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MATHEMATICAL MODELING FOR THE CRYSTALLIZATION PROCESS OF HYDROXYAPATITE OBTAINED BY PRECIPITATION IN AQUEOUS SOLUTION

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ABSTRACT. In the paper are presented the theoretical and experimental results concerning the influence of pH and temperature over the rate of the transformation: beta-whitlockite (beta-tricalcium phosphate) in hydroxyapatite (HAP). From the data of the kinetic studies were calculated the values of the rate constants and activation energies at pH = 8.5 – 12. Based on the obtained values for the activation energies it has been established that the process of transformation of beta-whitlockite in HAP could be described using a combined macrokinetic mechanism: transfer – mass transformation. The mathematical of the process has been elaborated and the numerical values of the constants from the mathematical model were determined. Based on the proposed model process simulations were made and the results show that the obtained values fit well with the experimental data, which confirms the model validation.

Keywords: *hydroxyapatite, macrokinetic mechanism, mathematical model*

INTRODUCTION

Due to its excellent properties like high biocompatibility, atoxicity and bone integration, HAP was accepted as biomaterial for biomedical purposes since 1920 and nowadays has many applications in medicine [1, 2, 3, 4].

Factors that affect the rate of adsorption of HAP in the human body are mostly determined by its chemical reactivity which depends on many different factors like: composition, particle size, defects, porosity, surface area and crystallinity [5]. On the other hand, these properties are greatly influenced on the route and conditions under which HAP is produced [6, 7].

HAP powder can be prepared in a variety of ways. The reactions could be classified in two categories:

a - solid phase reaction

b – precipitation

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Although many methods have been developed to synthesize apatites, the most prevalent method in preparation is still *precipitation* because of its ease in operation and tailoring composition, as well as in scaling up for mass production [8].

Among the precipitation methods, one of the most widely used is the precipitated method, uses as reactants calcium nitrate, bi - ammonium phosphate and ammonia solution.

The chemical reaction, which describes the process, is:

$$10\,Ca(NO_3)_2 \cdot 4H_2O + 6\,(NH_4)_2HPO_4 + 8NH_4OH \rightarrow \\ \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 20NH_4NO_3 + 6H_2O \quad (1)$$

In the literature are no quantitative data concerning how the main parameters of the synthesis (pH of the reaction environment and temperature) influence the rate of transformation of beta-whitlokite in hydroxyapatite. In this paper are presented the experimental results regarding the influence of the reaction environment, pH and temperature on the rate of transformation of beta-whitlokite in hydroxyapatite. These results obtained from the kinetic studies are the base for the mathematical model of the transformation of beta-whitlokite in hydroxyapatite.

MATHEMATICAL MODELING OF THE PREPARATION PROCESS OF HYDROXYAPATITE

The duration of the HAP obtaining procedure doesn't identify with the duration of the chemical reaction (1), because the chemical reaction between the calcium nitrate and bi - ammonia phosphate is an ionic reaction with a high rate. On the other hand, because the solubility of the reaction product is very low, the critical supersaturation will be quickly achieved which makes the separated solid phase (beta-whitlockite) be a metastabile one and in time will be converted in HAP.

In the second stage, after the chemical reaction is finished, the forming process of the new phase nuclei (HAP) will take place. That means that the obtaining process of HAP takes place in two stages, the total duration of the process being the sum of each stage.

The scheme for the obtaining process of HAP by precipitation can be presented as in Figure 1.

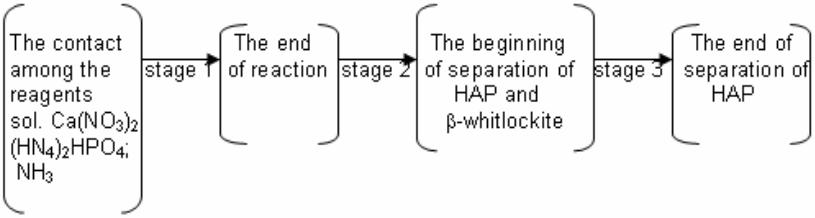

Figure 1. The scheme for the forming process of hydroxyapatite

This scheme suggests that the process of obtaining HAP could be realized after one of the following macrokinetic mechanisms:

a. mass transformation (chemical reaction – nuclei formation and growing)
b. mass transfer
c. combined model (mass transfer - mass transformation)

Because the rate of the chemical reaction is very high, the most probable macrokinetic mechanism for the obtaining process of HAP is a combined one, which includes not only processes of mass transformation but also processes of mass transfer (a, b). This combined mechanism could be presented directly using the balance equation (2) of the final reaction product (HAP):

$$n_{A_1'} = n_{A_{1\,[]l}'} + n^p_{A_1'} \cdot N_p \tag{2}$$

In the first stage of the reaction beta-whitlockite will be formed with metastable character, which will be transformed in time in HAP, in constant conditions of supersaturation.

