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Research of features phase formation of minerals of kidney stones

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Modeling methods allow to reveal features of processes of occurrence of new growths in a human body and action of the systems regulating their growth. At the same time studying of formation of some minerals in not to peculiar environment for them with accurately regulated conditions of a human body different (sometimes rather essentially) from conditions of the abiogenous environment, expands representation about genesis of minerals and [*Golovanova*, 2006)] promotes development of the general theory mineralforming. In the given work on the basis of thermodynamic and experimental modeling laws of formation of the basic phases nephritic are considered.

The method of thermodynamic modeling at all variety of solved specific targets, as a rule, means reception of the answer to one of following three basic questions:

1) whether there is a system at preset values of thermodynamic parameters in an equilibrium state and if isn't present as it is far from this condition

2) if the system is equilibrium, whether that is an equilibrium state stable;

3) what equilibrium chemical and phase structure of system under the set conditions.

Thermodynamic modeling of the spontaneous processes proceeding in considered systems, is reduced usually to stage-by-stage calculations of change of a condition of system in a direction of the equilibrium state calculated or set in advance. The methodological basis of the similar description of existential variability of processes is made by principles partial and local establish equilibrium. The concept of partial balance assumes that in nonequilibrium as a whole to the system characterized by set of chemical reactions and phase transitions, chemical and phase balance for separate (separate) chemical reactions or phases can be realized. It means that chemical (phase) balance is established in the given reaction much faster, than in other reactions (phases), and faster, than external parameters of system change. According to a principle of local (mosaic) balance, the system, as a whole nonequilibrium, can be equilibrium in each separate elementary volume of the final sizes. Thus balance is understood in the sense that within this volume it is possible to neglect gradients of intensive parameters. Thus, instead of limiting continuous representation of system (or continuous course of process) discrete approach is used. Besides, it is known that the interrelation of thermodynamic parameters expressed, in particular, by the fundamental equations of Gibbsa and criteria of stability is meant a balance establishment on each local site.

Thermodynamic calculation. Calculation of constants equilibrium in system a deposit-solution spent under the simplified scheme of balance between a deposit of MrAq and its sated solution:

$$\begin{tikzcd}
\mathrm{MpAq}\ (\text{тв}) \arrow[rr, leftrightarrow, "1"] \arrow[dr, leftrightarrow, "2"'] & & \mathrm{pM}^{m+}\ (\mathrm{solv}) + \mathrm{qA}^{n-}(\mathrm{solv}) \\
& \mathrm{MpAq}\ (\mathrm{solv}) \arrow[ur, leftrightarrow, "3"'] &
\end{tikzcd}$$

As prototypes of biological liquids used the hypothetical solutions, which ionic structure (inorganic macrocomponents), temperature and pH are close to urine [*Tiktinsky and Alexanders*, 2000].

The thermodynamic algorithm allows to calculate phase balance in multicomponent systems and quantitatively to estimate physical and chemical parameters of crystallization. For calculation carrying out values of thermodynamic products of solubility K^0_s slightly soluble connections which can be formed in investigated hypothetical solutions (urine) (tab. 1) have been used. Ionic force of a solution in an investigated range pH considered constant and equal to average value of the range calculated for studied biological system [*of Mountain ashes of Century A,* 1977].

Table 1. Thermodynamic products of solubility at 310 (SC-database, SCQUERY Version 1.37, 1993)

