Career Point International Journal of Research(CPIJR)
©2022 CPIJR | Volume 2 | Issue 1 | ISSN : 2583-1895

Application of Kamal Transformation to Certain Pharmacokinetic Equations

Chander Prakash Samar[1] , Dr. Hemlata Saxena[2]

Research Scholor, Department of mathematics, Career Point University Kota (Rajasthan), India cpsamar1986@gmail.com
Professor, Department of mathematics, Career Point University Kota (Rajasthan), India saxenadrhemlata@gmail.com

***Abstract*— In the present paper we consider mathematical model in term of a differential equation in field of pharmacy. Pharmacokinetic model is the one in which drugs in the body are in a dynamic state. Calculus is a significant mathematics tool for investigating drug movement quantitatively. Our Differential equation with in two compartments is used to relate the absorptions of drugs in various body organs over time. Integrated equations are regularly used to model the cumulative therapeutic or toxic reactions of medicine within the body. Differential calculus involves finding the rate at which a variable measure is changing. Solve this mathematical model with the help of Kamal transformation.**

***Keywords*— Derivatives, Differential Equation, Kamal Transform, Inverse Kamal Transform.**

Introduction

Drug concentration analysis in various biological compartments is performed using the pharmacokinetic models [9–11]. (plasma compartment, tissue compartment, deep-tissue compartment, and mammillary compartment). For the analysis of drug distribution in the biological body [12-14] one among them, the mammillary compartment model is usually used. According to the distribution of the drug in the body, this compartment model can be divided into one, two, three, four, etc. compartment models [15]. Pharmacokinetic parameters are required in the compartment model to predict drug disposition and biological half-life in order to study and comprehend distinct compartment models. The distribution and elimination processes are predicted by the pharmacokinetic parameters and biological half-life. To generate a pharmacological reaction, the drug must be present in the body at an effective concentration. There is no pharmacological response to treat the disease if the drug's plasma concentration declines below the effective concentration [16]. Moreover, a higher plasma drug concentration results in toxic effects. Therefore, while administering a drug to patients, the dose and dose interval are significant parameters. The pharmacokinetic factors are related to the dosage regimen (dose and dose interval) (absorption rate constant, elimination rate constant and biological half-life). The mammillary compartment model [17–18] states that when a drug is administered intravenously as a bolus dosage, all of the drugs are initially present in the plasma compartment (central compartment). However, as time passes and drugs are transported to the peripheral compartment, the concentration of drugs in the central compartment steadily decreases.

Complex rate expressions can be solved with easily using standard algebraic procedures according to the Laplace transform. Considering a one-compartment body model, it is accurate. If the two-compartment body model is involved, as we can see in [3], the anti-Laplace of the resulting convoluted transformations may only be obtained in a comprehensive table of Laplace transforms. Using a two-compartment pharmacokinetic model as well as the Kamal Transformation, this method for solving linear differential equations of the first order is illustrated.

We can take set A the function is defined Kamal Transform

$$A = \left\{ f: |f(t)| < Qe^{\frac{|t|}{\eta}} \text{ if } t \in (-1)^j.\ [0,\infty], j = 1,2; (Q, \eta_1, \eta_2 > 0) \right\}$$

Where Q is constant and η_1, η_2 can be finite or infinite [7]. The integral equation

$$G(p) = Kf(t) = \int_0^\infty e^{\frac{-t}{p}} f(t)dt, \quad p \in (\eta_1, \eta_2)$$

Kamal transform of the derivatives of the function

If $K\{F(t)\} = G(p)$

$$K\{F'(t)\} = \frac{1}{p}G(p) - F(0)$$

Pharmacokinetics describes the rate and extent of a drug's di stribution to various tissues and, consequently, the rate of th e drug's elimination.Pharmacokinetics can be reduced to mat hematical equations that describe how a drug is distributed a ll through the body, maintaining a net steady state as it move s from absorption and distribution through metabolism and-excretion.