In these conditions the balance equation (2) becomes:

$$n_{A_1'} = n^p_{A_1'} \cdot N_p \tag{3}$$

$$dn_{A_1'} = n^p_{A_1'} \cdot dN_p + N_p dn^p_{A_1'} \tag{4}$$

$$\frac{dn_{A_1'}}{V_T \cdot d\tau} = n^p_{A_1'} \cdot \frac{dN_p}{V_T \cdot d\tau} + N_p \cdot \frac{dn^p_{A_1'}}{V_T \cdot d\tau} \tag{5}$$

Using the relationships which express the number of moles of HAP from one particle $n^p_{A_1'}$ and the total number of moles of HAP ($n_{A_1'}$) from the total volume of the new formed phase ($V_{[]n}$):

$$n^p_{A_1'} = \frac{m_{A_1'}}{M_{A_1'}} = \overline{\rho_{A_1'}} \cdot v_p \; ; \quad n_{A_1'} = \overline{\rho_{A_1'}} \cdot V_{[]n} \tag{6}$$

equation (5) will be:

$$\overline{\rho_{A_1'}} \cdot \frac{dV_{[]n}}{V_T \cdot d\tau} = \overline{\rho_{A_1'}} \cdot \frac{dN_p}{V_T \cdot d\tau} + N_p \cdot \overline{\rho_{A_1'}} \cdot \frac{dv_p}{V_T \cdot d\tau} \tag{7}$$

If we note the volume of the new phase with $V_{[]n}$ and we considered that the total volume V_T is the sum of the two phase volumes: $V_T = V_{[]m} + V_{[]n} = V_{[]m} + v_{[]n} \cdot V_T$ and $v_{[]n} = \frac{V_{[]n}}{V_T}$:

$$V_T = \frac{V_{[]m}}{1 - v_{[]n}} \tag{8}$$

we obtain:

$$\frac{dv_{[]n}}{d\tau} = (1 - v_{[]n}) \cdot v_p \cdot \frac{dN_p}{V_{[]m} \cdot d\tau} + (1 - v_{[]n}) \cdot N_p \cdot \frac{dv_p}{V_{[]m} \cdot d\tau} \tag{9}$$

Equation (9) represents the nuclei forming and growing combined macrokinetic model, where the first right term expresses the rate of the nuclei formation and the second one the growing rate.

When the process is developing after this macrokinetic model and because the reaction rate is higher than the germs formation rate, solutions with high supersaturation will be formed.

MATHEMATICAL DESCRIPTION OF THE PROCESS

For the mathematical description of the process according to the macrokinetic model presented in equation (9) we must refer to the geometrical shape of the macro particles and to the τ signification (τ - the time to reach the final value of the volume fraction $v_{[]n}$ in case of the new phase).

Considering that the macroparticles are spherical, equation (9) can be written as follows [9]:

$$\frac{dv_{[]n}}{(1 - v_{[]n}) \cdot d\tau} = \frac{4}{3}\pi r^3 \cdot \frac{dN_p}{V_{[]n} \cdot d\tau} + \frac{N_p}{V_{[]m}} \cdot 4\pi r^2 \cdot \frac{dr}{d\tau} \tag{10}$$

where: $w_3 = \frac{dN_p}{V_{[]n} \cdot d\tau}$ and $w_2 = \frac{dr}{d\tau}$.

Because the process is developing at constant supersaturating, it is proposed that not only the rate of the germs formation but also the rate of transformation-growing are constant. Based on this hypothesis results that:

$$N_p = w_3 \cdot V_{[]n} \cdot \tau; \ (w_2 = \frac{r}{\tau}) \tag{11}$$

and equation (10) becomes:

$$\frac{dv_{[]n}}{(1 - v_{[]n}) \cdot d\tau} = \frac{16}{3}\pi \cdot w_2^3 \cdot w_3 \cdot \tau^3 \tag{12}$$

where w_3 expresses the germs forming rate and w_2 is their linear growing. When w_3 and w_2 are constant, equation (12) can be written as:

