

Synthesis of Hydroxyapatite Nanoparticles with Initiating Centres in Polymer Shell

O.M. Shevchuk*, M.R. Chobit, N.M. Bukartyk, G.O. Ogar, V.S. Tokarev

Lviv Polytechnic National University, 12, S. Bandery Str., 79052 Lviv, Ukraine

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This research work was devoted to the synthesis of hydroxyapatite nanoparticles with initiating centres in polymer shell. Macroinitiators comprised by heterofunctional copolymers containing either pendant peroxidic groups or benzoin pieces attached to the backbone chain were used as surface modifiers of hydroxyapatite. Their use in the stage of synthesis of the mineral particles makes possible a control over size and the surface properties of particles. The effect of copolymer nature and its concentration, as well as the synthesis conditions on hydroxyapatite particle size and the copolymer adsorption value was studied. Both types of functional groups namely peroxide and benzoin in structure of copolymers immobilized at the hydroxyapatite surface were used for initiation of polymerization processes at elevated temperature (in the first case) or under UV-irradiation (in another case). These techniques of bioceramics modification allowed to form polymer compatibilizing layer of proper structure and thickness bonded with the mineral particles that enhanced compatibility of mineral filler and polymer matrix of different nature and as a result obtaining composite materials with improved physico-mechanical properties.

Keywords: Hydroxyapatite, Nanoparticles, Macroinitiator of radical polymerization, Peroxide, Photoinitiator, Polymer composite.

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1. INTRODUCTION

Hydroxyapatite (HA) attracts much attention as a bone substitute material in orthopedics and stomatology due to its biocompatibility and bone bonding ability [1], while its wide usage is hindered by its low mechanical properties [2]. This problem can be solved via applying composite materials on the basis of HA and polymers (including bioactive polymers). However such composites usually possess insufficient biological activity because their filling degree with mineral particles is rather low (mostly less as 50%vol.). The problem arisen at obtaining of highly filled composites is caused by a poor adhesion between polymer matrix and hydrophilic surface of bioceramics resulting in delamination at the phase boundary and consequently in deterioration of the composite material mechanical properties.

Surface modification of mineral particle by polymers of diverse nature is one of the known technique used for compatibilization of the components in composite. Silanes, isocyanates, polyacids, and vinyl polymers are used to modify HA surface [3, 4]. Graft-polymerization initiated by the initiators immobilized beforehand at the filler surface is another method for formation of thin compatibilizing layers [5, 6]. This method allows to control the thickness of polymer layer, its functionality, and structure via changing the monomer nature and process conditions. Heterofunctional copolymers containing peroxidic and other initiating centres (so called macroinitiators) synthesized in Lviv Polytechnic National University can be adsorbed irreversibly on the surface of minerals and initiate graft-polymerization of vinyl monomer; this combination is a powerful instrument for design of polymer composites [7].

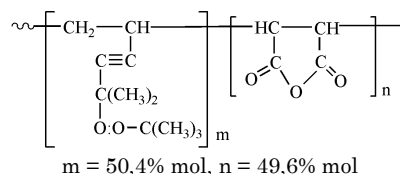
This work is devoted to study of the processes of obtaining the HA nanoparticles with functionalized polymer shell using two techniques: 1) adsorption modifica-

tion of HA nanoparticles with macroinitiators; 2) formation of thin polymer layer on the surface of HA via graft-polymerization of vinyl monomers initiated by macroinitiators previously adsorbed on its surface.

2. EXPERIMENTAL

2.1 Materials

Peroxide-containing macroinitiator (PMI) was synthesized via radical copolymerization of peroxidic monomer *5-tert-butylperoxy-5-methyl-1-hexene-3-yne* (PM) with maleic anhydride (MA) in ethyl acetate as described elsewhere [7].