I. TWO-COMPARTMENTAL MODEL EQUATION

See [3] for information on a medication that enters the body by an unique first order absorption process (normally via the oral or intramuscular routes) and distributes throughout the body using a two compartment model. The body was divided into central and peripheral compartments using the pharmacokinetic 2-compartment model. The plasma and tissues make up the central compartment (compartment 1), where the drug is distributed almost instantly. Wherever the drug supply is slower, as seen in [2], a tissue is present in the peripheral compartment (compartment 2).

Two Compartment Model

The differential equations below are used in a two-compartment model equation to determine how a drug is distributed and eliminated from the body

$$\frac{dy_1}{dt} = K_{21}y_2 - K_{12}y_1 - K_{10}y_1 \ \ldots \quad (1)$$

$$\frac{dy_2}{dt} = K_{12}y_1 - K_{21}y_2 \ \ldots \quad (2)$$

Taking kamal transform of (1) and (2) both the sides, can be transformed into linear equation

$$K\{y'_1\} = K_{21}K(y_2) - K_{12}K(y_1) - K_{10}K(y_1)$$

$$\frac{1}{p}y_1 - y_1(0) = K_{21}K(y_2) - K_{12}K(y_1) - K_{10}K(y_1)$$

$$\left(\frac{1}{p} + K_{12} + KL_{10}\right)y_1 - K_{21}y_2 = y_1(0) \ \ldots \quad (3)$$

$$K\{y'_2\} = K_{12}y_1 - K_{21}y_2$$

$$\frac{1}{p}y_2 - y_2(0) = K_{12}y_1 - K_{21}y_2$$

$$\left(\frac{1}{p} + K_{21}\right)y_2 - K_{12}y_1 = y_2(0) \ \ldots \quad (4)$$

Applying Crammer's Rule to solve equation (3) and (4)

$$\Delta = \begin{vmatrix} \frac{1}{p} + K_{12} + K_{10} & -K_{21} \\ -K_{12} & \frac{1}{p} + K_{21} \end{vmatrix} = \left(\frac{1}{p} + K_{12} + K_{10}\right)\left(\frac{1}{p} + K_{21}\right) - K_{21}K_{12}$$

$$\Delta_1 = \begin{vmatrix} y_1(0) & -K_{21} \\ 0 & \frac{1}{p} + K_{21} \end{vmatrix} = \left(\frac{1}{p} + K_{21}\right)y_1(0)$$

$$\Delta_2 = \begin{vmatrix} \frac{1}{p} + K_{12} + K_{10} & y_1(0) \\ -K_{12} & 0 \end{vmatrix} = K_{12}y_1(0)$$

$$y_1 = \frac{\Delta_1}{\Delta} = \frac{\left(\frac{1}{p} + K_{21}\right)y_1(0)}{\left(\frac{1}{p} + K_{12} + K_{10}\right)\left(\frac{1}{p} + K_{21}\right) - K_{21}K_{12}}$$

$$put \ \ K_{21} + K_{12} + K_{10} = a + b \ and \ \ K_{12}K_{10} = ab$$

$$y_1 = \frac{\Delta_1}{\Delta} = \frac{p\,(1 + pK_{21})y_1(0)}{(1 + ap)(1 + bp)}$$

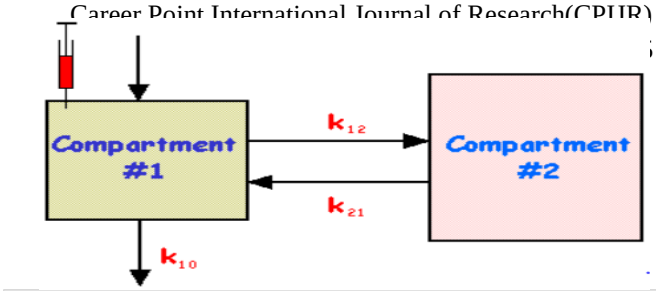
By using partial fraction method, we can write,

$$y_1 = \frac{(K_{21} - a)y_1(0)}{b(a - b)(1 + ap)} + \frac{(b - K_{21})y_1(0)}{b(a - b)(1 + ap)}$$

