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SOME OF BENEFITS NANOMATERIALS APPLICATIONS IN MEDICINE

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Abstract: Nanotehnology applied to biomedicine has an important place in research of nanomaterials. Size of nanomaterials particles is similar to the size of biological molecules and structures, a conclusion can be drawn that the application of nanomaterials *in vivo* and *in vitro* biomedical researches is possible. This paper is a short overview of medical applications of different nanomaterials such as carbon nanotubes, graphene, quantum dots, nanocapsules etc. The main nanocarriers systems such as liposomes, micelles and dendrimers also will be presented. Today, we are witnessing the great boom of magnetic particles as essential components in several areas of medical practice. The great advantages of using nanomaterials in biomedical areas lies in their ability to operate on the same small scale as all the intimate biochemical functions involved in the growth, development and ageing of the human body. Nano-pharamceuticals reveal enormous potential in drug delivery as carrier for spatial and temporal delivery of bioactive components and diagnostics. Additionally, it also provides smart materials for tissue engineering. This discipline is now well-established for drug delivery, diagnostics, prognostic and treatment of diseases through its nanoengineered tools.
Keywords: nanotechnology, biomedicine, nanopharmacy.

1. INTRODUCTION

Nanotechnology encompasses studies of the fundamental principles of molecules and structures of the dimension of 1-100 nm. Nanomaterials are of interest because of their unique magnetic, optical, mechanical, thermal and other properties [1]. Novel physical and chemical properties have potential of powerful impacts in our lives in many different ways. Nanomaterials have wide range of applications in the field of electronics, energy sectors, agriculture, food industry, medicines, molecular biology etc. Nanotechnology has huge potential to bring benefits in many areas of science. Government and private sectors worldwide invest large sums of money into nano research. However, nanotechnology is not independent technology and cannot be advanced by a single country or institution. This technology of the 21st century tend to be highly interdisciplinary, involving scientists from different countries and different area of research. Collaboration between scientists and countries is crucial for technology transfer to commercialize application. However, the process of transforming the results of scientific research into commercially viable products is long and complex. To achieve this, it is crucial to bridge the gap between generating new knowledge and turning into new products and services [2].

In this paper, biomedical application of nanomaterials will be presented and analyzed. Due to the fact that nanoparticles are similar to the size of biological structures, application of nanomaterials in biological research is possible [3]. Nanomedicine is capable of achieving great things, including advances in the treatment of cancer, diagnosis, prevention etc. The properties of nanomaterials are not always well characterized. Some of the key issue of nanomedicine are dealing with bioactivity, biocompatible, toxicity and nanobio interfacial

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properties. Numerous nanomedicine related applications are under development or in a research phase. Achieving full potential of nanomedicine may be years away [4].

Type of therapy is required when there is a discrepancy between a dose or concentration of a drug and its therapeutic results or toxic effects. Targeting cell or specific tissue by the means of individually designed carriers that are attached to drugs is a more reliable approach in drug delivery system. Such approach is known as cell or tissue specific targeting. Size reduction of targeted formulation and designing its pathways for suitable drug delivery system is a more fundamental and successful approach that forms the basis of nanotechnology. Recent advancement in nanotechnology has proven that nanoparticles acquire a great potential as drug carriers. Size reduction methods and technologies yield different types of nanostructures that exhibit unique physicochemical and biological properties.

These methods make the nanostructures favorable material for biomedical applications and thus acquire the importance in pharmaceutical sciences. In addition, these methods help in reducing toxicity, enhancing release, improving solubility and bioavailability and provide better formulation opportunities for drugs. Nanotechnology offers drugs in the nanometer size range which enhances the performance in a variety of dosage forms. Various advantages of nano sizing are mentioned below:

- Decreased fed/fasted variability
- Decreased patient-to-patient variability
- Enhanced solubility
- Increased oral bioavailability
- Increased rate of dissolution
- Increased surface area
- Less amount of dose required
- More rapid onset of therapeutic action

Recently, various novel and advance methods of cancer detection based on nanoparticles are being developed. These designed nanostructures are used as fluorescent materials, contrast agents, drugs with targeting antibodies and for molecular research tools. Recent modifications of nanoparticulate systems such as paramagnetic nanoparticles, quantum dots, nanoshells and nanosomes are widely used for diagnostic purposes.

