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RESEARCH ARTICLE

On model of transport of a medicinal product in an organism

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ABSTRACT

In this paper we introduce a model of transport of a medicinal product in a organism. The model based on estimation of spatio-temporal distribution of concentration of product. We introduce an analytical approach for analysis of the considered transport with account of changing of conditions. We consider a possibility to accelerate and decelerate of transport of the above medicinal product.

Keywords: transport of a medicinal product; spatio-temporal distribution of concentration of a medicinal product; changing of speed of transport of a medicinal product; analytical approach for analysis

INTRODUCTION

In the present time one can find fast increasing of quantity of new medicinal products as well as intensive development of old medicinal products with questionable efficacy and safety [1-5]. Usually influence of medicinal products on organism could be done experimentally. Some time required dose of the considered products with influence on organism could be estimated. At presents several models to analyze transport of medicinal products through organism already were elaborated. In this paper we consider a model for estimation of spatio-temporal distribution of concentration of a medicinal product. Based on the model we analyzed the above concentration with account possible changing of properties of organism.

Method of solution

In this section we consider a model for estimation and analysis of spatio-temporal distribution of concentration of a medicinal product in an organism with account possible changing of properties. We calculate the required distribution as solution of the second Fick's law in the following form

$$\frac{\partial C(x,t)}{\partial t}=\frac{\partial}{\partial x}\left[D(x,t)\frac{\partial C(x,t)}{\partial x}\right]-K(x,t)C(x,t)N(x,t), \qquad (1)$$

where $C(x,t)$ is the spatio-temporal distribution of concentration of the considered medicinal product; $D(x,t)$ is the diffusion coefficient of the product, which depends on tissue conditions in organism; $K(x,t)$ is the parameter of interaction of the considered product with another substances in organism; $N(x,t)$ is the concentration of other substances in organism, which interacting with infused product. Initial distribution of concentration of the considered medicinal product depends on type of infusion (single or continuous infusion). and could be written in the following form

$$C(x,0)=f_C(x). \tag{2}$$

Boundary values of concentration of the considered medicinal product also depends on type of infusion

for single infusion of product : $\left.\frac{\partial C(x,t)}{\partial x}\right|_{x=0}=0$, $C(L,t) = 0$; (3*a*)

for continuous infusion of product : $C(0,t) = C_0$, $C(L,t) = 0$, (3*b*)

where C_0 is the concentration of product in place of infusion. Next let us to solve the Eq. (1) with conditions (2) and (3) by method of averaging of function corrections [6-8]. First of all we transform Eq.(1) to the following integral form (for single or continuous infusion, respectively)

$$C(x,t)=C(x,t)+\frac{1}{L^2}\left\{\int_0^t\int_0^x D(v,\tau)\,C(v,\tau)\,d\,v\,d\,\tau-\int_0^t\int_0^x (x-v)C(v,\tau)\frac{\partial D(v,\tau)}{\partial v}d\,v\,d\,\tau+\right.$$

$$-\int_0^t\int_0^x (x-v)K(v,\tau)C(v,\tau)N(v,\tau)d\,v\,d\,\tau+\int_0^L (L-v)\,C(v,t)d\,v-\int_0^t\int_0^L D(v,\tau)C(v,\tau)d\,v\,d\,\tau+$$

$$\left.+\int_0^x (x-v)\,f(v)d\,v+\int_0^t\int_0^L (L-v)C(v,\tau)\frac{\partial D(v,\tau)}{\partial v}d\,v\,d\,\tau-\int_0^x (x-v)\,C(v,t)d\,v\right\}, \tag{4a}$$

$$C(x,t)=C(x,t)+\frac{1}{L^2}\left\{\int_0^t\int_0^x C(v,\tau)\frac{\partial D(v,\tau)}{\partial v}d\,v\,d\,\tau-\int_0^t\int_0^x (x-v)K(v,\tau)C(v,\tau)N(v,\tau)d\,v\,d\,\tau+\right.$$