Now by applying inverse Kamal transform, we have

$$y_1(t) = Ae^{-at} + Be^{-bt} \ \ldots \quad (5)$$

where $A = \frac{(K_{21}-a)y_1(0)}{b(a-b)}$, $B = \frac{(b-K_{21})y_1(0)}{b(a-b)}$



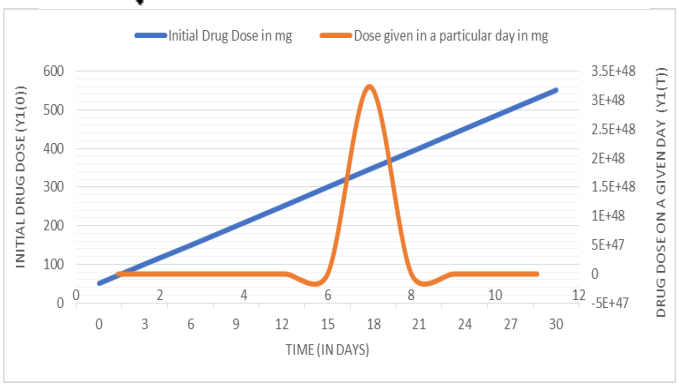
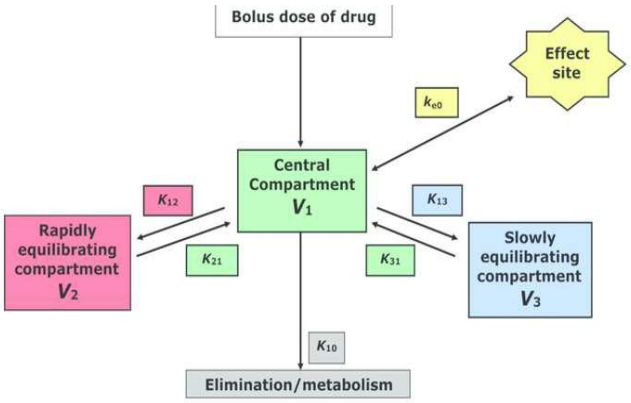


Fig 3.1

Fig 3.1 $Y_1(t)$ is the drug dose on a particular day is in mg. This figure depicts the dose over time graph.

II. COMPARTMENT MODEL EQUATION

The body was separated into a central compartment and two peripheral compartments using the pharmacokinetic three-compartment model. The plasma and tissues constitute up the central compartment (compartment 1), where the drug is essentially distributed instantly. Wherever the drug supply is slower than in compartment 1, tissues are located in the peripheral compartments (numbers 2 and 3).



In a 3- compartment model equations distribution and elimination of drug in the body is given by the differential equations as shown below

$$\frac{dy_1}{dt} = K_{21}y_2 - K_{31}y_3 - K_{12}y_1 - K_{10}y_1 \ \ldots \quad (6)$$

$$\frac{dy_2}{dt} = K_{12}y_1 - K_{21}y_2 \ \ldots \quad (7)$$

$$\frac{dy_3}{dt} = K_{13}y_1 - K_{31}y_3 \ \ldots \quad (8)$$

Taking Kamal transform of (1) and (2) both the sides, can be transformed into linear equation

$$K\{y'_1\} = K_{21}K(y_2) - K_{31}K(y_3) - K_{12}K(y_1) - K_{10}K(y_1)$$

$$\frac{1}{p}y_1 - y_1(0) = K_{21}y_2 - K_{31}y_3 - K_{12}y_1 - K_{10}y_1$$

$$\left(\frac{1}{p} + K_{12} + K_{10}\right)y_1 - K_{21}y_2 + K_{31}y_3 = y_1(0) \ldots \quad (9)$$

