 (15) (2002) 3247–3255.
[46]. M. Merodio, et al., Ocular disposition and tolerance of ganciclovir-loaded albumin nanoparticles after intravitreal injection in rats, Biomaterials 23 (7) (2002) 1587–1594.
[47]. M.M. Silva, et al., Chitosan nanoparticles as a mucoadhesive drug delivery system for ocular administration, Mar. Drugs 15 (12) (2017).
[48]. W. Yao, et al., Preparation and characterization of puerarin-dendrimer complexes as an ocular drug delivery system, Drug Dev. Ind. Pharm. 36 (9) (2010) 1027–1035.
[49]. C. Shi, et al., Nanoscale technologies in highly sensitive diagnosis of cardiovascular diseases, Front. Bioeng. Biotechnol. 8 (June) (2020) 1–18.
[50]. Y. Deng, et al., Application of the nano-drug delivery system in treatment of cardiovascular diseases, Front. Bioeng. Biotechnol. 7 (January) (2020) 1–18.
[51]. I.Y. Chen, J.C. Wu, Cardiovascular molecular imaging: focus on clinical translation, Circulation 123 (4) (2011) 425–443.
[52]. F.A. Jaffer, P. Libby, R. Weissleder, Molecular imaging of cardiovascular disease, Circulation 116 (9) (2007) 1052–1061.
[53]. E. Aikawa, et al., Osteogenesis associates with inflammation in early-stage atherosclerosis evaluated by molecular imaging in vivo, Circulation 116 (24) (2007) 2841–2850.
[54]. A. Saraste, S.G. Nekolla, M. Schwaiger, Cardiovascular molecular imaging: an overview, Cardiovasc. Res. 83 (4) (2009) 643–652.
[55]. S. Nakashiro, et al., Pioglitazone-incorporated nanoparticles prevent plaque destabilization and rupture by regulating monocyte/macrophage differentiation in ApoE-/- mice, Arterioscler. Thromb. Vasc. Biol. 36 (3) (2016) 491–500.
[56]. D. Peters, et al., Targeting atherosclerosis by using modular, multifunctional micelles, Proc. Natl. Acad. Sci. U.S.A. 106 (24) (2009) 9815–9819.
[57]. K. Zhu, et al., Nanoparticles-assisted stem cell therapy for ischemic heart disease, Stem Cell. Int. 2016 (2016), p. 1384658-1384658.
[58]. Z.M. Binsalamah, et al., Intramyocardial sustained delivery of placental growth factor using nanoparticles as a vehicle for delivery in the rat infarct model, Int. J. Nanomed. 6 (2011) 2667–2678.
[59]. K. Nakano, et al., Formulation of nanoparticle-eluting stents by a cationic electrodeposition coating technology: efficient nano-drug delivery via bioabsorbable polymeric nanoparticle-eluting stents in porcine coronary arteries, JACC Cardiovasc. Interv. 2 (4) (2009) 277–283.
[60]. B. Gorain, et al., Nanoemulsion strategy for olmesartan medoxomil improves oral absorption and extended antihypertensive activity in hypertensive rats, Colloids Surf. B Biointerfaces 115 (2014) 286–294. *Journal of Drug Delivery Science and Technology 63 (2021) 102487*
[61]. U. Shah, G. Joshi, K. Sawant, Improvement in antihypertensive and antianginal effects of felodipine by enhanced absorption from PLGA nanoparticles optimized by factorial design, Mater. Sci. Eng. C, Mater. Biol. Appl. 35 (2014) 153–163.
[62]. T. Niaz, et al., Antihypertensive nano-ceuticales based on chitosan biopolymer: physico-chemical evaluation and release kinetics, Carbohydr. Polym. 142 (2016) 268–274.
[63]. N.S. Ranpise, S.S. Korabu, V.N. Ghodake, Second generation lipid nanoparticles (NLC) as an oral drug carrier for delivery of lercanidipine hydrochloride, Colloids Surf. B Biointerfaces 116 (2014) 81–87.

[64]. D.A. Stout, et al., Mechanisms of greater cardiomyocyte functions on conductive nanoengineered composites for cardiovascular application, Int. J. Nanomed. 7 (2012) 5653–5669.