No	Malorastvorimoe connection	$pK^0_{s\,310}$	$K^0_{s\,310}$
1	$Ca\,(H_2PO_4)_2 \cdot H_2O$	1,14	$7{,}24 \cdot 10^{-2}$
2	$Ca\,(H_2PO_4)_2$	1,14	$7{,}24 \cdot 10^{-2}$
3	$CaHPO_4 \cdot 2H_2O$ (brushite)	6,60	$2{,}34 \cdot 10^{-7}$
4	$Ca_4H\,(PO_4)_3 \cdot 2.5\,H_2O$	47,95	$1{,}26 \cdot 10^{-96}$
5	α-$Ca_3\,(PO_4)_2$ (whitlockite)	25,50	$3{,}16 \cdot 10^{-26}$
6	β-$Ca_3\,(PO_4)_2$	29,50	$3{,}16 \cdot 10^{-30}$
7	$Ca_{10}\,(PO_4)_6\,(IT)_2$ (hydroxyapatite)	117,20	$6{,}3 \cdot 10^{-118}$
8	$CaC_2O_4 \cdot H_2O$ (whewellite)	8,65	$2{,}24 \cdot 10^{-09}$
9	$CaC_2O_4 \cdot 2H_2O$ (weddellite)	8,17	$6{,}76 \cdot 10^{-09}$
10	$CaC_2O_4 \cdot 3H_2O$	8,02	$9{,}55 \cdot 10^{-09}$
11	$CaCO_3$ (aragonite)	8,22	$6{,}03 \cdot 10^{-09}$
12	$CaCO_3$ (calcite)	8,35	$4{,}47 \cdot 10^{-09}$
13	$CaSO_4$ (anhydrite)	3,78	$1{,}66 \cdot 10^{-04}$
14	$C_{\text{ASO4·0,5ì2Ä}}$ (α)	4,09	$8{,}10 \cdot 10^{-05}$
15	$CaSO_4 \cdot 0{,}5H_2O$ (β) (bassanite)	3,89	$1{,}30 \cdot 10^{-04}$
16	$Ca\,(OH)_2$	5,26	$5{,}50 \cdot 10^{-06}$
17	$MgHPO_4 \cdot 3H_2O$ (newberyite)	5,82	$1{,}51 \cdot 10^{-06}$
18	$MgNH_4PO_4 \cdot 6H_2O$ (struvite)	13,15	$7{,}08 \cdot 10^{-14}$
19	$Mg_3\,(PO_4)_2$	19,3	$5{,}01 \cdot 10^{-20}$
20	MgC_2O_4	4,10	$7{,}94 \cdot 10^{-05}$
21	$MgCO_3 \cdot 3H_2O$ (magnesite)	4,67	$2{,}14 \cdot 10^{-05}$
22	$Mg\,(OH)_2$ (brucite)	10,74	$1{,}82 \cdot 10^{-11}$
23	$Ca_{10}\,(PO_4)_6F_2$ (apatite-(CaF))	120,86	$1.38 \cdot 10^{-121}$
24	CaF_2 (fluorite)	10,57	$2.69 \cdot 10^{-11}$

For an estimation of possibility of formation slightly soluble connections used the calculated values of indexes of supersaturation SI; (quantitatively) a supersaturation (S), created in a solution rather slightly soluble connections ($M_p\,A_{q-}$), counted on the equations:

$$S = \left[\frac{\left(a_{M^{m+}}\right)_s^{p^+} \cdot \left(a_{A^{a-}}\right)_s^{q-_-}}{\left(a_{M^{m+}}\right)_\infty^{p+} \cdot \left(a_{A^{a-}}\right)_\infty^{q-}} \right]^{\frac{1}{p_+ + q_-}} = \left(\frac{IAP}{K_s^0} \right)^{\frac{1}{p_+ + q_-}}, \ SI = \lg(S) \qquad (1),$$

Where IAP – ionic product activitts.

For definition of areas of stability slightly soluble phases of uric stones calculation with program use «Gbflow3» has been carried out. Given program utilize for thermodynamic modeling of gidpotepmalno-metasomatic processes by a method flowing different cells. Calculation establish equilibriumuses принцип minimization free energe Gibbsa of system. Chemical potentials BPK are set constant and identical to all cells of system, BPK in a problem should be linearly independent. Under the received data about structure of an equilibrium solution curves of saturation for all components of system in coordinates «pH – lg m_i» are under construction. On the resulted diagrams received as a result of calculations following designations are accepted: 1 whewellite; 2 – whewellite, brushite; 3 – brushite, hydroxyapatite; 4 – hydroxyapatite whewellite, hydroxyapatite; 6 – brushite; 7 – octacalcium phosphate; 8 – carbonate substitute hydroxyapatite; 9 – carbonate substitute hydroxyapatite, brushite, octacalcium phosphate; 10 – newberyite; 11 – brucite; 12 – brushite, newberyite; 13 – brushite, newberyite, magnesite; 14 – brushite, newberyite, magnesite, carbonate substitute hydroxyapatite; 15 – newberyite, magnesite, carbonate substitute hydroxyapatite; 16 – magnesite, carbonate substitute hydroxyapatite.

