VOL. 9, NO. 11, NOVEMBER 2014 ISSN 1819-6608
ARPN Journal of Engineering and Applied Sciences

www.arpnjournals.com

A THREE COMPARTMENT MATHEMATICAL MODEL OF LIVER

V. Anand[1] and N. Ch. Pattabhi Ramacharyulu[2]
[1]Faculty of Mathematics, R D colleges, Hanamkonda, Warangal, India
[2]Department of Mathematics, National Institute of Technology, Warangal, India
E-Mail: valupadas2@gmail.com

ABSTRACT

Mathematical modeling of pharmacokinetics is an important and growing field in drug development. Pharmacokinetics concerns with the distribution of drugs, chemicals or tracers by a fluid among the various compartment of human body. In this work we discuss the compartment mathematical model of liver function based on fundamental biological and pharmacological principles. Here we present behavior of thyroxin, iodine and bile over a period of time.

Keywords: liver, mathematical model, differential equations, pharmacokinetics, compartment model.

INTRODUCTION

Pharmacokinetics concerns with the distribution of drugs, chemicals or tracers by a fluid among the various compartment of human body [1]. The compartments could be fictitious spaces through which biomaterials pass through various locations (compartments of the body). The present investigation is on a three compartment model related to the liver in human body [2, 3, 4]. When a chemical, thyroxin is injected into the blood stream it is carried to the liver. The liver converts thyroxin to iodine, which is absorbed into the bile [5]. However, neither the conversion nor the absorption of which into the bile, would occur instantaneously. Some of the thyroxin (unconverted) reenters into the blood stream and gets recirculated. The Mathematical model is composed of three compartments: Compartment I, Compartment II and compartment III which represent blood vessels, liver and bile respectively as shown in the Figure-1.

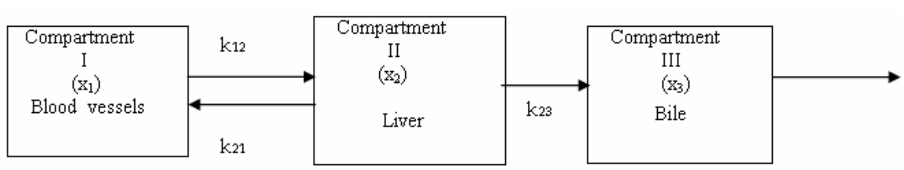

Figure-1. Mathematical model for liver.

Notations adopted:

$x_1(t)$ = the quantity of thyroxin in the blood vessel at the instant time 't'
$x_2(t)$ = the quantity of iodine in the liver
$x_3(t)$ = the quantity of iodine absorbed in to the bile
k_{12} = The rate of conversion of thyroxin into iodine
k_{21} = The rate of the quantity of unabsorbed thyroxin sent out for recycling from
Compartment II to compartment I
k_{23} = rate of absorption of Iodine from compartment II into bile compartment III

x_{10}, x_{20} and x_{30} are initial the values of x_1 , x_2 , x_3 respectively and the rate constants
x_{12} , x_{21} and x_{23} are all positive.

It is assumed that the rate $\dot{x}_1(t)$ at which thyroxin is converted to iodine as it transferred from compartment I to compartment II is proportional to concentration $x_1(t)$ of thyroxin in the compartment I.

MODEL BLOCK - DIAGRAMS AND MODEL EQUATIONS

The rate of change of thyroxin in compartment I $\dot{x}_1(t)$	= -	The rate of conversion of thyroxin into Iodine from compartment 1 to compartment II (k_{12} x_1)	+	The rate of reentry of uncovered thyroxin from compartment II to compartment I (k_{21} x_2)

$$\Rightarrow \frac{dx_1}{dt} = -k_{12}x_1 + k_{21}x_2\,,\ x_1(0) = x_{10} \tag{1}$$

VOL. 9, NO. 11, NOVEMBER 2014 ISSN 1819-6608
ARPN Journal of Engineering and Applied Sciences

www.arpnjournals.com

The rate of absorption of Iodine compartment II $\dot{x}_2(t)$	=	The rate of entry of thyroxin into compartment II from compartment I $(k_{12}x_1)$	-	The rate of reentry from compartment II to compartment I for reclying $(k_{21}x_2)$	-	The rate of transfer of Iodine from compartment II to compartment III $(k_{23}x_2)$

$$\Rightarrow \frac{dx_2}{dt} = k_{12}x_1 - (k_{21} + k_{23})x_2,\ x_2(0) = x_{20} \tag{2}$$

