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CRYSTAL GROWTH

Thermodynamics and Kinetics of Calcium Oxalate Crystallization in the Presence of Amino Acids

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Abstract—Specific features of the crystallization of calcium oxalates (CaC_2O_4) in the presence of amino acids have been established based on thermodynamic and experimental modeling. Phase formation in the Ca^{2+}–$C_2O_4^{2-}$–H_2O–amino acid system in a wide range of variation in the component concentrations and solution pH have been theoretically investigated. The influence of pH on the thermodynamic stability of crystallizing compounds is considered. The effect of amino acids of different structures on the formation of the CaC_2O_4 solid phase in a prototype of physiological solution is analyzed. The kinetic crystallization parameters (induction period and rate constant) and crystallite growth are determined.

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INTRODUCTION

The problem of the formation of pathogenic organomineral aggregates (OMAs) in human organism remains urgent throughout the world in view of the constant rise in the desease incidence, which amounts to 0.5–5.5% a year [1–5].

Urolithiasis, which leads to the OMA formation in urogenital organs, is a widely spread urological disease: it takes the second place in the world after the inflammatory nonspecific diseases of kidneys and uric ways and affects no less than 3% population. Urolithiasis may occur in any age; however, it is diagnosed for 70% patients in the most employable age (from 30 to 50 years), mainly for men [1, 2, 5–11]. The rise in the urolithiasis incidence is related both to the stronger influence of a number of unfavorable environmental factors on human organism and to the specific features of modern life (hypodynamia, abnormal food ration, etc.) [6, 10–12].

To date, the factors causing urolithiasis have been poorly studied. It is known that pathogenic OMAs have a complex and inhomogeneous composition [1–4]. However, the most widespread uric stones are oxalate stones, formed by two minerals: whewellite $CaC_2O_4 \cdot H_2O$ and weddelite $CaC_2O_4 \cdot 2H_2O$, with dominance of $CaC_2O_4 \cdot H_2O$ [[1–4, 8, 9, 13, 14].

According to the data of [1, 2, 8, 13–16], uric stones contain not only mineral but also organic component. The results obtained by different researchers indicate that the content of organic component in stones varies in a rather wide range: from several units to several tens wt %. Currently, there is no unified theory explaining the nature of the interaction between the mineral and organic components of uroliths. One can select three versions of this interaction (two of which correspond to active participation of organic material in the stone formation):

(i) direct participation of organic matrix in the stone formation through linking mineral-phase components and initiation of intrinsic mineralization;

(ii) slowdown and/or activation of the crystallization of mineral phases via selective adsorption interaction with these phases;

(iii) inactive participation due to the pathogenic formation of organic protein and inorganic components of stones in stone-forming solutions under the same external and internal factors (infection, protein metabolic disorder, etc.).

Many researchers emphasize that the specificity of the organic component controls to a great extent the phase formation in human organism [1, 2, 8, 13–21]. In this context, an urgent problem is to investigate the organic component of pathogenic OMAs.

To date, a large amount of data on the influence of the solution composition on the phase composition of precipitates and the crystallization kinetics of CaC_2O_4 have been accumulated [22–30]. Nevertheless, the information on the character of $CaC_2O_4 \cdot H_2O$ crystallization in physiological solutions of complex composition is insufficient. New data on the $CaC_2O_4 \cdot H_2O$ crystallization from solutions in the presence of amino acids are necessary both from a fundamental point of view (to gain insight into the nature of biomineraliza-

Table 1. Macrocomponents of physiological fluid prototype

Component ions	Average concentration, mmol/L
Sodium	100.0
Sodium	40.0
Calcium	3.4
Magnesium	8.2
Ammonia	35.0
Chlorides	117.0
Oxalates	0.31
Carbonates	16.5
Phosphates	23.0
Sulfates	53.5

tion processes) and for medicine (to prevent pathogenic OMA formation in human organism).

The purpose of this study was to analyze the thermodynamic and kinetics of calcium oxalate formation and reveal the effect of some amino acids on the phase formation processes.

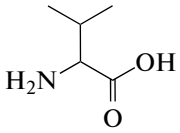
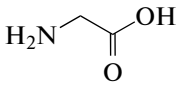
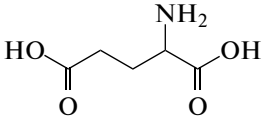
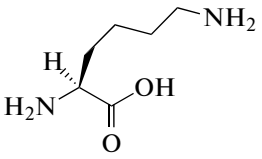
EXPERIMENTAL

Thermodynamic Modeling of the Calcium Oxalate Formation in the Presence of Physiological-Solution Components

When developing a thermodynamic model of the processes of phase formation in the Ca^{2+}–$C_2O_4^{2-}$–H_2O–amino acid system, a prototype of biological fluid was taken to be a hypothetical solution, whose mineral composition (inorganic macrocomponents), temperature, ionic strength, and pH corresponded to the average values of these parameters for urine of typical healthy adult human (Table 1) [9]. Amino acids were added to study the influence of the organic component on the formation of solid mineral phase (Table 2). This set of amino acids was chosen proceeding from their highest content both in the physiological solution and in uric stones and from the difference in their structures.

