Synthesis of bioactive materials for implants in the system $\text{Ca}_3(\text{PO}_4)_2$ - Ca_2GeO_4

Elizaveta A. Mukhanova^{1,2,*}, Vyacheslav G. Vetokhin¹, Alexander A. Rybalkin¹

¹Southern Federal University, 344006 Rostov-on-Don Bolshaya Sadovaya str. 105/42, Russia

²Don State Technical University, 344000 Rostov-on-Don pl. Gagarina 1, Russia

Abstract. Various modifications of Ge-substituted calcium phosphates were obtained using solid-phase synthesis, co-precipitation in solution, and combustion synthesis. Structural changes in the synthesis process are established using X-ray diffraction. The biological activity of the obtained samples in model fluids was estimated. It has been found that the synthesis method can lead to various structural modifications of calcium phosphate, which is a significant refinement to the phase diagram of the $\text{Ca}_3(\text{PO}_4)_2$ - Ca_2GeO_4 system described in the literature.

1 Introduction

Many calcium phosphates are used in implants or as a low release drug delivery systems [1–6]. The best known and widely used among them are hydroxyapatite $\text{Ca}_5(\text{PO}_4)_3(\text{OH})$ and β - $\text{Ca}_3(\text{PO}_4)_2$ (whitlockite) [5,7–10]. The substitution of calcium and phosphorous allows obtaining materials with improved properties. For example, the addition of silicon to hydroxyapatite and β -tricalcium-phosphate materials is being widely studied, due to the well-known influence of silicon on bone formation [11,12]. Amount of silicon in hydroxyapatite depends on a synthetic route while silico-carnotite has the constant concentration of Si^{4+} [13].

Ge^{4+} has some similarity to Si^{4+} -containing materials. And its compounds have some special properties. For example, the oral administration of Ge-132 increases interferon activity and exhibits antitumour activity against Ehrlich ascites tumours in mice. [14–17].

$\text{Ca}_5(\text{PO}_4)_2\text{GeO}_4$ with silico-carnotite structure was described in [18]. The authors obtained carnotite in system $\text{Ca}_3(\text{PO}_4)_2$ - Ca_2GeO_4 while cooling melt different composition from 1500 °C. The development of synthesis at lower temperatures is important and became the aim of our investigation. We analyzed opportunity to prepare calcium germinate-phosphate with the specific structure using solid-state reaction, combustion and co-precipitation techniques.

* Corresponding author: kand@sfedu.ru

2 Materials and methods of research

2.1 Preparation of Ge-substituted calcium phosphate

Ge-substituted calcium phosphates $\text{Ca}_5(\text{PO}_4)_2\text{GeO}_4$ were obtained by three different methods. In solid-state synthesis, we used as the initial reactants CaCO_3 , GeO_2 and $(\text{NH}_4)_2\text{HPO}_4$. The mixtures were prepared in an agate mortar, pressed into pellets and heated at 500 °C for 2 h to mild decompose of $(\text{NH}_4)_2\text{HPO}_4$ and activate CaCO_3 during it phase transition at $T = 590$ °C and then heated at 900, 1000 and 1100 °C during 2 hours each. The samples were repeatedly reground during synthesis. The samples were quenched in air.

For co-precipitation in the solution we used as the initial reactants GeO_2 , $\text{Ca}(\text{OH})_2$ and 2.1 M H_3PO_4 . The first step was to prepare a soluble form of ammonium germanate. GeO_2 was stirred under an ammonium hydroxide solution for 24 hours. The second step was to prepare the calcium phosphate solution by mixing 0.6 M solution of $\text{Ca}(\text{OH})_2$ and 2.1 M H_3PO_4 at pH~10-11. This solution was added to the $(\text{NH}_4)_2\text{Ge}_5\text{O}_{11}$ solution stirring constantly for 24 hours. The obtained precipitation was thermally treated at 1100°C for 2 hours.