Polymeric macrophotoinitiator (MPI) was obtained in accordance with [8] by attaching benzoin molecules to previously synthesized copolymer of methylmethacrylate with maleic anhydride (Fig. 1):

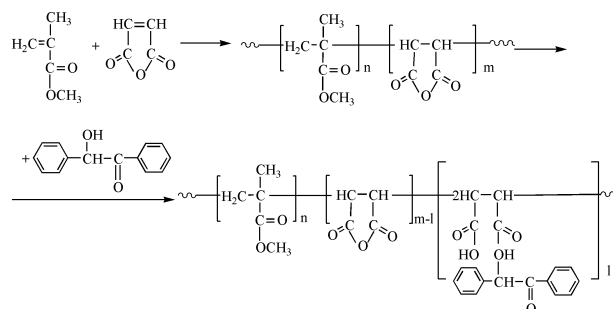
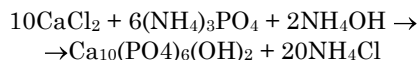


Fig. 1 – Scheme of MPI synthesis

* oshevch@polynet.lviv.ua

2.2 Synthesis

HA nanoparticles were obtained using sol-gel method as described in [9] in accordance with the reaction:



Adsorption of PMI and MPI onto HA surface was carried out from ethyl acetate solution at their different concentrations ($T = 298 \text{ K}$).

Grafting of polymer layers onto the surface of peroxidized HA was carried out via radical polymerization of corresponding monomers in dioxane initiated by peroxide fragments of PMI immobilized at the HA surface. No additional initiator was added to the system. The process was carried out in the sealed dilatometers; magnetic stirrer was used for stirring reaction mixture.

Photopolymerization of the composition on the basis of polyester resin PE-246, oligoesteracrylate TGM-3, photosensitizer eozine H, aerosile and HA nanoparticles with MPI adsorbed shell was carried out under UV-irradiation (DRT-400 mercury-quartz lamp, distance to photopolymeric composite film was 10cm, $T = 298 \text{ K}$, HA nanoparticle concentration – 2.8 %).

2.3 Analysis

The content of PM links as well as the content of adsorbed PMI at the surface of HA was determined using the results of chromatographic analysis of PM thermal decomposition products in accordance with known method [9]. The content of adsorbed PMI was determined gravimetrically.

Kinetics of graft polymerization was studied by dilatometric method. Additionally, gravimetric and gas-chromatography studies were performed. Photopolymerization kinetics was controlled by content of gel-fraction in composite.

The structure of the HA nanoparticles was determined from X-ray diffraction analysis (XRD) data ("DRON-30", CoKa irradiation) using Scherrer equation.

The hardness of photocured films was studied with the aid of M-3 pendulum device.

Molecular weight of polystyrene (pSt) and polymethylmethacrylate (pMMA) was estimated via determination of their intrinsic viscosity in benzene and acetone.

Thermogravimetric analysis of HA nanoparticles with grafted pMMA shell was carried out with the aid of "Q-1500D" derivatograph.

3. RESULTS AND DISCUSSION

Two approaches were realized to obtain HA nanoparticles with functionalized polymer shell: 1) Sol-gel synthesis of HA nanoparticles in water solution in the presence of PMI; 2) PMI or MPI adsorption at the surface of mineral nanoparticles synthesized beforehand.

The structure of obtained hydroxyapatite was proved by X-ray diffraction analysis data (Fig. 2).

Obtained data witnesses that the HA nanocrystals synthesized have an elongated shape with the size of about $9 \times 18 \text{ nm}$ in the case of the synthesis via ordi-

nary technique and $5 \times 14 \text{ nm}$ if the synthesis was carried out in the PMI presence. Evidently, PMI macromolecules while adsorbing at the surface of the seeds of HA crystalline phase restricted their growth serving in such a way as an exotemplate. Hence, the use of PMI during HA synthesis allowed to control the size and size distribution of synthesized nanoparticles.

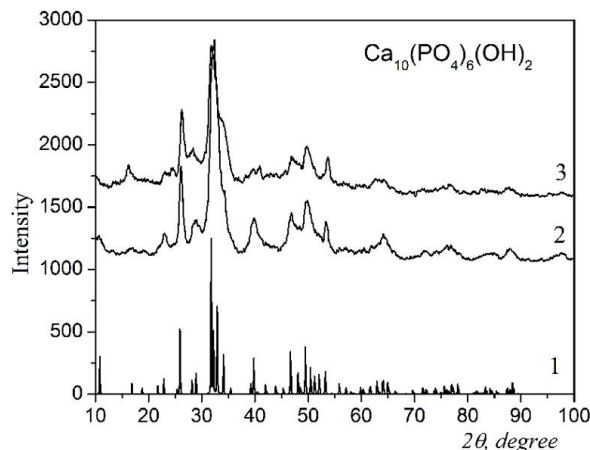


Fig. 2 – XRD spectra of HA samples: 1) etalon; 2) HA nanoparticles synthesized via standard technique; 3) HA nanoparticles synthesized in the presence of PMI