Technique of experiments. For verification of results of thermodynamic calculations a series of experiments on formation in prototypes of biological liquids (urine) has been spent. The ionic structure (inorganic macrocomponents), temperature, ionic force and pH the used solutions corresponded to environments in a human body. Synthesis of pathogenic phases by a sedimentation method included three series of the experiences, initial components different by initial concentration. In I series the structure of solutions corresponded minimum, in II – an average, in III – to the greatest possible concentration of components in a corresponding biological liquid. In each series studied behavior of system at temperature 37.0 0.5 °C and values pH, corresponding average and close to greatest possible to the sizes (pH – 6,45 and 7,45). To an establishment of phase structure of the synthesized material applied X-ray, IK-spectroscopy and methods of the chemical analysis.

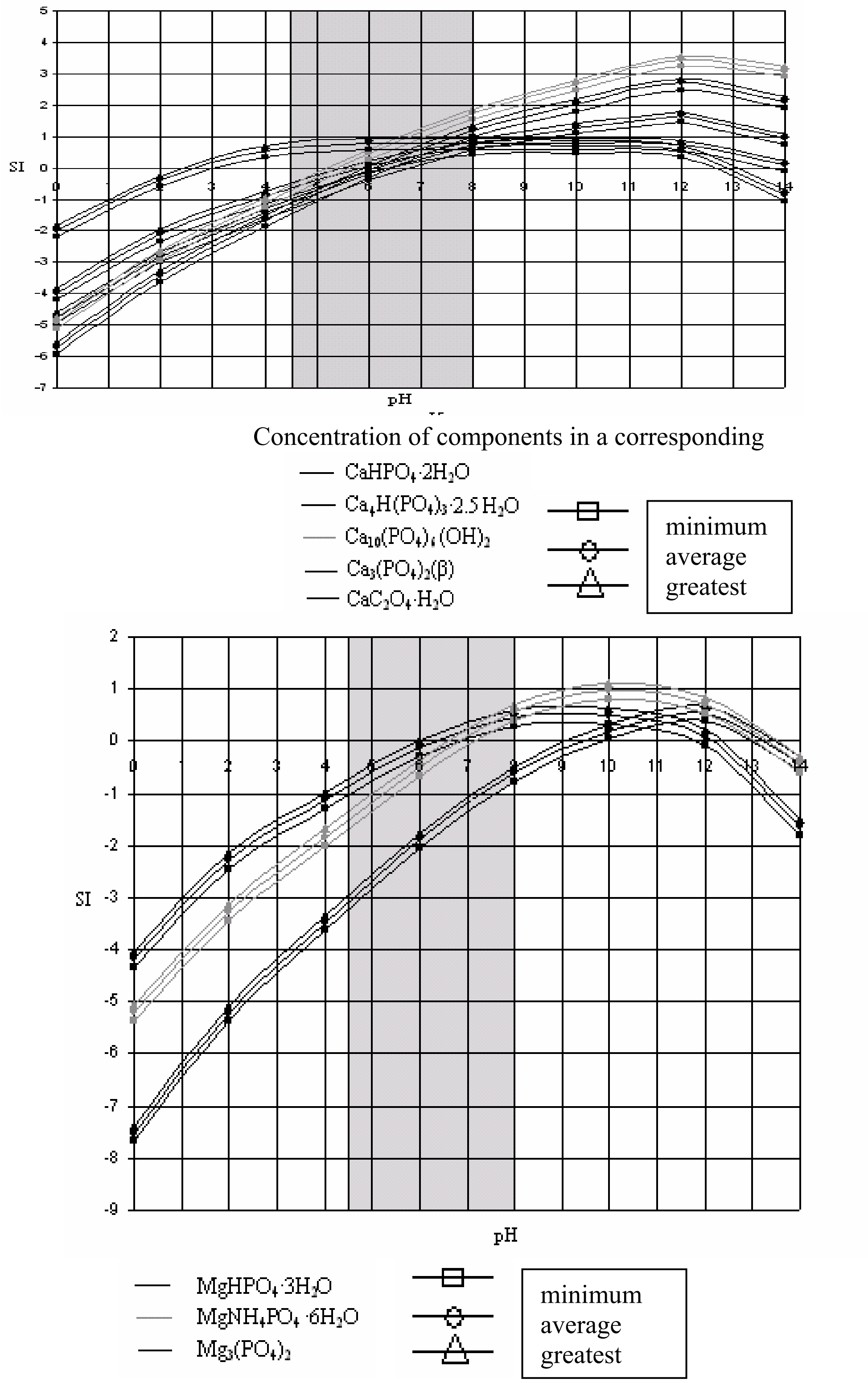

Fig. 1. Schedules of dependence of values of indexes of a supersaturation from pH a solution:a) for calcium salts, b)for magnesium phosphates

