Composite Hydrogel Materials of Biomedical Application with Fungibactericidal Properties

Nataliya Chopyk, Kateryna Vashchuk,
Sofiia Melnyk, Volodymyr Skorokhoda

Department of Chemical Technology of Plastics Processing,

Lviv Polytechnic National University, UKRAINE, Lviv,
S. Bandery street 12, E-mail: vskorohoda@yahoo.com

Abstract* — *The new porous compositions on the basis of hydroxyapatite filled copolymers of methacrylic esters and polyvinylpyrrolidone, which containing silver nanoparticles in the structure, were synthesized. Effect of pores forming agent nature, polyvinylpyrrolidone and hydroxyapatite amount on the composite properties was observed. In the composite structure silver nanoparticles are obtained via silver nitrate reduction by tertiary nitrogen of polyvinylpyrrolidone. The synthesized silver-containing composites possesses bactericidal properties .

Keywords – porous composition , polyvinylpyrrolidone, silver nanoparticles, bactericidal properties, porosity.

I. Introduction

Modern medicine and biotechnology pays great attention to research that focused on the development of new osteoplastic materials. These materials should provide effective regeneration of bone tissue after various kinds of operations, particularly in orthopedics and maxillofacial surgery. These applications require materials that can be produced on the basis of non-organic matrix of cattle natural bone tissue which contains chemical elements in the same form as in vital organism. Hydroxyapatite (HA) is the main mineral component of bone, tooth, enamel and dentin that plays an important role in many physiological processes. As potentially the most biologically compatible and active replacement of bone tissue the hydroxyapatite attracted great attention from scientific society [1]. Hydroxyapatite may be stable in contact with body fluids and become essentially integrated with the bone [2]. However, this material is brittle and its poor mechanical properties, such as compressive strength, elastic modulus and some fracture toughness, cannot be entirely compared to unique mechanical features of cortical and cancellous human bones [3]. The possibly most benefitial way to overcome this disadvantage is to design porous polymer-mineral composites [4,5] synthesized from calcium-phosphate materials (which have their composition similar to bone) and biocompatible polymeric matrix, mainly on the basis of 2-hydroxyethylmethacrylate (HEMA) with polyvinylpyrrolidone (PVP) copolymers.

The aim of the present work is to develop new compositions with antiseptic and antibacterial properties based on (co)polymers of HEMA with PVP capable being applied in medicine (in osteogenesis) and to investigate the effect of composition structure on the regulations of composites formation and properties.

II. Material and Methods

2-Hydroxyethylmethacrylate (Bisomer) were vacuum distilled before use; polyvinylpyrrolidone (M_W=28·10^3, AppliChem CmbH); hydroxyapatite ($Ca_{10-x}(PO_4)_6(OH)_2$) with the particles size of 0,05…1,25 mm was synthesized at the Department of Silicates Technology of Lviv Polytechnic National University.

The average diameter of pores (d_p) and polydispersivity index (*PDI*) were determined by size measuring of at least 200 pores using MBS-9 microscope. The structure of the composites was studied using transmission electron microscope (TEM) JEOL JEM 200 CX. The total porosity and composites density were determined using a Manehold method described in [6].

The compression strength was determined by the standard method using testing machine "Kimura" type RT-601U. UV spectroscopic studies was carried out on the Perkin-Elmer Lambda 20 UV-VIS spectrometer.

III. Result and Discussion

One of the main bioplastics requirements is the presence of through porous structure with controlled micro- and macropores sizes necessary for implant composite growth by bone tissue. Therefore, at first we studied the effect of nature of potential pores forming agents on the porous structure formation and composites conditional density. The basic polymer-monomer composition was the composition [HEMA]:[PVP] = 7:3 wt. p. with high reactivity and without demand of high curing temperature [7]. The pores forming agents were compounds of organic and inorganic nature: chloroform, methylene chloride, cyclopentane, hexane, calcium chloride, ammonium and potassium carbonate. The organic agents form pores at evaporation, calcium chloride – after its washing by water from a ready composite, ammonium and potassium carbonates – due to the decomposition and release of carbon dioxide at composite heating. Porous material is not formed only in the case of hexane. Concerning the inorganic forming agents (calcium chloride and ammonium carbonate), the high-porous composites were obtained with fine pores, the size of which does not exceed 0,4 mm. While using organic ones: chloroform, methylene chloride and cyclopentane the materials with satisfied size of pores (0,8…1,3 mm) are formed.

The value of porosity considerably depends on the components ratio. Porosity increases from 37 % for polyHEMA to 67…70 % for copolymer HEMA-PVP with PVP content of 30 wt. %. This fact reveals that PVP positively affects not only the kinetics of composite curing but pores forming as well. $AgN0_3$ do not affect the general porosity, though the polydispersivity index increases with the increase of their amount.

Photographs of the composites filled with HA are represented at Fig.1. They confirm the presence of developed micro- and macroporous structure favoring the effective growth of the composite by bone tissue. Composites, which incorporates contain more PVP, have greater porosity value (Fig.1a).