The influence of amino acids was taken into account by describing the complexing with calcium ions [31–35]; a correction characterizing the fraction of Ca^{2+} ions unbound into a complex was introduced to calculate the conditional products of solubilities,. When carrying out calculations, the acidity of the medium was also varied in a wide range (from 0 to 14) in order to establish the character and specificity of the dependences describing the state of the system. Under these conditions, the activity coefficients of ions (which take into account the electrostatic interaction) were calculated from the Davis equation [36].

Table 2. Amino acids used as additives and their characteristics [31]

Amino acid	Structure	pI	pK_a
DL-Valine (Val)		5.96	2.27 9.52
Glycine (Gly)		5.97	2.34 9.58
DL-Glutamic acid (Glu)		3.22	2.16 4.15 9.58
L-Lysine (Lys)		9.74	2.15 9.16 10.67

Here, pI is the isoelectric point (the acidity of the medium (pH) at which a certain molecule or surface does not possess an electric charge) and pK_a is the logarithm of acid dissociation constant.

In the calculations, the possibility and conditions of CaC_2O_4 precipitation were determined using the values of the thermodynamic solubility products corresponding to the data in the literature [37] and the database of stability constants (SC-database) for the complexes. The theoretical determination of the possibility and conditions for $CaC_2O_4 \cdot H_2O$ precipitation was based on calculating the thermodynamic parameters characterizing the degree of deviation of the system from equilibrium: conditional solubility products and the supersaturation indices (SIs) of the system.

Stability fields were constructed for thermodynamic description of the precipitate–solution equilibrium in a system where a sparingly soluble compound is formed. The construction of these diagrams implies establishment of a functional dependence, $pM^{q+} = f(pX^{q-}; \text{pH})$, for the parameter characterizing the minimum concentration of the cation entering in the precipitate composition, which must be provided to initiate the onset of phase precipitation at certain values of solution pH and anion concentration. The region located above the critical plane characterizes the conditions under which this phase cannot be thermodynamically formed. Based on these three-dimensional diagrams in the pM^{q+}–pX^{q-}–pH coordinates, conclusions on the stability of a given system were drawn, and the character of change in equilibrium under variation in conditions was predicted.

Study of the Calcium Oxalate Crystallization Kinetics

The study of the $CaC_2O_4 \cdot H_2O$ crystallization under nonequilibrium conditions (aimed at establishing the kinetics) was performed for a temperature of 37°C and three main values of the solution supersaturation: $\gamma = C_0/C_s = 5$, 7, and 10 (C_0 is the CaC_2O_4 concentration in a supersaturated solution and C_s is the calcium oxalate solubility at a temperature of 25°C, which is equal to 0.5×10^{-4} mol/L). Additional experiments were carried out at $\gamma = 12$, 15, 20, and 25 in order to obtain more complete information. The choice of the main γ values is substantiated by the existence of these supersaturations in biological media, specifically, in urine of a typical healthy adult human [1, 7].

Supersaturation with respect to CaC_2O_4 was provided due to the chemical reaction occurring when the initial solutions of readily soluble compounds of stoichiometric composition (calcium chloride and ammonium oxalate) were mixed:

$$Ca^{2+} + C_2O_4^{2-} \rightarrow CaC_2O_4.$$

Salts of analytic and reagent grades and distilled water were used as initial reagents. In each series of experiments, we prepared solutions containing cations and anions the joint presence of which (under given conditions) excludes the formation of poorly soluble compounds. Then the solutions were mixed in equivalent volumes.

The nucleation parameters were determined by the method based on measuring the induction periods (τ_{ind} is the time from the instant of merging two solutions to the precipitation onset (hidden period of the crystallization onset)). The induction time is known to be inversely proportional to the nucleation rate J: $\tau \sim 1/J$. In turn, the dependence of the nucleation rate on the solution supersaturation is expressed in terms of an exponential function containing interfacial energy σ:

$$J \sim \exp\left[-\frac{16\pi\sigma^3 v^2}{3k_B^3 T^3 (m\ln\gamma)^2}\right] = \exp\left[-\frac{B}{(\ln\gamma)^2}\right], \quad (1)$$

where v is the molecule volume, k_B is the Boltzmann constant, γ is the supersaturation, T is temperature, $m = 2$ is the number of ions into which the molecule dissociates in the solution, and B is a constant.

The induction time was determined visually by estimating the solution turbidity. The study was performed under laboratory conditions in a medium having a composition close to that of physiological solution of human urine.

