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Drug Diffusion from the Gastrointestinal Tract through the Body, Bloodstream, and Urinary Compartments: Mathematical Modeling Approach

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ABSTRACT: *This research involved the formulation of a mathematical system that mimics the diffusion of drug concentration from the gastrointestinal tract to the body and bloodstream compartments and the elimination through the urinary tract. The models are formulated separately as ordinary differential equations for the aforementioned compartments, where some pertinent entry parameters in the form of rates were obtained. We applied the Laplace method of solution to solve the formulated mathematical models for the drug concentration in the various compartments as mentioned. In order to investigate the effect of the drug concentration in the urinary and gastrointestinal tracts on the concentration in the body and bloodstream compartments, we solved the urinary tract and gastrointestinal models and substituted the results into the models representing the drug concentration in the body and bloodstream compartments, and those models were later solved to obtain the function representing the body and bloodstream compartments. The research further involved the numerical simulation of the various functions obtained by varying the various rates of diffusion on the drug concentration in the body and bloodstream compartments. The results revealed that the various diffusion rate changes affect the drug concentration level in the body and bloodstream compartments, respectively. The novelty of this research is the fact that we've been able to incorporate drug administration and concretion in the gastrointestinal and urinary tracts, which were not considered previously. This research is recommended for application by mathematicians and scientists alike who could be interested in understanding drug diffusion from one compartment to another with different rate constants.*

KEYWORDS: mathematical modeling, drug, diffusion, gastrointestinal tract, body, bloodstream, urinary and compartment diagram

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INTRODUCTION

Alcohol addiction is a phenomenon that has attracted the attention of several researchers and academics from a wide range of professions due to the devastating effects it has on many facets of human existence, Tireito (2022). Ethanol metabolism has primarily been based on single-dose experimental investigations to map the time course of ethanol elimination or from the perspective of highway safety according to Saha et al., (2015). When alcohol is used in repeated doses, further problems occur, Rota et al. (2014).

The model becomes more sophisticated and requires more analysis when several ingestions are simulated. As a result, both experimentalists and modelers have simply avoided multiple-dose investigations in favour of single-dose research Rota *et al*. (2014). Mathematical models, more specifically compartment models that examine the fluxes between the compartments, may handle such research rather readily, Plawecki et al., (2008). The majority of the compartment models that currently exist for alcohol removal are deterministic. Although such models offer a wealth of knowledge regarding the pharmacokinetics of ethanol, their effectiveness is hindered by the need to determine the model parameters, such as the anatomical structure of the assumed compartments, metabolic rates, as well as transient and steady state solutions. Stochastic models, which offer relevant information with little complexity, are a front-runner for modelling such phenomena due to the variability in the instants of alcohol consumption, absorption, and elimination times, which are random in nature. Based on the above mentioned challenges, there are other researchers who have venture into pharmacokinetics modelling. Shirley (2007) employed Markov or hidden Markov models in one study to analyze respondents' drinking patterns. Instead of being steady across time, these models are better suited to depict systems that undergo abrupt shifts. Wang et al. (2002) multivariate temporal models for alcohol intake were recommended in another investigation. Guang (1998) provided a stochastic model using queuing theory in another study to understand the harmful effects of ethanol on the body.

For the ethanol elimination process, a stochastic model was put up by Ghadirinejad *et al*. (2016). Their model was notable for accounting for numerous doses, zero and first order elimination, and other factors. Their findings were able to take into consideration changes in the quantity and timing of alcohol consumption.According to Plawecki *et al*. (2008), human-based compartment models that result in differential equation systems are typical mathematical models for blood alcohol content. Each variable in these models represents the amount of ethanol present in a particular organ or system, such as the vascular or digestive systems. A differential equation can be used to characterize the rate at which ethanol is absorbed, transported to another compartment, or metabolized. Models range in complexity from simple single-compartment models, Umulis *et al*. (2005) to more complex multi-compartment models (Ramchandani *et al*., 1999; Pieters *et al*., 1990) with three compartments or more.

