IOP Conf. Series: Materials Science and Engineering **133** (2016) 012029 doi:10.1088/1757-899X/133/1/012029

Morphological and physical - chemical issues of metal nanostructures used in medical field

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Abstract. In recent years applications of nanotechnology integrated into nanomedicine and bio-nanotechnology have attracted the attention of many researchers from different fields. Processes from chemical engineering especially nanostructured materials play an important role in medical and pharmaceutical development. Fundamental researches focused on finding simple, easily accomplished synthesis methods, morphological aspects and physico-chemical advanced characterization of nanomaterials. More over, by controlling synthesis conditions textural characteristics and physicochemical properties such as particle size, shape, surface, porosity, aggregation degree and composition can be tailored. Low cytotoxicity and antimicrobial effects of these nanostructured materials makes them be applied in medicine field. The major advantage of metal based nanoparticles is the use either for their antimicrobial properties or as drug-carriers having the potential to be active at low concentrations against infectious agents.

1. Introduction

In our century, microbes type virulent strains of bacteria have developed resistance to antibiotics that lead to a tremendous health impact and need to deliver solutions to this worldwide problem. The use of nanotechnology in medicine field, particularly nanomedicine, has already proved its major action on the pharmaceutical industry, especially in the antimicrobial field [1]. Over the last century antibiotics and vaccines arguably reduced human morbidity and mortality being considered the most important medical descoveries against infectious diseases [2,3].

Antimicrobial agents development represent a necessary help for classic medicine considering high resistant of pathogen micro-organisms. Researchers identified several inorganic, organic, and hybrid materials with possible uses in prevention and treatment of infections reporting the current information on the action mechanism of nano/microparticles based antimicrobial agents [4].

2. Materials and methods

Nowadays, a well-established branch of science called micro/nanomedicine, manages with tailoring small size devices, i.e. micro/nanoparticles, possessing unique properties for human health. Figure 1

shows a schematic exemplification of nano/ microparticles frequently used for drug delivery and therapeutic systems. Their biological properties are correlated to structural and functional characteristics.

There are studies specifying the relationship between cells and micro/ nanoparticles correlated to their structural and textural characteristics like size, shape, charge and functional groups having a considerable impact on their internalization.

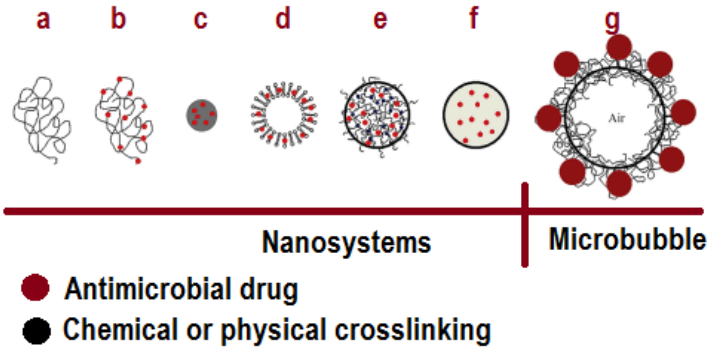

Figure 1. Exemple of nano/microsystems: a) antimicrobial polymers, b) polymer chains, c) inorganic nanoparticles, d) liposomes, e) polymeric nanoparticles, f) solid lipid nanoparticles loaded with antimicrobial drug, g) microbubbles loaded with nanoparticles.

Negative surface charge versus particles positive surface charge shows a significant reduction of particle association with cells [5].

3. Experimental part

Inorganic and hybrid materials were identified exhibiting antimicrobial activity depending on their physico- chemical and morpho-functional properties. Ionic form of metal based nanoparticles express antimicrobial ability compared to the metal, exhibiting an equivalent or superior antimicrobial effect [6-8]. Size, shape, porosity and surface properties are of great importance features inducing the antimicrobial efficacy of metal base nanoparticles. For example figure 2 shows TEM images of Ag nanoparticles revealing particles wide distribution ranging from 5 to 25 nm in diameter. Smaller particles are spherical in shape where as the larger ones are in an elongated form and shape that could be the result of the aggregation degree of the two or more particles together. Silver size and shape nanoparticles are also influenced by the concentration silver salt solution [9]. A major increase in the surface area consists in a stronger interaction of nanoparticles with the surrounding materials. Disadvantages of these material synthesis methods are represented by the toxicity of the reagents and the agglomeration and precipitation of nanoparticles [10].

