# MODELING SYSTEM FOR RESEARCH OF PROCESSES OF THE PATHOGENIC MINERALIZATION

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Recently interest to studying of minerals physiological and pathological origins (calcificate of mitral valves, uric, nephritic, tooth, salivary stones, etc.) has essentially increased. It is caused by growth number of the diseases connected with occurrence of stones in various bodies and fabrics. However by the present moment the problem of a pathological mineralization is insufficiently studied, in view of complexity of the object of research.

The basic inorganic part of bones, teeth and the majority of pathogenic formations in a human body is the mineral hydroxyapatite - $Ca_{10}(PO_4)_6(OH)_2$. In the chemical plan it is closest to a mineral making bone, is perfectly compatible to a muscular fabric and with an integument, after implantation it can grow together directly with a bone fabric in an organism.

By this time there is a considerable quantity of works devoted to synthesis hydroxyapatite [1-3, etc.]. It is necessary to notice that conditions at which carry out this or that synthesis, depend on the purposes and specificity of work of the researcher.

The way of synthesis hydroxyapatite in the environment of a synthetic biological liquid (SBF) in which quality plasma of blood of the person is chosen, is offered in the publication [4]. In the given work the way of synthesis hydroxyapatite for replacement of a bone fabric with use of the environment modeling structure of plasma of blood of the person (under the help data) is described, at physiological values pH and temperatures. Also stability of the received phases has been established at heating to $1600^0$C. The given way does not connect course of various pathological processes (including scale formation) with change of structure of a biological liquid, and also does not model biological system at deviations of structure of a biological liquid from norm.

**Purpose of work** is the working out a technique of synthesis hydroxyapatite for modeling of processes pathogenic biomineralization in a human body, and also receptions hydroxyapatite, as much as possible approached on structure to physiological to analogues for the biomedical purposes. An experiment technique. As the physiological environment for reception hydroxyapatite the saliva of the healthy adult average person has been chosen, which mineralization function is the major in relation to fabrics of a tooth (tab. 1).

**Table 1**

Mineral structure of human saliva [5], mmol/l

| Element | Minimum concentration | Maximum concentration | Medium concentration |
|---|---|---|---|
| Calcium | 1.0 | 2.0 | 1.5 |
| Sodium | 3.5 | 24.3 | 13.9 |
| Potassium | 14.4 | 37.9 | 26.2 |
| Magnesium | 0.4 | 0.9 | 0.7 |
| Ammonium | 1.2 | 6.0 | 3.6 |
| Chlorides | 8.5 | 16.9 | 12.7 |
| Carbonates | 4.5 | 10.2 | 7.4 |
| Phosphates | 3.2 | 8.1 | 5.6 |

In the experiment we used average values of a range of concentration of the basic inorganic components of human saliva. Supersaturation on ions $Ca^{2+}$ and $PO_4^{3-}$ in a solution has been created equal fifty (C(Ca) = 4.78 mmol/l, C($PO_4^{3-}$) = 23.7 mmol/l). As initial reagents used salts $CaCl_2 \cdot 2H_2O$, $(NH_4)_2HPO_4$, $K_2HPO_4 \cdot 3H_2O$, $MgCl_2 \cdot 6H_2O$, $NaHCO_3$, NaCl and distilled water. In the modeling solutions containing listed ions, there is no formation low soluble substances, except hydroxyapatite and the phases previous its formation (brushite – $CaHPO_4 \cdot 2H_2O$, calcium amorphous phosphate $Ca_x(PO_4)_y$ and octacalcium phosphate $Ca_8H_2(PO_4)_6 \cdot 5H_2O$).

Updating to the chosen value pH from a range of physiological values pH of human saliva (5.5; 6.0; 7.0; 8.0) spent after preparation of systems with the set concentration of the basic components. Ready solutions with total amount 1 liter, poured in conic flasks on 250 ml and left for crystallization at a room temperature for a time from 14 till 360 days. Deposits separated from a solution by filtering dried at 100ºC, weighed on analytical scales, and then analyzed by the IR-spectroscopy, RFA and atomno-issue spectroscopy with the inductive-connected plasma. Residual concentration of calcium and phosphate-ions in liquids phases defined by chemical methods.

