# Application of nanomaterials in medical sciences

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## Introduction

Nanotechnology deals with objects with at least one dimension not exceeding 100 nm [1]. The notion of nanotechnology is strictly related to Richard Feynman's lecture *There's plenty of room at the bottom*, given in 1959 at the California Institute of Technology. In his lecture Feynman outlined the theoretical foundations of the arrangement of structures based on individual atoms and particles. However, at that time the practical methods of implementing Feynman's ideas had not yet been discovered [1]. The term "nanotechnology" in modern meaning of the word was first used in 1974 by Norio Taniguchi to describe the total set of processes related to manipulating individual atoms or particles [2, 3]. The key milestone for the development of nanotechnology was the invention of the Scanning Tunnelling Microscope (STM) [4] in 1982 and the Atomic Force Microscope (AFM) in 1986 [5]. With those devices it became possible to observe structures on the atomic scale [2, 3]. The development of nanotechnology also benefited from Eric Drexler's 1986 book *Engines of Creation*, which introduced the knowledge of this branch of science to the general public [6]. Two major developments for the synthesis of nanostructures were the discovery of fullerene in 1985 [7] and obtaining carbon nanotubes in 1991 [8]. 2003 saw the first application of nanomaterials to the treatment of cancer [2].

Rapid development of nanotechnology and discoveries of new structures, varying in terms of shape and properties, forces the scientific world to constantly update the definition of "nanomaterials". The majority of currently applied definitions, based on the regulations of the European Parliament or other relevant European and American organizations dealing with nanotechnology, describe nanomaterials as structures of size not exceeding 100 nm, with specific composition and physico-chemical properties [9]. Nanostructures can form agglomerates that are larger than 100 nm, while retaining the specific properties of the original structure, hence the postulate voiced by Kreyling et al. [9] to introduce a new definition of nanomaterials, based on the specific volume of the surface area. The volume depends on the specific surface area and density of the structure. According to the authors, the limit value for categorizing the given structure as nanomaterial is 60 $m^2/cm^3$ [9].

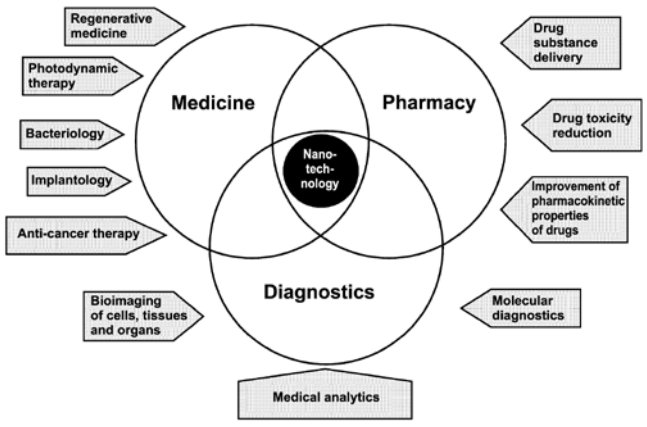


**Fig. 1. The scope of nanotechnology's impact on medical sciences**

Nanotechnology is an interdisciplinary branch of science, combining elements of physics, chemistry and technical sciences. Fields of practical application include i.a. medical and pharmaceutical sciences [10]. Nanotechnology is applied to medicine and related sciences i.a. in the rapidly developing research on the therapy of cancer, cell bioimaging, targeted therapy, drug delivery on the cellular level, and in the regeneration of tissues and organs [3]. Figure 1 outlines the practical application of nanotechnology to medicine, pharmacy and medical diagnostics. It should be pointed out that nanotechnology's contribution to the development of each of the fields presented below takes place simultaneously, whereby mutual impact and complementation of those fields should also be considered.

## Classification and properties of nanomaterials

Nanomaterials used in medicine can be classified either according to the character of the structure, chemical composition, dimensionality or application. In terms of the type of structure we can divide nanomaterials into: nanoparticles, quantum dots, nanotubes, dendrimers, micelle formations [10]. In terms of chemical classification, nanomaterials can be either organic or inorganic. Inorganic structures include metal oxide nanoparticles [11], semimetal oxides [12], metal nanoparticles [11], semiconductor quantum dots [13, 14] or carbon structures (nanotubes, graphene, fullerenes) [15]. Organic structures include polymer nanoparticles [16] or dendrimers [10]. Obviously, none of those classifications can be considered the only right one. We must take into consideration the fact that the majority of those structures are synthesized using organic substances, necessary for stabilizing the structure of the nanomaterial or its functionalization; therefore, nanomaterials usually have a hybrid nature. Figure 2 outlines the classification of nanomaterials in terms of structure type and chemical composition.

