MATHEMATICAL ANALYSIS OF A THREE COMPARTMENT CATENARY MODEL

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Abstract - Mathematical biology is a modern research area, forming part of biology and mathematics discipline. Mathematical modeling gives an idea how to transform physical situation into mathematical language in the form of differential equations. This paper is on pharmacokinetics which is considering a part of mathematical biology deals with distribution of drugs or tracers among the various compartments (parts) of the human body. In this model I explained the formation of differential equations and computed the distribution of drug concentration in three different compartments with respect to time.

Keywords – Pharmacokinetics, Catenary model, Eigen values, Routh-Hurwitz condition.

1: INTRODUCTION

In pharmacokinetics or drug kinetics or the distribution of a drug between various parts of the body, each part of the body is treated as one compartment [1]. These compartments are named as consisting of cells, intestinal fluids and blood vessels etc., [2,3] .Models of the type discussed are called compartment models, they are used extensively in medical, biological[4] and ecological studies. Mathematical models in pharmacokinetics [5,6,7,8] are also considered as Bio mathematical models. Because of chain like appearance of the graph (Fig1), such a compartment models called catenary model.

In this paper , I considered three compartments as one is central compartment (Blood vessels), second Intestinal fluid and third compartment is tissue compartment (cells). In this compartment model drug distributes most rapidly into first or central compartment, less rapidly into second and finally very slowly into the third compartment. In practice, an initial injection of labeled material into blood would not be instantaneously mixed, but it circulates and recirculates among the various compartments of the body.

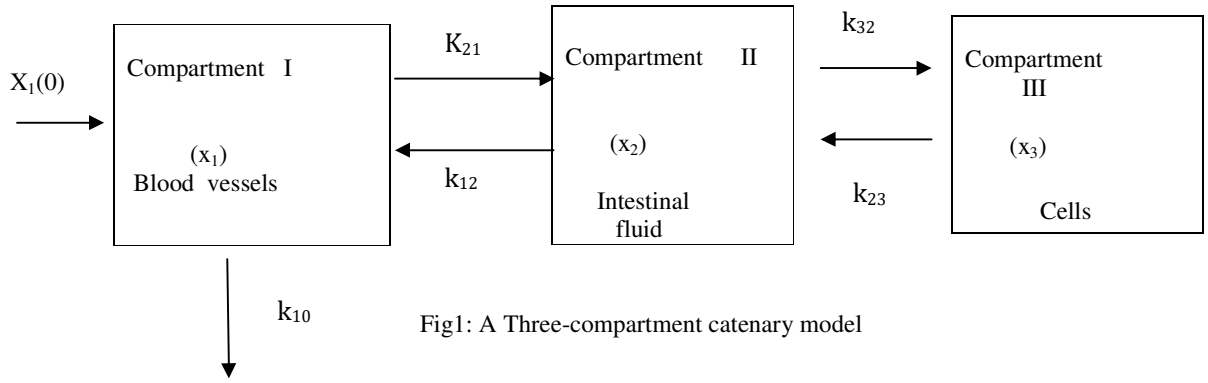

Fig1: A Three-compartment catenary model

2: MODEL BLOCK – DIAGRAMS and MODEL EQUATIONS

The rate of change of drug in compartment I:

The rate of change of drug in compartment I $\dot{x}_1(t)$	=	-	The rate of change of drug from Compartment I to Compartment II $(k_{12}+k_{10})x_1$	+	The rate of reentry of uncovered drug from compartment II to compartment I $(k_{21}\, x_2)$	

The rate of change of drug in compartment II:

The rate of change of drug in compartment II $\dot{x}_2(t)$	=	The rate of entry of drug into compartment II from compartment I $(k_{12}\, x_1)$	-	The rate of reentry of drug from compartment II to compartment I for recycling $(k_{21}\, x_2)$	-	The rate of entry of drug from compartment II to compartment III $(k_{23}\, x_2)$	+	The rate of transfer of drug from compartment II to compartment III $(k_{23}\, x_3)$

The rate of change of drug in compartment III

The rate of change of drug in compartment III $\dot{x}_3(t)$	=	The rate of transfer of drug from compartment II to Compartment III $(k_{23}\, x_2)$	-	The rate of reentry of drug from compartment III to Compartment II $(k_{32}\, x_2)$

The model equations for a three compartment model are given by the following set of three linear ordinary differential equations:

$$\frac{dx_1}{dt} = -(k_{12} + k_{10})x_1 + k_{21}x_2 \quad (1)$$

$$\frac{dx_2}{dt} = k_{12}x_1 - (k_{21} + k_{23})x_2 + k_{23}x_3 \quad (2)$$

$$\frac{dx_3}{dt} = k_{23}x_2 - k_{32}x_3 \quad (3)$$

Where k_{10},k_{12},k_{21}, k_{23} and k_{32} are positive transfer coefficients.