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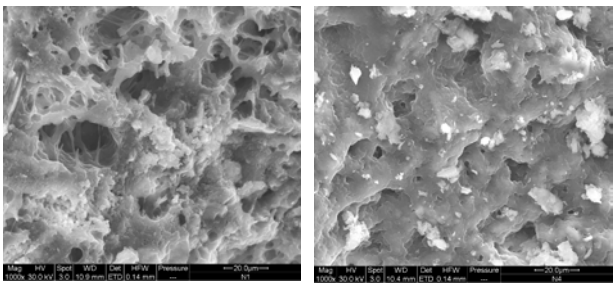

a) *b)*

Fig.1 Photographs of microporous structure of hydroxyapatite filled HEMA-PVP composites: [HEMA]:[PVP]:[HA], wt. p.: *a* – 6:4:7, *b* – 9:1:7.

The amount of the filler also affects the composite formation and its properties. The porous composite structure is not formed without HA or its content not exceeding 25% even at the optimum amount of pores forming agent. To our mind, foaming takes place before the composition curing. At the same time in the investigated range the decrease of material porosity is observed with the increase of filler amount. The most homogeneous porous material with the least conditional density is formed with HA amount of 70 wt. %.

In order to obtain silver nanoparticles and to provide the composites with antibacterial properties the reaction of silver recovery by interaction of its salts with tertiary nitrogen of PVP was investigated. The formation of silver by this reaction is confirmed with the presence of peak (420...430 nm) at UV spectra of products of interaction between $AgNO_3$ and PVP and with the results of the chemical analysis of reaction products.

The results of electron microscopy studies have shown that Argentum nitrate forms silver nanoparticles in the shape of different size polyhedrons. The size of nanoparticles depends on the nature of the reaction medium. In aqueous solution there are formed silver particles with an average diameter of 40...60 nm, whereas in mixtures of water with ethanol – 10...30 nm.

Reaction of Argentum reduction by interaction of its salts with tertiary nitrogen of PVP was used to provide antibacterial properties of composites during the composite formation. Temperature conditions of composites synthesis were justified on the basis of kinetic studies of polymerization [7]. The polymerization was initiated by BPO (1 wt. %).

During the synthesis composites with PVP and argentums salts change their color from weak-yellow to brown. It is also the indirect confirmation of silver nanoparticles formation while interaction between argentum nitrate and PVP tertiary nitrogen. This method has irrefutable advantages over other known methods when nanoparticles and hydrogels are prepared separately or when hydrogel is saturated with argentum salts or when silver nanoparticles are obtained via its reduction by amino-containing methacrylic monomer followed by its copolymerization with other monomers. Moreover, there is no necessity in toxic amino-containing reducers.

To confirm the possible practical application of the developed silver-containing composites in biomedical research industry their bactericidal and fungicidal properties were investigated. The research results are presented in Table 1.

TABLE 1

FUNGIBACTERICIDAL ACTIVITY OF SILVER-CONTAINING COMPOSITE (HEMA:PVP:HA:$AgNO_3$ = 7:3:7:0,6 WT. P., DIAMETER OF THE COMPOSITE SAMPLES 15 MM)

Diameter of the growth retardation zone, mm (%)		
E. coli	*S. aureus*	*A. niger*
24,4 (60)	26,0 (73)	20,0 (33)

As a result of comparative analysis of bactericidal and fungicidal properties of the obtained HEMA-PVP composites that contain silver nanoparticles and non-silver-containing composites on microorganisms it was found that the composites, containing silver nanoparticles, block the growth of bacteria, showing bactericidal activity.

Conclusion

Thus, new porous composites on the basis of hydroxyapatite filled copolymers of methacrylic esters and PVP were synthesized. The possibility of silver nanoparticles obtained during formation of the composite was confirmed. It is expected that these composites will possess antibacterial properties. The effect of origin and ratio of the initial components on the properties of porous filled composites was determined. These results will be used for optimization of compound ratio of the material for osteogenesis and its further investigations including medical and biological treatments.

References

[1] W. Suchanek, M. Yoshimura, “Processing and properties of hydroxyapatite-based biomaterials for use as hard tissue replacement implants”, J. Mat. Res., vol. 13, pp. 94-117, 1998.

[2] D.M. Roy, S.K. Linnehan, “Hydroxyapatite formed from coral skeletal carbonate by hydrothermal exchange”, Nature, vol. 247, pp. 220-222, 1974.

[3] K. Rezwana, Q.Z. Chena and J.J. Blakera, “Biodegradable and bioactive porous polymer/inorganic composite scaffolds for bone tissue engineering”, Biomaterials, vol. 27, pp. 3413-3431, 2006.

[4] S.S. Kim, M.S. Park and O. Jeon, “Poly(lactide-co-glycolide)/hydroxyapatite composite scaffolds for bone tissue engineering”, Biomaterials, vol. 27, pp. 1399-1409, 2006.

[5] V. Skorokhoda, N. Semenyuk, I. Dziaman and O. Suberlyak, “Mineral filled porous composites based on PVP copolymers with bactericidal properties”, Chemistry & Chemical Technology, vol. 10, no. 2, pp. 187-192, 2016.

[6] V. Dubyaga, L. Perepechkin and E. Katalevskyi, Polimernye membrany [Polymer membranes]: Per. s angl., Moskwa: Khimiya Publ, 1981.

[7] V. Skorokhoda, “Matrix polymerization of 2-hydroxy-ethylmethacrylate in the presence of polyvinylpyrrolidone”, Chemistry & Chemical Technology, vol., 4, no. 3, pp. 191-196, 2010.

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