ON DEVELOPMENT OF BLOOD CLOTS IN CONDITIONS OF BLOOD FLOW

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ABSTRACT

We introduce a model of evolution of blood clots in blood flow. The model is generalization of recently obtained experimental data. Also we introduce an analytical approach for analysis of the above evolution.

KEYWORDS

prognosis of blood clots; distribution of concentration of metobolites; analytical approach for analysis.

1. INTRODUCTION

One of most distributed diseases is atherosclerosis. During evolution of the disease one can find formation of single or multiply depositions [1-5]. Future development of these depositions leads to deformation and narrowing of the vessel lumen up to its blockage. In this situation it is attracted an interest prognosis of development depositions. In this paper we introduce and analyzed a model of evolution of blood clots in blood flow. Also we introduce an analytical approach for analysis of the above evolution.

2. METHOD OF SOLUTION

In this section we formulate a model to describe generation of blood clots. After the formulation we analyzed the model. The flow of a viscous liquid is described by the Navier-Stokes equations [6]

$$\frac{\partial \vec{v}}{\partial t} + (\vec{v} \cdot \nabla)\, \vec{v} = -\nabla \left(\frac{P}{\rho} \right) + \nu\, \Delta \vec{v}\,, \tag{1}$$

where $\vec{v}$ is the velocity of movement of liquid; ν is the kinematics viscosity; P is the pressure of liquid. Equations for components of velocity of flow with account cylindrical system of coordinate could be written as

$$\begin{cases} \dfrac{\partial v_r}{\partial t} = \nu \left\{ \dfrac{1}{r} \dfrac{\partial}{\partial r} \left[r \dfrac{\partial v_r(r,z,t)}{\partial r} \right] + \dfrac{\partial^2 v_r(r,z,t)}{\partial z^2} \right\} - v_r \dfrac{\partial v_r}{\partial r} - v_z \dfrac{\partial v_z}{\partial z} - \dfrac{\partial}{\partial r} \left(\dfrac{P}{\rho} \right) \\ \dfrac{\partial v_z}{\partial t} = \nu \left\{ \dfrac{1}{r} \dfrac{\partial}{\partial r} \left[r \dfrac{\partial v_z(r,z,t)}{\partial r} \right] + \dfrac{\partial^2 v_z(r,z,t)}{\partial z^2} \right\} - v_r \dfrac{\partial v_r}{\partial r} - v_z \dfrac{\partial v_z}{\partial z} - \dfrac{\partial}{\partial z} \left(\dfrac{P}{\rho} \right) \end{cases}$$

(1*a*)

Generation, decay and distribution of main metabolites could be described by the following equations

$$\begin{cases} \frac{\partial C_1(r,z,t)}{\partial t} = \nabla \left\{ D_1 \cdot \nabla C_1(r,z,t) - \vec{v}_1(r,z,t) \cdot C_1(r,z,t) \right\} - \\ \qquad - k_g C_1(r,z,t) C_2(r,z,t) + k_{r1} C_1(r,z,t) \\ \frac{\partial C_2(r,z,t)}{\partial t} = \nabla \left\{ D_2 \cdot \nabla C_2(r,z,t) - \vec{v}_2(r,z,t) \cdot C_2(r,z,t) \right\} - \\ \qquad - k_g C_1(r,z,t) C_2(r,z,t) + k_{r2} C_2(r,z,t) \end{cases}, \quad (2)$$

where $C_k(r,z,t)$ is the concentration of k-th metabolite; D_k is the diffusion coefficient of k-th metabolite; k_g is the parameter of interaction of metabolites; k_{rk} is the parameter of decay of metabolites; r, z and t are the current cylindrical coordinates and current time. We assume, that velocities of transport of every main metabolites could be described by the following relation: $\vec{v}_k = b_k \vec{v}$.

