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# Medical applications of nanotechnology

## Zastosowanie nanotechnologii w medycynie

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## Summary

Nanotechnologies are new areas of research focusing on affecting matter at the atomic and molecular levels. It is beyond doubt that modern medicine can benefit greatly from it; thus nanomedicine has become one of the main branches of nanotechnological research. Currently it focuses on developing new methods of preventing, diagnosing and treating various diseases. Nanomaterials show very high efficiency in destroying cancer cells and are already undergoing clinical trials. The results are so promising that nanomaterials might become an alternative to traditional cancer therapy, mostly due to the fact that they allow cancer cells to be targeted specifically and enable detailed imaging of tissues, making planning further therapy much easier. Nanoscience might also be a source of the needed breakthrough in the fight against atherosclerosis, since nanostructures may be used in both preventing and increasing the stability of atherosclerotic lesions. One area of interest is creating nanomaterials that are not only efficient, but also well tolerated by the human body. Other potential applications of nanotechnology in medicine include: nanoadjuvants with immunomodulatory properties used to deliver vaccine antigens; the nano-knife, an almost non-invasive method of destroying cancer cells with high voltage electricity; and carbon nanotubes, which are already a popular way of repairing damaged tissues and might be used to regenerate nerves in the future.

The aim of this article is to outline the potential uses of nanotechnology in medicine. Original articles and reviews have been used to present the new developments and directions of studies.

**Keywords:** **nanomedicine • nanotechnology • nanostructures • cancer treatment • nano-knife • nanotubes • immunoprophylaxis**

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**Abbreviations:** **AA1** – annexin A1, **Ac2-26** – amino acids 2–26, **CBSA** – cationic bovine serum albumin, **CNT-PGFs** – carbon nanotubes interfaced with glass fiber, **CNTs** – carbon nanotubes, **DCs** – dendritic cells, **FPR2/ALX** – receptor N-formyl peptide receptor 2, γ-PGA – Poly(γ-glutamic acid), γ-PGA-**Phe** – γ-PGA-graft-Phe copolymer, **HDFs** – human dermal fibroblasts, **HEV-71** – human enterovirus 71, **HPV** – human papilloma virus, **IRE** – irreversible electroporation, **ISCOMs** – immune stimulating complexes, **NIR** – near-infrared region, **PLGA** – poly(lactide-co-glycolide), **QDs** – quantum dots, **RE** – reversible electroporation, **SLNs** – solid lipid nanoparticles.

## Introduction

Recent years have brought considerable progress in nanotechnology – a highly advanced area of research that focuses on utilizing molecular and atomic techniques to create nano-scale products that might find usage in other fields of science. The "nano" term itself is derived from a Greek word for "dwarf". As such, it is not difficult to imagine that one nanometer is a very small measure of length, equal to one meter divided by one billion, that is $10^{-9}$ m. It is about the same size that a small glass ball would have in comparison to an object of the size of the Earth. Though at first nanoscience might not seem particularly exciting due to its small scale, it definitely has an enormous potential. Nanotechnology's basic concept relies on using atoms and molecules to build functional structures [1]. The first person to ever consider it as a research initiative that may revolutionize science was Richard Feynman, a Nobel Prize winner in the field of physics. During one of his speeches in 1959, he hypothesized that molecular machines might be able to build with unbelievable, atomic precision [72].

Nanomedicine is without doubt one of the main areas of interest in nanotechnological studies [73], mostly due to the fact that nanoscience may lead to the long awaited breakthroughs in the fight against various diseases such as cancer or atherosclerosis. Each of the three main branches of nanotechnology – nanomaterials, molecular nanotechnology and biotechnology – might become a source of extremely valuable discoveries and solutions for modern medicine. Nano-scale products have already been widely accepted as biocompatible materials and analytic methods. They are also used in surgical and dental practice, studying nerve cells and performing biomolecular research. The second branch of nanotechnology focuses on mechanical systems, designed and created at a molecular level, that might potentially find usage in medicine. As for biotechnology, its very basic concept, often viewed as using biological systems in technological and industrial processes, has been expanded by including genetic engineering and creating artificial representations of organic life. The application of nanoscience has already been very beneficial to modern medicine, mostly due to the increase in range and efficiency of available treatment options [20].