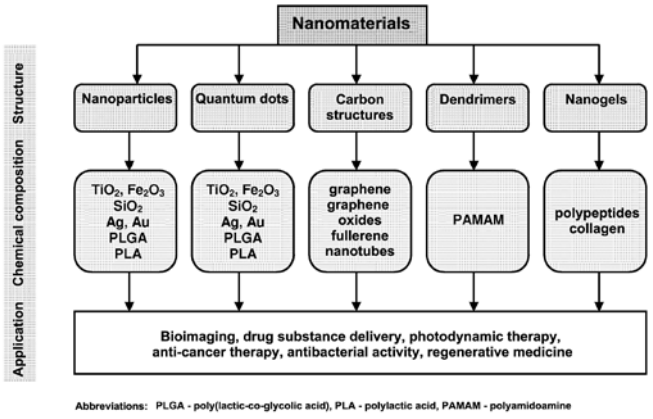


**Fig. 2. The classification of nanomaterials in terms of structure type and chemical composition**

Due to their size, high surface area to volume ratio and the capability of surface modifications, nanomaterials exhibit unique magnetic, optical or biological properties, allowing us to track and adjust processes taking place on cellular level [17].

Considering the properties of quantum dots and inorganic nanoparticles, we can adopt a certain common structural framework for those nanostructures, outlined in Figure 3.

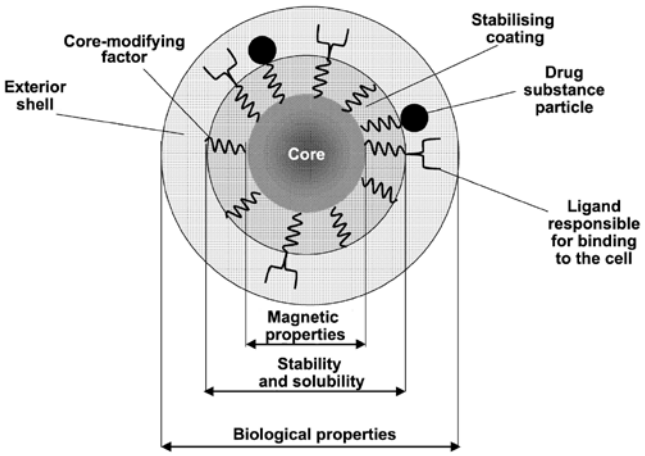


**Fig. 3. Schematic representation of quantum dots or nanoparticles construction**

The key element of those substances is the core, giving the nanomaterial its specific magnetic or optical properties. The next layer is the organic coating that stabilizes the structure, is responsible for its hydrophilic character and allows for further functionalization [18÷20]. The organic coating is further enclosed in a layer that may be composed of ligands responsible for selective binding of the quantum dot or nanoparticle to certain cells or tissues (the so-called targeted therapy). The exterior layer of the nanostructure can also contain a bioactive substance. In such case, the usability of the nanomaterial is expanded by a therapeutic function [18÷20]. Table 1 provides some examples of nanomaterials, their compositions and properties.

**Table 1**

**Composition and properties of certain nanostructures**

| Structure type | Composition | Properties | References |
|---|---|---|---|
| Quantum dots | CdTe nanocrystal core, stabilizing ligand: 3-thiopropionic acid, bound ligand: lectin | High fluorescence efficiency, stable fluorescence, selective binding to cells | [21] |
| Mesoporous silica nanoparticles | Spherical porous nanoparticles (diameter approx. 100 nm), containing surfactant-dispersed doxorubicin) | pH-dependent release of drug substance, cancer cell penetration capacity | [22] |
| Silver nanoparticles | Ampicillin-modified surface area of silver nanoparticles | Synergic antibacterial activity of silver nanoparticles and the antibiotic | [23] |
| Graphene, graphene derivatives | Surface area of graphene and its derivatives modified with enzymes, antibodies and polymers | Formations (electrodes) sensitive to concentrations of various substrates | [15] |
| Dendrimers | Synthetic polyamidamine polymers with branched chains and common central core | Nucleic acid binding capacity | [1] |
| Iron-cobalt nanoparticles | Spherical FeCo nanoparticles, coated with graphite, functionalized with polyoxyethylene glycol and biocompatible phospholipide | Capacity to penetrate the cell and interact with the exterior magnetic field | [19] |
| Carbon nanotubes | Single-walled carbon nanotubes, functionalized with folic acid | Capacity to absorb near-infrared radiation (NIR) | [17] |