The equations (1), (2), (3) can be put into the of matrix form

The system of equations can be written as $\frac{dX}{dt} = AX$ (4)

$$\frac{d}{dt}\begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} = \begin{bmatrix} -(k_{12} + k_{10}) & k_{21} & 0 \\ k_{12} & -(k_{21} + k_{23}) & k_{32} \\ 0 & k_{23} & -k_{32} \end{bmatrix}\begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} \quad (5)$$

Where X= $\begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix}$ and A= $\begin{bmatrix} -(k_{12}+k_{10}) & k_{21} & 0 \\ k_{12} & -(k_{21}+k_{23}) & k_{32} \\ 0 & k_{23} & -k_{32} \end{bmatrix}$

Let $X = X_0 e^{\lambda t}$ be a trial solution with initial conditions $X(0) = [x_{10} \quad x_{20} \quad x_{30}]^T$

The exponent ' λ' satisfies the characteristic equation of A :

$$\det[A - \lambda I] = 0$$

The characteristic equation for the system is:

$$\lambda^3 + (k_{10} + k_{12} + k_{21} + k_{23} + k_{32})\lambda^2 + [k_{12}k_{23} + (k_{21} + k_{23})k_{10} + (k_{12} + k_{21} + k_{10})k_{32}]\lambda + k_{21}k_{23}k_{10} = 0 \quad (6)$$

Equation (6) is a cubic polynomial of the form

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0 \quad (7)$$

It is evident that $a_1 > 0$ and $a_3 (= k_{21} + k_{23} + k_{10}) > 0$

Clearly the relation $a_1 a_2 > a_3$ satisfies $\Rightarrow$ $a_3(a_1 a_2 - a_3) > 0$

If $a_1>0$, $a_3>0$, and $a_3(a_1a_2-a_3)>0$ are necessary and sufficient conditions to satisfies Routh-Hurwitz condition. Hence equation (7) satisfies Routh-Hurwitz condition.

Hence, the three Eigen roots $\lambda_1,\lambda_2,\lambda_3$ of the characteristic equation (7) are necessary and sufficient conditions for all roots of the characteristic equation to have negative real part.

Therefore, let the solution for $x_1(t)$ is

$$x_1(t) = c_1e^{\lambda_1 t} + c_2e^{\lambda_2 t} + c_3e^{\lambda_3 t} \tag{7}$$

$$\dot{x}_1(t) = c_1\lambda_1e^{\lambda_1 t} + \lambda_2c_2e^{\lambda_2 t} + \lambda_3c_3e^{\lambda_3 t} \tag{8}$$

Now from the equation (1), we can write

$$x_2(t) = \frac{1}{k_{21}}\left[\dot{x}_1(t) + (k_{12}+k_{10})x_1\right]$$

$$= \frac{1}{k_{21}}\left[\begin{array}{l} c_1\lambda_1e^{\lambda_1 t} + \lambda_2c_2e^{\lambda_2 t} + \lambda_3c_3e^{\lambda_3 t} \\ +(c_1e^{\lambda_1 t} + c_2e^{\lambda_2 t} + c_3e^{\lambda_3 t})(k_{12}+k_{10}) \end{array}\right]$$

$$= \frac{1}{k_{21}}\left[\begin{array}{l} (k_{12}+k_{10}+\lambda_1)c_1e^{\lambda_1 t} + (k_{12}+k_{10}+\lambda_2)c_2e^{\lambda_2 t} \\ +(k_{12}+k_{10}+\lambda_3)c_3e^{\lambda_3 t} \\ \end{array}\right] \tag{9}$$