Nanotechnology, as a field of science uniting the most recent achievements of chemistry, biology, physics, mechanics and computer sciences, is also a promising area of research in material manufacturing. Materials based on nanoparticles are expected to provide a breakthrough in many branches of industry. For example, fighting pathogenic microorganisms, testing products, water and the natural environment [65] and creating new packaging materials are among the major applications of nanotechnology in the food industry. Scientists believe that in the future, food will become not only a great source of nutrients with desired sensory qualities, but will also contribute to the general well-being and health of the consumers. This is mostly due to the expectation that in the future, food production will be based on an individualized approach to the end product and defining the correlation between genes, diet and consumer's health [36]. Although nanomaterials have been on the market for a few years, the full scope of their effects on the human body has not been discovered yet. Due to this reason, it is essential that we remain careful with nanomaterials' usage while further studies are conducted to determine their safety [65]. Nanotechnology is also used in construction [63], designing computer applications [15] and textile manufacture [49].

The aim of this article is to present the potential benefits of using nanotechnology in medical sciences.

## Types of nanomaterials

There are many types of nanoparticles: organic, inorganic, nanocrystals, nanotubes, polymeric structures such as dendrimers, etc. They are used primarily in research and drug delivery systems [32]. The most notable types of nanomaterials and their properties are listed below.

1. Nanotubes – this group consists of both organic and inorganic compounds that are formed into single- or multi-walled structures composed of self-assembling sheets of atoms arranged into tubes [32]. In 1952 the Russians Radushkevich and Lukyanovich presented images of carbon nanotubes as seen under the transmission electron microscope (TEM) [55]. The works on these materials accelerated in 1991, when Iijima published his findings on nanotubes growing without the need for a catalyst [51]. Carbon nanotubes (CNTs) are large, cylindrical molecules built by hexagonally placed carbon atoms. Their wall consists of one or more layers of graphene. Due to their high external surface area, CNTs are capable of achieving considerable loading capacity of chemotherapeutics. Moreover, their ability to undergo cellular internalization is essential to CNTs' extraordinary importance in biomedicine [13].

2. Nanocrystals – crystals smaller than 1 μm [7]. Nanocrystals can be used as a versatile method of improving the pharmacodynamic and pharmacokinetic properties of poorly soluble medications [22]. Moreover, these nanoparticles increase the bioavailability and solubility of other substances [7,23]. In comparison to conventional fluorophores, nanocrystals are more photochemically stable as they possess a narrow, tunable, symmetric emission spectrum [8]. Nanocrystals are built much like an onion, with a core surrounded by a shell, the latter providing a physical barrier between the external environment and the optically active core. Such a structure makes them less sensitive to photo-oxidation and medium changes [56]. The first products utilizing nanocrystals have already appeared on the market [31].

3. Dendrimers – the first studies regarding these nanomaterials were published in the late 1970s and early

1980s [69], and the term "dendrimer" was introduced by Tomalia [68]. In terms of their chemical structure, these nanomaterials are branched, tridimensional polymers that resemble a sphere. Their internal structure consists of a multifunctional core and branches of dendrimers called dendrons that fan out from the core. Dendrons are capped with free functional groups that might be swapped for other substituents in order to modify the chemical and physical properties of the whole structure. Various pharmacologically active molecules can be encased within the interior cavities of dendrimers or connected to their surface groups [60,64].

4. Liposomes – their history begins with Bangham publishing the results of his research in 1964 [6]. Liposomes were proposed as a potential drug delivery system for the first time in the 1970s [24]. These nanomaterials are described as spherical vesicles with the particle sizes ranging from 30 nm to several micrometers. Liposomes consist of one or more lipid bilayers located outside the aqueous units with polar groups headed both towards the exterior and interior aqueous phases. Liposomes might encase both hydrophobic and hydrophilic substances, prevent the degradation of their contents and release them for a set purpose [4]. Medications utilizing these nanomaterials as carriers that have already been made available include analgesics, anticancer and antifungal drugs [37].