The crystal growth was studied by the conductometric method, which implies measurement of the concentration of solutions during their crystallization. It is based on the principle of determining the electrical conductivity of solution in a Kohlrausch cell. An Anion-4154 conductometer [25] was applied to this end. Based on the conductometric data, the degree of crystallization completeness α was determined as a function of time:

$$\alpha = \frac{C_0 - C_\tau}{C_0 - C_s}. \quad (2)$$

Here, C_0 is the initial concentration of CaC_2O_4 in a supersaturated solution, C_τ is the CaC_2O_4 concentration at instant τ, and C_s is the CaC_2O_4 solubility at a temperature of 25°C.

To determine the kinetic parameters of CaC_2O_4 crystal growth based on the dependence $\alpha = f(\tau)$, we calculated the precipitation rate as a function of current absolute supersaturation from the formula

$$\frac{d\alpha}{d\tau} = kA(C_\tau - C_s)^n, \quad (3)$$

where A is the total surface area of precipitate, k is the crystallization constant, and n is the crystallization order. The total surface area for particles of constant shape can be estimated from the expression

$$A = \beta N_\tau^{1/3} V_\tau^{2/3}, \quad (4)$$

where β is the shape factor, N_τ is the total number of particles, and V_τ is the precipitate volume by the instant τ. Taking into account that $\alpha = V_\tau/V_{max}$ and V_{max} is the maximum precipitate volume at complete supersaturation removal and carrying out necessary transformations, we obtain the following formula for calculating the kinetic characteristics of CaC_2O_4 crystallization (on the assumption that the number of particles is constant: $N_\tau = N = \text{const}$):

$$\left(\frac{d\alpha}{d\tau}\right)\alpha^{-2/3} = k'(C_\tau - C_s)^n, \quad (5)$$

where k' contains all constants (V_{max}, β, N, and k) and is time-independent under given initial conditions. Logarithmation yields the following relation:

$$\log\left(\frac{d\alpha}{d\tau}\right) - \frac{2}{3}\log\alpha = \log k' + n\log(C_\tau - C_s). \quad (6)$$

Plotting in the coordinates $\log(d\alpha/d\tau) - 2/3\log\alpha = f(\log(C_\tau - C_s))$ should yield a straight line. The segment cut by this line on the ordinate axis gives the value of $\log k'$, and the slope of this line corresponds to the crystallization order n.

Nucleation and crystallization kinetics were investigated both in CaC_2O_4 solutions without organic components and in solutions with amino acids added in a concentration of 0.004 mol/L, which corresponds to their concentration in a physiological solution [7, 31].

To gain information about the interaction of amino acids with $CaC_2O_4 \cdot H_2O$ crystals, we performed experiments on the adsorption of amino acids on synthesized samples of monohydrate CaC_2O_4.

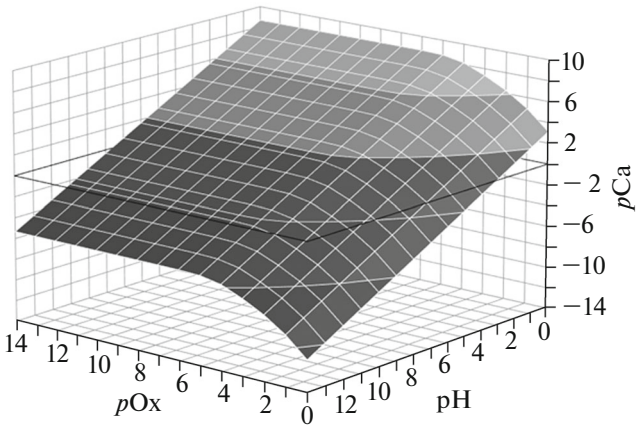


Fig. 1. Stability field in the formation of a poorly soluble compound in the Ca^{2+}–$C_2O_4^{2-}$–H_2O system; *p*Ca and *p*Ox are, respectively, the concentrations of calcium and oxalate ions and pH is the hydrogen ion activity (acidity of the medium).

The adsorption on the adsorbent surface was determined from the difference in the concentrations of dissolved amino acid before and after the contact with $CaC_2O_4 \cdot H_2O$. A series of glutamic acid and lysine solutions with concentrations from 2 to 20 mmol/L were prepared to this end by dissolving weights in a solution of ammonium oxalate dihydrate. Then an equivalent number of calcium chloride solution, corresponding to a supersaturation of 50, was added and the pH value was corrected to 5.5 ± 0.05 using sodium hydroxide and hydrochloric acid solutions. At this pH value the adsorption of amino acids on $CaC_2O_4 \cdot H_2O$ is maximally efficient [13]. The adsorption vessels were tightly closed and kept for 48 h. After this time the solutions were filtered, and the concentration of amino acids in filtrates was determined.

The amino acid concentration was found by an analysis based on the transformation of amino acids into a soluble copper salt using a biuret test with subsequent photometric determination. Measurements were performed on a KFK-2 photocolorimeter. The optical density of standard solutions is determined in the range including a wavelength of 670 nm. Cells with a 1-cm-thick light-absorbing layer are used for measurements.