In this paper for simplification of testing of the introduced model we consider interaction of two metabolites. Increasing of number of metabolites leads to increasing of quantity of analogous equations, but not to qualitatively new results. Boundary and initial conditions for the required functions could be written as

$$C_k(r,0,t) = C_{0k},\ C_k(r,0,t) = 0,\ \left.\frac{\partial C_k(r,z,t)}{\partial r}\right|_{r=R} = 0,\ \left.\frac{\partial v_r(r,z,t)}{\partial r}\right|_{r=0} = 0,$$

$$\left.\frac{\partial v_r(r,z,t)}{\partial r}\right|_{r=R} = 0,$$

$$C_k(0,z,t) \neq \infty,\ C_k(r,z,0) = C_0\delta(z+L),\ v_r(r,0,t) = 0,\ v_r(r,L,t) = 0,\ v_r(0,z,t) \neq \infty,$$

$$v_z(r,0,t) = V_0,\ v_z(r,0,t) = 0,\ v_z(r,L,t) = 0,\ v_z(0,z,t) \neq \infty,\ v_r(r,z,0) = 0,\ v_z(r,0,0) = V_0. \quad (3)$$

Now we calculate solutions of equations (1) and (2) with conditions (3) by method of averaging of functions corrections [6-8]. In the framework of this method we substitute not yet known average values of the required concentrations α_{Ck1} and velocities ($\beta = r,z$) instead of the above functions in the right sides of the equations (1) and (2). The replacement gives a possibility to determine the first-order approximations of concentrations of metabolites and velocities of their transport in the following form

$$v_{r1} = V_0 - \frac{\partial}{\partial r}\int_0^t \frac{P}{\rho} d\tau,\ v_{z1} = V_0 - \frac{\partial}{\partial z}\int_0^t \frac{P}{\rho} d\tau, \quad (4)$$

$$\begin{cases} C_{11}(r,z,t) = C_{01} - \alpha_{C11}\int\limits_0^t \left\{ \frac{1}{r}\frac{\partial\left[r\,v_{r1}(r,z,\tau)\right]}{\partial r} + \frac{\partial v_{z1}(r,z,\tau)}{\partial z} \right\} d\tau - \\ \qquad -\alpha_{C11}\alpha_{C21}\int\limits_0^t k_g\, d\tau + \alpha_{C11}\int\limits_0^t k_{r1} d\tau \\ C_{21}(r,z,t) = C_{02} - \alpha_{C21}\int\limits_0^t \left\{ \frac{1}{r}\frac{\partial\left[r\,v_{r2}(r,z,\tau)\right]}{\partial r} + \frac{\partial v_{z2}(r,z,\tau)}{\partial z} \right\} d\tau - \\ \qquad -\alpha_{C11}\alpha_{C21}\int\limits_0^t k_g\, d\tau + \alpha_{C21}\int\limits_0^t k_{r2} d\tau \end{cases} \tag{5}$$

The above average values α_1 were determined by using the following standard relation [6-8]

$$\alpha_1 = \frac{2}{R^2\Theta}\int\limits_0^\Theta \int\limits_0^R r \int\limits_0^L f_1(r,z,t)\, d\,r\, d\,z\, d\,t\,. \tag{6}$$

Substitution of relations (4) and (5) into relation (6) gives a possibility to obtain relations to determine required average values in the following final form

$$\alpha_{vr1} = V_0 - \frac{2}{R^2 L\Theta}\left[R\int\limits_0^\Theta (\Theta - t)\int\limits_0^L \frac{P}{\rho} d\,z\,d\,r\,d\,t - \int\limits_0^\Theta (\Theta - t)\int\limits_0^R\int\limits_0^L \frac{P}{\rho} d\,z\,d\,r\,d\,t \right],$$

$$\alpha_{vz1} = V_0 - \frac{2}{R^2 L\Theta}\int\limits_0^\Theta (\Theta - t)\int\limits_0^R\int\limits_0^L \frac{r}{\rho}\left[P(L) - P(0)\right] d\,z\,d\,r\,d\,t, \tag{7}$$

$$\alpha_{C11} = C_{01} \Bigg/ \left[\frac{2}{R^2 L\Theta}\int\limits_0^\Theta (\Theta - t)\int\limits_0^R\int\limits_0^L \left\{ \frac{\partial\left[r\,v_{r1}(r,z,t)\right]}{\partial r} + r\frac{\partial v_{z1}(r,z,t)}{\partial z} \right\} d\,r\,d\,z\,d\,t - \right.$$
$$\left. - \frac{2}{R^2 L\Theta}\int\limits_0^\Theta (\Theta - t)\int\limits_0^R r\int\limits_0^L k_{r1}\, d\,r\,d\,z\,d\,t + \frac{2\alpha_{C21}}{R^2 L\Theta}\int\limits_0^\Theta (\Theta - t)\int\limits_0^R r\int\limits_0^L k_g\, d\,r\,d\,z\,d\,t + 1 \right],$$