Nanotechnology provides the better safety profile against drugs with high toxic potential and these nanoforms can be directed to act specifically at the target tissue by active as well as passive means. In addition, other modalities of therapy such as heat induced ablation of cancer cells by nanoshells and gene therapy are also being developed. Optimization of nanoparticles based drug delivery approaches concerns the early detection of cancer cells and/or specific tumor biomarkers, and the enhancement of the efficacy of the treatments applied [17].

2. BIOMEDICAL APPLICATION OF NANOMATERIALS

Biomedical nanotechnology presents revolutionary opportunities in the fight against many diseases. An area with near-term potential is detecting molecules associated with diseases such as cancer, diabetes mellitus, neurodegenerative diseases, as well as detecting microorganisms and viruses associated with infections, such as pathogenic bacteria, fungi, and HIV viruses. Macroscale devices constructed from exquisitely sensitive nanoscale components, such as micro-/nanocantilevers, nanotubes, and nanowires, can detect even the rarest biomolecular signals at a very early stage of the disease. Development of these devices is in the proof-of-concept phase, though entering the market may be sooner than expected. However, a different approach of molecular sensing *in vivo* involves the use of implantable sensors which is still hampered by unwanted biofouling impairing long-term stability of continuous sensors caused by blood components and factors of the immune system. Nanotechnology might yield nano-structured surfaces preventing this non-specific protein adsorption [5].

The above described advances in medical diagnostics are rivalled by the progress made in therapeutics enabled by nanotechnology. Especially in the field of cancer therapy, promising applications are being developed. Several novel nanoparticles will respond to externally applied physical stimuli in ways that make them suitable therapeutics or therapeutic delivery systems. For example, magnetic iron oxide nanoparticles, gold-coated silica nanoshells, and carbon nanotubes can transform electro-magnetic energy into heat causing a temperature increase lethal to cancer cells merely by increasing the magnetic field or by irradiation with an external laser source of near-infra red light at the very location where these nanoparticles are bound to or internalised within tumour cells. Moreover, the delivery of chemotherapy and photosensitisers to tumours, and activating them *in situ* is possible. Also in other areas, drug delivery is one of the major application fields for nanotechnology.

Nanoparticle-mediated transport across the blood-brain barrier could not only provide an effective treatment for brain tumours, but also for other central nervous system related-diseases such as

Alzheimer's and Parkinson's. Furthermore, non-viral gene delivery systems for gene therapy, nanoneedles for cell surgery and delivery of molecules into the cell nucleus, nanocrystalline silver particles with antimicrobial activity or haemostatic agents on wound care products, microchip-based drug delivery systems for programmable drug release, and nanoporous drug eluting coatings on stents are examples of new nanotechnology materials and devices in drug delivery applications [6]. In the future, a modular approach to construct delivery systems which combine targeting, imaging and therapeutic functionalities into multifunctional nanoplatforms may allow for new refined non-invasive procedures. These nanoplatforms would localise to target cells, enable diagnostics and subsequently deliver therapeutics with great precision. Such modular approaches to nanodevice construction can potentially be more powerful than current treatment modalities, but are inherently more complex than existing small molecule or protein therapeutics (Figure 1). Another important field of application for nanotechnology are biomaterials used for example in orthopaedic or dental implants or as scaffolds for tissue engineered products. Together with the control of nanoporosity allowing vascularisation and the growth of cells inside the biomaterial, the nano-structured surfaces of biomaterials also allow the creation of novel types of scaffolds for tissue-engineered products. A promising approach for the latter application are nanofibres produced using self-assembling peptides with engineering functionality and biodegradability.