The study of PMI adsorption at the surface of nano-HA synthesized via ordinary technique revealed its extremely high adsorption capacity $A = 136 \text{ mg/g}$, that was connected with high specific surface area of the HA nanoparticles synthesized which was equal to $170\text{--}180 \text{ m}^2/\text{g}$. At the same time the amount of PMI adsorbed in the case of HA particle nucleation in the presence of 25 % PMI was much higher reaching 182 mg/g that can be explained by greater specific surface of HA particles in the later case ($S_{sp} = 290 \text{ m}^2/\text{g}$).

The dependence of PMI adsorption value and corresponding thickness of reactive polymer layer on the concentration of initial reagents at synthesis of nano-HA is shown in Table 1. A decrease of concentrations of both calcium chloride and triammonium phosphate in reaction mixture brought about an increase in the values of irreversible PMI adsorption. This phenomenon is obviously caused by rise of the HA overall surface accessible for PMI macromolecules due to diminishing of HA particle size.

Table 1 – Dependence of the PMI adsorption value (A) and the content of peroxide group $[\text{O}_{act}]$ on the HA surface on synthesis conditions of nano-HA ($C_{PMI} = 10 \%$ with respect to HA).

$C_{\text{CaCl}_2}, \%$	$C_{(\text{NH}_4)_3\text{PO}_4}, \%$	$A, \text{ mg/g}$	$[\text{O}_{act}], \%$
2.50	2.00	56.9	0.30
0.83	0.66	70.1	0.37

MPI adsorption at the surface of HA nanoparticles from ethyl acetate and methanol solutions was studied (Fig. 3). Importantly the adsorption isotherms of MMA-MMA copolymer did not differ from MPI isotherms. So, the conclusion was drawn that an introduction of benzoin pieces into the structure of this copolymer do not influence on the character of adsorbate macromolecule interaction with adsorbent surface.

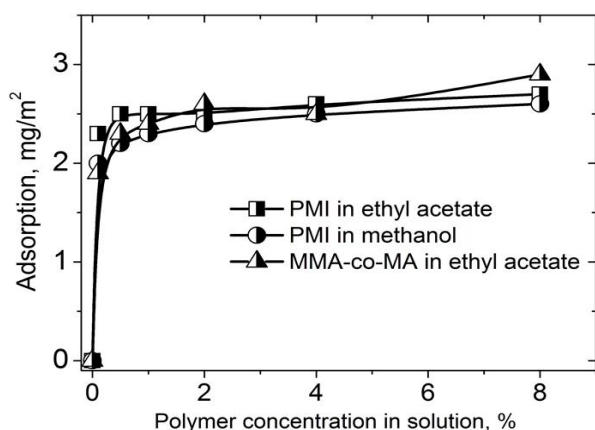


Fig 3 – Isotherms of MPI and MMA-co-MA adsorption onto HA in different solvents

The characteristic transition of the adsorption curves from a sharp rise to saturation took place at copolymer concentration of about 0.5 % and further increase in its concentration did not give an essential gain in adsorption value. We supposed that formation of ionic bonds due to interaction of carboxylic groups of copolymer macromolecules reached the interface firstly with the basic groups at the HA surface should shield the adsorbing centres making a barrier for their chemical interaction with other MPI macromolecules reaching the particles later. Chemical bonding hindered also conformational changes in the MPI macromolecules at the surface and consequently rearrangement of adsorption layer.

The surface modification of HA by PMI allowed to initiate polymerization of vinyl monomers in order to create compatibilizing polymer layer of certain nature and controlled thickness on the surface. Obtained data witnessed that radical polymerization of styrene and methyl methacrylate initiated from the HA nanoparticle surface by peroxide groups of the PMI immobilized proceeded with quite high rates up to high conversions (85%) (Fig. 4, 5, Table 2).