$$\alpha_{C21} = \frac{-b \pm \sqrt{b^2 - 4a\,c}}{2a}, \tag{8}$$

where

$$a = \frac{2}{R^2 L\Theta}\int\limits_0^\Theta (\Theta - t)\int\limits_0^R r\int\limits_0^L k_g\, d\,r\,d\,z\,d\,t \left[1 + \frac{2}{R^2 L\Theta}\int\limits_0^\Theta (\Theta - t)\int\limits_0^R\int\limits_0^L \left\{ \frac{\partial\left[r\,v_{r1}(r,z,t)\right]}{\partial r} + \right.\right.$$
$$\left.\left. + r\frac{\partial v_{z1}(r,z,t)}{\partial z} \right\} d\,r\,d\,z\,d\,t - \frac{2}{R^2 L\Theta}\int\limits_0^\Theta (\Theta - t)\int\limits_0^R r\int\limits_0^L k_{r1}\, d\,r\,d\,z\,d\,t \right],$$

$$b = \left\{ \left[1 + \frac{2}{R^2 L\Theta}\int\limits_0^\Theta (\Theta - t) \times \right.\right.$$

$$\times\int_0^R\int_0^L\left\{\frac{\partial\left[r\,v_{r1}(r,z,t)\right]}{\partial r}+r\,\frac{\partial v_{z1}(r,z,t)}{\partial z}\right\}d\,r\,d\,z\,d\,t-\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r1}\,d\,r\,d\,z\,d\,t\;\Bigg]\times$$

$$\times\Bigg[1+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\left\{\frac{\partial\left[r\,v_{r1}(r,z,t)\right]}{\partial r}+r\,\frac{\partial v_{z1}(r,z,t)}{\partial z}\right\}d\,r\,d\,z\,d\,t-\frac{2}{R^2L\,\Theta}\int_0^\Theta(\Theta-t)\times$$

$$\times\int_0^R r\int_0^L k_{r1}\,d\,r\,d\,z\,d\,t\,\Bigg]+\frac{2C_{01}}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_g\,d\,r\,d\,z\,d\,t-\frac{2\,C_{02}}{R^2L\,\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_g\,d\,r\,d\,z\,d\,t\Bigg\}$$

,

$$c=C_{02}\Bigg[\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r1}\,d\,r\,d\,z\,d\,t-1-\int_0^\Theta\int_0^R\int_0^L\left\{\frac{\partial\left[r\,v_{r1}(r,z,t)\right]}{\partial r}+r\,\frac{\partial v_{z1}(r,z,t)}{\partial z}\right\}d\,r\,d\,z\,\times$$

$$\times\,2(\Theta-t)\,d\,t/R^2L\Theta\,\Bigg].$$

The second-order approximations of concentrations of metabolites and velocities of their transport could be determined by the following standard replacement $\rho\ (r,z,t)\to\alpha_{2\rho}+\rho_1\ (r,z,t)$ [6-8]

$$v_{r2}(r,z,t)=V_0+\frac{\nu}{r}\frac{\partial}{\partial r}\left[r\,\frac{\partial}{\partial r}\int_0^t v_{r1}(r,z,\tau)\,d\,\tau\right]-\alpha_{vr2}\,\frac{\partial}{\partial r}\int_0^t v_{r1}(r,z,\tau)\,d\,\tau-\frac{\partial}{\partial r}\int_0^t\frac{P}{\rho}d\,\tau-$$

$$-\int_0^t v_{r1}(r,z,\tau)\frac{\partial v_{r1}(r,z,\tau)}{\partial r}d\,\tau-\alpha_{vz2}\,\frac{\partial}{\partial z}\int_0^t v_{z1}(r,z,\tau)\,d\,\tau-\int_0^t v_{z1}(r,z,\tau)\frac{\partial v_{z1}(r,z,\tau)}{\partial z}d\,\tau+$$