Equation (9) written as

$$\dot{x}_2(t) = \frac{1}{k_{21}}\left[\begin{array}{l} (k_{12}+k_{10}+\lambda_1)c_1\lambda_1e^{\lambda_1 t} + (k_{12}+k_{10}+\lambda_2)c_2\lambda_2e^{\lambda_2 t} \\ +(k_{12}+k_{10}+\lambda_3)c_3\lambda_3e^{\lambda_3 t} \\ \end{array}\right] \tag{10}$$

Now from the equation (2), we can write

$$x_3(t) = \frac{1}{k_{32}}\left[\dot{x}_2(t) - k_{12}x_1 + (k_{23}+k_{21})x_2\right]$$

$$= \frac{1}{k_{21}k_{32}} \begin{bmatrix} \begin{bmatrix} (k_{12}+k_{10}+\lambda_1)c_1\lambda_1 e^{\lambda_1 t} + (k_{12}+k_{10}+\lambda_2)c_2\lambda_2 e^{\lambda_2 t} \\ +(k_{12}+k_{10}+\lambda_3)c_3\lambda_3 e^{\lambda_3 t} \end{bmatrix} \\ -k_{21}k_{12}\left(c_1 e^{\lambda_1 t} + c_2 e^{\lambda_2 t} + c_3 e^{\lambda_3 t}\right) \\ +(k_{23}+k_{21}) \begin{bmatrix} (k_{12}+k_{10}+\lambda_1)c_1 e^{\lambda_1 t} \\ +(k_{12}+k_{10}+\lambda_2)c_2 e^{\lambda_2 t} \\ +(k_{12}+k_{10}+\lambda_3)c_3 e^{\lambda_3 t} \end{bmatrix} \end{bmatrix} \quad (11)$$

3: NUMERICAL COMPUTATION

Let the Initial values: x_{10}=50, x_{20}=30, x_{30}=10

Consider the random values of transfer coefficients (k_{10}, k_{12}, k_{21}, k_{23}, k_{32}) as follows