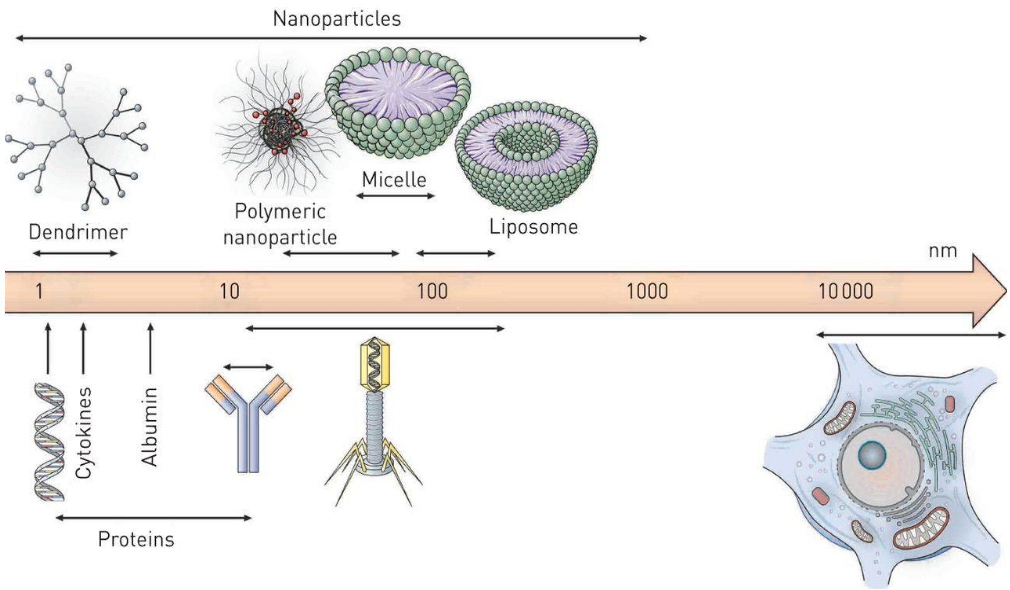

Figure 1. Medical nanoparticles for next generation drug delivery [7]

Medical devices for *in vitro* diagnostics, such as gene-, protein- or lab-on-a-chip devices, do not have any of the safety concerns associated with nanoparticles introduced into the body. Numerous devices and systems for sequencing single molecules of DNA are feasible. Nanopores are finding use as new nanoscale technology for cancer detection enabling ultrarapid and real-time DNA sequencers. In general, developments in protein-chips and labon-a-chip devices are more challenging compared to gene-chips and these devices are anticipated to play an important role in medicine of the future, which will be personalised and will combine diagnostics with therapeutics into a new emerging medical area called theranostics [7].

3. NANOPARTICLES AND MAGNETISM

Nanoparticles can be made from different materials such as metals, metal oxide, inorganic materials, polymeric materials and lipids. They can be amorphous or crystalline. Today we are witnessing the great boom of nanocrystaline magnetic particles as essential components in several areas of medical practice. These nanoparticles have two or three dimensions under 100 nm, which brings a high surface-to-volume ration and gives them attractive properties for biomedical application. As a particle size decreases, total surface area increases, which means that more atoms are on the particle surface and nanoparticles are more reactive compared to bulk materials.

A bulk ferromagnet tends to minimize the internal energy by spontaneously splitting into magnetic domains, which are regions containing magnetic moments in one direction. A ferromagnetic particles of iron-oxide with a radius under 30 nm are a single domain particles. It means that magnetization does not vary under magnetic field. For a given size of volume and no external magnetic field acting on the material, no domain will be present. The system is single domain in which the sample is uniformly magnetized with a single superspin. If we further reduce the size of a single domain nanoparticles, in the absence of a magnetic field, there will be a critical size above which the thermal energy will overcome the anisotropy barrier causing fluctuating of magnetization. Such fluctuations represents paramagnetic state, but magnetic moment is several order of magnitude higher. Then, the experiment will show an "unblocked" magnetization typical for the particle in a superparamagnetic state which is closely connected with the time of measurement.

The characteristic time of the thermal fluctuation of the magnetization is called relaxation time. When the relaxation time is much longer than the time of observation of the moment, magnetic moment of nanoparticle is stable and exhibits ferro or ferri ordering – „blocked" state. Superparamagnetic nanoparticles can be obtained by various physical and chemical methods. The most described synthesis routes comprise the aqueous ferrous and ferric salts alkaline co-precipitation, the thermal decomposition of organometallic complexes, the alkaline hydrolysis in a polyol solvent and the post-synthesis hydrothermal treatment [12−14].