$$+\nu\,\frac{\partial^2}{\partial z^2}\int_0^t v_{r1}(r,z,\tau)d\,\tau \tag{9}$$

$$v_{z2}(r,z,t)=V_0+\frac{\nu}{r}\frac{\partial}{\partial r}\left[r\,\frac{\partial}{\partial r}\int_0^t v_{z1}(r,z,\tau)\,d\,\tau\right]-\alpha_{vr2}\,\frac{\partial}{\partial r}\int_0^t v_{r1}(r,z,\tau)\,d\,\tau-\frac{\partial}{\partial r}\int_0^t\frac{P}{\rho}d\,\tau-$$

$$-\int_0^t v_{r1}(r,z,\tau)\frac{\partial v_{r1}(r,z,\tau)}{\partial r}d\,\tau-\alpha_{vz2}\,\frac{\partial}{\partial z}\int_0^t v_{z1}(r,z,\tau)\,d\,\tau-\int_0^t v_{r1}(r,z,\tau)\frac{\partial v_{z1}(r,z,\tau)}{\partial z}d\,\tau+$$

$$+\nu\,\frac{\partial^2}{\partial z^2}\int_0^t v_{z1}(r,z,\tau)d\,\tau$$

$$C_{12}(r,z,t)=\frac{1}{r}\frac{\partial}{\partial\,r}\left[r\int_0^t D_1\,\frac{\partial C_{11}(r,z,\tau)}{\partial\,r}d\,\tau\right]+\frac{\partial}{\partial\,z}\left[\int_0^t D_1\,\frac{\partial C_{11}(r,z,\tau)}{\partial\,z}d\,\tau\right]-\frac{\alpha_{C12}}{r}\times$$

$$\times\frac{\partial}{\partial r}\left[\int_0^t r\cdot v_r(r,z,\tau)d\tau\right]-\frac{1}{r}\frac{\partial}{\partial r}\left[r\cdot\int_0^t C_{11}(r,z,\tau)\cdot v_r(r,z,\tau)d\tau\right]-\alpha_{C12}\alpha_{C22}\int_0^t k_g\,d\tau-$$

$$-\frac{\partial}{\partial z}\int_0^t\left[v_z(r,z,\tau)\cdot C_{11}(r,z,\tau)\right]d\tau-\alpha_{C12}\int_0^t k_g C_{21}(r,z,\tau)\,d\tau-\alpha_{C22}\int_0^t k_g C_{11}(r,z,\tau)d\tau-$$

$$-\int_0^t k_g C_{11}(r,z,\tau)C_{21}(r,z,\tau)\,d\tau-\alpha_{C12}\frac{\partial}{\partial z}\int_0^t v_z(r,z,\tau)d\tau+\int_0^t k_{r1}C_{11}(r,z,\tau)d\tau+C_{01}+$$

$$+\alpha_{C12}\int_0^t k_{r1}d\tau \tag{10}$$

$$C_{22}(r,z,t)=\frac{1}{r}\frac{\partial}{\partial r}\left[r\int_0^t D_1\frac{\partial C_{21}(r,z,\tau)}{\partial r}d\tau\right]+\frac{\partial}{\partial z}\left[\int_0^t D_1\frac{\partial C_{21}(r,z,\tau)}{\partial z}d\tau\right]-\frac{\alpha_{C22}}{r}\times$$

$$\times\frac{\partial}{\partial r}\left[\int_0^t r\cdot v_r(r,z,\tau)\,d\tau\right]-\frac{1}{r}\frac{\partial}{\partial r}\left[r\cdot\int_0^t C_{11}(r,z,\tau)\cdot v_r(r,z,\tau)d\tau\right]+\alpha_{C12}\int_0^t k_{r1}d\tau-$$

$$-\frac{\partial}{\partial z}\int_0^t\left[v_z(r,z,\tau)\cdot C_{11}(r,z,\tau)\right]d\tau-\alpha_{C22}\frac{\partial}{\partial z}\int_0^t v_z(r,z,\tau)d\tau-\alpha_{C12}\alpha_{C22}\int_0^t k_g\,d\tau-$$

