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Metal and Calcium-Phosphate Nanoparticles for Biomedical Applications

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Nanoparticle research is currently an area of intense scientific research due to variety of potential applications in optics, electronics, biotechnology, health care, biomedical, chemical, and pharmaceutical fields. The physical sizes of these materials create a strong possibility for their interaction with biological systems. Biological systems themselves contain various components that have nanometer dimensions (proteins, nucleic acids, membranes), therefore nanopaticles can be useful both for in vivo and in vitro biological researches and applications. Among the metallic nanoparticles (NPs), the most important materials in nanomedicine are gold, silver, copper, iron, cobalt, nickel, platinum, magnesium, palladium and rhodium.

Keywords: Nanoparticles, Biomedicine, Nanomedecine, Calcium Phosphate

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1. INTRODUCTION

The application of nanomaterials in biomedicine has led to the development of diagnostic devices, contrast agents, analytical tools, physical therapy applications, and drug delivery vehicles. In all the nanomaterials with antibacterial properties, metallic nanoparticles are the best. Nanoparticles of Cu, Co, Ni, Ag have shown catalytical properties and they are used in synthesis of various pigments. Copper nanoparticles can significantly increase bone density, increase binding strength, and improving organisational forms, and are significant in osteoporosis prevention and treatment. Nanoscale magnetic particles are playing increasingly important role as tools in biotechnology and medicine, as well as for studding biological systems. These biomedical applications of magnetic nanoparticles include target drug delivery as magnetic vectors can be directed to the target of interest using either external or internal magnetic field, magnetic contrast agents in magnetic resonance imaging (MRI), hyperthermia agents for localized damage of the tumor tissue using high frequency magnetic field, and cell and biomolecule separation. Composites comprising the calcium phosphates and natural biopolymers are widely used in the manufacturing of orthopaedic biomaterials. The hydroxyapatite is used as a component of synthetic materials for orthopaedy and stomatology for a long time.

2. METAL NANOPARTICLES

Main areas of nanoparticles applications need controllable fabrication of nanostructures with a high degree of regularity and uniformity in order to control their properties precisely. Thus, it's very important to develop technology for efficient formation of ordered arrays of nanoparticles on substrate surface with tunable forms, size and distance between structural elements. There are different methods of NPs obtaining, most often they are grown by wet-chemical methods through reduction of their salts. In this work a bottom-up magnetron sputtering method under conditions close to thermodynamic equilibrium is used for obtaining NPs of Cu, Ni, Ti, Cr and Al. Characteristic peculiarities of quiasi-equilibrium conditions are: the condensation process occurs at sufficiently low supersaturation to provide a proximity to phase equilibrium between condensate and depositing substance; this supersaturation remains stable in the course of the time to guarantee steady-state conditions of the condensation process.

Self-assembling of metal nanosystems was performed in technological setup equipped with three direct current magnetron sputterers. One of them was used for sputtering of depositing material. As a working gas argon was used at pressure more then 10 Pa. Argon was subjected to deep purification via the absorption of chemically active gases during the process of additional Ti sputtering by two lateral magnetrons. The partial pressure of the chemically active residual gases (mainly O_2, H_2 and N_2) was $8 \cdot 10^{-8}$ Pa. Fresh KCl cleavages were used as the substrates. The reduction of the free path length at the increased working gas pressures allowed us to average the energy of the ion-sputtered atoms, as well as to ensure the equiprobable arrival of the substance onto different facets of the growing crystals near the growth surface.

Approaching to equilibrium was achieved by heating of the growth surface under the plasma action. In this case, the average energy of the ion-sputtered atoms is one order of magnitude higher than the energy of thermally evaporated atoms and is equal to about 5 – 8 eV, which corresponds to a particle temperature of ~ 38000 K. Moreover, it is known that the incomplete thermal accommodation needs the energy of condensed atoms corresponding to a temperature above 6000 K. Hence, the incomplete thermal accommodation enhances the reevaporation of adatoms and, thus, makes it possible to achieve near-equilibrium conditions at relatively low substrate temperatures.

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We have established that modern conventional notions of the metal condensation mechanism under Volmer–Weber conditions are limited only by sufficiently high supersaturations and that the cluster nanosystems can be formed under the conditions closest to the equilibrium ones. In this case, the near-equilibrium condensation and the Ostwald ripening, which are maintained by the effect of the particles on the growth surface, are the necessary prerequisites of the self-organization of the statistical uniformity of nanosystems.

3. CHITOSAN/HYDROXYAPATITE SCAFFOLDS

It is well known that bone tissue of human and animals is made of protein matrix individual for each living organism and mineral component which is inorganic compound of calcium and phosphor, in other words hydroxyapatite (HP). That is why different implants produced on the basis of HP are widely used in orthopaedics and traumatology. Thus, creation of new artificial materials on the basis of HP with advanced properties and characteristics close to human bone tissue are of great interest to scientists. It is worth noting, that artificial HP implants have very high biocompatibility. Composite nanostructured materials made of natural biopolymers and hydrogel nanoreactor matrixes have much more better mechanical properties than pure HP and strength of the nanocomposite can be comparable with natural bone.

Nanocomposites comprising calcium phosphates and natural biopolymers are widely used as biomaterials for bone tissue repair and engineering. Chitosan/hydroxyapatite scaffolds could be used for bone regeneration in case the application of auto- or allografts is impossible. There are several ways to produce such composite materials. Most of them involve two major stages: first, the synthesis of an organic polymeric scaffold of pure or chemically treated and modified chitosan and, second, mineralization of the scaffold in simulated body fluid (the biomimetic way) or in saturated matrix solutions.

The objective of this work was to characterize and study in vivo biodegradation of simple chitosan/hydroxyapatite scaffolds that were obtained in aqueous medium from chitosan solution and soluble precursor salts by a one step coprecipitation method. A study of in vivo behavior of the materials was then performed using model linear rats. For these experiments 48 linear laboratory rats at the age of 4 months were used. The Ukrainian National Act of animal protection against cruel treatment (Act No 3447-IV 21.02.2006) regulating the care and use of laboratory animals has been observed. At the middle one-third of right tibia of the animals perforated defects were made with a stomatological borer, diameter 2 mm, in the sterile operating room. The width of a tibial diaphysis of adult rats is at the average from 4.2 to 4.7 mm. When a perforating bone defect is modeled, it is necessary to preserve integrity of bone, which causes the intramembranous type of bone regeneration.

A model defect in this case cannot be wider than 2 mm. The 50/50 chitosan-hydroxyapatite scaffolds were chosen for in vivo evaluation. In the experimental group of animals cylindrical ChAp rods were implanted into traumas, diameter of the rods was equal to the width of the wound channel. The control group was comprised of the rats with the analogous tibial defects, which were not filled with the investigated material. The animals were taken out of the experiment after 5, 10, 15, and 24 days after implantation and histological and histo-morphometric analyses of decalcified specimens were performed to evaluate the stages of biodegradation processes. Calcified specimens were examined by scanning electron microscopy with X-ray microanalysis to compare elemental composition and morphological characteristics of the implant and the bone during integration. To obtain porous materials, a lyophilization procedure was applied to wet (not dried completely) substances by using the vacuum chamber VUP-5M in which a glass sample-holder cooled with liquid nitrogen had been mounted. The frozen samples were dried under 10^{-3} Pa overnight. Porous chitosan/hydroxyapatite scaffolds have shown osteoconductive properties and have been replaced in the in vivo experiments by newly formed bone tissue.

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