Bunonyo and Amadi (2023) employed system of mathematical model to analyze the concentration of alcohol in the GI tract and bloodstream. Their models were solved analytically and some of the useful entry parameters were obtained. According to their findings, alcohol content in a compartment rises as the pace of alcohol movement in that compartment increases. Smith et al. (1993) looked at the rate at which ethanol left the circulation in healthy males and females as well as in alcohol abusers. Following the oral administration of ethanol (0.8 g/kg body weight) in the form of whiskey, blood alcohol levels were estimated over the course of three hours. In Meem (2022) employed a mathematical model for alcohol issues, there are four demographic classes represented by his model: potential drinkers, occasional drinkers, heavy drinkers, and recovered and abstainers. Sensitivity analysis of the basic reproduction number shows that focusing solely on alcoholics is less effective in the long run at preventing the spread of alcoholism than encouraging and supporting potential drinkers to refrain from adopting drinking habits and occasional drinkers to stop drinking. A mathematical model of alcohol misuse created by Sharma and Samanta (2015) has four compartments that correspond to the four demographic classes, moderate, and infrequent drinkers, heavy drinkers, drinkers under treatment, and temporarily recovered class. To comprehend the dispersion of medication administration in the human body via oral and intravenous routes, Khanday *et al*. (2017) created mathematical models, using Fick's principle and the law of mass action, three models were created based on the diffusion process. To find the answer to the ordinary differential equations relating to the rate of change of concentration in various compartments, including blood and tissue medium, the Laplace transform and eigenvalues methods were applied. According to the findings, the drug concentration gradually rises in the other compartments while falling in the first.

Rockerbie and Rockerbie (1995) developed a mathematical model using an iterative algorithm based on the Widmark formula and used it to simulate a continuous spectrum of the expected blood alcohol concentration from start of alcohol dosage to time of specific event in numerical and graphic form. The 2-compartment model employed by Norberg et al. (2000) consists of the peripheral compartment, which houses the remaining body fluids in other tissues, and the central compartment, which in this case contains the blood plasma and the tissues that are in quick equilibrium with it (liver and kidney). When the alcohol concentration dropped to levels about 0.10 gl-1 and lower, they demonstrated that the rate of alcohol elimination transitioned to a linear phase on their semi-logarithmic.

Using a mathematical model, Hongzhi (2023) investigated how alcohol diffuses throughout the body. Under the fundamental presumption that the body's process for transferring alcohol is separated into four stages (alcohol-stomach-body-fluids-body), a mathematical model is developed, and numerical simulation is used to verify the diffusion process when consuming in various ways. Pieters *et al*. (1990) used a three-compartment model to describe the pharmacokinetics of alcohol following oral delivery.

Moore (2022) forecast blood ethanol concentration levels over time for a variety of drinking and eating scenarios by included the process of food digestion in the model. Four categories of drinkers were defined by Baker *et al*. (2014): very heavy drinkers, heavy drinkers, binge drinkers, and light drinkers. The average daily intake of very heavy drinkers (VHD) is more than 3 g/kg, and more than 10% of their daily intakes are higher than 4 g/kg. Heavy drinkers (HD) continue to consume more than 3 g/kg per day on more than 20% of their drinking days.
However, this study is an extension of Bunonyo *et al*. (2023), whose investigation is limited to the drug concentration in the body and bloodstream compartments without consideration of how the elimination and metabolic rate affect the gastrointestinal and urinary tracts. In this research we shall adopt the Laplace method in solving the models we would be formulating.

MATERIALS AND METHODS

This study investigates the administration of drugs and the concentration of drug from one compartment to another, as seen in Figure 1. The diffusion of drugs from one compartment to another is with specific rate of diffusion because of the complexity of different human body system. The compartment diagram helps us with the formulation of the first order ordinary differential equations that mimics the diffusion and concentration of drugs from the gastrointestinal tract, the body, the bloodstream and the urinary tracts respectively.

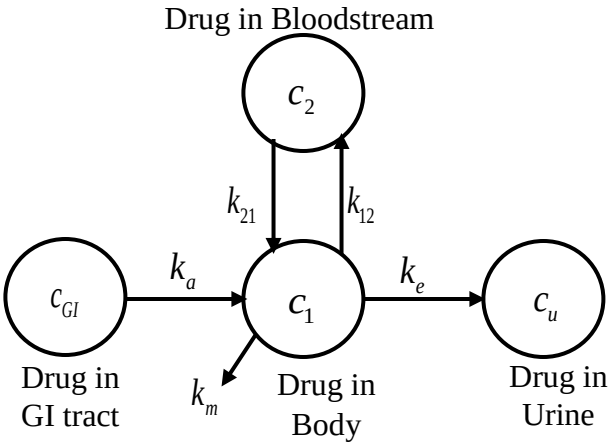

Figure1 Diagram showing drug diffusion from one compartment to another with different rate