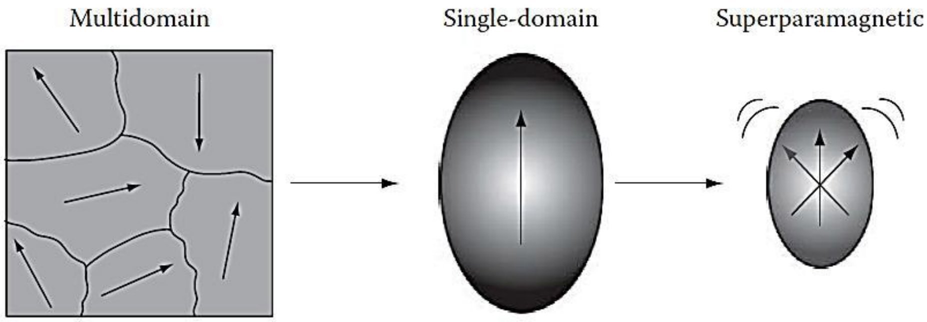

Figure 2. Magnetic behaviors derived from the scale reduction in magnetic materials

For magnetic targeting, a drug or therapeutic radionuclide is bound to a magnetic compound, introduced in the body, and then concentrated in the target area by means of a magnetic field (using an internally implanted permanent magnet or an externally applied field). Depending on the application, the particles then release the drug or give rise to a local effect (irradiation from radioactive microspheres or hyperthermia with magnetic NPs). Drug release can proceed by simple diffusion or take place through mechanisms requiring enzymatic activity or changes in physiological conditions such as pH, osmolality, or temperature; drug release can also be magnetically triggered from the drug-conjugated magnetic NPs [13].

The key parameters in the behavior of magnetic NPs are related to surface chemistry, size (magnetic core, hydrodynamic volume, and size distribution), and magnetic properties (magnetic moment, remanence, coercivity). The surface chemistry is especially important to avoid the action of the reticuloendothelial system (RES), which is part of the immune system, and increase the half-life in the blood stream. Coating the NPs with a neutral and hydrophilic compound (i.e. polyethylene glycol (PEG), polysaccharides, dysopsonins (HSA), etc.) increases the circulatory half-life from minutes to hours or days. Another possibility is to reduce the particle size; however, despite all efforts, complete evasion of the RES does not seem feasible and unwanted migration to other areas in the body could cause toxicological problems. In addition to cancer treatment, magnetic NPs can also be used in anemic chronic kidney disease and disorders associated with the musculoskeletal system (i.e. local inflammatory processes, side effects). For those disorders, superparamagnetic Fe oxide NPs (SPION), in conjunction with external magnetic fields, seem a suitable alternative for drug delivery to inflammatory sites by maintaining appropriate local concentrations while reducing overall dosage and side effects [15].

The biocompatibility and magnetic properties make iron oxide nanoparticles good candidate for application in magnetic hyperthermia. Magnetic hyperthermia can be described in a following manner: Firstly, magnetic nanoparticles have to be injected into the human body. Once these particles are situated and later disseminated in a tumor area, external AC magnetic field is used. Nanoparticles are used to convert heat from the electromagnetic radiation. The produced heat causes enhancement of the temperature in the tumor area, which ruins or completely devastates cancerous cells. Contrary to cells affected by a tumor, healthy cells are more resistant to high temperatures.

Cancerous cells can be destructed without huge influence on a healthy tissue by increasing a local temperature of the tumor region (to about 42 − 46°C). This enables very effective and localized cancer treatment avoiding harm which is occurred by another medical therapies like chemotherapy or radiotherapy [15−16].