Uric stones. Proceeding from the received indexes of a supersaturation (fig. 1) it is established that in investigated solutions *thermodynamic* formation of following phases is probable: brushite $CaHPO_4 \cdot 2H_2O$; whitlockite Ca_3 (PO_4) $_2$; hydroxyapatite Sa_{10} (PO_4) $_6$ (IT) $_2$; whewellite $CaC_2O_4 \cdot H_2O$;

weddellite $CaC_2O_4 \cdot 2H_2O$; koaksit $CaC_2O_4 \cdot 3H_2O$; calcite $CaCO_3$; newberyite $MgHPO_4 \cdot 3H_2O$, and struvite $MgNH_4PO_4 \cdot 6H_2O$.

From listed above a number of connections in all studied range pH = 4,5–8,0 formation only oxalates of calcium of various degree hydration is possible, thus $CaC_2O_4 \cdot H_2O$ (whewellite) is the stablest updating that proves to be true experimental data on crystallization of oxalates at pH = 4,8–7,0. In solutions with pH 4,5–5,6 sedimentation slightly soluble calcium and magnesium phosphates thermodynamic is impossible. This fact is confirmed with the data of experiment specifying that formation hydroxyapatite proceeds in a solution, value pH which is shifted in the alkaline party (pH = 6,5–7,8). Comparing the indexes of a supersaturation calculated for phosphates of calcium various stoichiomete of structure (at pH 5,2–8,0), it is possible to assert that the greatest degree of a supersaturation takes place for hydroxyapatite At pH <6,5 on decrease of values SI analyzed phosphates of calcium can be ranged abreast: $CaHPO_4 \cdot 2H_2O >$ β-Ca_3 (PO_4) $_2>$ Ca_4H (PO_4) $_3 \cdot 2{,}5H_2O$. At pH> 7,5 sequence looks like: β-Ca_3 (PO_4) $_2>$ Ca_4H (PO_4) $_3 \cdot 2{,}5$ $H_2O >$ $CaHPO_4 \cdot 2H_2O$. Magnesium phosphates (for example, struvite) can be formed in investigated solutions only at pH> 6,0.

At definition of areas of stability slightly soluble phases of uric stones under the program «Gbflow3» following results are received.

System «Ca^2 – PO_4^{3-} – $C_2O_4^{2-}$ – H_2O».

Calculation on sedimentation model (fig. 2a) has shown that a solution supersaturate rather whewellite in area pH from 4,1 to 5,7. In a range 5,7 – 5,9 paragenesis « whewellite – brushite » and « brushite – hydroxyapatite » is steady. At great values pH steady is only hydroxyapatite.

At dissolution modeling equimolar mixes whewellite and hydroxyapatite (fig. 2б) it is revealed that hydroxyapatite it is dissolved at pH <6,0, and уевеллит at pH> 8,5. Thus, the range of their coexistence coincides with area of values pH "normal" urine of the person that explains frequent occurrence of this paragenesis as a part of uric stones.

Systems «Ca^2 – PO_4^{3-} – H_2O» and «Ca^2 – PO_4^{3-} – CO_3^{2-} – H_2O»

Sedimentation modeling in system «Ca^2 – PO_4^{3-} – H_2O» (fig. 3a) has shown that brushite is steady only at pH 5,6 – 5,8. Increase pH leads to transition brushite in hydroxyapatite In system «Ca^2 – PO_4^{3-} – CO_3^{2-} – H_2O» (3б) the stability area brushite extends to pH 7,5.