Assumptions

Before we can go ahead and formulate the system of mathematical models, let's consider the following assumptions:

- The concentration of drugs in the body compartment can be affected by the increasing rate of inter-compartmental distribution.
- The concentration of drugs in the bloodstream compartment is affected by the inter-compartmental distribution rates.
- The elimination rate affects the drug concentration in the body and bloodstream compartments.
- The first-order rate constant affects the drug concentration in the body and bloodstream compartments.
- The metabolic rate constant affects the drug concentration in the body and bloodstream compartments.
- The volume and dosage of the drug contribute to its concentration in the body and bloodstream compartments.

Definition of Parameters

c_1 : Concentration of drug in the human body compartment

c_2 : Concentration of drug in bloodstream compartment

c_u : Concentration of drug in urinary tract

c_{GI} : Concentration of drug in gastrointestinal tract

k_{12}, k_{21} : Inter-compartmental distribution rate constant

k_e : Excretion rate constant

k_m : Metabolic rate constant

k_a : First order rate constant

V : Volume of drug in the compartments

D : Drug dosage in the compartments

Model Formulation

The formation of the system of mathematical models of the problem under investigation follows the above compartment diagram in Figure 1, Bunonyo *et al*. (2023) and Bunonyo and Amadi (2023), where the system of models is formulated as:

$$\frac{dc_1}{dt} = k_a c_{GI} + k_a c_1 + k_{21} c_2 - k_{12} c_1 - k_e c_1 - k_m c_1 + k_e c_u \quad (1)$$

$$\frac{dc_2}{dt} = k_{12} c_1 - k_{21} c_2 \quad (2)$$

$$\frac{dc_u}{dt} = -k_e c_1 + k_e c_u \quad (3)$$

$$\frac{dc_{GI}}{dt} = -k_a c_{GI} \quad (4)$$

Equations (1)-(4) are subject to certain initial conditions, they are:

$$\left.\begin{aligned} c_1(0) &= 0 \\ c_2(0) &= 0 \\ c_{\mathrm{GI}}(0) &= \frac{D}{V} \\ c_u(0) &= 0 \end{aligned}\right\} \tag{5}$$

Methods of Solution

Considering the concentration of the administered drug via the GI on other compartments, we have to solve equation (4) first, that is:

$$\frac{dc_{GI}}{dt} = -k_a c_{GI} \tag{6}$$

Recalling that the Laplace method can be stated as:

$$L\{c_{GI}(t)\} = c_{GI}(s) = \int_0^\infty e^{-st} c_{GI}(t)dt \tag{7}$$

Applying equation (7) on equation (6), we have:

$$L\left\{\frac{dc_{GI}}{dt}\right\} + k_a L\{c_{GI}\} = 0 \tag{8}$$

$$(s + k_a)c_{GI} - c_{GI}(0) = 0 \tag{9}$$

Simplifying equation (9) with the initial condition in equation (5), we have:

$$(s + k_a)c_{GI} = \frac{D}{V} \tag{10}$$

Simplifying equation (16), we have the following:

$$c_{GI}(s) = \frac{D}{V(s + k_a)} \tag{11}$$

Taking the inverse of the Laplace transform in equation (11), we have:

$$c_{GI}(t) = L^{-1}\{c_{GI}(s)\} \tag{12}$$

Applying equation (12) in solving equation (11), we have:

$$c_{GI}(t) = L^{-1}\{c_{GI}(s)\} = L^{-1}\left\{\frac{D}{V(s + k_a)}\right\} \tag{13}$$

Simplifying equation (13), we have:

$$c_{GI}(t) = L^{-1}\{c_{GI}(s)\} = \frac{D}{V} L^{-1}\left\{\frac{1}{(s + k_a)}\right\} \tag{14}$$