The rate of change of material in compartment III compartment II $\dot{x}_3(t)$	=	The rate of transfer compartment II to Compartment III $(k_{23}x_2)$

$$\Rightarrow \frac{dx_3}{dt} = k_{23}x_2,\ x_3(0) = x_{30} \tag{3}$$

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

$$\frac{d}{dt}[X] = AX \tag{4}$$

where $A = \begin{bmatrix} -k_{12} & k_{21} & 0 \\ k_{12} & -(k_{21}+k_{23}) & 0 \\ 0 & k_{23} & 0 \end{bmatrix}$ and $X = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix}$ (5)

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

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

$$\det|A - \lambda I| = 0$$

$$i,e;\lambda\left[\lambda^2 + (k_{12}+k_{21}+k_{23})\lambda + k_{12}k_{23}\right] = 0 \tag{6}$$

the roots of which are λ=0 and $\lambda_2, \lambda_3 = -k \pm M$ (7)

where

$$k = \frac{k_{12}+k_{21}+k_{23}}{2}$$

and

$$M = \sqrt{k^2 - k_{12}k_{23}}$$

$$= \sqrt{\frac{(k_{12}-k_{23})^2 + k_{21}(k_{12}+k_{21})}{4}} > 0 \tag{8}$$

Evidently M is real and less than k. Hence λ_2 and λ_3 are both real and negative roots.

The solutions of equations (1), (2), (3) can be written as

$$x_1(t) = A + Be^{\lambda_2 t} + Ce^{\lambda_3 t} \tag{9}$$

$$x_2(t) = \frac{1}{k_{21}}\left[Ak_{12} + B(\lambda_2 + k_{12})e^{\lambda_2 t} + C(\lambda_3 + k_{12})e^{\lambda_3 t}\right] \tag{10}$$

$$x_3(t) = \frac{k_{23}}{k_{21}}\left[Atk_{12} + \frac{B(\lambda_2+k_{12})e^{\lambda_2 t}}{\lambda_2} + \frac{C(\lambda_3+k_{12})e^{\lambda_3 t}}{\lambda_3} + E\right] \tag{11}$$

where A, B, C and E are arbitrary constants. Using the initial conditions, we get the values of the constants

$$A = 0 \tag{12}$$

$$B = \frac{x_{10}(k_{12}+\lambda_3) - k_{21}x_{20}}{\lambda_3 - \lambda_2} \tag{13}$$

$$C = \frac{k_{21}x_{20} - (k_{12}+\lambda_2)x_{10}}{\lambda_3 - \lambda_2} \tag{14}$$

and

$$E = \frac{k_{21}}{k_{23}}(x_{10} + x_{20} + x_{30}) \tag{15}$$

Substituting these values in (1.1), (1.2), (1.3) we get after some simplification

$$x_1(t) = \frac{x_{10}(k_{12}+\lambda_3) - k_{21}x_{20}}{\lambda_3 - \lambda_2}e^{\lambda_2 t} + \frac{k_{21}x_{20} - (k_{12}+\lambda_2)x_{10}}{\lambda_3 - \lambda_2}e^{\lambda_3 t}$$

$$= \frac{e^{-kt}}{M}\left[\{k_{21}x_{20} - x_{10}(k_{12}+k)\}\sinh Mt + (Mx_{10})\cosh Mt\right] \tag{16}$$

VOL. 9, NO. 11, NOVEMBER 2014 ISSN 1819-6608
ARPN Journal of Engineering and Applied Sciences

$$x_2(t) = \frac{1}{k_{21}}\left[\frac{x_{10}(k_{12}+\lambda_3)-k_{21}x_{20}}{\lambda_3-\lambda_2}(\lambda_2+k_{12})e^{\lambda_2 t} + \frac{k_{21}x_{20}-x_{10}(k_{12}+\lambda_2)}{\lambda_3-\lambda_2}(\lambda_3+k_{12})e^{\lambda_3 t}\right]$$

$$= \frac{e^{-kt}}{M}\left[(2x_{10}k_{12}-kx_{20})\sinh Mt + (Mx_{20})\cosh Mt\right] \tag{17}$$