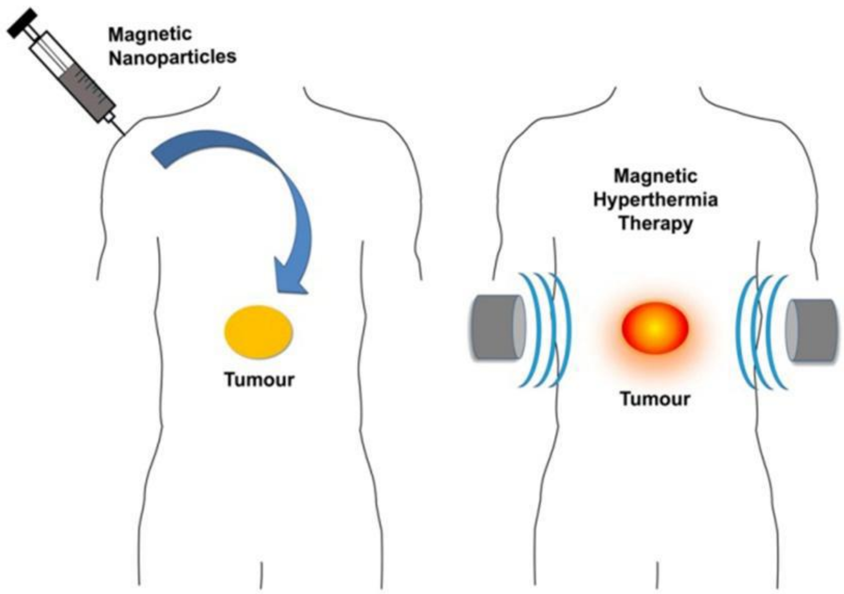

Figure 3. Magnetic hyperthermia therapy

4. CONCLUSION

Nanomedicine can be applied in biomedicine in many different ways and has potential to revolutionize global health. Some of biomedical applications are already available but many of them is in a research phase. This rapidly developing discipline is helping to realize our dream of fighting against many complex diseases such as cancer. On the other hand, nanoparticles can cause harmful effects. It is worth to mention that there are potential side effects and possible risks on living organism. The main risk that has been indentified to date is toxicity of nanomaterials. Researchers from different disciplines should collaborate in order to achieve commercialized application and analyze unknown risks. Many different nanomaterial-based platforms have been developed to improve drug delivery to tumor tissue, expand diagnostic and enhance the therapeutic efficacy while minimizing possible side-effects, but only a few have found their way into clinical application. Magnetic drug delivery constitutes a promising technology to treat cancer, and several products are already on the market. The limitations inherent in the use of external magnetic fields can, in some cases, be circumvented by means of internal magnets located in the proximity of the target by minimally invasive surgery. For nanomedicine (and nanotechnology) to truly become a global mega trend, the hype must be separated from reality. In addition, societal, environmental, and ethical concerns will need to be addressed as scientific advances occur.

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НЕКЕ ПРЕДНОСТИ ПРИМЈЕНЕ НАНОМАТЕРИЈАЛА У МЕДИЦИНИ

Сажетак: Нанотехнологија која се примјењује у биомедицини има важно мјесто у истраживању наноматеријала. Величина честица наноматеријала слична је величини биолошких молекула и структура, те се може закључити да је примјена наноматеријала у in vivo и in vitro биомедицинским истраживањима могућа. Овај рад представља кратак преглед медицинских примјена различитих наноматеријала као што су нанотубе угљеника, графен, квантне тачке, нанокапсуле итд. Такође ће бити представљени главни развојни наносистеми попут липозома, мицела и дендрима. Данас смо свједоци великог пораста употребе магнетних честица као суштинских компоненти у неколико области медицинске праксе. Велике предности коришћења наноматеријала у биомедицинским областима леже у њиховој способности да раде на истом нивоу као и све биохемијске функције укључене у раст, развој и старење људског тијела. Нанофарамција открива огроман потенцијал у преносу лијекова као носиоца просторно и временски биоактивних компоненти, као и дијагностике. Поред тога, откривају се и паметни материјали за ткивни инжењеринг. Ова дисциплина је сада добро утврђена за пренос лијекова, дијагностику, прогностику и лијечење болести путем наноенгинералних алата.

Кључне ријечи: нанотехнологија, биомедицина, нанофармација.

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