Kinetic curves of this process had rather ordinary shapes typical for a common radical polymerization,

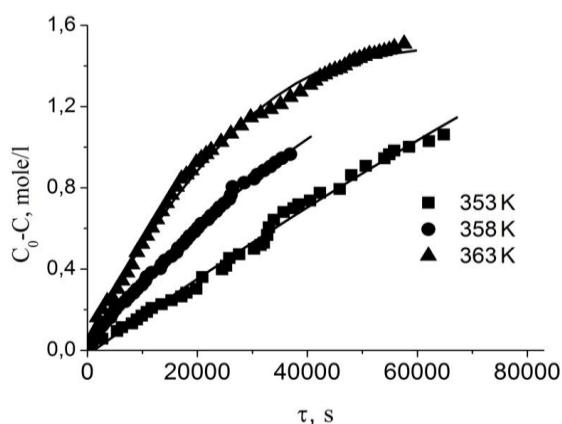


Fig. 4 – Temperature effect on kinetics of the MMA polymerization initiated by PMI immobilized at the HA nanoparticles

while this process had some features caused evidently by the presence in the system of solid highly dispersed phase as well as by immobilization of the initiator at the phase boundary. Reaction order with respect to initiator (n) was close to 1 that is much higher than value predicted for radical polymerization (typically $n = 0.5$). We supposed that in spite of low overall concentration of peroxide groups in this system, fixation of PMI macromolecules in adsorption layers caused a sharp increase of concentration of initiating centres in reaction zone. Under these conditions the main part of growing polymer chains were terminated via chain transfer reactions to peroxidic and other functional groups of immobilized PMI. This led to an increase of reaction order to the values higher than 0.5.

Table 2 – Characteristics of MMA polymerization initiated from the surface of peroxidized HA.

T, K	$C_{0.o}$, mole/l	$W_{pol} \cdot 10^5$, mole/(l·s)	$k_{pol} \cdot 10^4$, $10^{0.5}/(\text{mole}^{0.5} \cdot \text{s})$	E_a , kJ/mol	MW_{pMMA} , g/mole
353	0.012	1.9	5.8	80.6	85400
358	0.012	3.2	9.7		56800
363	0.012	4.4	13.4		27700
363	0.006	1.9	13.2		16600
363	0.024	7.0	13.2		32800

Another feature consisted in an increase of pMMA molecular weight with rising concentration of peroxidized HA in the system in contrast to typical regularities, while the temperature enhancement caused its diminishing (Table 2). The explanation could be as follows. The polymerization occurred mainly in the area close to the surface of HA nanoparticles where chain termination reactions were suppressed as a result of diffusion control. Thus, HA concentration enhancement caused an enlargement of area of this reaction zone that was a reason for a rise of pMMA average molecular weight.

The rates of styrene polymerization initiated from the HA surface peroxidized were lower than in case of methyl methacrylate (Fig. 5). This coincided with the literature data [10] reporting on higher ratio of the constants of chain growth and termination ($k_p/k_t^{0.5}$) for MMA as compared to styrene.

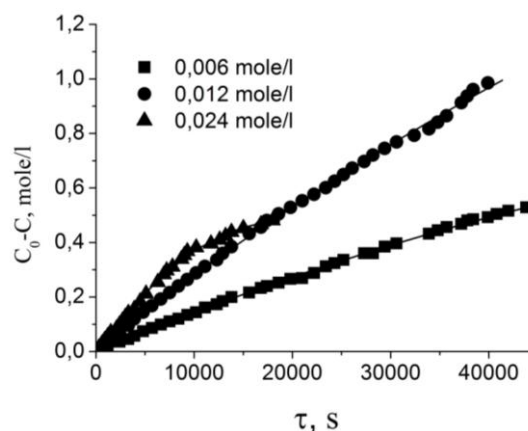


Fig. 5 – Dependence of St polymerization kinetics on the concentration of immobilized peroxide groups in the system