$$K\{y'_2\} = K_{12}y_1 - K_{21}y_2$$

$$\frac{1}{p}y_2 - y_2(0) = K_{12}y_1 - K_{21}y_2$$

$$\left(\frac{1}{p} + K_{21}\right)y_2 - K_{12}y_1 = y_2(0) \ldots \quad (10)$$

$$K\{y'_3\} = K_{13}y_1 - K_{31}y_3$$

$$\frac{1}{p}y_3 - y_3(0) = K_{13}y_1 - K_{31}y_3$$

$$\left(\frac{1}{p} + K_{31}\right)y_3 - K_{13}y_1 = y_3(0) \ldots \quad (11)$$

Applying Crammer's Rule to solve equation (9), (10) and (11) to find the value of y_1

$$\Delta = \begin{vmatrix} \frac{1}{p} + K_{12} + K_{10} & -K_{21} & K_{31} \\ -K_{12} & \frac{1}{p} + K_{21} & 0 \\ -K_{13} & 0 & \frac{1}{p} + K_{31} \end{vmatrix}$$

$$\Delta = \left(\frac{1}{p} + K_{12} + K_{10}\right)\left(\frac{1}{p} + K_{21}\right)\left(\frac{1}{p} + K_{31}\right) + K_{21}\left(\frac{-K_{12}}{p} - K_{12}K_{31}\right) + K_{31}\left(\frac{K_{13}}{p} + K_{21}K_{13}\right)$$

$$\Delta = \frac{1}{p^3} + \frac{1}{p^2}(K_{12} + K_{10} + K_{21} + K_{31}) + \frac{1}{p}(K_{10}K_{21} + K_{12}K_{31} + K_{10}K_{31} + K_{21}K_{31} + K_{13}K_{31}) + K_{10}K_{21}K_{31} + K_{13}K_{21}K_{31}$$

Put $K_{12} + K_{10} + K_{21} + K_{31} = a + b + c,$

$$K_{10}K_{21} + K_{12}K_{31} + K_{10}K_{31} + K_{21}K_{31} + K_{13}K_{31} = ab + bc + ca$$

$$K_{10}K_{21}K_{31} + K_{13}K_{21}K_{31} = abc$$

$$\Delta = \frac{1}{p^3} + \frac{1}{p^2}(a + b + c) + \frac{1}{p}(ab + bc + ca) + abc$$

$$\Delta = \frac{1 + p(a + b + c) + p^2(ab + bc + ca) + p^3}{p^3}$$

$$\Delta = \frac{(1 + ap)(1 + bp)(1 + cp)}{p^3}$$

$$\Delta_1 = \begin{vmatrix} y_1(0) & -K_{21} & K_{31} \\ 0 & \frac{1}{p} + K_{21} & 0 \\ 0 & 0 & \frac{1}{p} + K_{31} \end{vmatrix} = \left(\frac{1}{p} + K_{21}\right)\left(\frac{1}{p} + K_{31}\right)y_1(0)$$

$$y_1 = \frac{\Delta_1}{\Delta} = \frac{\left(\frac{1}{p} + K_{21}\right)\left(\frac{1}{p} + K_{31}\right)y_1(0)}{\frac{1}{p^3} + \frac{1}{p^2}(a + b + c) + \frac{1}{p}(ab + bc + ca) + abc}$$

$$y_1 = \frac{\Delta_1}{\Delta} = \frac{p(1 + pK_{21})(1 + pK_{31})y_1(0)}{1 + p(a + b + c) + p^2(ab + bc + ca) + p^3}$$

$$y_1 = \frac{\Delta_1}{\Delta} = \frac{p(1 + pK_{21})(1 + pK_{31})y_1(0)}{(1 + ap)(1 + bp)(1 + cp)}$$