[65]. M. Kumar, et al., Chitosan IFN-gamma-pDNA nanoparticle (CIN) therapy for allergic asthma, Genet. Vaccine Ther. 1 (1) (2003), 3-3.
[66]. A.E. John, et al., Discovery of a potent nanoparticle P-selectin antagonist with anti-inflammatory effects in allergic airway disease, Faseb. J. 17 (15) (2003) 2296–2298, official publication of the Federation of American Societies for Experimental Biology.
[67]. A. Bhardwaj, et al., Development and characterization of ligand-appended liposomes for multiple drug therapy for pulmonary tuberculosis, Artif. Cells Nanomed. Biotechnol. 41 (1) (2013) 52–59.
[68]. M.D. Shin, et al., COVID-19 vaccine development and a potential nanomaterial path forward, Nat. Nanotechnol. 15 (8) (2020) 646–655.
[69]. H.K. Verma, et al., Current updates on the European and WHO registered clinical trials of coronavirus disease 2019 (COVID-19), Biomed. J. 43 (5) (2020) 424–433.
[70]. B. Gopalan, et al., Nanoparticle based systemic gene therapy for lung cancer: molecular mechanisms and strategies to suppress nanoparticle-mediated inflammatory response, Technol. Canc. Res. Treat. 3 (6) (2004) 647–657.
[71]. S. Prabha, V. Labhasetwar, Nanoparticle-mediated wild-type p53 gene delivery results in sustained antiproliferative activity in breast cancer cells, Mol. Pharm. 1 (3) (2004) 211–219.
[72]. J.R. Antonio, et al., Nanotechnol. Dermatol. 89 (1) (2014) 126–136.
[73]. M. Zhou, et al., Peptide-labeled quantum dots for imaging GPCRs in whole cells and as single molecules, Bioconjugate Chem. 18 (2) (2007) 323–332.
[74]. D. Papakostas, et al., Nanoparticles in dermatology, Arch. Dermatol. Res. 303 (8) (2011) 533–550.
[75]. M. Cui, et al., Nanodelivery systems for topical management of skin disorders, Mol. Pharm. 18 (2) (2020) 491–505.
[76]. H. Lboutounne, et al., Sustained ex vivo skin antiseptic activity of chlorhexidine in poly(epsilon-caprolactone) nanocapsule encapsulated form and as a digluconate, J. Contr. Release 82 (2–3) (2002) 319–334, official journal of the Controlled Release Society.
[77]. H. Lboutounne, et al., Characterization of transport of chlorhexidine-loaded nanocapsules through hairless and wistar rat skin, Skin Pharmacol. Physiol. 17 (4) (2004) 176–182.
[78]. Y.-H. Tsuang, et al., Studies of photokilling of bacteria using titanium dioxide nanoparticles, Artif. Organs 32 (2) (2008) 167–174.
[79]. X. Chen, H.J. Schluesener, Nanosilver: a nanoproduct in medical application, Toxicol. Lett. 176 (1) (2008) 1–12.
[80]. E. Makrantonaki, R. Ganceviciene, C. Zouboulis, An update on the role of the sebaceous gland in the pathogenesis of acne, Derm. Endocrinol. 3 (1) (2011) 41–49.
[81]. G.A. Castro, et al., Formation of ion pairing as an alternative to improve encapsulation and stability and to reduce skin irritation of retinoic acid loaded in solid lipid nanoparticles, Int. J. Pharmaceut. 381 (1) (2009) 77–83.
[82]. G.A. Castro, et al., Comedolytic effect and reduced skin irritation of a new formulation of all-trans retinoic acid-loaded solid lipid nanoparticles for topical treatment of acne, Arch. Dermatol. Res. 303 (7) (2011) 513–520.
[83]. B. Jain, et al., Development and characterization of minoxidil-loaded liposomal system for delivery to pilosebaceous units, J. Liposome Res. 20 (2) (2010) 105–114.
[84]. E.A.A. Neel, et al., Nanotechnology in dentistry: prevention, diagnosis, and therapy, Int. J. Nanomed. 10 (2015) 6371–6394.
[85]. S.T. Ozak, P. Ozkan, Nanotechnology and dentistry, Eur. J. Dermatol. 7 (1) (2013) 145–151.