$$+\int_0^x (x-v)\,f(v)d\,v-\int_0^t D(x,\tau)C(x,\tau)d\,\tau+C_0\int_0^t D(x,\tau)d\,\tau-\frac{x}{L}\left[\int_0^t\int_0^L C(v,\tau)\frac{\partial D(v,\tau)}{\partial v}d\,v\,d\,\tau-\right.$$

$$\left.-\int_0^t\int_0^L (L-v)K(v,\tau)C(v,\tau)N(v,\tau)d\,v\,d\,\tau+\int_0^L (L-v)\,f(v)d\,v-\int_0^L (L-v)C(v,t)d\,v\right]-$$

$$\left.-\int_0^x (x-v)\,C(v,t)d\,v\right\}. \tag{4b}$$

In the framework of the considered method we substitute not yet known average value of the required concentration α_1 instead of the above concentration in the right sides of Eqs. (4). The substitution gives a possibility to obtain equations to calculate the first-order approximations of concentration of the considered product in the following form (for single or continuous infusion, respectively)

$$C_1(x,t)=\alpha_1+\frac{1}{L^2}\left[\int_0^x (x-v)\,f(v)\,d\,v-\alpha_1\int_0^t\int_0^x (x-v)K(v,\tau)N(v,\tau)\,d\,v\,d\,\tau+\alpha_1\frac{L^2-x^2}{2}\right], \tag{5a}$$

$$C_1(x,t)=\alpha_1+\frac{1}{L^2}\left\{\alpha_1\int_0^t[D(x,\tau)-D(0,\tau)]d\,\tau-\alpha_1\int_0^t\int_0^x (x-v)K(v,\tau)N(v,\tau)\,d\,v\,d\,\tau+\right.$$
$$+\int_0^x (x-v)\,f(v)\,d\,v-\alpha_1\int_0^t D(x,\tau)\,d\,\tau+C_0\int_0^t D(x,\tau)d\,\tau-\left[\alpha_1\int_0^t[D(L,\tau)-D(0,\tau)]d\,\tau-\right.$$
$$\left.\left.-\alpha_1\int_0^t\int_0^L (L-v)K(v,\tau)N(v,\tau)d\,v\,d\,\tau+\int_0^L (L-v)\,f(v)\,d\,v\right]\frac{x}{L}-\alpha_1(L+x)\frac{x}{2}\right\}. \tag{5b}$$

Average value of concentration of medical product α_1 could be obtain by the following standard relation [6-8]

$$\alpha_1=\frac{1}{L\Theta}\int_0^\Theta\int_0^L C_1(x,t)\,d\,x\,d\,t. \tag{6}$$

Substitution of relations (5) into relation (6) gives a possibility to obtain relations to determine average value α_1 in the final form (for single or continuous infusion, respectively)

$$\alpha_1=\Theta\int_0^L\left(L^2-x^2\right)f(x)\,d\,x\left[\int_0^\Theta(\Theta-t)\int_0^L\left(L^2-x^2\right)K(x,t)N(x,t)\,d\,x\,d\,t-\frac{2}{3}\Theta L^3-\right.$$
$$\left.-2\int_0^\Theta(\Theta-t)\int_0^L x(L-x)K(x,t)N(x,t)\,d\,x\,d\,t\right]^{-1}, \tag{7a}$$

$$\alpha_1=\left[2\Theta\int_0^L\int_0^x(x-v)\,f(v)d\,v\,d\,x+\Theta L\int_0^L(L-x)\,f(x)d\,x+2C_0\int_0^\Theta(\Theta-t)\int_0^L D(x,t)\,d\,x\,d\,t\right]\times$$
$$\times\left[\int_0^\Theta(\Theta-t)\int_0^L\left(L^2-x^2\right)K(x,t)N(x,t)\,d\,x\,d\,t+\int_0^\Theta(\Theta-t)\int_0^L D(x,t)\,d\,x\,d\,t+L^3\frac{5\Theta}{12}-\right.$$
$$-\int_0^\Theta(\Theta-t)\int_0^L x(L-x)K(x,t)N(x,t)\,d\,x\,d\,t+\frac{L}{2}\int_0^\Theta(\Theta-t)\int_0^L(L-x)K(x,t)N(x,t)d\,x\,d\,t-$$
$$\left.-\int_0^\Theta(\Theta-t)\int_0^L D(x,t)\,d\,x\,d\,t\right]. \tag{7b}$$

