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ON SOME PATHOLOGIES CONNECTED WITH THE CRYSTALLIZATION PROCESS AT THE HUMAN BODY (GALLSTONES FORMATION)

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Abstract. In the paper the gallstones formation process is considered from the mathematical point of view. The process is described by the nonlinear reaction-diffusion equation with the appropriate initial-boundary conditions. The solutions are obtained in the explicit form. Numerical examples are given.

Keywords and phrases: Gallstone, reaction-diffusion equation, crystallization.

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Gallbladder is a small important organ for the human body, which is reservoir for bile. Bile is produced by the liver and is an important substance for the digestion of lipids in the intestine. Bile helps to emulsify lipids in the food and inhibits fat to aggregate into large particles. Also bile salts destroy microbes. Besides its digestive function, bile helps in excretion of bilirubin, a byproduct of red blood cells (RBC) recycled by the liver. Each day about 12 to 18 g bile acids are produced into the intestine. Bile acids are recycled each day. About 800mg cholesterol is produced by body per day. Half of this cholesterol is used for the synthesis about 400-600 mg of bile acid. Human adults secrete about 12 to 18 g of bile acids each day after meals. The bile pool size is about 4 to 6 g. Gallbladder bile is 97% water, 0.7% bile salts, 0.2 % bilirubin, 0.51% fats (cholesterol, fatty acids and lecithin), 200 meq/I inorganic salts [1,2,3,4].

Biliary obstruction is caused by different dietary disorders (for instance high consumption of sugar and fat), abnormal metabolism,various of dietary factors. As a result the gallstones are formed. Biliary obstruction blocks the bile ducts, gallbladder becomes supersaturated by bile and bilirubin polymers serve as a seeds which promotes crystallization process at the gallbladder. Gallstones may result from increased saturation of cholesterol or bilirubin. Lower concentration of bile acids or phospholipids reduce cholesterol solubility and lead to microcrystal formation. The stones in gallbladder are of different types yellow (with cholesterol), brown (with Mn), black (with Fe and Cu ions) [1,2,3,4].

When the stones are formed in the human body, they can be measured in the laboratory by MRI. The process of stones formation is crystallization process, which depend on the body temperature, pressure and some substances such as bilirubin, cholesterol, Mn, Fe, Cu. This process is described by the reaction-diffusion equation with the appropriate initial-boundary conditions [1].

Let us consider a single prismatic type gallstone formation. The crystallization process depends on time, temperature, pressure and amount of bile at the gallbladder. The formation and circulation of bile is a periodic process. We consider one period and admit that gallbladder serve as crystallizer in gallstones formation. Also we admit, that the temperature and pressure at the human body is constant. The crystallization process can be described by the nonlinear reaction-diffusion equation and this process takes place in a small area V_0 near seed, whilst out of this area ordinary diffusion equation is valid [5,6,7]

$$\frac{\partial U}{\partial t} = D\Delta U - \beta(U,t); \quad (x,y,z) \in V_0, \tag{1}$$

$$\frac{\partial U}{\partial t} = D\Delta U; \quad (x,y,z) \in V - V_0, \tag{2}$$

with the initial-boundary conditions

$$\int_V U(x,y,z,0)dxdydz = C_0, \quad U|_S = 0, \quad 0 < t < t_0, \tag{3}$$

where U is substance supersaturation, C_0 is initial supersaturation, D is the diffusion coefficient, β is a velocity of the chemical reaction (i.e. nucleation process), which is generally a non-linear function of U and t, S is a boundary of gallbladder. It is obvious that the boundary S_0 of V_0 is a jump surface for the function U.

From the experimental results it is known, that [6]

$$\beta(U,t) = \beta_0 U^2, \tag{4}$$

where β_0 is a constant. So, according to (1), (4) we have to solve the non-linear parabolic equation

$$\frac{\partial U}{\partial t} = D\Delta U - \beta_0 U^2 \tag{5}$$

with initial condition (3).

Let us seek solutions of (5) in the form

$$U(x,y,z,t) = R\sin^2\psi + C^*, \tag{6}$$

where ψ is a function forth order of which is negligible, R is some parameter, C^* is a constant second order of which is negligible. Putting (6) into (5) taking into the account previous prepositions and the formulas

$$\sin 2\psi \approx 2\psi - \frac{4\psi^3}{3}, \quad \cos 2\psi \approx 1 - 2\psi^2, \tag{7}$$

we obtain

$$\begin{aligned} &DR\left(2\psi - \frac{4\psi^3}{3}\right)\Delta\psi + 2DR(1-2\psi^2)(\nabla\psi)^2 = \beta_0(R^2\psi^4 + 2RC^*\psi^2) \\ &+R\left(2\psi - \frac{4\psi^3}{3}\right)\frac{\partial\psi}{\partial t}. \end{aligned} \tag{8}$$

Under our assumptions from (7) and (8) we obtain

$$\begin{aligned} &\left(2\psi - \frac{4\psi^3}{3}\right)\Delta\psi + 2(1-2\psi^2)(\nabla\psi)^2 = 2\frac{\beta_0}{D}C^*\psi^2 + \\ &\frac{1}{D}\left(2\psi - \frac{4\psi^3}{3}\right)\frac{\partial\psi}{\partial t}. \end{aligned} \tag{9}$$

We will find the solution of (9) in the form

$$\psi = e^{-\alpha|x|-\delta|y|-\gamma|z|-\theta t - D_0}, \tag{10}$$

where D_0 is some positive constant, $\alpha, \delta, \gamma, \theta$ are non-negative constants.