$$-\alpha_{C12}\int_0^t k_g C_{21}(r,z,\tau)d\tau-\alpha_{C22}\int_0^t k_g C_{11}(r,z,\tau)d\tau-\int_0^t k_g C_{11}(r,z,\tau)\,C_{21}(r,z,\tau)\,d\tau+$$

$$+C_{02}+\int_0^t k_{r1}C_{11}(r,z,\tau)\,d\tau\,.$$

Average values of the second-order approximations of the considered functions were determined by using the following standard relations [6-8]

$$\alpha_2=\frac{2}{R^2L\Theta}\int_0^\Theta\int_0^R r\int_0^L\left[\rho_2(r,z,t)-\rho_1(r,z,t)\right]d\,r\,d\,z\,d\,t. \tag{11}$$

Substitution of relations (9) and (10) into relation (11) gives a possibility to obtain the following relations to determine required average values α_2

$$\alpha_{vr2}=\left\{\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\nu\frac{\partial}{\partial r}\left[r\frac{\partial v_{r1}(r,z,t)}{\partial r}\right]d\,r\,d\,z\,d\,t-\int_0^\Theta\int_0^R\int_0^L\frac{\partial v_{z1}(r,z,t)}{\partial z}d\,r\,d\,z\times\right.$$

$$\times(\Theta-t)\,d\,t\frac{2\alpha_{vz2}}{R^2L\Theta}-\frac{1}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{r1}^2(r,z,t)}{\partial r}d\,r\,d\,z\,d\,t+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\nu\times$$

$$\times\frac{\partial^2 v_{r1}(r,z,t)}{\partial z^2}d\,r\,d\,z\,d\,t-\frac{1}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\nu\frac{\partial v_{z1}^2(r,z,t)}{\partial z}d\,r\,d\,z\,d\,t\Bigg\}\times$$

$$\times\left[1+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{r1}(r,z,t)}{\partial r}d\,r\,d\,z\,d\,t\right]^{-1},\qquad(12)$$

$$\alpha_{vz2}=\left\{\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\nu\frac{\partial}{\partial r}\left[r\frac{\partial v_{z1}(r,z,t)}{\partial r}\right]d\,r\,d\,z\,d\,t+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\nu\times\right.$$

$$\times\frac{\partial^2 v_{z1}(r,z,t)}{\partial z^2}d\,r\,d\,z\,d\,t-\frac{1}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{r1}^2(r,z,t)}{\partial r}d\,r\,d\,z\,d\,t-\frac{1}{R^2L\Theta}\int_0^\Theta(\Theta-t)\times$$

$$\times\int_0^R\int_0^L\nu\frac{\partial v_{z1}^2(r,z,t)}{\partial z}d\,r\,d\,z\,d\,t-\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{r1}(r,z,t)}{\partial r}d\,r\,d\,z\,d\,t\left\{\frac{2}{R^2L\Theta}\times\right.$$

$$\times\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\nu\frac{\partial}{\partial r}\left[r\frac{\partial v_{r1}(r,z,t)}{\partial r}\right]d\,r\,d\,z\,d\,t+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\nu\frac{\partial^2 v_{r1}(r,z,t)}{\partial z^2}d\,r\,d\,z\,d\,t-$$

$$-\frac{1}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{r1}^2(r,z,t)}{\partial r}d\,r\,d\,z\,d\,t-\frac{1}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\nu\frac{\partial v_{z1}^2(r,z,t)}{\partial z}d\,r\,d\,z\,d\,t\Bigg\}\times$$

$$\times\left[1+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{r1}(r,z,t)}{\partial r}d\,r\,d\,z\,d\,t\right]^{-1}\Bigg\}\left\{\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{z1}(r,z,t)}{\partial z}d\,r\,d\,z\,d\,t\times\right.$$

$$\times\frac{2}{R^2L\Theta}+1-\frac{4}{R^4L^2\Theta^2}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{r1}(r,z,t)}{\partial r}d\,r\,d\,z\,d\,t\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{z1}(r,z,t)}{\partial z}d\,r\,d\,z\,d\,t\times$$

$$\left.\times\left[1+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R\int_0^L\frac{\partial v_{r1}(r,z,t)}{\partial r}d\,r\,d\,z\,d\,t\right]^{-1}\right\}^{-1},$$