The second-order approximation of the considered concentration in the framework of the method of averaging of function corrections could be determined by using the following standard procedure: replacement of the considered concentration in the right sides of Eqs. (4) on the sum $C(x,t)\to\alpha_2+C_1(x,t)$ [6-8]. The replacement gives a possibility to obtain the following equations to determine the concentration of the considered medicinal product (for single or continuous infusion, respectively)

$$C_2(x,t)=\alpha_2+C_1(x,t)+\frac{1}{L^2}\left\{\int_0^t\int_0^x D(v,\tau)\,[\alpha_2+C_1(v,\tau)]d\,v\,d\,\tau-\int_0^t\int_0^x(x-v)[\alpha_2+C_1(v,\tau)]\times\right.$$
$$\times\frac{\partial D(v,\tau)}{\partial v}d\,v\,d\,\tau+\int_0^x(x-v)\,f(v)d\,v-\int_0^t\int_0^x(x-v)K(v,\tau)[\alpha_2+C_1(v,\tau)]N(v,\tau)d\,v\,d\,\tau+$$
$$+\int_0^L(L-v)\,[\alpha_2+C_1(v,t)]d\,v+\int_0^t\int_0^L(L-v)[\alpha_2+C_1(v,\tau)]\frac{\partial D(v,\tau)}{\partial v}d\,v\,d\,\tau-\int_0^x[\alpha_2+C_1(v,t)]\times$$
$$\left.\times(x-v)\,d\,v-\int_0^t\int_0^L D(v,\tau)[\alpha_2+C_1(v,\tau)]d\,v\,d\,\tau\right\}, \tag{8a}$$

$$C_2(x,t)=\alpha_2+C_1(x,t)+\frac{1}{L^2}\left\{\int_0^t\int_0^x[\alpha_2+C_1(v,\tau)]\frac{\partial D(v,\tau)}{\partial v}d\,v\,d\,\tau+\int_0^x(x-v)\,f\,(v)\,d\,v-\right.$$
$$-\int_0^t\int_0^x(x-v)K(v,\tau)\,[\alpha_2+C_1(v,\tau)]N(v,\tau)d\,v\,d\,\tau-\int_0^t D(x,\tau)[\alpha_2+C_1(x,\tau)]d\,\tau+$$
$$+C_0\int_0^t D(x,\tau)d\,\tau-\int_0^x(x-v)[\alpha_2+C_1(v,t)]d\,v-\frac{x}{L}\left[\int_0^t\int_0^L[\alpha_2+C_1(v,\tau)]\frac{\partial D(v,\tau)}{\partial v}d\,v\;d\,\tau-\right.$$
$$-\int_0^t\int_0^L(L-v)K(v,\tau)[\alpha_2+C_1(v,\tau)]N(v,\tau)d\,v\,d\,\tau+\int_0^L(L-v)\,f\,(v)d\,v-\int_0^L(L-v)\,\times$$
$$\left.\left.\times\left[\alpha_2+C_1(v,t)\right]d\,v\right]\right\}. \tag{8b}$$

Average value of the second-order approximation of the above concentration α_2 could be calculated by using the following standard relation [6-8]

$$\alpha_2=\frac{1}{L\Theta}\int_0^\Theta\int_0^L[C_2(x,t)-C_1(x,t)]\,d\,x\,d\,t\,. \tag{9}$$