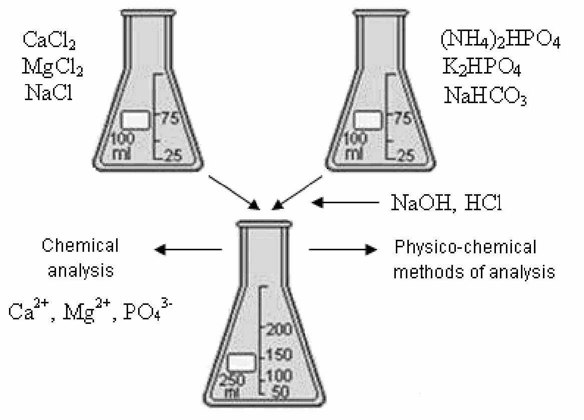


**Fig.1.** The scheme of modeling experiment

**Results and discussion.** Formation of the low soluble phases $CaHPO_4 \cdot 2H_2O$ (brushite); $Ca_8H_2(PO_4)_6 \cdot 5H_2O$ (octacalcium phosphate) and $Ca_{10}(PO_4)_6(OH)_2$ (hydroxyapatite) is the most possibly in the solutions modeling structure of human saliva by preliminary thermodynamic calculation [6].

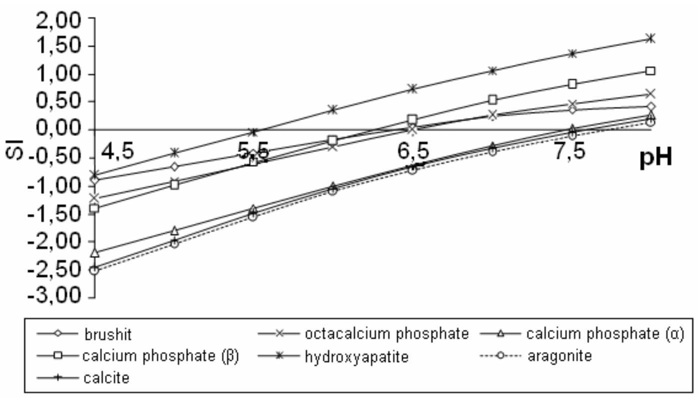


**Fig. 2.** Dependence of an index supersaturation from pH a solution for average values of a range of concentration of an oral liquid

Hydroxyapatite has the greatest degree of supersaturation in studied systems (pH 5.2 – 8.0) which were calculated for calcium phosphates with various stoichiometric structures within the limits of the chosen thermodynamic model.

It is known that brushite crystallizes at lower values pH, than apatite, and according to our thermodynamic calculations, it is a metastable phase. Results of modeling experiment have shown, at the first stage of our research brushite or a mix of brushite and whitlokite are formed in all range of pH. There is a transition of brushite in thermodynamically more stable phase – hydroxyapatite at increase in time of crystallization, and speed of this transition depends from pH a solution (tab. 2). At all samples amorphous component is present to what essential increase of a background in area 10º-20º reflexion corners testifies.

**Table 2**

Results of modeling experiment

<table>
<tr><th>pH</th><th>14 days</th><th>90 days</th><th>180 days</th><th>360 days</th></tr>
<tr><td>5.50±0.05</td><td>brushite + hydroxyapatite</td><td colspan="3">hydroxyapatite</td></tr>
<tr><td>6.00±0.05</td><td colspan="2">brushite + hydroxyapatite</td><td colspan="2">hydroxyapatite</td></tr>
<tr><td>7.00±0.05</td><td colspan="3">calcium amorphous phosphate + whitlokite</td><td>hydroxyapatite</td></tr>
<tr><td>8.00±0.05</td><td colspan="4">calcium amorphous phosphate</td></tr>
</table>

Thus, results of experimental modeling of process of formation hydroxyapatite, the basic mineral component of a dental and other stones, from prototypes of biological liquids coincide with the data of thermodynamic calculation, and also really observable phase structure pathogenic mineral formation in oral cavities. Hence, it is possible to draw a conclusion, the offered method of modeling can be applied to studying of biological liquids, including a saliva, and also reception hydroxyapatite.

**Conclusions.** The described technique of synthesis hydroxyapatite allows in vitro, using accessible reactants and the equipment, to study difficult processes of phase formation which proceed in a mouth of the human, and also to receive apatite, on structure approached to the biogenic. The given way can be used for reception hydroxyapatite biomedical appointment as one of components cements, materials for implantation, fabric engineering, etc. And also on the basis of the offered technique working out of medical preparations for preventive maintenance and treatment of caries and formation of scales is possible.

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