The adsorption of amino acids was verified using IR spectroscopy. The samples were prepared by pressing pellets with KBr. The spectra were recorded in the range from 4000 to 470 cm^{-1} on an FT-801 spectrophotometer. Interpretation was performed using the ZaIR 3.5 software, whose database contains more than 130 thousands of spectra.

Experimental Modeling of the Formation of the $CaC_2O_4 \cdot H_2O$ Solid Phase in the Presence of Amino Acids

A series of model experiments was performed under laboratory conditions to establish the regularities of the formation of minerals from solutions, whose ion composition, pH, and temperature are close to the corresponding values typical of biological fluid.

In each experiment pH values were corrected to the physiological value (6.5 ± 0.05) by adding a 30% solution of sodium hydroxide or hydrochloric acid (concentrated). After mixing equivalent volumes of solutions, a solution with a specified supersaturation and calculated concentration of components was obtained.

We used compositions of model solutions of human urine with a supersaturation $\gamma = 350$. Glycine and glutamic acid in concentration of 0.2 mol/L (a value exceeding the physiological one by a factor of 50) were added to the model system to study the influence of amino acids on the $CaC_2O_4 \cdot H_2O$ crystallization. To analyze the temporal behavior of the CaC_2O_4 crystallization parameters in the presence of amino acids, we performed three series of experiments, differing by the time of controlled synthesis of solid phases (7, 14, or 21 days).

X-Ray Diffraction

X-ray diffraction of the precipitates was performed by the powder method on a DRON-3 diffractometer. A qualitative analysis of the phase composition of samples was carried out by comparing the experimental values of interplanar spacings and relative intensities of diffraction peaks with the set of corresponding values for each expected phase in the International Powder Diffraction File Database PDF-2 and the WWW-MINCRYST Database (Crystallographic and Crystallochemical Database for Minerals and Their Structural Analogs). The detection limit was 0.5–5 wt %. Quantitative phase analysis was performed using the Search-Match software [38]. The sensitivity of X-ray diffraction analysis in these measurements was 3%.

RESULTS AND DISCUSSION

Results of Thermodynamic Modeling of the CaC_2O_4 Formation in the Presence of Physiological Solution Components

Based on the obtained thermodynamic values of solubility products at 310 K, we found functional dependences in the form $pCa^{2+} = f(pC_2O_4^{2-}; \text{pH})$ and plotted three-dimensional diagrams ("stability fields") for calcium oxalate monohydrate $CaC_2O_4 \cdot H_2O$ (Fig. 1).

To estimate the influence of the acidity of the medium and the concentration of added amino acids on the possibility of forming a sparingly soluble com-

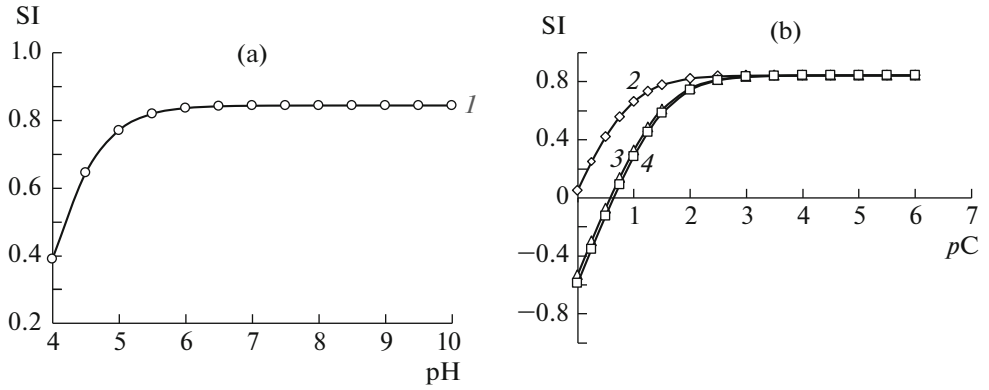


Fig. 2. Dependences of the supersaturation index SI log(γ) of $CaC_2O_4 \cdot H_2O$ (a) on the pH of the solution and (b) on the amino acid concentration *p*C: (*1*) without additives and (*2–4*) with (*2*) L-lysine, (*3*) glycine, and (*4*) DL-glutamic acid.

pound in the solution, we plotted graphical dependences (Fig. 2) of the supersaturation index (SI = log γ) [9] on two parameters: SI = *f*(*p*H) and SI = *f*(*pC*). It is assumed that, if SI > 0, the precipitation of this phase from the solution is thermodynamically more likely.

The acidity of the medium affects most strongly the thermodynamic stability of materials, the state of the system, and the crystallization processes. In particular, the driving force of $CaC_2O_4 \cdot H_2O$ crystallization significantly increases with an increase in pH. The reason is that a rise in pH leads to an increase in the relative concentration of $C_2O_4^{2-}$ in the system; therefore, one can observe a positive correlation between the supersaturation of the medium and pH.