5. Solid lipid nanoparticles (SLNs) – these nanomaterials consist of solid lipids stabilized with an emulsifying layer in an aqueous dispersion. In a way, they resemble nanoemulsions that have had the inner liquid lipids replaced by solid ones. The use of the latter type of lipids contributes to the improved control over drug release, mostly due to the fact that that drug mobility is generally lower in solid lipids than it is within an oily phase [48]. Physiological lipids such as fatty acids, steroids, mono-, di- or triglyceride mixtures and waxes are among the most commonly used ones. SLNs are stabilized by biocompatible surfactants [9]. The main advantages of SLNs include: protecting chemically labile and sensitive drug molecules from degradation in the external environment and during their passage through the intestines, improvement of the bioavailability of highly lipophilic molecules, using biodegradable and physiological lipids to produce nanoparticles and, with a proper scaling, the low cost of industrial production [14].

## Nanoparticles with annexin – a breakthrough in treating atherosclerosis?

Cardiovascular diseases have been among the major causes of death in the world for many years [74]. The most important factor that makes them so dangerous is atherosclerosis – a slowly progressing pathology that reduces the lumen of arteries. This in turn may lead to critically decreased blood flow through the vital organs, which results in their failure.

Fredman [19] et al. have tried to influence three pathomechanisms that play a vital role in atherosclerosis: damage of the arterial wall, non-resolving inflammatory response, and the risk of unstable lesions rupturing and releasing clot-promoting material to the bloodstream. In regular immunological processes, there are various substances that have the ability to mediate the resolution of the inflammatory response. Annexin A1 (AA1), a glucocorticoid-regulated protein, is among these natural anti-inflammatory mechanisms. In order to influence the progression of atherosclerosis, Fredman [19] et al. developed nanoparticles filled with AA1 molecules and injected them into the mouse bloodstream. The pro-resolving effects of AA1, mediated through its N-formyl peptide receptor 2 (FPR2/ALX), can also be achieved by an amino-terminal peptide encompassing amino acids 2–26 (Ac2-26). The mice were injected with nanoparticles that targeted collagen IV and contained Ac2-26. More than 70% of nanoparticles have reached advanced lesions and had their potential in treating chronic atherosclerosis evaluated. It was discovered that mice with preexisting lesions responded to Col IV-Ac2-26 injections and showed a considerable improvement in plaque properties, including oxidative stress suppression, increase in the protective collagen layer (associated with a decrease in collagenase activity) and reduced plaque necrosis. Due to the fact that mice lacking FPR2/ALX in myeloid cells were not affected by the injections, it was concluded that nanoparticles with resolution-mediating substances could activate receptors in myeloid cells to stabilize atherosclerotic lesions [19].

Leoni [40] et al. researched other aspects of AA1 infused nanoparticles' therapeutic potential, namely the possibility of using a similar method to the one studied by Fredman [19] et al. in treating chronic epithelial damage in inflammatory bowel diseases such as Crohn's disease [40].

## Potential application of nanotechnology in cancer therapy

Despite the recent advances in medical sciences, neoplasms, alongside cardiovascular diseases, remain among the most significant causes of premature deaths [75]. Thus, developing new anti-cancer treatment possibilities has become a priority for researchers. Nanomedicine is one of the upcoming forms of therapy that concentrates on alternative methods of delivering drugs and increasing their efficiency, while also reducing the side effects to healthy tissues. Due to the complicated nature of cancer drug resistance and the need to consider a variety of mechanisms, developing new treatment options is extremely difficult [47].

Surgical intervention, radiotherapy and chemotherapy are the currently available ways of treating cancer. While effective in many cases, they often cause severe systemic damage and destroy a considerable amount of tissues surrounding the tumor. Despite the fact that full

recovery is not always possible, previously mentioned side effects are considered acceptable due to the lack of better options. Among the newly developed treatment possibilities, there are a few that were designed specifically to make them less damaging to the patient's healthy tissues. One of them is the nanoshells that are currently undergoing clinical trials. These extremely small nanoparticles covered with gold can specifically target cancer cells by penetrating deep inside the tissues and can also be tuned to absorb in the near-infrared region (NIR) [43]. When injected, nanoshells have the ability to accumulate in the neoplastic tissue and cause ablation of the tumor when irradiated with an NIR laser either through the skin or by using an optical fiber inserted into, for example, the lungs. Increasing neoplasm specificity might be achieved by using special tumor-targeting moieties. Due to the fact that nanoparticles scatter light, they might also be used in imaging techniques such as dark-field microscopy and optical coherence tomography [52].