Substitution of relations (8) into relation (9) gives a possibility to obtain the following relations for the required average value α_2 (for single or continuous infusion, respectively)

$$\alpha_2=\left[\frac{1}{2}\int_0^\Theta(\Theta-t)\int_0^L(L+x)^2\,C_1(x,t)\frac{\partial D(x,t)}{\partial x}d\,x\,d\,t-\int_0^\Theta(\Theta-t)\int_0^L(x-v)D(x,t)C_1(x,t)\,d\,x\,d\,t+\right.$$
$$+2\int_0^\Theta(\Theta-t)\int_0^L x^2\,C_1(x,t)\frac{\partial D(x,t)}{\partial x}d\,x\,d\,t-\frac{1}{2}\int_0^\Theta(\Theta-t)\int_0^L(L+x)^2\,K(x,t)C_1(x,t)N(x,t)d\,x\,d\,t-$$
$$-2\int_0^\Theta(\Theta-t)\int_0^L x^2K(x,t)C_1(x,t)N(x,t)d\,x\,d\,t-\frac{1}{2}\int_0^\Theta(\Theta-t)\int_0^L\left(L^2-x^2\right)C_1(x,t)\frac{\partial D(x,t)}{\partial x}d\,x\,d\,t-$$
$$-\int_0^\Theta\int_0^L x(L-x)\,f\,(x)d\,x\,d\,t-L\int_0^\Theta\int_0^L(L-x)C_1(x,t)d\,x\,d\,t+L\int_0^\Theta\int_0^L(L-x)D(x,t)C_1(x,t)\,d\,x\,\times$$
$$\times(\Theta-t)\,d\,t+\frac{1}{2}\int_0^\Theta(\Theta-t)\int_0^L\left(L^2+x^2\right)D(x,t)C_1(x,t)d\,x\,d\,t+2\int_0^\Theta\int_0^L x^2\,C_1(x,t)D(x,t)\,d\,x\,\times$$
$$\left.\times(\Theta-t)\,d\,t\right]\left[\int_0^\Theta(\Theta-t)\int_0^L(x-v)D(x,t)\,d\,x\,d\,t-\frac{1}{2}\int_0^\Theta(\Theta-t)\int_0^L(L+x)^2\,\frac{\partial D(x,t)}{\partial x}d\,x\,d\,t\,+\right.$$
$$+\frac{1}{2}\int_0^\Theta(\Theta-t)\int_0^L(L+x)^2\,K(x,t)N(x,t)\,d\,x\,d\,t+2\int_0^\Theta(\Theta-t)\int_0^L x^2K(x,t)N(x,t)\,d\,x\,d\,t+$$
$$\left.+\Theta^2\,\frac{L^3}{4}+2\int_0^\Theta(\Theta-t)\int_0^L x^2\,\frac{\partial D(x,t)}{\partial x}d\,x\,d\,t\right]^{-1}, \tag{10a}$$

$$\alpha_2=\left[\frac{1}{2}\int_0^\Theta(\Theta-t)\int_0^L(L-x)^2\,K(x,t)C_1(x,t)N(x,t)\,d\,x\,d\,t+\int_0^\Theta(\Theta-t)\int_0^L x^2\,K(x,t)\,C_1(x,t)\,\times\right.$$
$$\times\,N(x,t)\,d\,x\,d\,t-\int_0^\Theta(\Theta-t)\int_0^L(L-x)C_1(x,t)\frac{\partial D(x,t)}{\partial x}d\,x\,d\,t-\frac{\Theta}{2}\int_0^L(L-x)^2\,f\,(x)d\,x-$$
$$-\Theta\int_0^L x^2\,f\,(x)\,d\,x+C_0\int_0^\Theta(\Theta-t)\int_0^L D(x,t)\,d\,x\,d\,t+\int_0^\Theta(\Theta-t)\int_0^L D(x,t)C_1(x,t)d\,x\,d\,t+$$