The effect of amino acids on the formation of mineral solid phase during complexing in the system was found to be insignificant (because of the small stability constants of complexes with calcium ions for all amino acids under consideration).

Note that the thus constructed thermodynamic model demonstrates a possibility of forming phases proceeding from only the data on their thermodynamic stability in the standard state and disregards, in particular, the kinetic factors affecting the solid phase formation under real conditions. Therefore, to determine the possibility of forming poorly soluble compounds in a solution whose ion composition (inorganic macrocomponents), temperature, and pH are close to the parameters typical of biological fluid, it is necessary to carry out a model experiment under laboratory conditions.

Study of the CaC_2O_4 Crystallization Kinetics

In the first stage we analyzed the influence of supersaturation on the induction period of CaC_2O_4 monohydrate in the absence of foreign additives. We obtained a linear dependence: $\ln\tau = f((\ln\gamma)^{-2})$. This atypical relation is a sum of two exponential dependences with different exponential factors. The surface energy σ (entering the constant *B*) in two portions of the kinetic curve was found to be 15.3 and 36.0 mJ/m^2; these values correspond to the heterogeneous and homogeneous nucleation, respectively.

The influence of organic additives (amino acids) on the induction period of $CaC_2O_4 \cdot H_2O$ turned out to be fairly diverse and dependent on the acid type. The induction periods of CaC_2O_4 monohydrate in the presence of the amino acids under study are shown in the diagram in Fig. 3.

It can be seen in Fig. 3 that amino acids may either slow down the $CaC_2O_4 \cdot H_2O$ crystallization (DL-glutamic acid, glycine, L-lysine) or activate it (DL-valine). The slowdown effect of amino acids is related to their adsorption on the active surface centers of newly formed crystals. The adsorption occurs due to the interaction between the positively charged surface of CaC_2O_4 crystals and the amino acid, which is in the most likely form under given conditions. In this case, one would expect a stronger slowdown effect lead to an

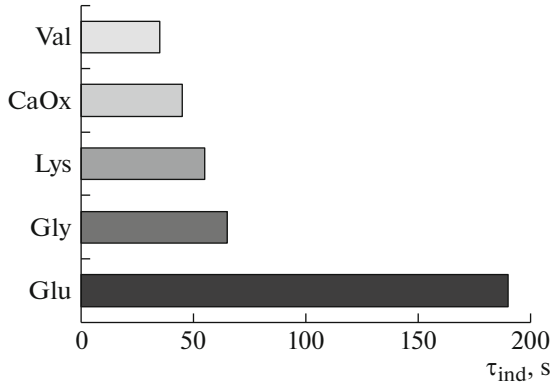


Fig. 3. Influence of amino acids on the induction period τ_{ind} of $CaC_2O_4 \cdot H_2O$ nucleation: calcium oxalate without additives (CaOx) and with additives of (Val) valine, (Lys) lysine, (Gly) glycine, and (Glu) glutamic acid.

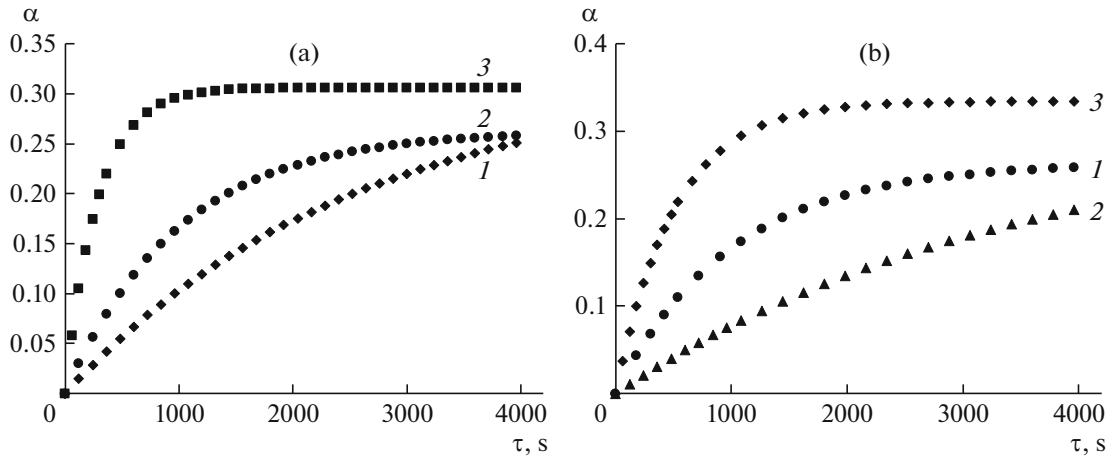


Fig. 4. Crystallization kinetics curves (α is the degree of crystallization) for calcium oxalate (a) without additives of amino acids at different supersaturations, γ = (*1*) 5, (*2*) 7, and (*3*) 10, and (b) at γ = 7 (*1*) without additives and (*2*, *3*) in the presence of (*2*) L-lysine and (*3*) DL-valine.

