SYNTHESIS AND CHARACTERIZATION OF COMPOSITES BASED ON CALCIUM PHOSPHATES AND POLY(VINYL ALCOHOL) FOR BIOMEDICAL APPLICATION

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СИНТЕЗ И ИССЛЕДОВАНИЕ КОМПОЗИТНЫХ МАТЕРИАЛОВ НА ОСНОВЕ ФОСФАТОВ КАЛЬЦИЯ И ПОЛИВИНИЛОВОГО СПИРТА ДЛЯ ИСПОЛЬЗОВАНИЯ В БИОМЕДИЦИНЕ

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Аннотация. Композитные материалы получены in situ на основе поливинилового спирта, фосфатов кальция и гидроксиапатита, синтезированного под воздействием микроволнового излучения, циклическим замораживанием – оттаиванием. Синтез фосфатов кальция проводился in situ в присутствии поливинилового спирта при нагревании и перемешивании в течении восьми часов также с последующим циклическим замораживанием - оттаиванием. С использованием методов газоадсорбционного, рентгенофазового анализов, а также ИК-спектроскопии и сканирующей электронной микроскопии был установлен состав композитов, их структура, морфология и свойства их поверхности. Также установлено, что введение поливинилового спирта не оказывает влияния на процесс фазообразования и формирования кристаллической структуры.

Introduction. Bone is known as a natural-organic composite material of complex structure. Basically, it consists of nano-scale inorganic crystals that filter collagen fibrils and water. Inorganic phase predominates (69%) and is represented by hydroxyapatite (HA; $Ca_{10}(PO_4)_6(OH)_2$). Hydroxyapatite crystals within natural bone are rod-shaped 40–60 nm in length, 10–20 nm in width, and 1–3 nm in thickness. Synthesized hydroxyapatite is of scientific interest due to biocompability and osteoconductive properties. It is widely used for hard-tissue scaffolds, bone-grafting, prosthetic replacement, and bone drug delivery agents. High degrees of crystallinity and chemical stability are desirable properties for bone repairing / augmentation materials. Besides, being non-toxic and biodegradable, hydroxyapatite is suitable for biomedical materials. In recent years, particular attention has been paid to the preparation of HA bioceramics with porous morphology. Porous HA exhibits strong bonding to the bone; the pores provide mechanical interlock leading to material firm fixation. Bone tissue grows well into the pores increasing strength of the HA implant. Dimension and morphology of pores have proved to be crucial factors for an efficient osteointegration.

Nevertheless, poor mechanical properties of the synthesized hydroxyapatite (e.g., high elastic modulus and low fracture toughness) restrict its applications. Therefore, in recent years numerous attempts at material and techniques development have been made in order to impart suitable biological and mechanical properties to

synthetic composites so that they become applicable in the realm of natural bone replacement. Composites of HA with polymers enhance mechanical properties of HA and help to retain its useful bioactive properties.

Polymers offer many prospects depending on chemical composition and structure of the former (hydrophilic/hydrophobic ratio, toughness/flexibility, etc.), but very few have demonstrated good bioactive properties to ensure the implant osteointegration. Polymers that contain polar functional groups – e.g., carboxyl (-COOH), hydroxyl (-OH), alkyl ($-CH_2$), dihydrophosphate ($-H_2PO_4^-$) – have appeared to be ionizable side groups providing greater affinity to Ca^{2+} ions and the hydroxyapatite crystals nucleation within a solution. There have been made the attempts at *in situ* mineralization technique with poly(lactic acid), poly(acrylic acid), chitosan, collagen, and gelatin due to their calcium-binding properties. Another polymer with potential biomedical application is poly(vinyl alcohol) (PVA). PVA is a polar hydrophilic biocompatible polymer possessing excellent physical and mechanical properties of absorption and exudation of body fluid; which has led to its applications as a biomaterial.

Polymers can also form hydrogels – swollen networks of hydrophilic polymer and water via physical or chemical crosslinking, which exhibit the ability to swell in water, as well as retain a significant fraction of water in its interior structure without further dissolution. Their physical properties resemble those of human tissues and are easily attached onto the underlying bone. Poly(vinyl alcohol) hydrogel has been widely studied, which has resulted in manifestation of numerous properties, namely, stability, availability and low cost of the molding, and sufficient biocompatibility. On the other hand, PVA displays poor mechanical resistance. The shortcomings could be eliminated by adding hydroxyapatite as the reinforced phase to PVA composite or hydrogel.