Other studies that were performed include the potential application of nanoparticles bound with antibodies via polyethylene glycol in breast cancer therapy. In vitro tests have confirmed the possibility of using nanoshells to induce selective cell death through photothermal ablation in response to NIR light. Breast cancer cells with the expression of HER-2 have been seeded separately or next to human dermal fibroblasts (HDFs) prior to incubation with nanoparticles bound with anti-HER-2 antibodies. Irradiating the HER-2 positive cells with NIR light caused their death, while similar treatment left the HDFs mostly undamaged due to the fact that they did not bind with nanoshells at high levels [44].

Drug delivery is also achieved by using organic compounds. Natural protein polymers composed mostly of gelatin and albumins have shown considerable promise in regard to building effective nano-carrier systems. Various clinical trials have proven the conventional paclitaxel formulations to be worse than an albumin-bound paclitaxel formulation, mostly due to the fact that the latter is better tolerated by patients. Cationic bovine serum albumin (CBSA) has been tested as a potential method of transporting siRNA in metastatic lung cancer therapy. One of the biggest advantages of this system is that CBSA can form stable nanoparticles with siRNA, protecting it from degradation and increasing the chances of its successful delivery and accumulation in the lungs. Systemic application of Bcl-2 siRNA using the described method has proven to provide an efficient gene-silencing effect and induce apoptosis of cancer cells in a mouse model [42].

Delivering versatile payloads by using molecular and cellular targeting has been described as having a higher efficacy, safety and specificity than other systems. Chemotherapeutics and imaging agents used to achieve these results have favorable pharmacokinetics, and thus they are often considered to represent a new era of "cancer nanomedicine". Despite their versatility, the usage of these nano-compounds is highly limited due to their high cost and lack of appropriate legal regulations. Thus, it is essential that the application of nanomedicine in the fight against cancer must have concrete indications of its necessity, relying on proving that a considerable clinical improvement will be achieved due to the properties of these substances [12].

## Nano-knife – treating inoperable neoplasms

The nano-knife is a device that has been used in modern medicine only for a few years, but it has already proven capable of efficiently destroying tumor cells. This method relies on subjecting cancer cells to changing electrical fields with a voltage up to 3000 V. The duration of this exposure lasts only micro- or milliseconds. The electric current that flows between the electrodes located at the edges and in the centre of the tumor causes the unique form of biological effect called irreversible electroporation (IRE) [58]. IRE is a new, non-thermal type of ablation that relies on creating irreversible holes (pores) in a cellular membrane. That in turn leads to the death of the affected cell, which usually occurs after 16-18 hours in the mechanism of apoptosis caused by an increase in membrane permeability [16,39]. Reversibility of this phenomenon is tied to physical parameters of the electrical current that flows through the living cells. Depending on the applied voltage, the number of impulses and their duration, the cell might undergo changes to its permeability that are either reversible (reversible electroporation [RE], applied voltage equal to 300-600 V) or irreversible (irreversible electroporation [IRE], applied voltage equal to 1500-3000 V) [58].

Electrogene therapy uses pores that were created in the RE mechanism to modify the cell genome by inserting new genes in vivo into its inner compartments [53]. Electrochemotherapy also relies on increased cellular membrane permeability. These methods make it possible to increase the effectiveness of administered concentrations of anti-cancer substances which drastically, ranging from a several to a few hundred times, increases their cytotoxic effect. Some naturally insoluble drugs such as bleomycin might be used in combination with electroporation to cause the ablation of cancer tissue [50].

When comparing the nano-knife to the traditional types of ablation such as thermo- or cryoablation, it is easy to notice the remarkability of this method. The most notable advantages include considerably shorter duration of the surgical procedure and lack of negative thermal effect on the healthy tissues when compared to thermoablation [39]. What really makes the nano-knife stand out from the other methods of causing ablation is the fact that the device preserves living structures containing collagen fibers such as blood vessels, bile ducts or pancreatic ducts [39,58]. Moreover, the collagenous

matrix of the tissue also remains intact, which translates into much better regeneration of the organ after cell destruction [58]. All of these features open up the possibility of destroying tumors that are situated in the direct proximity of previously listed collagenous structures without the risk of damaging them. This fact plays a vital role in treating neoplasms that are located in the liver hilum and the head and tail of the pancreas – locations where using thermoablation is usually impossible [58]. Up until this point, the nano-knife has been used to operate on changes in the liver, pancreas [61], prostate gland [71], kidneys, lungs, lymph nodes and lesser pelvis, though the last three locations have not been operated on using this method too often [61].