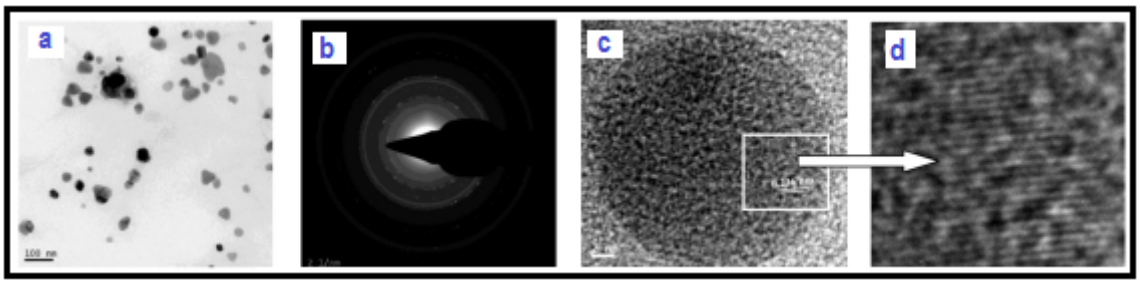

Figure 2. TEM and HRTEM images of silver nanoparticles on the GrO sheets at different salt concentrations: a) 8×10^{-3} moldm^{-3} $AgNO_3$, b) 1×10^{-3} moldm^{-3} $AgNO_3$, c) HRTEM with fringe spacing, d) enlarge image of fringe spacing.

Other uses of nanocomposite materials refer to coating medical devices and production of antimicrobial cotton textiles already being demonstrated to reduce postoperative infections [11]. Bionanotechnology use plants and micro-organisms such as bacteria, yeasts, fungi, and actinomycetes for fabrication of inorganic nanoparticles [12].

Multidisciplinary nano-scaled molecules used in diagnosis and treatment of different diseases are represented by metal oxide nanoparticles already applied as effective antimicrobial agents. Metal oxide nanoparticles are well known to target some cellular signaling pathways. Combination of metal oxides with other therapeutic agents enhances their bioavailability and efficacy. These remarkable nanomaterials have been used due to their various action mechanisms as antioxidant, anticancer, antimicrobial, and anti- inflammatory agents [13].

A serious threat to public health worldwide is considered to be the emergence of antibiotic-resistant microbial strains. Advanced nano-biotechnology enable the researchers to synthesize specific nanoparticulated metal oxide with well establish properties as antimicrobial activity. Zinc oxide nanoparticles were proven to inhibit the growth of wide spectrum bacterial strains such as gram-negative E. coli and Pseudomonas aeruginosa as well as gram-positive Staphylococcus aureus [14].