Materials and methods. Various methods of HA - PVA composites have been developed recently, including the production methods of composite hydrogels, films, polymer-coated ceramics, composite scaffolds, and powders. The primary target of the current paper is to describe synthesis of poly(vinyl alcohol) – hydroxyapatite hydrogels and composites with different HA and PVA ratios, as well as the characteristics of obtained compounds.

Hydroxyapatite – poly(vinyl alcohol) composite materials were obtained in forms of both hydrogel and powders with different ratio of components by means of adding hydroxyapatite powder to PVA water solution. Another synthetic route was carried out by mixing reagents for hydroxyapatite with PVA water solution on continuous heating and stirring throughout eight-hour period. In both methods suspensions were washed with distilled water, dried, and divided in halves – whereas one half was calcined with subsequent white powders obtainment, and another half was being processed through several freezing-thawing cycles with subsequent hydrogels obtainment.

The composition of all of the samples was characterized by X-ray diffraction (XRD) on Rigaku Miniflex 600 diffractometer ($Cu_{K\alpha}$- radiation $2\theta = 10\,°–90\,°$, scan step 0,02 °, scan rate d of 10 °/min). JCPDS PDF data were used to index diffraction peaks, evaluate the crystallite size, and determine the quantitative phase composition of the samples. The specific surface area of the synthesized composites powders was determined by BET analysis of low-temperature nitrogen sorption isotherms obtained using a TriStar II automatic gas adsorption analyzer. Surface morphology was examined via scanning electron microscope on a Hitachi TM-3000 instrument operated at an acceleration voltage of 15 kV with surface charge elimination, using a QUANTAX 70 energy dispersive spectrometer system for elemental analysis. IR-spectra of samples were performed using Agilent Cary 630 Fourier at frequency range of 400–4000 cm^{-1}.

Conclusions. XRD results have indicated that a variety of calcium phosphates – such as monetite ($Ca(HPO_4)$) and brushite ($Ca(HPO_4) \cdot 2H_2O$) – was formed in the samples prepared by mixing reagents for hydroxyapatite and PVA, and hydroxyapatite phase was not indicated in neither of the samples. Still, the samples appeared to have well-crystallized structure. Composites obtained by mixing HA with PVA are more amorphous, yet, they do contain hydroxyapatite crystalline phase.
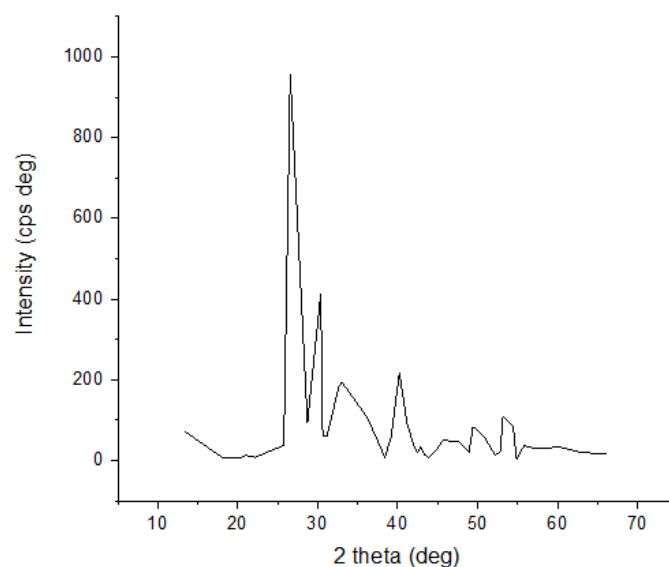

Fig. 1. XRD-graph of Monentite – PVA composite

According to BET analysis, both types of composites are considerably mesoporous, which is consistent with biomaterials characteristics. HA composites display more developed surface and lower porosity. However, calcium phosphates composites possess larger pores and manifest lower values of a specific surface area.

Table 1

BET-analysis results

Sample	Degasification, vacuum	Specific surface area, m^2/g (ratio error $\Delta \pm 10\%$)	Porosity, cm^3/g	Average pore size, nm
К. 1. С.	2h, 200°C	79,9	0,237	11,9
К. 1. С.	2h, 150 °C	67,8	0,188	11,1
К. 2. Г. 1	2h, 150 °C	13,5	0,098	28,9
К. 2. Г. 5	2h, 150 °C	-	0,03 (approx.)	-
К. 2. Г. 25	2h, 150 °C	3,2	0,019	25,5

IR-spectra reflect composition of the obtained samples while spectra of composites obtained by mixing do not contain absorption bands of polyvinyl alcohol although the presence of phosphate groups has been indicated.