By using partial fraction method, we can write,

$$y_1 = \frac{(K_{21} - a)(a - K_{31})y_1(0)}{a(a - b)(a - c)(1 + ap)} + \frac{(K_{21} - b)(b - K_{31})y_1(0)}{b(b - a)(b - c)(1 + bp)} + \frac{(K_{21} - c)(c - K_{31})y_1(0)}{c(c - a)(c - b)(1 + cp)}$$

Now by applying inverse Kamal transform, we have

$$y_1(t) = \alpha e^{-at} + \beta e^{-bt} + \gamma e^{-ct} \ldots \quad (12)$$

where

$$\alpha = \frac{(K_{21} - a)(a - K_{31})y_1(0)}{a(a - b)(a - c)}, \beta = \frac{(K_{21} - b)(b - K_{31}y_1(0))}{b(b - a)(b - c)}, \gamma = \frac{(K_{21} - c)(c - K_{31})y_1(0)}{c(c - a)(c - b)}$$

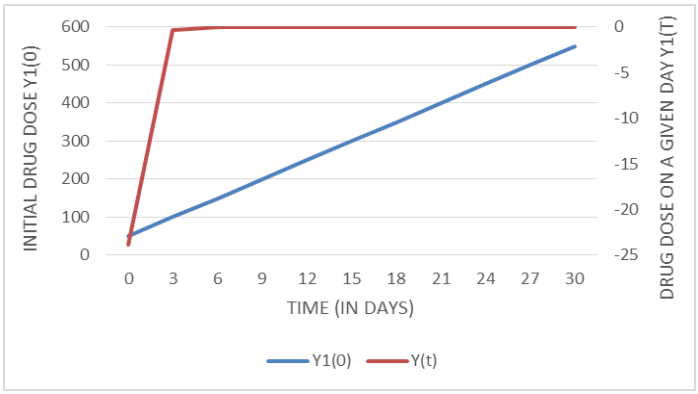


Fig 3.1

Fig 3.1 $Y_1(0)$ and $Y_1(t)$ are the drug dose initially and on a particular day respectively and are in mg. This figure depicts the dose over time graph.

Application to derive pharmacokinetic equations

After the intravenous injection of a drug to a patient, it distributing in the body and also eliminates in the body as first order kinetics is set into the differential.

$$\frac{dY}{dt} = Y' = -kY,$$

Where Y is the total amount of drug in the body of a patient in time t

Taking Kamal transform of both sides

$$\frac{1}{p}Y - Y(0) = -kY$$

$$\frac{1}{p}Y + kY = Y(0)$$

$$\frac{(1 + pk)Y}{P} = Y(0)$$

$$Y = \frac{p\,Y(0)}{(1+pk)},$$ p-Kamal transform operator

Then taking inverse Kamal transform of both sides

$$K^{-1}(Y) = K^{-1}\left\{\frac{p\,Y(0)}{(1 + pk)}\right\}$$

$$Y = Y(0)\,e^{-Kt}$$

Where $Y(0)$ amount of drug given to the patient when time is zero.

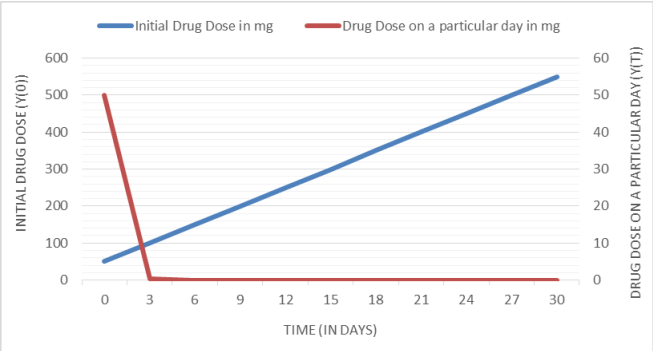


Fig 3.2

Fig 3.2 Y(0) and Y(t) are the drug dose initially and on a particular day respectively and are in mg. This figure depicts the dose over time graph.