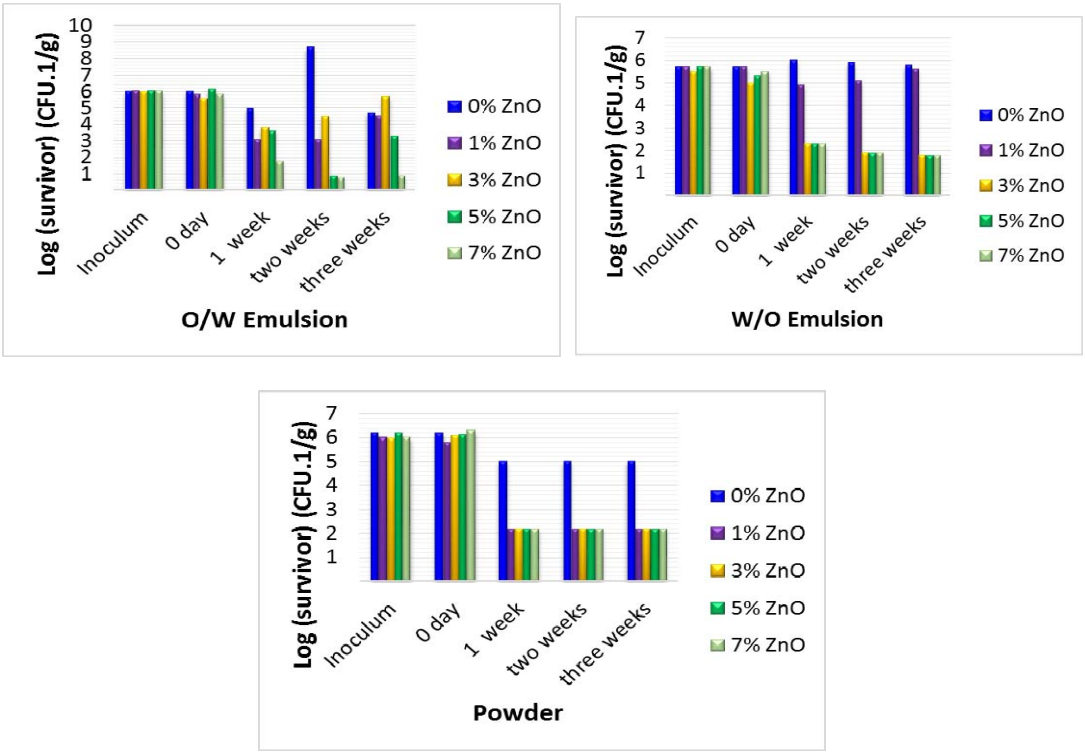

Figure 3. Test results of zinc oxides effect on P. aeruginosa in the oil-in-water emulsion, in the water-in-oil emulsion and in the dry powder.

Decreasing metal oxide nanoparticles size led to distortion and damage of bacterial cell membrane. More over, leakage of intracellular contents and possible death of bacteria demonstrate the antibacterial effects of these outstanding materials [15]. Different concentrations of ZnO nanoparticles in the anhydrous product were tested concerning P. aeruginosa as shown in figure 3.

4. Results and discussions

Results concerning P. aeruginosa bacterial strain revealed that bacterial population finally exceeded the control without zinc oxide nanoparticles at 28 days and decreased over 7 days, but then proliferated again during storage after 32 days [16].

Metal oxide nanoparticles known to possess a unique electronic structure provides a surface for direct free radical scavenging activity promising to act as an antioxidant therapeutic agent (Fig. 4).

Researchers found in a study of nerve cells (HT22), that CeO2/or Y2O3 nanoparticles, protect nerve cells suggesting that small size metal oxides could be the modulator of the oxidative stress in the biological systems [17].

Recent studies revealed that synthesized copper oxide nanoparticles using a thermal plasma technique have showed a minimum inhibitory concentration in the range 100 - 5000 µg/ml against drug resistant bacterial strains [18]. Other researches found that photo-activation of TiO2 nanoparticles using the ultra violet (UV) radiations, support the bactericidal effect which might be due to loss of respiratory activity caused by peroxidation of the polyunsaturated phospholipids of cell membrane [19].