The function (10) will be the solution of (8) if the following conditions are satisfied

$$2(\alpha^2+\delta^2+\gamma^2) = \frac{\beta_0}{D}C^* - \frac{1}{D}\theta, \;\; C^* > \frac{\theta}{\beta_0}. \tag{11}$$

According to (6), (9), (10), (11) the solution of (1) will be given by

$$U(x,y,z,t) = R\sin^2 e^{-\alpha|x|-\delta|y|-\gamma|z|-\theta t - D_0} + C^*, \;\; (x,y,z)\in V_0,$$

where the constants $R, C^*\alpha, \delta, \gamma, \theta$ satisfy the conditions (11), C^* is a constant second order of which is negligible, the constant D_0 is chosen for the desired accuracy in such a way that e^{-4D_0} is negligible (for example, for $D_0 = 4, e^{-16} \approx 10^{-8}$).The solution of the linear equation (2) satisfying the condition (3) will be given by [5]

$$U(x,y,z,t) = Re^{-\theta t}\cos[R_0(\theta/D)^{1/2}(|x|+|y|+|z|-a_0)], \;\; (x,y,z)\in V-V_0, \;\; U|_S = 0,$$

where $2a_0$ is a diameter of V_0, $3a - a_0 = (\pi/2)(\theta/D)^{-1/2}$, $3a$ is a diameter of gallbladder, near the boundary of gallbladder $R_0(\theta/D)^{1/2}(|x|+|y|+|z|-a_0) = \pi/2$, R_0 is the definite constants and is chosen accordingly.

Note. By the same model (formulas (1),(2),(3)) can be described the formation of urinary stones and stones at kidney. In this case the stones are formed meanly by means of uric acid and calcium oxalate with the different diffusion coefficients.

Below in Fig.1 and Fig.2 the distribution of supersaturation is constructed by using Maple and the following data $V_0 = 1\times 1\times 1$; $C_0 = 4\times 10^{-3}$; $\beta_0 = 2.5$; $D = 240^{-1}$; $C^* = 10^{-3}$; $R = 4\times 10^{-3}$; $\alpha = \delta = 0.5\times 10^{-3/2}$; $\theta = 10^{-4}/6$ (we have taken a non-dimensional value).

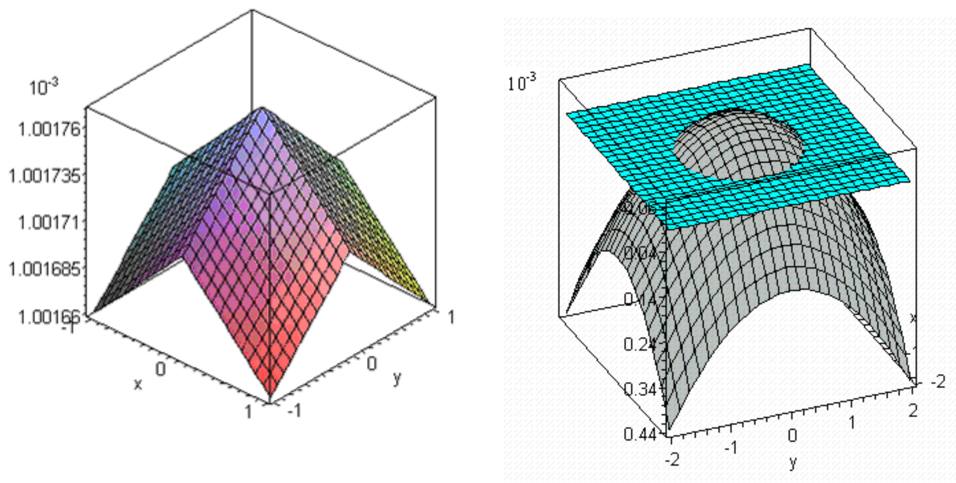

Fig.1. The distribution of the supersaturation for $t = 1$, in the areas V_0 and $V - V_0$ respectively.

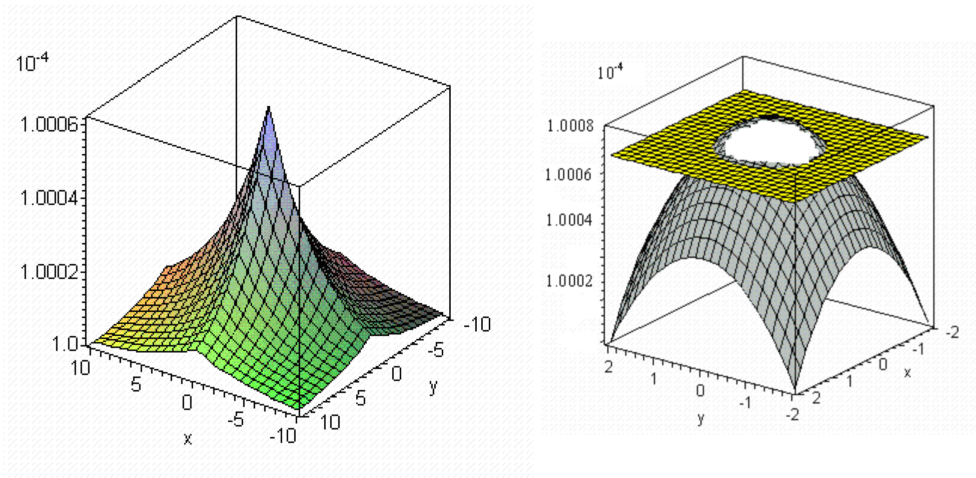

Fig.2. The distribution of the supersaturation for $t = 4$, in the areas V_0 and $V - V_0$ respectively.

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