Simplifying equation (14), we have:

$$c_{GI}(t) = L^{-1}\{c_{GI}(s)\} = \frac{D}{V}L^{-1}\left\{\frac{1}{(s+k_a)}\right\} = \frac{D}{V}e^{-k_a t} \quad (15)$$

where $L^{-1}\left\{\frac{1}{(s+k_a)}\right\} = e^{-k_a t}$

To solve the model the model representing drug concentration in the urinary tract, we shall solve as follows:

$$L\left\{\frac{dc_u}{dt}\right\} - k_e L\{c_u\} = -k_e L\{c_1\} \quad (16)$$

Simplifying equation (23), we have:

$$sc_u(s) - c_u(0) - k_e c_u(s) = -k_e c_1(s) \quad (17)$$

Simplifying equation (24) further, we have:

$$(s-k_e)c_u(s) = -k_e c_1(s) \quad (18)$$

Simplifying equation (25), we have:

$$c_u(s) = -k_e \frac{c_1(s)}{(s-k_e)} \quad (19)$$

Solving equation (2) using the Laplace method, which is:

$$L\left\{\frac{dc_2}{dt}\right\} + k_{21}L\{c_2\} = k_{12}L\{c_1\} \quad (20)$$

Simplifying equation (27), we have:

$$sc_2(s) - c_2(0) + k_{21}c_2(s) = k_{12}c_1(s) \quad (21)$$

Simplifying equation (28), we have:

$$(s+k_{21})c_2(s) = k_{12}c_1(s) \quad (22)$$

Simplifying equation (29), we have:

$$c_2(s) = k_{12}\frac{c_1(s)}{(s+k_{21})} \quad (23)$$

Solving the model representing the drug concentration in the body, we apply the Laplace method on equation (1), which is:

$$L\left\{\frac{dc_1}{dt}\right\} = k_a L\{c_{GI}\} + k_a L\{c_1\} + k_{21}L\{c_2\} - k_{12}L\{c_1\} - k_e L\{c_1\} - k_m L\{c_1\} + k_e L\{c_u\} \quad (24)$$

Simplifying equation (31), we have:

$$sc_1(s) - c_1(0) = k_a c_{GI}(s) + k_a c_1(s) + k_{21}c_2(s) - k_{12}c_1(s) - k_e c_1(s) - k_m c_1(s) + k_e c_u(s) \quad (25)$$

Simplifying equation (32), we have:

$$sc_1(s) - k_a c_1(s) + k_{12} c_1(s) + k_e c_1(s) + k_m c_1(s) - k_e c_u(s) = k_a c_{GI}(s) + k_{21} c_2(s) \quad (26)$$

Substituting equations (17), (26) and (30) into equation (33), we have:

$$\left[s - k_a + k_{12} + k_e + k_m + k_e^2 \frac{1}{(s - k_e)} - k_{21} k_{12} \frac{1}{(s + k_{21})} \right] c_1(s) = \frac{D k_a}{V(s + k_a)} \quad (27)$$

Simplifying equation (27), we have:

$$\left[s + k_\delta + k_e^2 \frac{1}{(s - k_e)} - k_{21} k_{12} \frac{1}{(s + k_{21})} \right] c_1(s) = \frac{D k_a}{V(s + k_a)} \quad (28)$$

where $k_\delta = -k_a + k_{12} + k_e + k_m$

Simplifying equation (28), we have:

$$c_1(s) = \frac{\frac{D k_a}{V(s + k_a)}}{\left[s + k_\delta + k_e^2 \frac{1}{(s - k_e)} - k_{21} k_{12} \frac{1}{(s + k_{21})} \right]} \quad (29)$$

Simplifying equation (29), we have:

$$c_1(s) = \frac{D k_a}{V(s + k_a)} \frac{1}{\left[s + k_\delta + k_e^2 \frac{1}{(s - k_e)} - k_{21} k_{12} \frac{1}{(s + k_{21})} \right]} \quad (30)$$

Simplifying equation (30), we have:

$$c_1(s) = \frac{\beta_0}{\left[s(s + k_a) + k_\delta (s + k_a) + k_e^2 \frac{(s + k_a)}{(s - k_e)} - k_{21} k_{12} \frac{(s + k_a)}{(s + k_{21})} \right]} \quad (31)$$

where $\beta_0 = \frac{D k_a}{V}$

$$c_1(s) = \frac{\beta_0}{\left[s(s + k_a) + k_\delta (s + k_a) + k_e^2 \frac{(s + k_a)}{(s - k_e)} - k_{21} k_{12} \frac{(s + k_a)}{(s + k_{21})} \right]} \quad (32)$$

Simplifying equation (32), we have:

$$c_1(t) = L^{-1}\{c_1(s)\} = \beta_0 L^{-1} \left\{ \frac{1}{\left[s(s + k_a) + k_\delta (s + k_a) + k_e^2 \frac{(s + k_a)}{(s - k_e)} - k_{21} k_{12} \frac{(s + k_a)}{(s + k_{21})} \right]} \right\} \quad (33)$$