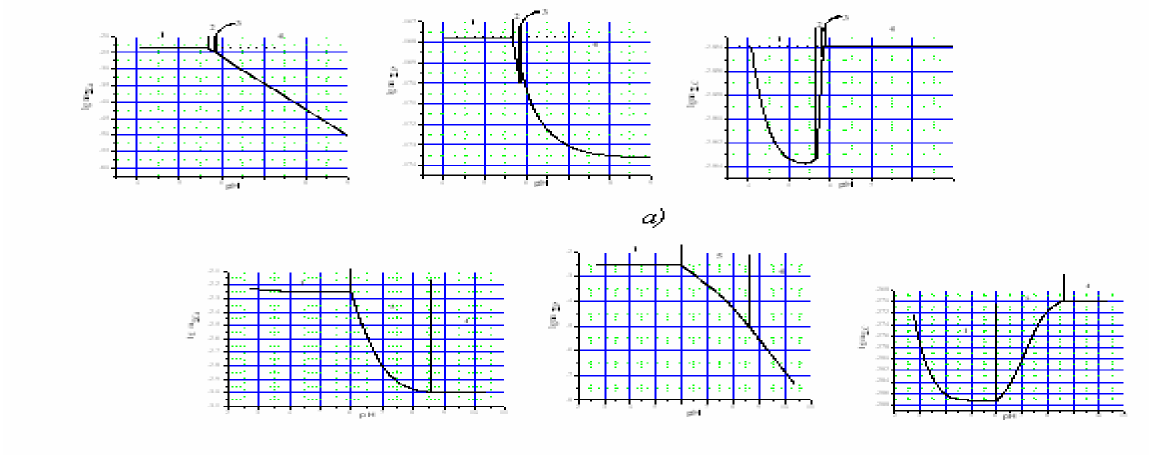

Fig. 2. The diagram pH-lg m_i systems «Ca^2 – PO_4^{3-} – $C_2O_4^{2-}$ – H_2O»: Sedimentation (a); dissolution (b)

In a narrow range 7,5–7,6 it is steady octacalcium phosphate which as a part of nephroliths meets extremely seldom. The further increase pH leads to formation carbonate substitute hydroxyapatite.

Results ***of modeling experiment*** have shown that hydroxyapatite in small quantities has been received practically in all experiences. The basic phases in the allocated deposits were brushite and amorphous phosphate of calcium (fig. 4).

Proceeding from thermodynamic calculations these phases in experimental conditions are metastable, i.e. balance rather hydroxyapatite has not been reached. As a whole, the received results well explain wide prevalence hydroxyapatite which is present practically at all nephroliths of the person though it is frequent in insignificant quantities. According to thermodynamic calculations in system «Ca^2 – PO_4^{3-} – $C_2O_4^{2-}$ – H_2O» at values pH = 6,5 and 7,5 it is steady hydroxyapatite that will be coordinated with results of experiment.

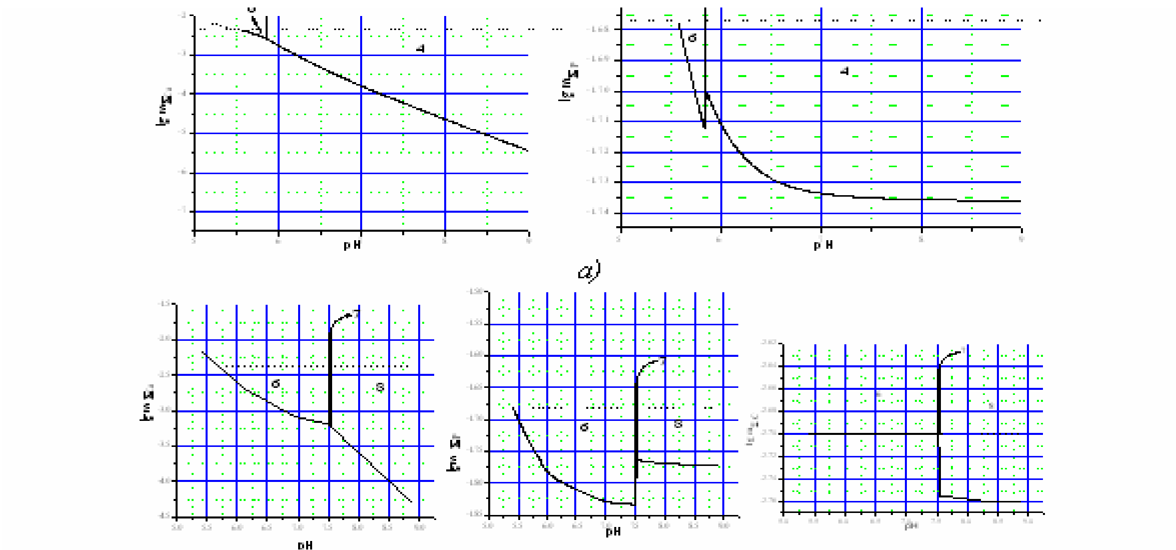

Fig. 3. The diagram pH-lg m_i systems: «Ca^2 – PO_4^{3-} – H_2O» (a); «Ca^2 – PO_4^{3-} – CO_3^{2-} – H_2O» (b)