## Regenerative medicine – carbon nanotubes

The considerable progress in regenerative medicine that has occurred in recent years has been significantly accelerated by the new technologies and possibilities enabled by the advances in nanomedicine. A perfect example of this is the new scaffolds and grafts. Their revolutionary design allows for a greater regenerative effect on both cells and tissues. The results of research regarding the usage of nanomaterials have been published based on the studies conducted on the following tissues: bone, cartilage, nervous system, skin and heart muscle [10]. Among the materials that have been used are carbon nanotubes (CNTs). Their unique properties have opened up the possibility for the application of CNTs in therapies that focus on repairing damaged tissues, especially those that require electrical stimuli [2].

Ahn [2] et al. studied the impact that CNTs interfaced with glass fiber (CNT-PGFs) had on transected sciatic nerves in rats. It was discovered that CNT-PGFs were effective in stimulating the active regeneration of the damaged nerve by inducing growth of the dorsal root ganglion neurites along the aligned CNT-PGFs and considerably increasing the maximum neurite length. It was observed that within 16 weeks after the procedure, the method brought significant improvement to the number of regenerating axons crossing the scaffold, the cross-sectional area of the re-innervated muscles and the electrophysiological readings. Although the research conducted by Ahn [2] et al. was only a first in vivo attempt at using CNTs to induce sciatic nerve regeneration, the results are very promising and strongly support the possibility of using CNT-PGFs scaffolds at the interface between peripheral neural tissues and the nerve conduit [2]. Another important property of the CNTs is that they can transport proteins through the cell membrane in order to induce their naturally mediated effect. A group of CNTs, called amino-functionalized CNTs, are biocompatible, capable of dissolving in water solutions and present both high reactivity and low toxicity, which allows them to potentially be used in therapies promoting nerve cell growth. Chen [11] et al. conducted a study on CNTs to evaluate their biological activity, physicochemical properties and cytotoxicity towards pheochromocytoma cells in rats and dorsal root ganglions in chicken embryos. It was observed that using an amino-functionalized CNT complex with nerve growth factor was less toxic to pheochromocytoma cells and promoted both their and chicken dorsal root ganglion regeneration [12]. It is beyond any doubt that functionalizing CNTs with appropriate molecules represents an incredibly promising strategy for achieving better biological compatibility and inducing selective nerve regeneration [30].

## Immunoprophylaxis

Vaccines are often considered to be among the greatest achievements of modern medicine. Though they were at first only an interesting novelty, currently it is difficult to imagine everyday medical practice without this highly effective method of active immunoprophylaxis. This is mostly due to the fact that the introduction of vaccines caused a considerable decrease in the incidence and mortality rate of many infectious diseases and in some cases even paved the way for the eradication of certain dangerous illnesses.

Recent discoveries show that the nanomaterials might prove to be very efficient antigen delivery systems, primarily because they can provide sustained and controlled release profiles. Other important advantages of nanotechnology based carriers include high bioavailability and targeting possibilities. Furthermore, nanomaterials possess immunomodulatory effects that might be used to promote and shape the humoral immune response. Using nanotechnological adjuvants can greatly benefit the outcomes of vaccination, mostly due to the combination of their efficient delivery function and the immune-regulating properties [78].