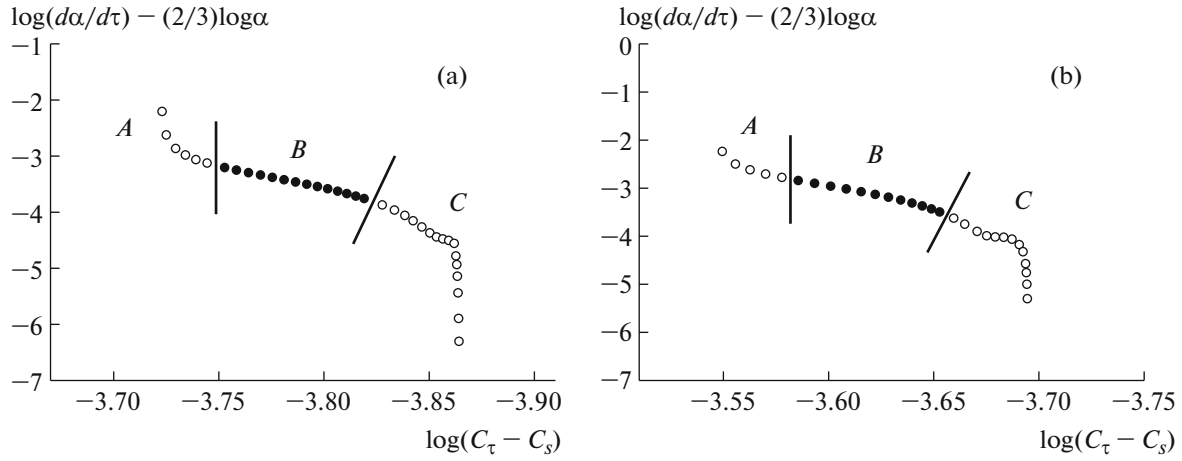


Fig. 5. Determination of the crystallization kinetics parameters $\log\left(\frac{d\alpha}{d\tau}\right) - \frac{2}{3}\log\alpha$ for $CaC_2O_4 \cdot H_2O$ at γ = 7: (a) without additives and (b) in the presence of glycine. C_τ is the calcium oxalate concentration at an instant τ and C_s is the calcium oxalate solubility; the bars are conditional boundaries of portions in the kinetic curves.

increase in the amino acid content in kidney stones. This holds true at least for the main amino acids [16, 24, 27].

A comparative analysis of the effect of amino acids under study on the induction period shows that this effect is likely related to the main characteristics of the amino acids, determining their adsorption on the $CaC_2O_4 \cdot H_2O$ crystal surface [39]: their structure (in particular, the number of carboxyl groups) and the protolytic properties (amino acid dissociation reactions), which determine the state and form of existence of amino acids in solution at different pH values.

Thus, the opposite effect of amino acids with similar structures and properties on the $CaC_2O_4 \cdot H_2O$ nucleation can be explained by the fact that both the slowdown and activation of nucleation are implemented due to the same mechanism: strong bonding of amino acid with calcium ions on the nucleus surface (slowdown) or in the solution (activation).

Then we obtained the kinetic characteristics of $CaC_2O_4 \cdot H_2O$ crystallization; their analysis (Fig. 4) showed that the degree of transformation α monotonically increases with time, and the crystallization is gradually slowed down, up to complete stop.

Table 3. Kinetic characteristics of $CaC_2O_4 \cdot H_2O$ crystallization in the presence of amino acids

Additive	Induction period τ_{ind}, s	Supersaturation					
		5		7		10	
		n	$\log k'$	n	$\log k'$	n	$\log k'$
CaC_2O_4	45	7.9	26.5	10.1	33.1	12.0	38.6
DL-Glutamic acid	186	5.4	16.3	7.5	23.9	9.1	28.6
Glycine	68	7.1	23.5	10.0	32.8	9.9	31.0
L-Lysine	52	5.3	16.9	7.5	23.6	9.3	28.4
DL-Valine	35	8.0	27.0	10.2	34.1	11.6	36.9

Here, n is the crystallization order and k' is the crystallization constant.

The kinetic curves were used to plot dependences in the form $\log(d\alpha/d\tau) - 2/3\log\alpha = f(\log(C_\tau - C_s))$, where one can select several linear portions with different slopes (Fig. 5). Portion A corresponds to an increase in the total number of particles due to the formation of crystallization nuclei, portion B corresponds to the growth of the particles formed without an increase in their total number, and portion C describes the secondary processes: decrease in the total number of particles due to the dissolution of small crystals and growth of larger ones and the particle aggregation [25]. Portion B is most interesting for revealing kinetics; therefore, it was used to calculate the main kinetic characteristics of CaC_2O_4 crystallization. The intersection of this segment with the ordinate axis yields the precipitation reaction rate constant, and its slope determines the crystallization order.

The $\log k'$ and n constants, found by processing experimental data, are listed in Table 3.