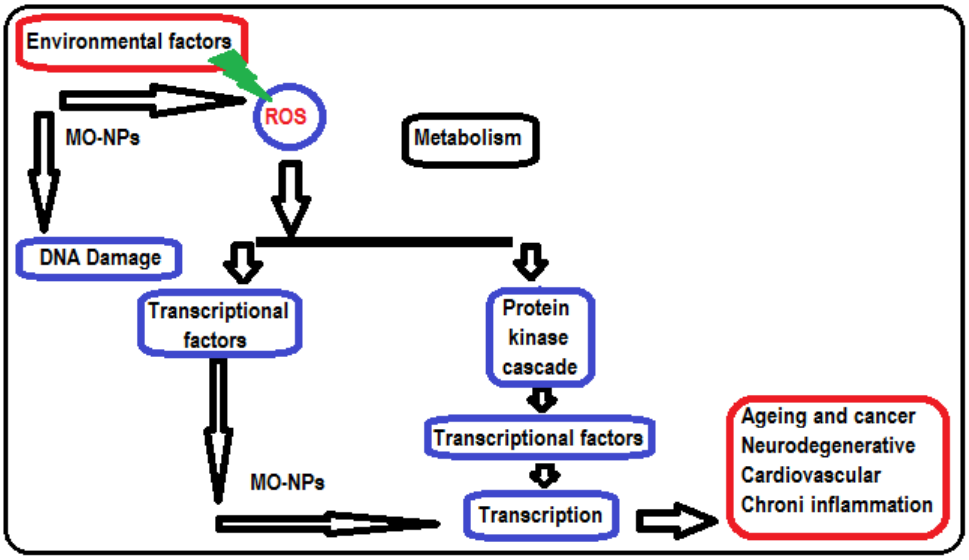

Figure 4. Brief representation of the direct free radical scavenging potential of metal oxide nanoparticles.

Among aluminum, silicon, titanium and zinc oxide nanoparticles against bacterial strains of Bacillus subtilis, E. coli and Pseudomonas fluorescens, ZnO nanoparticles were found to be more potent with 100% motility followed by SiO2 and Al2O3 nanoaprticles [20].

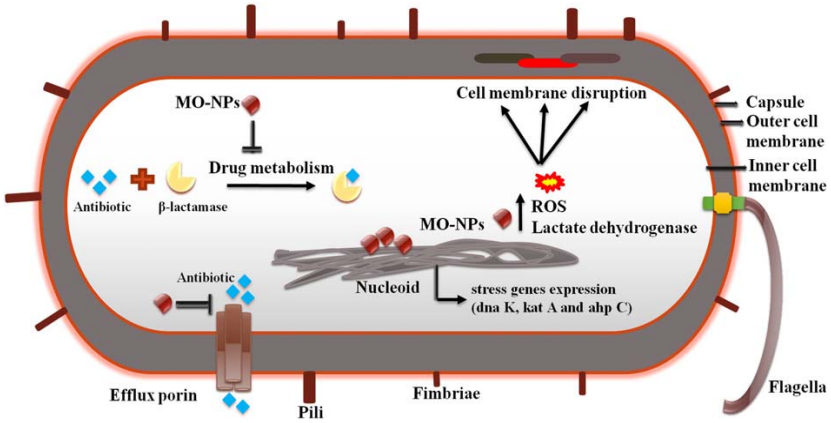

Figure 5. Representation of possible antibacterial mechanism of metal oxide nanoparticles activity.

The mechanism of antimicrobial action of metal oxide nanoparticles is not completely understood, it may depends on chemical composition, surface changes and intrinsic properties of nanomaterials along with the preponderant bacterial species. Nanoparticles were proved to be assigned to the microbial cell with electrostatic interactions consisting of cell wall damage concomitant with the increase in permeability of the cell [21, 22]. Figure 5 shows electrostatic interactions of metal oxide nanoparticles followed by reactive oxygen species (ROS) generation and activation of oxidative stress genes and the inhibitory effect of these nanoparticulate materials on drug resistance mechanisms mediated by β-lactamases and antibiotic efflux pumps.

Mutagenic potential of ZnO, CuO, TiO2, Al2O3, and Co3O4, and type metal oxides was investigated and reported significant colony inhibition activity of CuO nanoparticles. Generally, metal and metal oxide nanoparticles are known to destroy cell wall due to the interaction with the thiol (–SH) group of membrane proteins. Further more, metal oxide nanoparticles can deactivate the β-lactamases preventing the evolution of antibiotic resistance [23].

5. Conclusions

Remarkable morphology properties, physical-chemical characteristics, biological applications of metal nanoparticles significantly improve classic medicine. Metal and metal oxide nanoparticles incorporated into matrices act as active components in nanocomposites being biocompatible and suited for biomedical applications. In order to perform controlled release of drugs, by incorporating specific functional groups into matrices chemical engineering research has a major impact on nanomedicine research. Over the last few years nanosized materials have considerable evolved bringing to nanomedicine unprecedented advances in the diagnosis, imaging and treatment of a variety of hard to treat diseases. Nowadays, around 250 nanoproducts exist in various stages of development, including different compositions, nanostructures, physicochemical characteristics, surface functionality and morphology. Thus, nanomedicine researches will have to exceed chemical engineering and consider new medical aspects including in vivo studies and clinical trials.

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