Other nanostructures that might potentially be used as adjutants are: polymeric nanoparticles, liposomes, particles resembling a virus, immune stimulating complexes (ISCOMs) [26] and nanoemulsions [62]. One of the most important advantages of these nanoparticles is that some of them are capable of entering antigen-presenting cells and thus have the ability to regulate the immune response. This might prove to be a decisive factor in inducing a Th1-type response against intracellular pathogens. The properties of these nanostructures make them a viable delivery method, both on the surface of mucosa and through intradermal applications [26]. The studies have shown that the nanoparticles that are poly-(D,L-lactic acid-co-glycolic acid) copolymers (PLGAs) have an increased ability to deliver antigens to dendritic cells (DCs) [17]. It was discovered that γ-PGA-graft-Phe copolymer (γ-PGA-Phe) nanoparticles [3], PLGAs and liposomes [45] undergo successful phagocytosis by DCs in cultures through endocytosis. Additionally, it was revealed that the most optimal particle size for uptake by DCs was 500 nm or less [18]. Nanostructures that were absorbed by DCs stimulate the growth of these cells and increase the expression of a few cell surface markers, including co-stimulating CD40, CD80,

CD83, CD86, and MHC class I and II particles [67]. The researchers suspect that the nanoparticles themselves are not the only factor that has an effect on DCs' activation, as the properties of the polymers used in the nanostructures' production seem to also have a role in this process [33]. The results of the most recent studies unequivocally show that DCs are the most important component of immune response regulation [5,67]. That is why successful delivery of the antigen to their interior is a key to developing more efficient vaccines [21]. A vaccine antigen can be placed inside the nanostructure, which makes it easier to deliver it to cells that undergo fast degradation in the human body or cells that induce only a short and localized immune response. Moreover, antigens located on the surface of nanostructures can be recognized and presented by the immune system much like the antigens of pathogens [26]. Genetic immunization utilizes plasmid DNA from bacteria, viruses, protozoan or cancer cells. Liposomes that contain DNA can protect it from nucleases and direct the genetic material to the antigen-presenting cells in lymph nodes draining the injected site [25]. An article describing the clinical trials of anti-influenza vaccines using nanoemulsion W805EC as an adjuvant was published in 2012 [62]. An oil-in-water nanoemulsion consists of a surfactant, a solvent, soybean oil and water. The drop size is estimated to be around 400 nm [28]. Applied intranasally as an adjuvant, it increases the uptake of the antigen by the epithelium and dendritic cells in the nasal mucosa [27]. The nanoemulsion is safe for both animals [46] and humans. Moreover, it increases immunogenicity of the antigen [62].

The major concerns regarding the application of nanotechnological vaccine carriers include the risk of toxicity, production difficulties and presenting antigens in their native form [26]. Despite these limitations, the effectiveness of nano-vaccines has been proven in an animal model with major pathogens including H5N1 influenza virus [57], human enterovirus 71 (HEV-71) [59] and human papilloma virus (HPV) [66].

## Nanotechnology in diagnostics

Biosensing applications constitute an area where nanomaterials have already proven to be a promising option for future developments. Due to the unique properties of these materials, the overall performance of existing techniques has been clearly improved, while the detection limits have been lowered by several orders of magnitude. Magnetic nanoparticles, semi-conductor quantum dots, gold nanoparticles, carbon nanotubes, nanodiamonds, polymer nanoparticles and graphene are the most notable materials that are currently the object of studies. It has been shown that the fluorescent labels in biosensor devices might potentially be replaced by magnetic nanoparticles. The main advantage of their application is that the analyte can be concentrated before the detection process begins. Magnetic nanoparticles with a modified receptor unit that interacts with specific targets may be added to the analyte solution. Application of the external magnetic field causes the nanoparticles to create agglomerates that can easily be separated from the solution. Magnetic resonance imaging can greatly benefit from nanoparticles since they represent a promising, highly sensitive transduction technique [29].

Quantum dots (QDs) are inorganic nanomaterials composed of a zinc sulfide shell and cadmium selenide core that act as semi-conductor crystals. One of their most interesting properties is that they can be adjusted to fluoresce with a different color range or wavelength depending on the materials or size of crystals that have been used. In contrast to organic fluorophores that possess a narrow absorption band and a broad fluorescent spectrum, these extraordinarily photostable materials are not only capable of efficiently absorbing light over a broad spectrum and have spectrally tunable and narrow emission profiles, but also exhibit a longer fluorescence lifetime. This allows the excitation and emission lights to be separated. Due to this property, the output signal's measuring efficiency is maximized. Other advantages of QDs include the lack of substantial photobleaching effect and the ability to fluoresce at a single or multiple narrow wavelengths at the same time. These nanomaterials can be used both as donors and receptors of light energy. In medicine, it is possible to utilize QDs to detect glucose binding with a receptor molecule bound to the QDs [34].