First, we should note the large values of the nucleation order n for $CaC_2O_4 \cdot H_2O$ crystallization. Apparently, this is a consequence of the proximity of the exponential law describing the crystal growth kinetics within the mechanism of two-dimensional nucleation to a power-law dependence. For the high supersaturations in use, this growth mechanism is quite realistic. One can see that the crystallization rate increases with an increase in the initial supersaturation. This relationship can be explained by both the increase in the total number of crystallization centers and the rise in the mean crystal growth rate.

The presence of amino acids in solution differently affects (as in the case of nucleation) the $CaC_2O_4 \cdot H_2O$ crystallization. Glutamic acid, lysine, and glycine have a slowdown effect, while the effect of valine is clearly activating.

The slowdown effect of amino acids can be most naturally explained by their adsorption on growing $CaC_2O_4 \cdot H_2O$ crystals. Analyzing the structure of

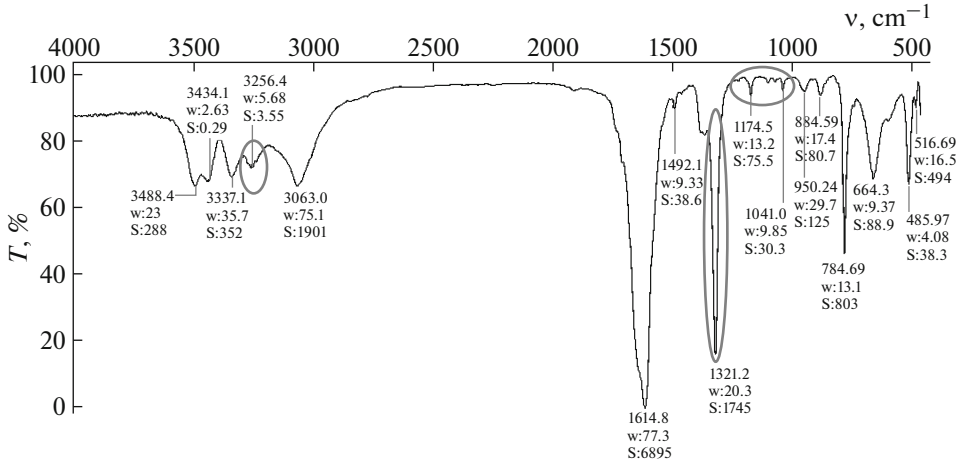


Fig. 6. IR spectrum of synthesized $CaC_2O_4 \cdot H_2O$ powder after the adsorption experiment with glutamic acid. The amino acid absorption bands are indicated.

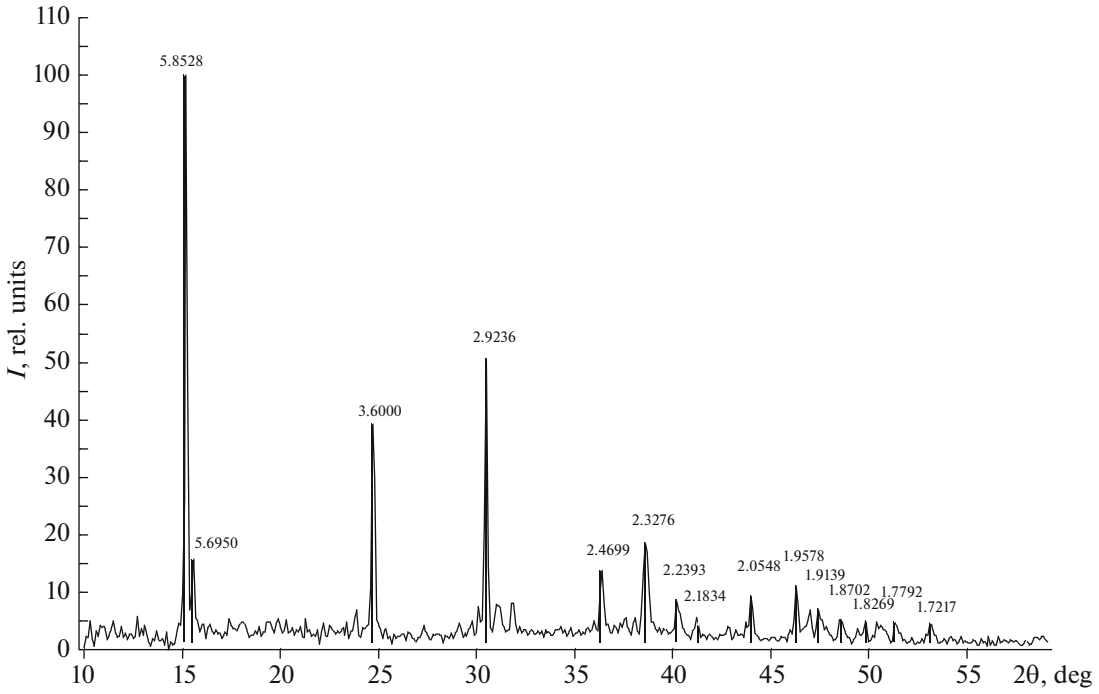


Fig. 7. X-ray diffraction pattern of $CaC_2O_4 \cdot H_2O$.

amino acids and their state in the solution (Table 2), one can conclude that the slowdown of the whewellite crystal growth is enhanced with an increase in the length of hydrocarbon radical, increase in the number of carboxyl groups in amino acid, and their presence in the solution in the form of charged ions at physiological pH values.