[86]. I.M.F. Abiodun Solanke, D.M. Ajayi, A.O. Arigbede, Nanotechnology and its application in dentistry, Ann. Med. Health Sci. Res. 4 (9) (2014), 171-171.
[87]. M. Saeedi, et al., Applications of nanotechnology in drug delivery to the central nervous system, Biomed. Pharmacother. 111 (December 2018) (2019) 666–675.
[88]. J.R. Kanwar, et al., Nanoparticles in the treatment and diagnosis of neurological disorders: untamed dragon with fire power to heal, Nanomed. Nanotechnol. Biol. Med. 8 (4) (2012) 399–414.
[89]. F. Dilnawaz, S.K. Sahoo, Therapeutic approaches of magnetic nanoparticles for the central nervous system, Drug Discov. Today 20 (10) (2015) 1256–1264.
[90]. Z. Fan, D. Chen, C.X. Deng, Improving ultrasound gene transfection efficiency by controlling ultrasound excitation of microbubbles, J. Contr. Release 170 (3) (2013) 401–413, official journal of the Controlled Release Society.

[91]. K.K. Jain, Role of nanotechnology in developing new therapies for diseases of the nervous system, Nanomedicine 1 (1) (2006) 9–12.
[92]. P. Ambesh, D.G. Angeli, Nanotechnology in neurology: genesis, current status, and future prospects, Ann. Indian Acad. Neurol. 18 (4) (2015) 382–386.
[93]. J.T. Seil, T.J. Webster, Decreased astroglial cell adhesion and proliferation on zinc oxide nanoparticle polyurethane composites, Int. J. Nanomed. 3 (4) (2008) 523–531.
[94]. I.L. Bergin, F.A. Witzmann, Nanoparticle toxicity by the gastrointestinal route: evidence and knowledge gaps, Int. J. Biomed. Nanosci. Nanotechnol. (IJBNN) 3 (1–2) (2013), 10.1504/IJBNN.2013.054515.
[95]. H.K. Verma, N. Merchant, L. Bhaskar, Tumor Necrosis factor-alpha gene promoter (TNF-alpha G-308A) polymorphisms increase the risk of hepatocellular carcinoma in Asians: a meta-analysis, Crit. Rev. Oncog. 25 (1) (2020) 11–20.
[96]. G. Brakmane, M. Winslet, A.M. Seifalian, Systematic review: the applications of nanotechnology in gastroenterology, Aliment Pharmacol. Therapeut. 36 (3) (2012) 213–221.
[97]. H. Laroui, et al., Nanomedicine in GI, Am. J. Physiol. Gastrointest. Liver Physiol. 300 (3) (2011) 371–383.
[98]. A. Lamprecht, Nanomedicines in gastroenterology and hepatology, Nat. Rev. Gastroenterol. Hepatol. 12 (4) (2015) 195–204.
[99]. L.H. Reddy, P. Couvreur, Nanotechnology for therapy and imaging of liver diseases, J. Hepatol. 55 (6) (2011) 1461–1466.
[100]. H. Sharma, et al., Nanomedicine : a new therapeutic approach in liver diseases, Austin J. Nanomed. Nanotechnol. 7 (1) (2019).
[101]. M.F. Yanik, et al., Neurosurgery: functional regeneration after laser axotomy, Nature 432 (7019) (2004) 822.
[102]. E.D. Kirson, Y. Yaari, A novel technique for micro-dissection of neuronal processes, J. Neurosci. Methods 98 (2) (2000) 119–122.
[103]. T. Kubik, K. Bogunia-Kubik, M. Sugisaka, Nanotechnology on duty in medical applications, Curr. Pharmaceut. Biotechnol. 6 (1) (2005) 17–33.
[104]. S. Shrivastava, D. Dash, Applying nanotechnology to human health: revolution in biomedical sciences, J. Nanotechnol. 2009 (2009) 184702.
[105]. K. Ma, et al., Electrospun nanofiber scaffolds for rapid and rich capture of bone marrow-derived hematopoietic stem cells, Biomaterials 29 (13) (2008) 2096–2103.
[106]. A. Chaubey, et al., Surface patterning: tool to modulate stem cell differentiation in an adipose system, J. Biomed. Mater. Res. B Appl. Biomater. 84 (1) (2008) 70–78.