Despite the fact that glucose and other biosensors have been improved over the years, they still share the same general structure of enzyme electrodes with the devices used in the distant past. Researchers have experimented with many methods of modifying the electrodes, but using certain nanomaterials, such as gold nanoparticles or carbon nanotubes, has proven to be one of the most promising concepts. This is mostly due to the fact that these nanomaterials possess certain advantageous qualities, such as their ability to improve the electron transfer between the electrode and the redox centre of the enzyme while maintaining a friendly platform for immobilizing enzymes. These properties are the main reason behind improved response times and higher sensitivity of electrodes that were modified with nanotechnology. It was also observed that the immobilization of enzymes often improved their stability by minimizing enzyme unfolding. Nanosensor devices are perfectly suited for various in-vivo and in-situ measurements due to their extremely low invasiveness resulting from their nanoscale size [54].

## Toxicity

Despite the considerable amount of research regarding the topic, it is difficult to evaluate the exact danger associated with the application of nanotechnology in medicine since nanomaterials are a very varied group and so it is extremely difficult for scientists to select a singular, common criterion. Nanoparticles, depending on the

materials used in their production, possess a different structure, surface area, solubility, cytotoxicity, and physical and chemical properties [38].

Although the potential benefits of using nanotubes in pharmacological sciences seem promising, the toxicity reports are inconclusive. The mechanisms that are at the basis of CNT toxicity include DNA mutations (disruption of the mitotic spindle and errors in chromosome numbers), malignant transformations, inflammatory responses, oxidative stress, interstitial fibrosis and the formation of granulomas [35,41].

Despite the fact that gold is biologically inert and in normal circumstances should not cause damage to the human organism, when used in high doses or over a long duration, it might prove to be toxic, as it has a relatively low clearance rate and tends to accumulate in the tissues and bloodstream. Thus it is essential that methods of targeting specific, diseased cells and tissues be developed before gold nanoparticles are allowed to be commonly used in medicine [76]. Research on animal models has shown that 10 and 60 nm glycol-coated gold nanoparticles present too high toxicity levels to be a viable option for medical applications, while 5 and 30 nm particles have proven to be sufficiently safe for such uses. The main concern is the increase in alanine and aspartate transaminase levels in biochemistry results that indicates mild liver damage [77].

As shown in certain cell culture experiments, the QDs undergo intracellular localization depending on their design and can release free cadmium and radical species into the solution. These factors are the main reason behind their toxicity. Animal trials have shown that once administered through an intravascular injection, the QDs tend to infiltrate the liver and spleen tissues. However, dots that are above 6 nm in size undergo minimal excretion and appear to be generally safe to animals. Dosing is the only feasible explanation for the discrepancy in toxicity that was observed in various in vivo and in vitro studies. The main issue, however, is that because QDs accumulate and are retained inside tissues, their long-term toxicity could not be evaluated yet [70].

## Conclusions

1. Nanotechnology is a source of new materials that present a significant opportunity for new developments in various branches of medicine.

2. Chemotherapeutics based on nanotechnology and new imaging techniques represent a new era of "cancer nanomedicine", but their introduction to common clinical practice is often very expensive and hindered by legal regulations.

3. Nanoparticles filled with AA1 inhibit the further growth and improve the stability of atherosclerotic lesions. They might also be used in treating damaged mucosa in people suffering from inflammatory bowel diseases.

4. Nanomedicine focuses on alternative ways of drug administration and increasing the efficacy of cancer treatment. One of the new methods involves nanoshells that infiltrate the cancer tissue and cause photothermal ablation of the tumor when irradiated with NIR light.

5. The nano-knife is a new, non-thermal method of cancer cell ablation that utilizes the unique phenomenon of irreversible electroporation in response to a changing electrical field.

6. Nanotechnology has significantly accelerated the growth of regenerative medicine. CNTs, due to their properties and low toxicity, might be used to reverse nerve damage.

7. Nanoadjuvants represent a chance to develop a new generation of vaccines with more favorable properties.

8. Evaluating the detrimental effects of nanomaterials is difficult, because they represent a very varied group. Some reports regarding their toxicity have already been published. Further studies are needed before nanomaterials can be authorized for common application in human treatments.

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