$$\frac{dv_{[]n}}{(1-v_{[]n})\cdot d\tau} = K_3 \cdot \tau^3 \tag{13}$$

The integration of equation (13) in the limits:

$$\tau = 0\ ;\ \ V_{[]n} = 0\ ;\ \ \tau = \tau;\ \ V_{[]n} = V_{[]n}$$

Leads to the equation (14):

$$\eta = 1 - e^{-K_3 \cdot \tau^4} \tag{14}$$

In conditions of forming and growing needle like HAP macroparticles: $v_p = l\ ;\ w_2 = \frac{l}{\tau}$, equation (10) becomes:

$$\frac{dv_{[]n}}{(1-v_{[]n})\cdot d\tau} = 2\cdot w_2 \cdot w_3 \cdot \tau \tag{15}$$

which by integration:

$$\eta = 1 - e^{-K_2 \cdot \tau^2} \tag{16}$$

In the case that the particles don't grow any more, w_2=0, equation (10) becomes:

$$\frac{dv_{[]n}}{\left(1-v_{[]n}\right)\cdot d\tau} = v_g \cdot w_3 \tag{17}$$

Integration of equation (17) leads to:

$$\eta = 1 - e^{-K_1 \cdot \tau} \tag{18}$$

Equations (13), (15) and (17) allow the calculation of the time for the fraction $v_{[]n} \equiv \eta$ of the new formed phase (HAP) to reach a certain value (within 0÷1). To use these equations experimental measurements are needed, which allow the validation of the kinetic mechanism and also the numerical values for K_1, K_2 and K_3.

RESULTS AND DISCUSSION

The results presented in Table 1 describe the evolution in time of the transformation of beta-whitlockite in hydroxyapatite. Data form Table 1 were used for the determination of K_1, K_2 and K_3 constants from the (14), (16) and (18) equations. For this purpose these three equations were plotted: $-\ln(1-\eta) = f(\tau)$, Figure 2 (a – c).