Simplifying equation (33), we have:

$$c_1(t) = L^{-1}\{c_1(s)\} = \beta_0 L^{-1}\left\{\frac{(s-k_e)(s+k_{21})}{(s+k_a)\begin{bmatrix} s(s-k_e)(s+k_{21})+k_\delta(s-k_e)(s+k_{21}) \\ +k_e^2(s+k_{21})-k_{21}k_{12}(s-k_e) \end{bmatrix}}\right\} \quad (34)$$

Further simplification of equation (34), we obtained:

$$c_1(t) = \beta_0 L^{-1}\left\{\frac{s^2+(k_{21}-k_e)s-k_{21}k_e}{\begin{bmatrix} s^2(s+k_a)(s+(k_{21}+k_\delta-k_e))+\left[k_\delta(k_{21}-k_e)+k_e^2-k_ek_{21}-k_{21}k_{12}\right](s+k_a)s \\ +\left(k_e^2k_{21}+k_{21}k_{12}k_e-k_\delta k_ek_{21}\right)(s+k_a) \end{bmatrix}}\right\} \quad (35)$$

Equation (35) is simplified to:

$$c_1(t) = L^{-1}\{c_1(s)\} = \beta_0 L^{-1}\left\{\frac{s^2+k_\lambda s-k_{21}k_e}{(s+k_a)\left(s^3+k_\beta s^2+k_\gamma s+k_\phi\right)}\right\} \quad (36)$$

where

$$k_\beta = (k_{21}+k_\delta-k_e), k_\gamma = k_\delta(k_{21}-k_e)+k_e^2-k_ek_{21}-k_{21}k_{12}, k_\phi = \left(k_e^2k_{21}+k_{21}k_{12}k_e-k_\delta k_ek_{21}\right), k_\lambda = (k_{21}-k_e)$$

Express $$\frac{s^2+k_\lambda s-k_{21}k_e}{(s+k_a)(s-r_1)(s-r_2)(s-r_3)} \equiv \frac{A}{(s+k_a)}+\frac{B}{(s-r_1)}+\frac{C}{(s-r_2)}+\frac{D}{(s-r_3)} \quad (37)$$

If we express $\left(s^3+k_\beta s^2+k_\gamma s+k_\phi\right) \equiv (s-r_1)(s-r_2)(s-r_3)$, then equation (36) becomes:

$$L^{-1}\{c_1(s)\} = \beta_0 L^{-1}\left\{\frac{s^2+k_\lambda s-k_{21}k_e}{(s+k_a)(s-r_1)(s-r_2)(s-r_3)}\right\} \quad (38)$$

Simplifying equation (38), we have:

$$\frac{s^2+k_\lambda s-k_{21}k_e}{(s+k_a)(s-r_1)(s-r_2)(s-r_3)} \equiv \frac{A}{(s+k_a)}+\frac{B}{(s-r_1)}+\frac{C}{(s-r_2)}+\frac{D}{(s-r_3)} \quad (39)$$

Substituting equation (39) into equation (538), we have:

$$L^{-1}\{c_1(s)\} = \beta_0 L^{-1}\left\{\frac{A}{(s+k_a)}+\frac{B}{(s-r_1)}+\frac{C}{(s-r_2)}+\frac{D}{(s-r_3)}\right\} \quad (40)$$

Simplifying equation (39), we have:

$$\frac{s^2+k_\lambda s-k_{21}k_e}{(s+k_a)(s-r_1)(s-r_2)(s-r_3)}\equiv\frac{A}{(s+k_a)}+\frac{B(s-r_2)(s-r_3)+C(s-r_3)(s-r_1)+D(s-r_2)(s-r_1)}{(s-r_1)(s-r_2)(s-r_3)} \tag{41}$$

Simplifying equation (41), we have:

$$\frac{s^2+k_\lambda s-k_{21}k_e}{(s+k_a)(s-r_1)(s-r_2)(s-r_3)}\equiv\frac{\begin{bmatrix}A(s-r_1)(s-r_2)(s-r_3)+B(s-r_2)(s-r_3)(s+k_a)\\+C(s-r_3)(s-r_1)(s+k_a)+D(s-r_2)(s-r_1)(s+k_a)\end{bmatrix}}{(s+k_a)(s-r_1)(s-r_2)(s-r_3)} \tag{42}$$