CONCLUSION

In this work, we have discussed two systems of two compartments and three compartments pharmacokinetic models of these models solve with the help of Kamal transform. Both models are represented in term of first order differential equation. Kamal transform is powerful tool to solve the differential equations. These models can be extensively used for any type of drug diffusion problems which are arising in pharmacokinetic studies. This study has a good number of applications in drug control drug dosage and other related problems.

REFERENCES

[1] Jayesh Jain, Dr. Ajazul Haque, Ramashankar Prajapati, Shiksha Singh: Application of Mathematics to Certain Pharmacokinetic Equations, International Journal of Engineering Research & Science, Vol-6, Issue-3, March-2020.

[2] Basic Physics of Nuclear Medicine/Dynamic Studies in Nuclear Medicine (Wikibook).

[3] Tadeusz W£Adys£Aw Hermann: Application Of Laplace Transforms To A Pharmacokinetic Open Two-Compartment Body Model Acta Poloniae Pharmaceutica ñ Drug Research, Vol. 74 No. 5 pp. 1527-1531, 2017

[4] Dokoumetzidis, A. and Macheras, P. Fractional kinetics in drug absorption and disposition processes. J. Pharmacokinet. Pharmacodyn. 36, pp. 165-178, 2009.

[5] Abdelilah kamal HS. The new integral transform kamal transform Advances in Theoretical and Applied mathematics, 11(4), pp. 451-458, 2016.

[6] Sudhanshu Aggarwal, Raman Chauhan, Nidhi Sharma. A new application of kamal transform for solving linear volterra integral equation. International journal of latest technology in engineering, management & applied science, Vol.7, issue 4, April 2018.

[7] Gupta S.P. "Statistical Methods" Sultan Chand & Sons, New Delhi.

[8] Prasad G. Textbook of "Differential Calculus" Pothishala Pvt. Ltd, Allahabad.

[9] Mager DE, Jusko WJ. General pharmacokinetic model for drugs exhibiting target-mediated drug disposition. J Pharm Pharm 2001; Vol. 28, pp. 507-532.

[10] Himmelstein KJ, Lutz RJ. A review of the applications of physiologically based pharmacokinetic modeling. J Pharm Biopharm 1979,Vol. 7, pp. 127-145.

[11] de Biasi J. Four open mammillary and catenary compartment models for pharmacokinetics studies. J Biomed Eng 1989, Vol. 11, pp. 467-470.

[12] Gibaldi M, Perrier B. Phai-macokinetics. New York: Dekker, 1975, 1982, pp. 494.

[13] Cherruault Y, Sarin VB. General treatment of linear mammillary models. Int J Biomed Comput 1985, Vol. 16,pp. 119-126.

[14] Withers RT, Laforgia J, Heymsfield SB. Critical appraisal of the estimation of body composition via two - , three - , and four - compartment models. Am J Hum Biol 1999 Vol. 11, pp. 175-185.

[15] Vaughan DP, Trainor A. Derivation of general equations for linear mammillary models when the drug is administered by different routes. J Pharm Biopharm 1975, Vol. 3, pp. 203-218.

[16] Shargel L, Yu AB, Wu-Pong S. Applied Bio-pharmaceutics and Pharmacokinetics. 7th ed. New York, United States: Access Pharmacy; 2017.

[17] Evans WC. Linear systems: Compartmental modeling, and estimability issues in iaq studies. In: Tichenor B, editor. Characterizing Sources of Indoor Air Pollution and Related Sink Effects, ASTM STP No. 1287, 1996, pp. 239-262.

[18] Leslie Z. Benet: General treatment of linear mammillary models with elimination from any compartment as used in pharmacokinetics. J Pharm Sci 1972, Vol. 61, pp. 536-541.

[19] Samar, C.P., and Saxena, H., 2021, "Solution of Generalized Fractional Kinetic Equation by Laplace and Kamal Transformation", International Journal of Mathematics Trends and Technology, Vol. 67, Issue 6, pp. 38-43.