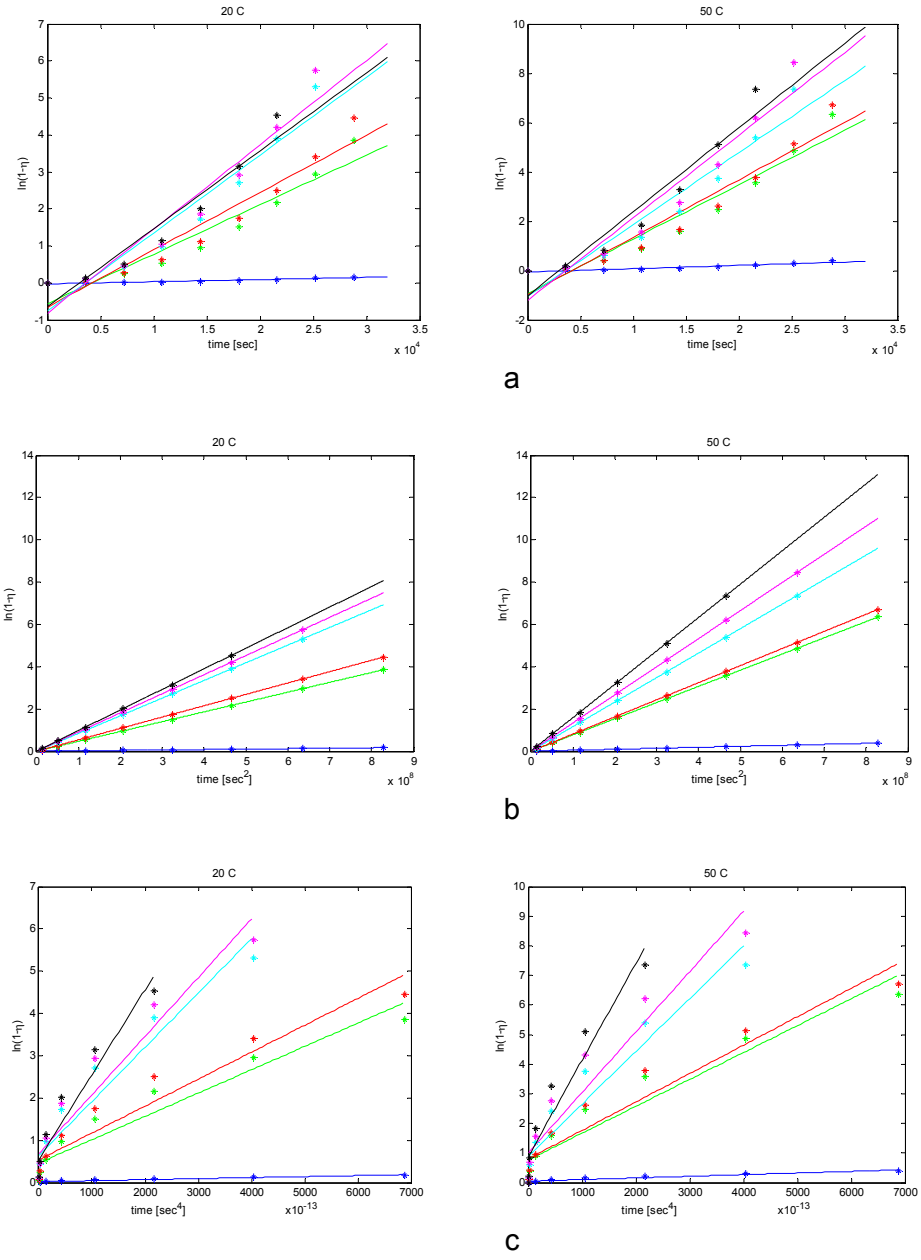

Figure 2. a: $-\ln(1-\eta)-\tau$; b: $-\ln(1-\eta)-\tau^2$; c: $-\ln(1-\eta)-\tau^4$

Table 1. The experimental results of the transformation grade of beta-whitlockite in time and at 20 ^{0}C and 50 ^{0}C for different pH values

pH	Time [s] / η	0	3600	7200	10800	14400	18000	21600	25200	28800	32400
8.5	20ºC	0	0.003	0.009	0.021	0.042	0.063	0.092	0.120	0.158	0.191
	50ºC	0	0.005	0.025	0.052	0.090	0.142	0.190	0.250	0.328	0.390
9.1	20ºC	0	0.055	0.215	0.415	0.620	0.775	0.880	0.945	0.981	0.991
	50ºC	0	0.092	0.330	0.590	0.800	0.910	0.971	0.990	1.000	-
9.7	20ºC	0	0.068	0.240	0.470	0.670	0.820	0.920	0.962	0.980	1.000
	50ºC	0	0.102	0.340	0.610	0.815	0.920	0.977	0.990	1.000	-
10.2	20ºC	0	0.101	0.350	0.620	0.820	0.940	0.981	0.996	1.000	-
	50ºC	0	0.136	0.450	0.740	0.910	0.978	0.996	1.000	-	-
11.3	20ºC	0	0.110	0.370	0.650	0.840	0.950	0.986	0.996	1.000	-
	50ºC	0	0.157	0.490	0.790	0.931	0.982	0.997	1.000	-	-
12	20ºC	0	0.119	0.400	0.680	0.860	0.960	0.989	1.000	-	-
	50ºC	0	0.187	0.560	0.840	0.960	0.995	1.000	-	-	-

From the slope were determined the numerical values of the K constants, presented in Table 2.

Tablel 2. The values of K constant

pH	20 ^{0}C			50 ^{0}C		
	K_1	K_2	K_3	K_1	K_2	K_3
8.5	6.583E-06	2.032E-10	1.920E-19	1.513E-05	4.671E-10	4.412E-19
9.1	1.510E-04	4.649E-09	4.392E-18	2.480E-04	7.655E-09	7.232E-18
9.7	1.740E-04	5.372E-09	5.075E-18	2.620E-04	8.089E-09	7.641E-18
10.2	2.410E-04	8.356E-09	9.915E-18	3.340E-04	1.158E-08	1.374E-17
11.3	2.600E-04	9.036E-09	1.072E-17	3.830E-04	1.329E-08	1.577E-17
12	2.450E-04	9.728E-09	1.494E-17	3.980E-04	1.579E-08	2.425E-17

In order to identify the mathematical model which describes the process the process simulation was needed. For this purpose the numerical values of the K_1, K_2 and K_3 from Table 2 were used and different times were calculated relating to the transformation grade of beta-whitlockite in HAP and compared with the experimental results. The results obtained at 20 ^{0}C and 50 ^{0}C for pH=9.7 are presented in Figure 3 (the simulations were made for all pH values, but in this article are presented only the relevant simulation results).

The analysis of the results show a very good fit of the experimental results with those calculated for equation (16), where the errors for the majority of the results don't exceed 2%. In the mathematical models expressed by equations (14) and (18) the deviations from the experimental values are high.