[107]. S. Ber, G. Torun Kose, ¨ V. Hasirci, Bone tissue engineering on patterned collagen films: an in vitro study, Biomaterials 26 (14) (2005) 1977–1986.
[108]. H. Kenar, et al., Chemical and topographical modification of PHBV surface to promote osteoblast alignment and confinement, J. Biomed. Mater. Res. 85 (4) (2008) 1001–1010.
[109]. A. Khademhosseini, et al., Microfluidic patterning for fabrication of contractile cardiac organoids, Biomed. Microdevices 9 (2) (2007) 149–157.
[110]. I. Steinhauser, et al., Trastuzumab-modified nanoparticles: optimisation of preparation and uptake in cancer cells, Biomaterials 27 (28) (2006) 4975–4983. *Journal of Drug Delivery Science and Technology 63 (2021) 102487*
[111]. Gonzalez-Fern ´ ´andez, Antibody-conjugated nanoparticles for biomedical applications, J. Nanomater. (2009) 439389, 2009.
[112]. M. Fujita, et al., Brain tumor tandem targeting using a combination of monoclonal antibodies attached to biopoly(beta-L-malic acid), J. Contr. Release 122 (3) (2007) 356–363, official journal of the Controlled Release Society.
[113]. A. Aigner, Tumor-targeting nanosystems for the delivery of siRNA, Nanomedicine 2 (4) (2007) 569–572.
[114]. J.D. Heidel, et al., Administration in non-human primates of escalating intravenous doses of targeted nanoparticles containing ribonucleotide reductase subunit M2 siRNA, Proc. Natl. Acad. Sci. Unit. States Am. 104 (14) (2007) 5715–5721.
[115]. C. Ogino, et al., Recognition and effective degradation of 17β-estradiol by anti estradiol-antibody-immobilized TiO2 nanoparticles, J. Biosci. Bioeng. 104 (4) (2007) 339–342.
[116]. A. Debin, et al., Intranasal immunization with recombinant antigens associated with new cationic particles induces strong mucosal as well as systemic antibody and CTL responses, Vaccine 20 (21–22) (2002) 2752–2763.
[117]. P. Yingchoncharoen, D.S. Kalinowski, D.R. Richardson, Lipid-based drug delivery systems in cancer therapy: what is available and what is yet to come, Pharmacol. Rev. 68 (3) (2016) 701–787.

[118]. L. Van Hoecke, K. Roose, How mRNA therapeutics are entering the monoclonal antibody field, J. Transl. Med. 17 (1) (2019), 54-54.
[119]. A.K. Goyal, G. Rath, T. Garg, Nanotechnological Approaches for Genetic Immunization. DNA and RNA Nanobiotechnologies in Medicine: Diagnosis and Treatment of Diseases, 2013, pp. 67–120.
[120]. M.A. Walling, J.A. Novak, J.R.E. Shepard, Quantum dots for live cell and in vivo imaging, Int. J. Mol. Sci. 10 (2) (2009) 441–491.
[121]. R. Agarwal, et al., Delivery and tracking of quantum dot peptide bioconjugates in an intact developing avian brain, ACS Chem. Neurosci. 6 (3) (2015) 494–504.
[122]. J.S. Suk, et al., PEGylation as a strategy for improving nanoparticle-based drug and gene delivery, Adv. Drug Deliv. Rev. 99 (Pt A) (2016) 28–51.
[123]. B. Issa, et al., Magnetic nanoparticles: surface effects and properties related to biomedicine applications, Int. J. Mol. Sci. 14 (11) (2013) 21266–21305.
[124]. D. Elgrabli, et al., Biodistribution and clearance of TiO2 nanoparticles in rats after intravenous injection, PloS One 10 (4) (2015) e0124490-e0124490.
[125]. T.G. Smijs, S. Pavel, Titanium dioxide and zinc oxide nanoparticles in sunscreens: focus on their safety and effectiveness, Nanotechnol. Sci. Appl. 4 (2011) 95–112.
[126]. J.K. Patra, et al., Nano based drug delivery systems: recent developments and future prospects, J. Nanobiotechnol. 16 (1) (2018), 71-71.