**Application of nanomaterials**

Due to their unique physico-chemical properties, nanomaterials have a broad scope of application in medical and related sciences. Those structures are used i.a. in the imaging of pathological lesions of tissues and organs, biomarker identification or tissue regeneration. The latest developments in nanotechnological engineering are applied to the therapy of conditions including: cancers, cardiovascular diseases, neurological diseases and more [24].

Bioimaging of tissues and organs usually involves quantum dots and nanoparticles. The necessary condition of bioimaging is the functionalization of the nanostructure with an appropriate ligand, specific for the receptor of bioimaged cells [25]. Certain optical properties of the nanomaterial (e.g. fluorescence) make certain cell or tissue areas visible when exposed to radiation at excitation wavelength [14]. Compared to traditional dyes used in bioimaging (rhodamine, fluoroscein), quantum dots are characterized by higher photostability, wide absorption band, narrow and symmetrical band of fluorescence emission, high quantum efficiency of fluorescence and long fluorescence lifetime [26]. All of the above properties make quantum dots very popular in cancer cell imaging. Structures of this type, composed of a CdSe [27] and InP [28] cores, have been used in fluorescent bioimaging of KB cells (human epidermal nasopharyngeal carcinoma). An example of bioimaging combined with potential therapeutic effect was the synthesis of magnetic iron-cobalt nanoparticles coated with gold by Patra et al. [29]. The gold coating in this case acted as inhibitor of the proangiogenic VEGF-165 (Vascular Endothelial Growth Factor), while the core of the structure (Fe-Co) enabled the Magnetic Resonance Imaging (MRI). Apart from quantum dots and nanoparticles, bioimaging also uses single-walled carbon nanotubes. The modification of the surface area of this type of structure with polyoxyethylated phospholipide ensures the proper level of solubility of the structure, while labelling with $^{64}Cu$ allows for imaging cells and tissues using Positron-Emission Tomography (PET) [19].

Another field of application for nanostructures is the drug delivery on cellular level. This method of active substance administration improves the pharmacokinetic properties of the drug, which translates into better dissolution kinetics, quicker absorption and achieving the therapeutic concentration in the target tissue [1]. Zhang et al. [12] used spherical mesoporous silica nanoparticles as the carrier for sparingly water-soluble telmisartan in order to improve its dissolution kinetics. He et al. [22] obtained a drug delivery system based on mesoporous silica nanoparticles, exhibiting a pH-responsive kinetics of releasing doxorubicin directly to cancer cells. In this case the acidic environment of cancer cells favoured the accelerated release of the drug from the porous matrix [22].

One of the known methods of ensuring a therapeutic effect combined with simultaneous control of the therapeutic process through monitoring the fluorescence (bioimaging) is the coupling of anti-cancer drugs with quantum dots. An example of this method is the encapsulation of quantum dots in chitosan containing folic acid (targeting ligand) and doxorubicin as the drug substance [30].

The unique architecture of nanomaterials allows them to imitate natural tissues and provide appropriate extracellular environment for their growth and development [31]. Certain nanomaterials may function as the internal scaffold for the damaged tissues, facilitating their regeneration. In the case of bone structure regeneration those materials, aside from providing support, may also function as the carriers for the drug substance [31]. Traditional materials used in regenerative medicine have a limited durability, caused by inflammation occurring around the implant, infection or osteolysis. Thus, it seems justified to look for nanostructures with properties similar to the internal architecture of the bone or cartilaginous tissue [32]. The key factor in the choice of the specific nanomaterial is the

appropriate properties of the surface area of the nanostructure, such as topography, chemical similarity or surface wettability [32]. Bone tissue regeneration has successfully employed the nanohydroxyapatite in the form of granules (approx. 70 nm in diameter), participating in the bone mineralization, proliferation and increasing the adhesion of osteogenic cells. Also, hydroxyapatite in the form of tantalum-coated granules has been used, as well as nanomaterials in the form of fibres created through self-assembled amphiphillic peptides (Arg-Gly-Asp) [32].