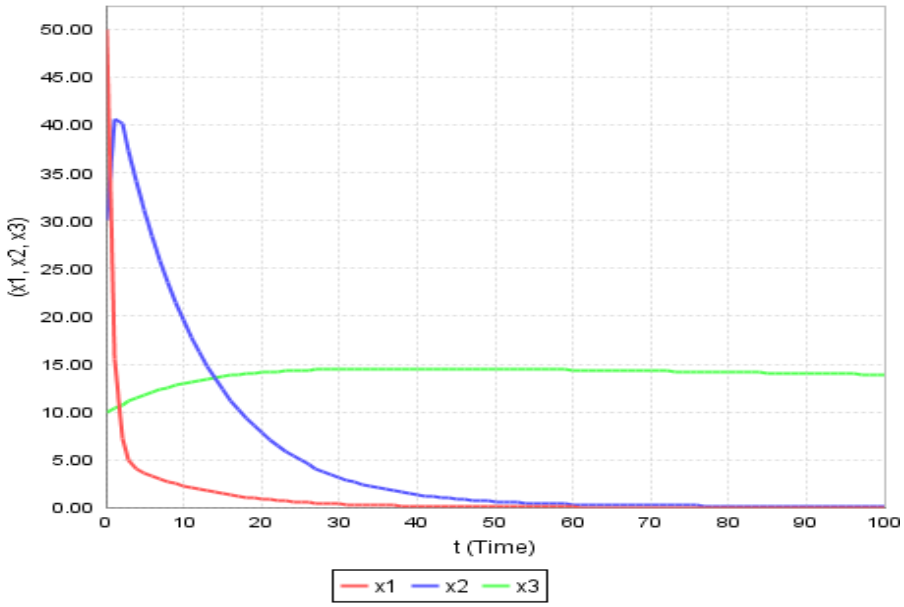

Fig1: K_{10} =0 .185, k_{12}=0 .175, k_{21}= 0.15, k_{23}= 0.01, k_{32}=0 .001

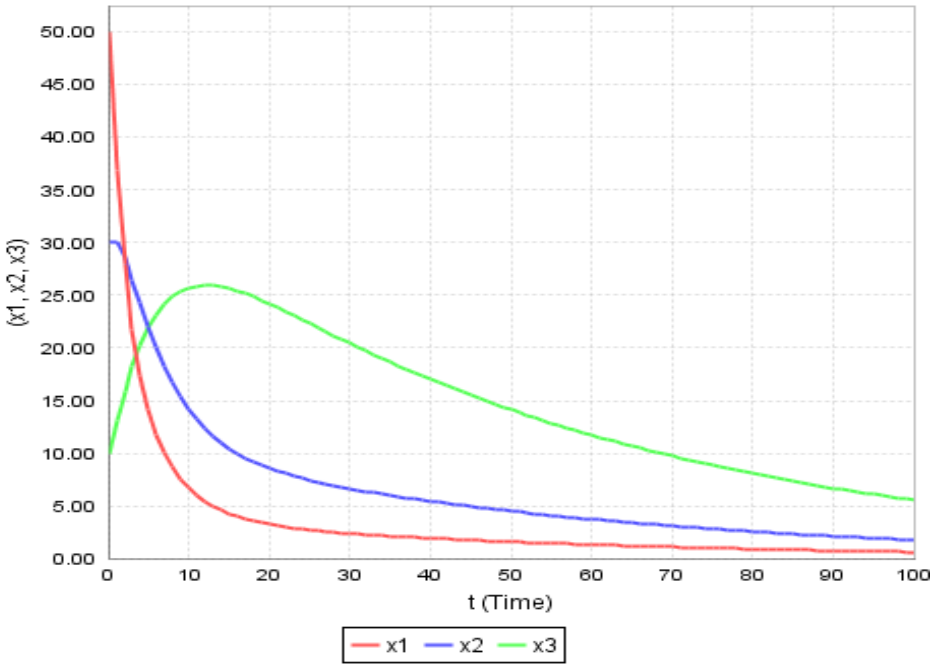

Fig2: K_{10}=0.233, K_{12}=0.166, K_{21}=0.136, K_{23}=0.123, K_{32}=0.05

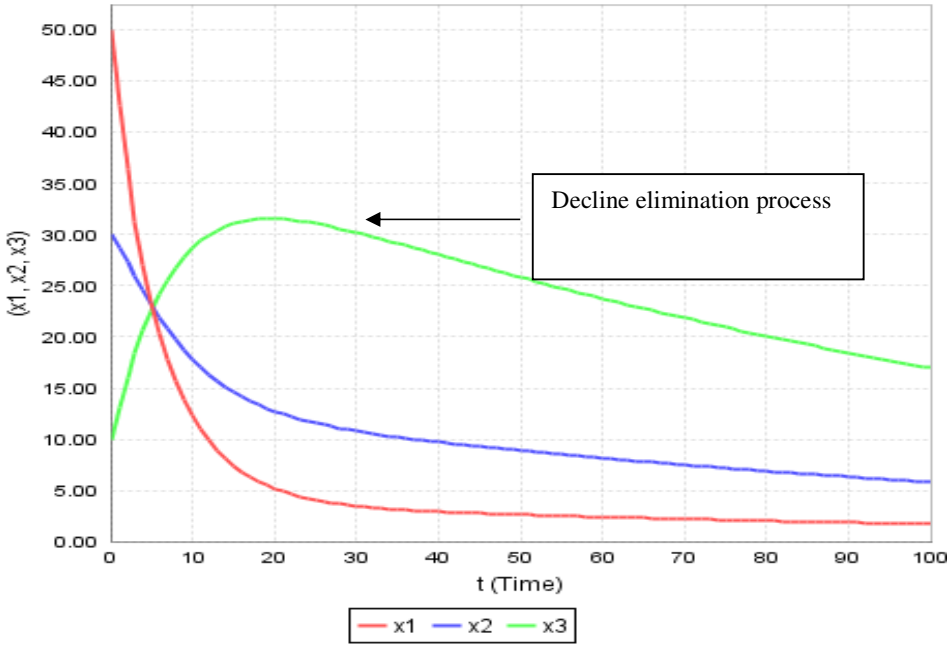

Fig3:K_{10}=0.12, K_{12}=0.075, K_{21}=0.055, K_{23}=0.127, K_{32}=0.052

4: CONCLUSIONS

From the figure1, it is observed that drug concentration in the second compartment sudden rise and slowly decreases and comes to stable over a time period. From the figure2, it is identified that drug concentration in the third compartment gradually increases and slowly decreases and comes to stable over a time and also it is noticed that from the figure3, the elimination process in the compartments has a common meeting time.

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