$$+2\int_0^{\Theta}\int_0^{L}x^2C_1(x,t)\,d\,x\,d\,t-\frac{L}{2}\int_0^{\Theta}(\Theta-t)\int_0^{L}(L-x)K(x,t)C_1(x,t)N(x,t)\,d\,x\,d\,t+\frac{1}{2}\int_0^{\Theta}\int_0^{L}\left(L^2-x^2\right)\times$$

$$\times C_1(x,t)\,d\,x\,d\,t+\Theta\int_0^{L}(L-v)\,f(v)\,d\,v-\int_0^{\Theta}\int_0^{L}x(L-x)C_1(x,t)\,d\,x\,d\,t+\frac{L}{2}\int_0^{\Theta}(\Theta-t)\int_0^{L}C_1(x,t)\times$$

$$\times\frac{\partial D(x,t)}{\partial x}\,d\,x\,d\,t\Bigg]\Bigg[\int_0^{\Theta}(\Theta-t)\int_0^{L}D(x,t)\,d\,x\,d\,t-\frac{1}{2}\int_0^{\Theta}(\Theta-t)\int_0^{L}(L-x)^2\,K(x,t)N(x,t)\,d\,x\,d\,t-$$

$$-\Theta\frac{L^3}{3}-\int_0^{\Theta}(\Theta-t)\int_0^{L}x^2\,K(x,t)N(x,t)\,d\,x\,d\,t+\frac{L}{2}\int_0^{\Theta}(\Theta-t)\int_0^{L}(L-x)K(x,t)N(x,t)\,d\,x\,d\,t-$$

$$-\int_0^{\Theta}(\Theta-t)\int_0^{L}D(x,t)\,d\,x\,d\,t\Bigg]^{-1}. \qquad (10b)$$

Spatio-temporal distribution of concentration of medicinal product 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.

DISCUSSION

In this section we present an analysis of spatio-temporal distribution of concentration of medicinal product in organism. Figs. 1 and 2 shows typical dependences of the considered concentration on time. Figs. 3 and 4 shows typical dependences of the considered concentration on coordinate. The obtained dependences qualitatively coincides with analogous experimental distributions. Increasing of temperature of organism leads to acceleration of interaction of the considered medicinal product with other substances of the organism.

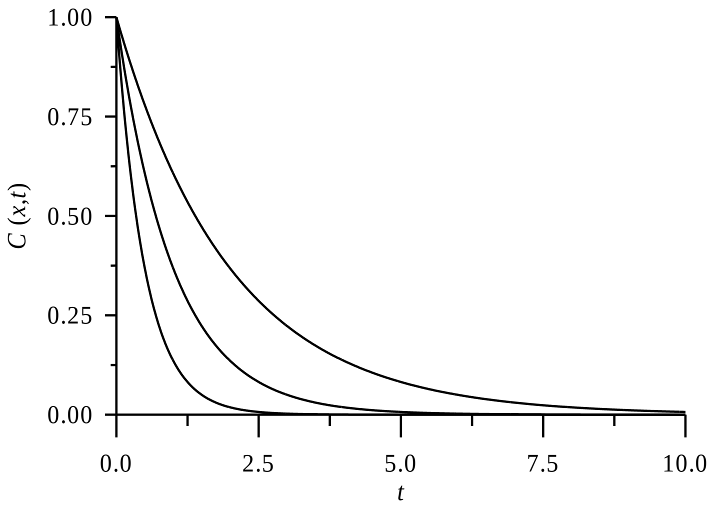

Fig 1: Typical dependences of concentration of considered product on time at a single infusion of medicinal product