$$x_3(t) = \frac{k_{23}}{k_{21}}\left[\frac{x_{10}(k_{12}+\lambda_3)-k_{21}x_{20}}{(\lambda_3-\lambda_2)\lambda_2}(\lambda_2+k_{12})e^{\lambda_2 t} + \frac{k_{21}x_{20}-x_{10}(k_{12}+\lambda_2)}{(\lambda_3-\lambda_2)\lambda_3}(\lambda_3+k_{12})e^{\lambda_3 t}\right] + (x_{10}+x_{20}+x_{30})$$

$$= \frac{e^{-kt}}{M}\left[\{k_{23}x_{20}-k(x_{10}+x_{20})\}\sinh Mt - M(x_{10}+x_{20})\cosh Mt\right] + (x_{10}+x_{20}+x_{30}) \tag{18}$$

The variations of $x_1(t)$, $x_2(t)$ and $x_3(t)$ Vrs 't' are illustrated for a select range of values of k_{12}, k_{21}, k_{23} (vide Figure-2 to Figure-5) and for the initial values $x_{10} = 150$, $x_{20} = 125$ and $x_{30} = 65$ of thyroxin, iodine and bile, respectively.

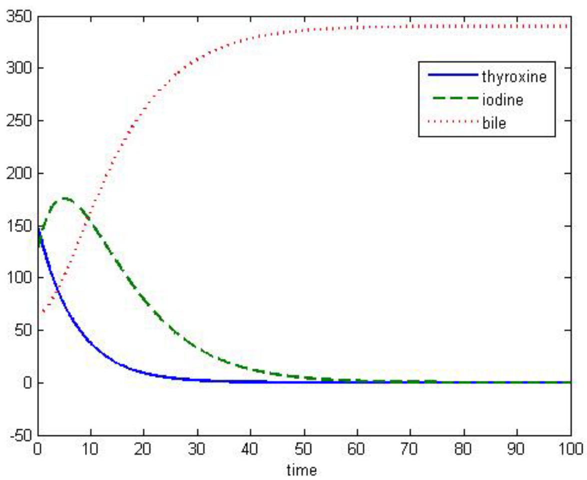

Figure-2. Variation of thyroxin, iodine, bile for the transfer coefficients k12=0.185 k_{21}=0.056 and k_{23}=0.006.

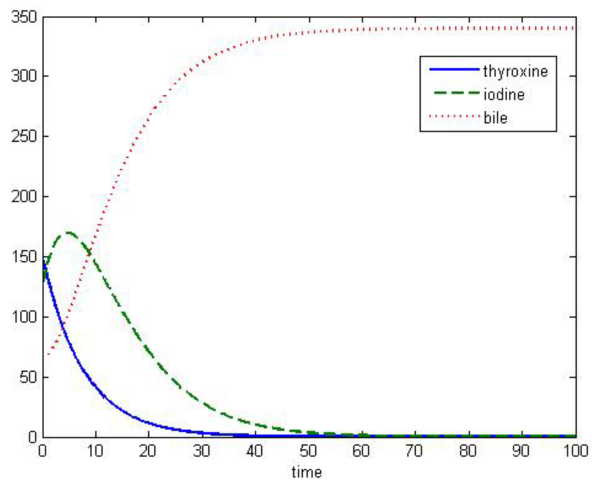

Figure-3. Variation of thyroxin, iodine bile for for the transfer coefficients k12=0.185 k_{21}=0.0511 and k_{32}=0.0001.

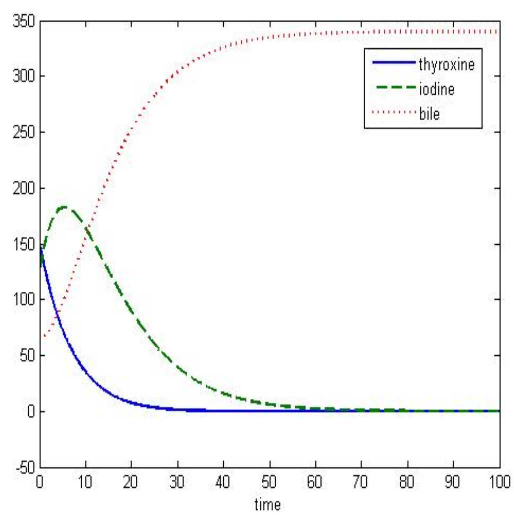

Figure-4. Variation of thyroxin, iodine, bile for the transfer coefficients k_{12}=0.185, k_{21}=0.0511 and k_{23}=0.0001.