$$\alpha_{C12}=\left\{\frac{2C_{01}}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R D_1(r,0,t)d\,r\,d\,t-\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{11}(r,z,t)C_{21}(r,z,t)\,d\,r\,d\,z\,d\,t-\right.$$

$$-\alpha_{C22}\left[\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{11}(r,z,t)d\,r\,d\,z\,d\,t+\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{11}(r,z,t)d\,r\,d\,z\,d\,t\right]-$$

$$\left.-C_{01}\frac{V_0\Theta}{2L}+\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r1}C_{11}(r,z,t)\,d\,r\,d\,z\,d\,t\right\}\left[\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{21}(r,z,t)d\,r\,d\,z\,d\,t+\right.$$

$$+1+\frac{V_0\Theta}{2L}-\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r1}d\,r\,d\,z\,d\,t+\frac{2\alpha_{C22}}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_g\,d\,r\,d\,z\,d\,t\Bigg]^{-1}, \quad (13)$$

$$\alpha_{C22}=\frac{\sqrt{b^2-4ac}-b}{2a}.$$

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$$a=\frac{2}{R^2L\Theta}\left[\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{11}(r,z,t)d\,r\,d\,z\,d\,t-\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r2}d\,r\,d\,z\,d\,t+\right.$$

$$\left.+1+C_{02}\frac{V_0\Theta}{2L}\right]\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_g\,d\,r\,d\,z\,d\,t,$$

$$b=\left[1+C_{02}\frac{V_0\Theta}{2L}+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_g\times\right.$$

$$\left.\times C_{11}(r,z,t)d\,r\,d\,z\,d\,t-\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r2}d\,r\,d\,z\,d\,t\right]\left[1-\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r1}d\,r\,d\,z\,d\,t+\right.$$

$$\left.+\frac{V_0\Theta}{2L}+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{21}(r,z,t)d\,r\,d\,z\,d\,t\right]-\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_g\,d\,r\,d\,z\,d\,t\times$$

$$\times\left[\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r2}C_{21}(r,z,t)\,d\,r\,d\,z\,d\,t-\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{11}(r,z,t)C_{21}(r,z,t)\,d\,r\,d\,z\,d\,t+\right.$$

$$\left.+\frac{2C_{02}}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R D_2(r,0,t)\,d\,r\,d\,t-C_{02}\frac{V_0\Theta}{2L}\right]+\left[\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{11}(r,z,t)d\,r\,d\,z\,d\,t\times\right.$$

$$\left.\times\frac{2}{R^2L\Theta}+\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{11}(r,z,t)d\,r\,d\,z\,d\,t\right],$$

$$c=\left\{\left[\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r2}C_{21}(r,z,t)\,d\,r\,d\,z\,d\,t-\right.\right.$$

$$\left.-\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{11}(r,z,t)C_{21}(r,z,t)\,d\,r\,d\,z\,d\,t\right]+\frac{2C_{02}}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R D_2(r,0,t)\,d\,r\,d\,t-$$

$$\left.-C_{02}\frac{V_0\Theta}{2L}\right\}\left[1+\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{21}(r,z,t)d\,r\,d\,z\,d\,t-\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r1}d\,r\,d\,z\,d\,t+\right.$$

$$\left.+\frac{V_0\Theta}{2L}\right]+\left[\frac{2}{R^2L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{21}(r,z,t)\,d\,r\,d\,z\,d\,t+\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_gC_{21}(r,z,t)d\,r\,d\,z\,d\,t+\right.$$

$$+\frac{2}{R^2 L\Theta}\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_g\,d\,r\,d\,z\,d\,t\Bigg]\Bigg[\frac{2C_{01}}{R^2 L\Theta}\int_0^\Theta(\Theta-t)\int_0^R D_1(r,0,t)d\,r\,d\,t-\int_0^\Theta\int_0^R r\int_0^L k_g C_{11}(r,z,t)\times$$

$$\times C_{21}(r,z,t)\,d\,r\,d\,z(\Theta-t)d\,t-C_{01}\frac{V_0\Theta}{2L}+\int_0^\Theta(\Theta-t)\int_0^R r\int_0^L k_{r1}C_{11}(r,z,t)\,d\,r\,d\,z\,d\,t\Bigg].$$

Spatio-temporal distributions of concentrations of metabolites and velocities of their transport was analyzed analytically by using the second-order approximation in the framework of method of averaging of function corrections. The approximation is usually enough good approximation for to make qualitative analysis and to obtain some quantitative results. All obtained results have been checked by comparison with results of numerical simulations.