Aside from applications related directly to the therapy of the given disease, nanomaterials also play a significant role in medical diagnostics and analytics. Unique electrical properties of carbon structures such as graphene, graphene derivatives (oxides) or nanotubes make those substances highly useful as components of sensors [15]. The obtained formations (electrodes) exhibited sensitivity i.a. to the concentration of nucleic acids, proteins, saccharides, antibodies, hormones, drugs and other substances. Electrodes that are selective against the bioactive particles play an important role also in medical diagnostics [15].

**Toxicity of nanomaterials**

Considerable progress in development of new nanostructures and their broad scope of applications force the scientists to study in detail the impact of new substances on living organisms. Certain properties of nanomaterials that are generally recognized as unique, such as small size, large specific surface area or surface activity, may trigger the toxicity of nanomaterials [33]. The major factors determining the toxicity of those substances also include the size distribution of nanoparticles, their shape, chemical composition, electron properties, reactivity of surface groups and aggregation capacity [34].

The majority of nanomaterials subjected to genotoxicity tests with the use of the comet assay, micronucleus DNA tests [33] or MTT (*3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-tetrazolium bromide*) assay of cell viability [11] showed high toxicity levels. However, the results of *in vivo* tests have not always confirmed the results of *in vitro* tests [11]. The differences in results are caused mainly by disruptions of the analytical procedure by nanomaterials themselves (e.g. reactions with reagents) [11]. In order to provide an objective assessment of the toxicity of the given material, an individual analytical procedure is required, taking into consideration the specific nature of the analyzed structure. It should also be pointed out that the development of nanotechnology should be accompanied by corresponding development of test methods of nanostructures, especially in terms of safety of application [35].

**Conclusion**

Due to their small sizes, surface area modification capacity and unique biological properties, nanomaterials have a broad scope of application in medicine, pharmacy and medical diagnostics. Those structures are used i.a. as carriers for drug substances, in magnetic and fluorescent bioimaging, as elements of measuring sensors, and sometimes they exhibit therapeutic activity themselves (antimicrobial activity). Given their properties, significantly different from the matter that surrounds us, the nanomaterials are still and intriguing and mysterious subject. Proper use of the knowledge on those structures and the ability to put them to practical use in treatment, diagnostics and disease prevention will benefit the health and quality of life of the patients.

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# International Symposium on Electronic/Optic Functional Molecules

## 11-13 March 2012, Shanghai, China

**Official Information:**

The international symposium aims to provide a forum for discussing innovative research and development in the research field of Electronic/Optic Functional Molecules and their applications, including organic electronics, organic optics, chemosensors, molecular machines and their bio-applications, and so on. An objective of the international symposium is to honor Prof. Klaus Müllen, one of the pioneers of the field of organic electronics and optic materials, on the occasion of his 65th birthday. The symposium will be held on Mar 11-13, 2012, in East China University of Science and Technology, Shanghai, China. The Chairman is Prof. He Tian. For more details about the symposium and registration, please visit the homepage of the symposium (http://hyxy.ecust.edu.cn/iseofm/).

**Confirmed plenary lecturers (to be continued)**

1) Prof. Takuzo Aida, University of Tokyo, Japan
2) Prof. Eric V. Anslyn, University of Texas at Austin, USA
3) Prof. Jean-Luc Brédas, Georgia Tech, USA
4) Prof. Alan Heeger, UCSB, USA, Nobel Prizer winner
5) Prof. Klaus Müllen, MPI, Mainz, Germany
6) Prof. Peter Stang, Univ. Utah, USA
7) Prof. Xi Zhang, Tsinghua University, China

**Invited lecturers (more to come)**

1) Harry L. Anderson, UK
2) Peter Bäuerle, Germany
3) Uwe H. F. Bunz, USA
4) Yves Henri Geerts, Belguim
5) Stefan Hecht, Gremany
6) Emil J. W. List, Austria
7) Seth Marder, USA
8) Soo Young Park, South Korea
9) Paolo Samori, France
10) Ullrich Scherf, Germany
11) Licheng Sun, Sweden
12) Mark D. Watson, USA
13) Jean Roncali, France
14) Thorri Gunnlaugsson,Ireland
15) Tomas Torres, Spain
16) Hiroyuki Furuta, Japan
17) Yuliang Li, China
18) Lixiang Wang, China
19) Steven J. Langford, Australia
20) Joyoon Yoon, Korea.

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