For combustion method, we used GeO_2 , CaCO_3 , H_3PO_4 , and $\text{C}_2\text{H}_5\text{OH}$. We prepared $(\text{NH}_4)_2\text{Ge}_5\text{O}_{11}$ solution as described previously. CaCO_3 was dissolved in HNO_3 . Three solutions were mixed together. We added citric acid and ethylene glycol in ethanol to form a mixed solution, with the Ge^{4+} and a Ca^{2+} -to-citric acid molar ratio of 1:2 and the ethylene glycol-to citric acid molar ratio of 1.2:1 [19]. During these procedures, the solution was continuously stirred using a magnetic agitator for a few days. Then, the stabilized sol was poured into a glass beaker and stirred constantly to transform a dried gel at 80 °C. The beaker was transferred to a muffle furnace preheated at 900 °C, and by heating, the dried gel simultaneously burnt in a self-propagating combustion manner until all the gels were burnt out completely to form a white powder. After burnt out at 900 °C for 2 h, the specimens were sintered at different temperatures 1000 and 1100 °C for 2 h in the air.

2.2 Characterization Techniques

The phases presented in the samples were identified by X-ray powder diffraction. The data were collected with an ARL X'TRA diffractometer in Ni-filtered CuK_α -radiation.

3 Results and discussion

The XRD pattern of the sample prepared by a solid-state reaction is shown on Fig. 1. The main phase has a structure of $\beta\text{-Ca}_3(\text{PO}_4)_2$ whitlockite. The samples prepared by co-precipitation and combustion techniques are shown in Fig. 2. The main phase in both cases has a structure of hydroxyapatite. Sample from co-precipitation reaction has higher crystallinity.

To discuss the effect of the synthetic route on a preferable structure we need to compare structure to each other. Fig. 3 a-c presents all structure types: whitlockite (Fig. 4a), hydroxyapatite (4b) and silico-carnotite (4c). All structures have similar densities. PO_4 tetrahedra are isolated in all of them but coordination number of calcium ion is different. Calcium in silico-carnotite has 7 nearest oxygen, in hydroxyapatite 7 and 9 neighbors and in $\beta\text{-Ca}_3(\text{PO}_4)_2$ – 10 and 12 oxygens. And based on this fact the phase diagram of $\text{Ca}_3(\text{PO}_4)_2\text{-Ca}_2\text{GeO}_4$ need to refine. All samples have the identical composition and the main factor which affect on the sustainability of structure type is a synthetic route. The

temperature above 1500 °C is preferable to silicocarnotite type. The lower temperatures lead to whitlockite (in solid state) or hydroxyapatite (in solutions). One more factor which influences on hydroxyapatite formation is pH – all reaction in solution took place at pH=10-11, while other phosphates form at another pH. And whitlockite looks like more stable phase under 1200 while except additional conditions. In all structures, this material can have bioactivity as structure analogs and considering of know application of germanium compounds in medicine.

Fig. 1. XRD patterns of $\text{Ca}_5(\text{PO}_4)_2\text{GeO}_4$ obtained by solid-state reaction.

Fig. 2. XRD patterns of $\text{Ca}_5(\text{PO}_4)_2\text{GeO}_4$ obtained by combustion method (a) and co-precipitation method (b).

4 Conclusion

We suggested that only synthesis at temperatures above 1200 °C led to a silico-carnotite structure. Under this condition despite on well-known phase diagram whitlockite or hydroxyapatite structure became preferable. This fact supplements well-known phase diagram $\text{Ca}_3(\text{PO}_4)_2\text{-Ca}_2\text{GeO}_4$ system. In our further studies, we will calculate the enthalpies of reaction and formation of different structures using atomistic modeling and CALPHAD methods.

Fig. 3. Crystal structures of calcium phosphates: a) whitlockite $\beta\text{-Ca}_3(\text{PO}_4)_2$; b) hydroxyapatite $\text{Ca}_5(\text{PO}_4)_3\text{OH}$; c) silico-carnotite $\text{Ca}_5(\text{PO}_4)_2\text{SiO}_4$

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