3. DISCUSSION

In this section we analyzed spatio-temporal distribution of concentrations of metabolites. Figs. 1 and 2 shows typical dependences of the above concentrations on time and coordinate. These figures show, that concentrations of metabolites could be increased or decreased at different conditions of transport.

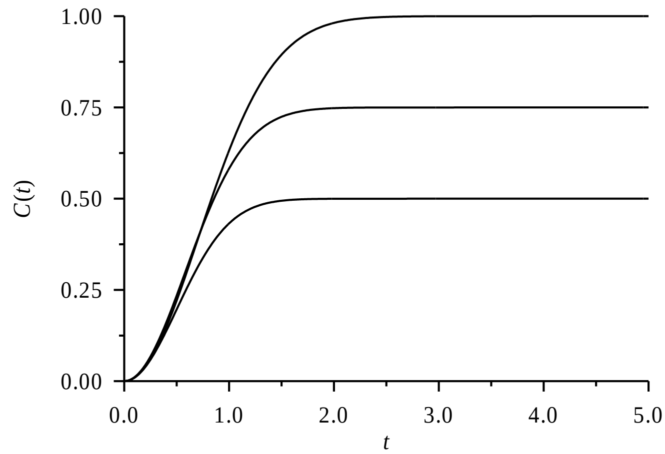

Fig. 1*a*. Typical dependences of concentrations of metabolites on time

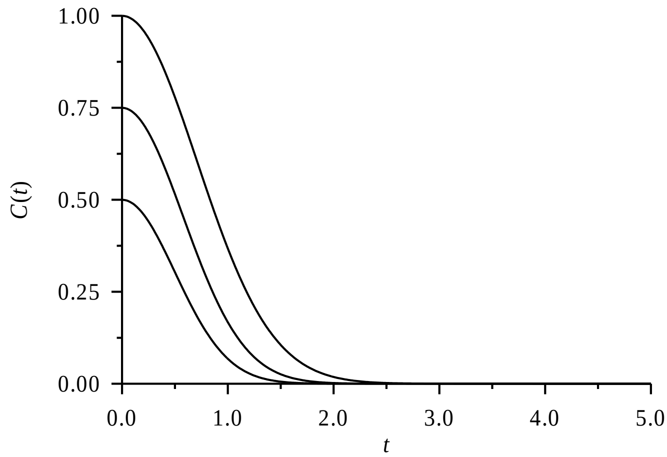

Fig. 1*b*. Typical dependences of concentrations of metabolites on time

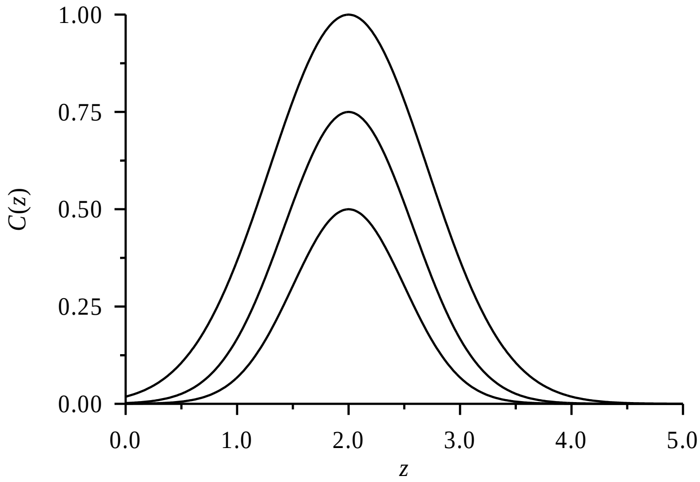

Fig. 2. Typical dependences of concentrations of metabolites on coordinate

Conclusion

We introduce a model of evolution of blood clots in blood flow. The model gives a possibility to take into account changing of conditions of blood clots in space and time as well as nonlinearity of the considered process. Also we introduce an analytical approach for analysis of the of blood clots.

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