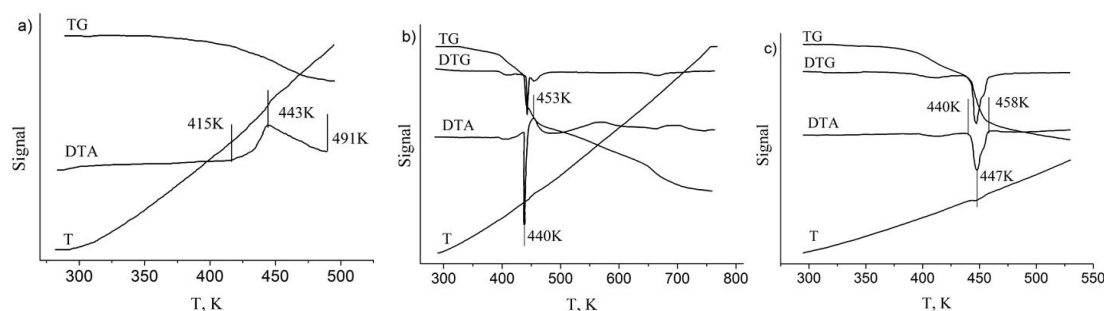


Fig. 6 – Derivatograms of PMI (a), HA modified by PMI (b), HA after MMA graft polymerization

For St polymerization the influence of dispersed HA surface on both the process kinetics and physico-chemical characteristics of polymer obtained was very similar to that for MMA polymerization, indeed the order with respect to initiator was higher than 0.5 and pSt molecular weight increased with the rise of peroxidized HA concentration. At the same time pSt molecular weights were higher than for pMMA; this fact is explained by difference in mechanisms of the chain termination reaction attributed to these monomers namely recombination for St and mainly disproportionation for MMA.

Comparison of derivatographic curves of PMI, HA nanoparticles modified by PMI, and HA nanoparticles with grafted pMMA layer (Fig. 6) showed that in contrast to the latter, two first samples demonstrated exothermic effects on DTA curves in the range of 440-458 K attributed to decomposition of peroxidic groups. That means peroxidic fragments decomposed almost completely at the surface of HA nanoparticles modified during the graft polymerization process; and this phenomenon could be explained by essentially higher decay rates of PMI immobilized at solid surface as compared to this process in solution. Absence of active peroxidic groups (being the free radical sources) in samples of HA nanoparticles with grafted pMMA made them a good candidates for the use as an orthopedic material.

Nano-hydroxyapatite surface-modified by MPI was used for obtaining the polyester composites capable of curing at room temperature under UV-irradiation. The synthesized MPI itself as well as immobilized at the surface of nanoparticles appeared to be more effective photoinitiator comparing to initial benzoin (Fig. 7). Immobilization of photoinitiating groups on the HA nanoparticles enhanced properties of photocomposites as compared with a low-molecular photoinitiator benzoin and MPI on its base. Faster hardening and more as twice higher hardness of composite with MPI immobi-

lized was observed, evidently due to better compatibility and more even distribution of the surface-modified HA nanoparticles in the polymer matrix. On the other hand filling of polyester composites by HA nanoparticles should improve their biocompatibility.

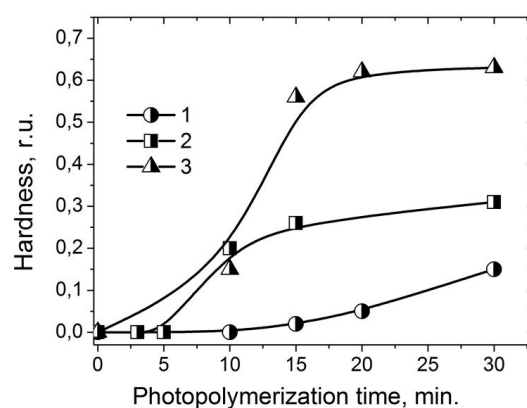


Fig. 7 – Effect of the photoinitiator nature on hardening kinetics of photopolymer composite film: benzoin (1); MPI (2); MPI immobilized on HA nanoparticles (3)

4. CONCLUSIONS

The method of the synthesis of nano-hydroxyapatite from a water salt solution in the presence of macroinitiators was elaborated that allowed simultaneously to control over size and to modify the surface of nanoparticles. Immobilization of the macroinitiators containing either peroxidic groups or benzoin pieces in their structure made possibility to carry out the radical graft polymerization initiated from the surface of modified nanoparticles and to design the structure and thickness of polymer shell bonded to the surface of nanoparticles. As a result improvements in physico-mechanical properties of filled polymer composites on the basis of nano-hydroxyapatite were achieved.

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