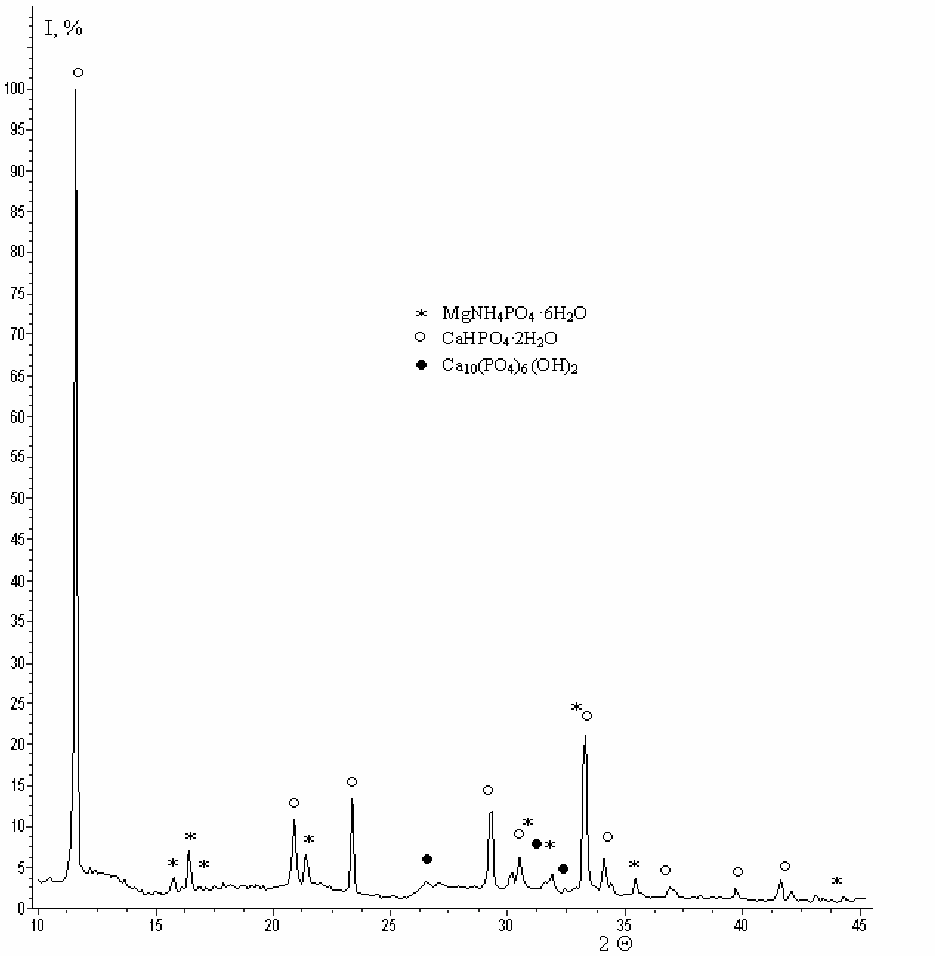

Fig. 4. The roentgenogram of the sample: received at sedimentation from a prototype of a biological liquid with initial value pH = 6,45 after 30 days of crystallization

As a whole, results of theoretical and experimental modeling of formation of the basic mineral phases of nephroliths will well be coordinated and supplement the friend from the friend. According to the received data the size pH a solution makes much more essential impact on structure of a formed firm phase, than a variation of initial concentration of its components. According to thermodynamic calculations a biological solution пересыщен concerning the basic phases of nephroliths (whewellite and hydroxyapatite). It is possible to explain that urolithic illness is shown at the limited number of people stabilization of a solution by connections of the albuminous nature and amino acids.

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