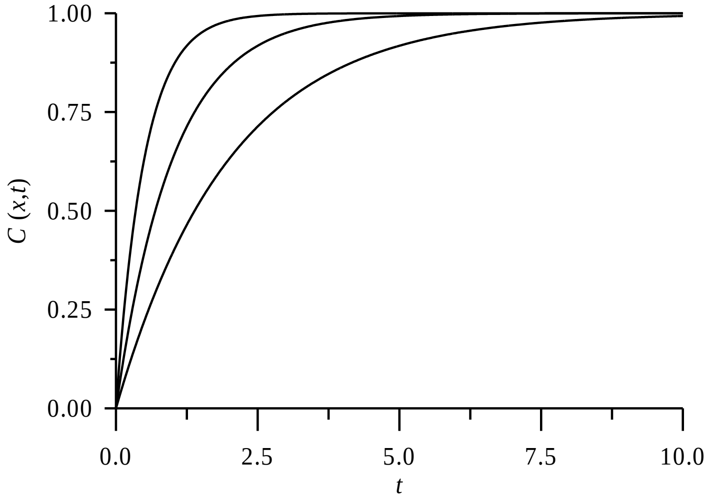

Fig 2: Typical dependences of concentration of considered product on time at continuous infusion of medicinal product

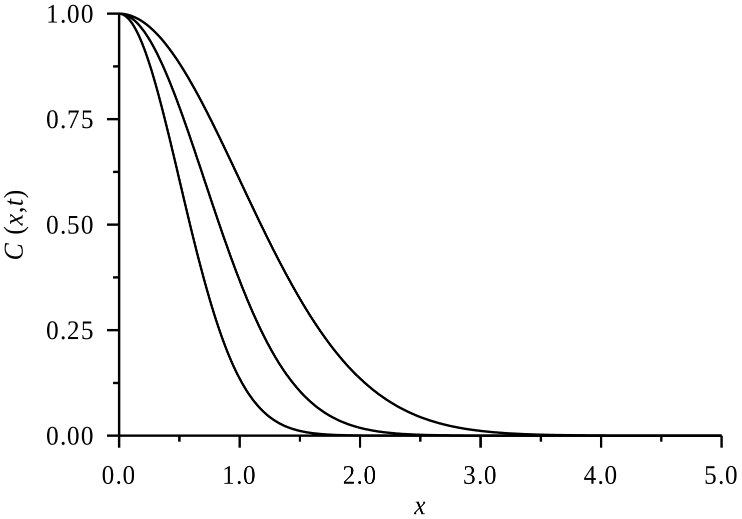

Fig 3: Typical dependences of concentration of considered product on coordinate at a single infusion of medicinal product

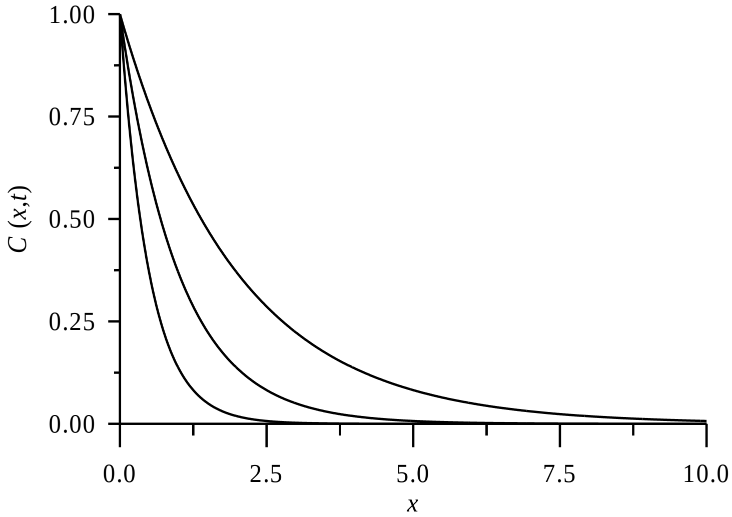

Fig. 4: Typical dependences of concentration of considered product on coordinate at continuous infusion of medicinal product

CONCLUSION

In this paper we consider analysis of transport of a medicinal product in an organisms. The analysis based on estimation of spatio-temporal distribution of concentration of the above product. We introduce an analytical approach for analysis of the above transport with account changing of it's conditions. We consider possibility to accelerate and decelerate transport of medicinal product in organisms.

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