VOL. 9, NO. 11, NOVEMBER 2014 ISSN 1819-6608
ARPN Journal of Engineering and Applied Sciences

www.arpnjournals.com

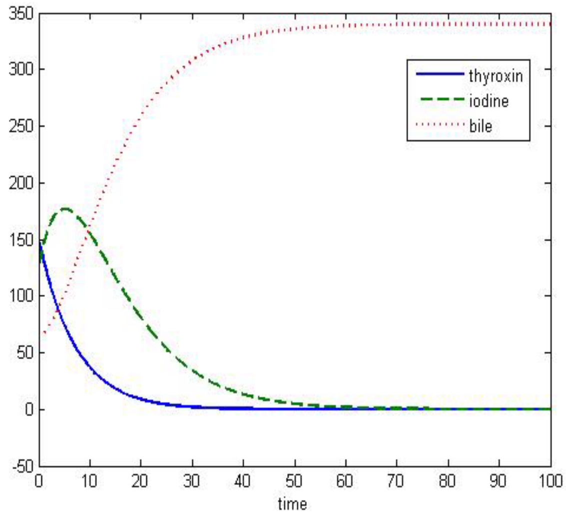

Figure-5. Variation of thyroxin, iodine, bile for the transfer coefficients k_{12}=0.185, k_{21}=0.055 and k_{23}=0.0005.

CONCLUSIONS

Thyroxin monotonically decreases reaching zero level. Iodine initially rises to reach a maximum and falls asymptotically to approach to zero as is the case with thyroxin. The bile increase monotonically approaches asymptotic level.

Incipient variations of $x_1(t)$, $x_2(t)$ and $x_3(t)$ (i.e.; variations for small range time't')

It is know

$\cosh Mt = 1 + \frac{(kt)^2}{2!} + O(t^3)$ and $\sinh Mt = kt + O(t^3)$

Neglecting term of O (t^3), we get

$$x_1 = x_{10} + (k_{21}x_{20} - x_{10}k_{12})t + \frac{1}{2}\left[(k_{12}+k_{21})(x_{10}k_{12} - k_{21}x_{20})\right] t^2 \qquad (19)$$

$$x_2 = x_{20} + (k_{12}x_{10} - kx_{20})2t + \frac{1}{2}\left[x_{20}(k_{12}k_{23} + k^2) - 2kk_{12}x_{10}\right]t^2 \qquad (20)$$

$$x_3 = x_{30} + (x_{20}k_{23})t + \frac{k_{23}}{2}\left[(x_{10}k_{12}) - (k_{12}+k_{23})x_{20}\right]t^2 \qquad (21)$$

The variations of $x_1(t)$, $x_2(t)$ and $x_3(t)$ Vrs small time 't' are illustrated for a select range of values of k_{12}, k_{21}, k_{23} (vide Figure-6 to Figure-9) and for the initial values $x_{10} = 150$, $x_{20} = 125$ and $x_{30} = 65$ of thyroxin, iodine and bile, respectively.

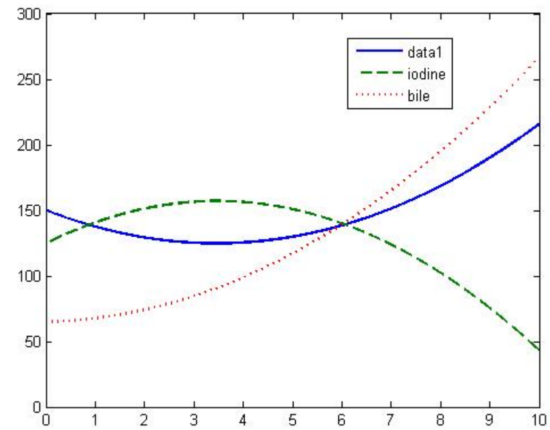

Figure-6. k_{12}=0.185, k_{21}=0.105, k_{23}=0.006.

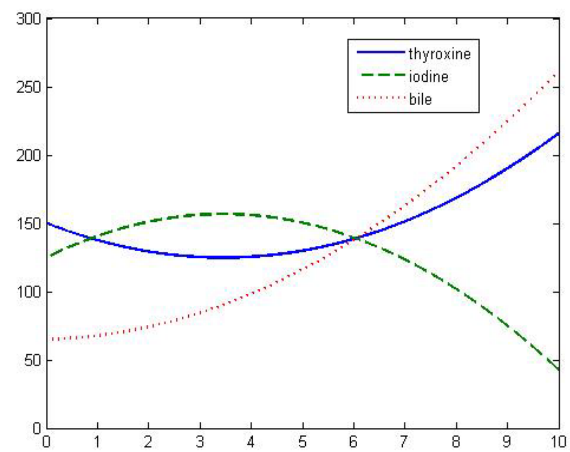

Figure-7. k_{12}=0.185, k_{21}=0.105, k_{23}=0.007.