At the same time, amino acids may serve a new centers of $CaC_2O_4 \cdot H_2O$ nucleation, which increase the number of crystals due to their ability of binding calcium ions [30, 40]. In addition, being adsorbed on the crystal surface, amino acids can stimulate two-dimensional nucleation, thus increasing the crystal growth rate. These effects explain the activating effect of amino acids on the $CaC_2O_4 \cdot H_2O$ crystallization.

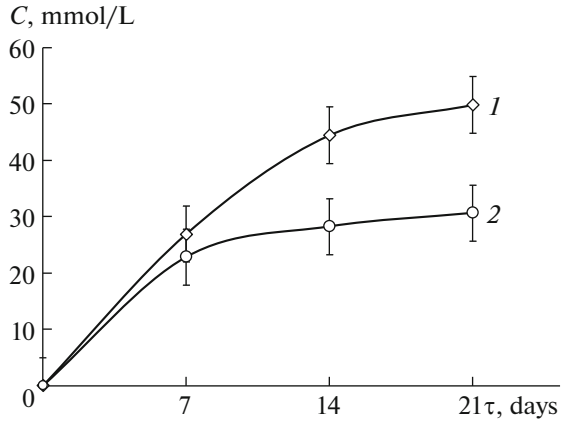


Fig. 8. Residual concentrations C of amino acids in the solution above the precipitate after the $CaC_2O_4 \cdot H_2O$ solid phase ·synthesis: (*1*) glycine and (*2*) DL-glutamic acid.

To confirm the possibility of the adsorption effect of amino acids on the whewellite crystallization, we studied the adsorption of glutamic acid and lysine on synthesized CaC_2O_4 monohydrate. IR spectroscopy showed that these amino acids are indeed adsorbed on whewellite powders: the adsorbent spectra contain bands at 1200–1000, 3300–3200, and 1400–1300 cm^{-1}, which are characteristic of amino acids (Fig. 6). The main adsorptions are adequately described within the Langmuir model.

An X-ray diffraction analysis of the solid phases formed during crystallization from a model solution showed that the amino acids do not affect the phase composition of the precipitate, because the precipitate was $CaC_2O_4 \cdot H_2O$ in all cases [25, 29] and no other impurity phases were revealed (Fig. 7).

A study of the $CaC_2O_4 \cdot H_2O$ crystallization in the presence of amino acids in a model experiment under laboratory conditions showed that an increase in the synthesis time leads to a rise in the concentration of amino acids in the mother solution above the precipitate (Fig. 8).

Apparently, this is related to the competition between the processes of the $CaC_2O_4 \cdot H_2O$ solid phase formation, adsorption of amino acids on the surface,

and complexing of amino acids with calcium ions. In particular, in the course of crystallization, the equilibrium shifts towards the thermodynamically more preferred process: $CaC_2O_4 \cdot H_2O$ formation, which is accompanied by the destruction of previously formed complexes of amino acids with calcium ions in the solution and their release to the solution.

CONCLUSIONS

Phase formation in the Ca^{2+}–$C_2O_4^{2-}$–H_2O–amino acid system were found. It was established that the role of amino acids as an impurity in the formation of mineral solid phase during complexing in the system is insignificant because of the small stability constants of the complexes with calcium ions. The nature of the crystallizing compounds, their thermodynamic stability, and precipitation reaction depth are mainly determined by the acidity of the medium.

The study of the processes of $CaC_2O_4 \cdot H_2O$ nucleation in model solutions without impurities and with additives of amino acids showed the following: (i) the transition from heterogeneous to homogeneous nucleation with an increase in supersaturation γ above 12 is observed in solutions without additives and (ii) the effect of amino acids on the nucleation of calcium oxalate monohydrate can be either slowdown or activating.

The analysis of the $CaC_2O_4 \cdot H_2O$ crystallization kinetics in the presence of additives of amino acids showed the following: (i) whewellite crystals grow according to the mechanism of two-dimensional nucleation; (ii) the effect of amino acids can be either slowdown or activating; (iii) amino acids affect the whewellite crystal growth in the same way as they affect the induction times of $CaC_2O_4 \cdot H_2O$ nucleation; and (iv) both effects can be explained in terms of the adsorption of amino acids on whewellite crystals: the slowdown is caused by blocking growth points, while the activation is due to the formation of two-dimensional nucleation centers on the crystal surface.`

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