At pH = 8.5 the proposed model fits well with experimental data only until 20 % conversion (at 20 ^{0}C) and until 40 % (at 50 ^{0}C).

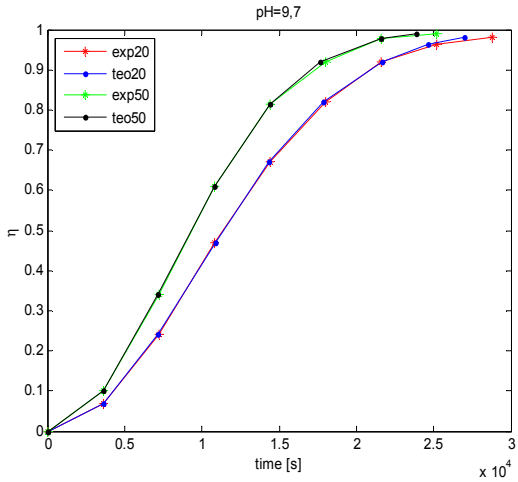

Figure 3. The variation of conversion in time at 20 ^{0}C and 50 ^{0}C at pH = 9.7

CONCLUSIONS

Based on the kinetic study regarding the transformation process of beta-whitlockite in HAP the mathematical model of this process was established. The implementation of the model for three particular cases led to equations, which were used to calculate the numerical values of K_1, K_2 and K_3 constants, based on experimental data. The process simulation using the mathematical model indicate that this could be described using the equation: $\eta = 1 - e^{-K_2 \cdot \tau^2}$, which corresponds to a combined macrokinetic mechanism: transfer (transfer of Ca^{2+} and PO_4^{3-} ions towards the HAP crystal surface) – mass transformation (formation and growing of HAP nuclei)

EXPERIMENTAL SECTION

For the synthesis of HAP and the kinetic study for the transformation of beta-whitlockite in hydroxyapatite, reactants of analytical purity were used: calcium nitrate tetra hydrate, bi-ammonia phosphate and ammonia solution 28 %.The concentration of the calcium nitrate solution was 0.5 mol/L and by adding ammonia solution the pH was turned to the value of 8.5. The concentration of the bi-ammonia phosphate solution was 0.3 mol/L and to this solution was added the necessary amount of ammonia to reach the pH values presented in Table 1. In all the experiments the phosphate solution

was added in drops over the calcium nitrate solution. The ammonia losses were avoided by fixing a closed ascending refrigerator and a hydraulic closing to the reaction vessel. The temperature was measured and maintained constant with a thermostat. From time to time, during the reaction, samples were taken, filtered, washed with distillated water and dried at 105 ^{0}C until constant weight. The dried samples were crushed into fine powders with $d_p < 50\mu m$ and were heated for 2 hours at 1000 ^{0}C.

Determination of the phase composition using XRD

The quantitative analysis of the phases was made using DRON-3 by measuring the integrated intensity of the peaks. Knowing the absorption mass coefficients in a bi-phase system, the amount of HAP was determined using the equation:

$$\frac{I_1}{I_1^0} = \frac{w_1 \cdot \mu_1}{w_1(\mu_1 - \mu_2) + \mu_2} \tag{18}$$

The evolution in time of the process was followed up using the transformation grade of the beta-whitlockite in HAP.

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NOMENCLATURE

I_1	integrated intensity of pure phase in mixture
I_1^0	integrated intensity of pure phase
$m_{A_1'}$	mass of HAP (kg)
μ_1,μ_2	mass absorption coefficients
w_1	mass fraction of phase
n_{A_1}	mols of HAP formed in reaction (mol)
$n_{A_{1[]l}}$	mols of HAP formed in the liquid phase (mol)
$n^p_{A_1}$	mols of HAP in one macroparticle (mol)
N_p	number of macroparticles (-)
r^2	particle radius (m)
l	particle length (m)
w_3	rate of germs forming (m/s)
w_2	rate of germs growing (m/s)
K	rate constant (-)
$V_{[]n}$	the volume fraction of the new phase (m^3)
$V_{[]m}$	the volume fraction of the new phase (m^3)
V_T	total volume of the new formed phase (m^3)

Greek symbols

$\overline{\rho_{A_1'}}$	molar density (kmol/ m^3)
τ	time (s)
v_p	stoechiometric coefficient of macroparticles (-)
$v_{[]n}$	stoechiometric coefficient of the new phase (-)