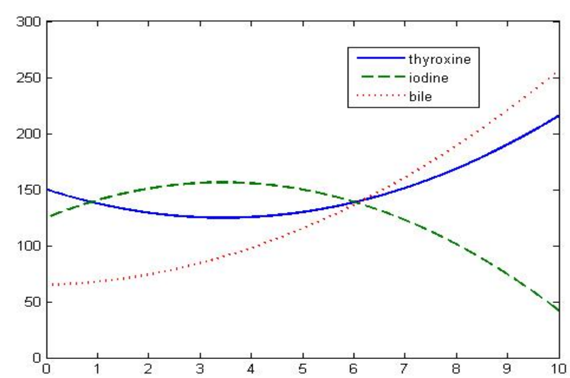

Figure-8. k_{12}=0.185, k_{21}=0.105, k_{23}=0.008.

VOL. 9, NO. 11, NOVEMBER 2014 ISSN 1819-6608
ARPN Journal of Engineering and Applied Sciences

www.arpnjournals.com

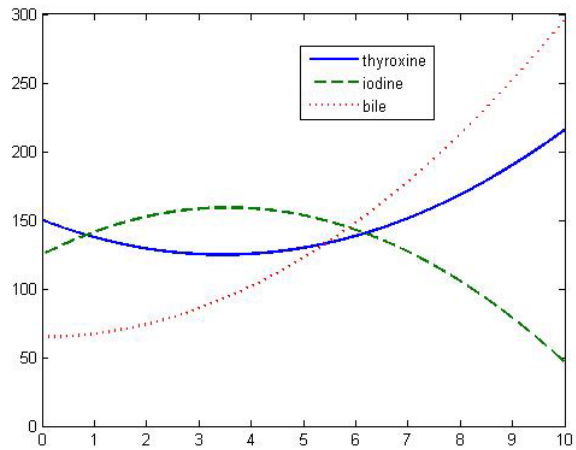

Figure-9. k_{12}=0.185, k_{21}=0.105, k_{23}=0.0001.

Asymptotic variation of $x_1(t)$, $x_2(t)$ and $x_3(t)$ (variation for large range time't')

In this case e^{Mt} dominates over e^{-Mt} (since M>0) and

$\cosh Mt \approx \frac{e^{Mt}}{2}$ and $\sinh Mt \approx \frac{e^{Mt}}{2}$

Hence the asymptotic expression for $x_1(t)$, $x_2(t)$, $x_3(t)$ are

$$x_1 = \frac{e^{-t(K-M)}}{2M}\left[(x_{20}k_{21} + x_{10}(M + K - k_{12})\right] \qquad (22)$$

$$x_2 = \frac{e^{-t(K-M)}}{2M}\left[(2x_{10}k_{12} + x_{20}(M - K)\right] \qquad (23)$$

$$x_3 = \frac{e^{-t(K-M)}}{2M}\left[(x_{20}k_{23} - (x_{10} + x_{20})(M + K)\right] + (x_{10} + x_{20} + x_{30}) \qquad (24)$$

CONCLUSIONS

For large range time 't', each of $x_1(t)$, $x_2(t)$ and $x_3(t)$ decrease exponentially with the Characteristic time $\frac{1}{k - \sqrt{k^2 - k_{12}k_{23}}}$.

REFERENCES

[1] J.N. Kapur. 1985. Mathematical models in Biology and Medicine. Affiliated east-west press pvt. Ltd. pp. 316-317.

[2] Evert C.F and M.F. Randal. 1970. Formulation and computation of compartment models. J. pharm. Sci. 9(3): 102-114.

[3] Jacquez John A. 1972. Compartment analysis in biology and medicine. New York:Elsevier Scientific publishing company.

[4] J.M. Watt and Andrew Young. 1962. An attempt to simulate the liver on a computer. Computer. Journal. 5: 221-227.

[5] Geoffery Gordon. 1999. System simulation. Prentice-hal India. pp. 34-36.