Upon further simplification of equation (42), we have:

$$s^2+k_\lambda s-k_{21}k_e\equiv\begin{bmatrix}A(s-r_1)(s-r_2)(s-r_3)+B(s-r_2)(s-r_3)(s+k_a)\\+C(s-r_3)(s-r_1)(s+k_a)+D(s-r_2)(s-r_1)(s+k_a)\end{bmatrix} \tag{43}$$

From equation (43), we have:

$$(A+B+C+D)=0 \tag{44}$$

$$-A(r_3+r_2+r_1)-B(r_3-k_a+r_2)-C(r_1-k_a+r_3)-D(r_1-k_a+r_2)=1 \tag{45}$$

$$A(r_2r_3+r_1r_3+r_1r_2)-B(r_3k_a-r_3r_2+r_2k_a)-C(r_1k_a-r_1r_3+r_3k_a)-D(r_1k_a+r_1r_2-r_2k_a)=k_\lambda \tag{46}$$

$$-Ar_1r_2r_3+Br_2r_3k_a+Cr_3r_1k_a+Dr_2r_1k_a=-k_{21}k_e \tag{47}$$

Equations (44)-(47) can be expressed as:

$$\begin{pmatrix}1 & 1 & 1 & 1\\(-r_2r_3-r_1r_3-r_1r_2) & (k_a-r_2-r_3) & (k_a-r_1-r_3) & (k_a-r_1-r_2)\\(r_2r_3+r_1r_3+r_1r_2) & (r_3r_2-r_3k_a-r_2k_a) & (r_1r_3-r_1k_a-r_3k_a) & (r_2k_a-r_1k_a-r_1r_2)\\-r_1r_2r_3 & r_2r_3k_a & r_3r_1k_a & r_2r_1k_a\end{pmatrix}\begin{pmatrix}A\\B\\C\\D\end{pmatrix}=\begin{pmatrix}0\\1\\k_\lambda\\-k_{21}k_e\end{pmatrix} \tag{48}$$

Further simplification of equation (48), we have:

$$\begin{pmatrix}1 & 1 & 1 & 1\\r_{\alpha1} & r_{\beta1} & r_{\phi1} & r_{\lambda1}\\r_{\alpha2} & r_{\beta2} & r_{\phi2} & r_{\lambda2}\\-r_1r_2r_3 & r_2r_3k_a & r_3r_1k_a & r_2r_1k_a\end{pmatrix}\begin{pmatrix}A\\B\\C\\D\end{pmatrix}=\begin{pmatrix}0\\1\\k_\lambda\\-k_{21}k_e\end{pmatrix} \tag{49}$$

where $r_{\alpha1}=(-r_2r_3-r_1r_3-r_1r_2), r_{\beta1}=(k_a-r_2-r_3), r_{\phi1}=(k_a-r_1-r_3), r_{\lambda1}=(k_a-r_1-r_2),$

$r_{\alpha2}=(r_2r_3+r_1r_3+r_1r_2), r_{\beta2}=(r_3r_2-r_3k_a-r_2k_a), r_{\phi2}=(r_1r_3-r_1k_a-r_3k_a), r_{\lambda2}=(r_2k_a-r_1k_a-r_1r_2)$

Recall that $\left(s^3+k_\beta s^2+k_\gamma s+k_\phi\right)\equiv\left(s-r_1\right)\left(s-r_2\right)\left(s-r_3\right)$ (50)

Solving equation (50), where r_1, r_2 and r_3 denotes the roots of the equation (50). To obtain the roots, we adopt Wolfram Mathematica, which are:

$$r_1=\frac{k_\beta}{3}+\frac{2^{1/3}\left(k_\beta^2-3k_\gamma\right)}{3\left(-2k_\beta^3+9k_\beta k_\gamma-27k_\phi+\sqrt{-4\left(k_\beta^2-3k_\gamma\right)^3+\left(2k_\beta^3-9k_\beta k_\gamma+27k_\phi\right)^2}\right)^{1/3}}+\frac{\left(-2k_\beta^3+9k_\beta k_\gamma-27k_\phi+\sqrt{-4\left(k_\beta^2-3k_\gamma\right)^3+\left(2k_\beta^3-9k_\beta k_\gamma+27k_\phi\right)^2}\right)^{1/3}}{3\times 2^{1/3}} \quad (51)$$

$$r_2=-\frac{k_\beta}{3}+\frac{\left(1+\sqrt[i]{3}\right)\left(-k_\beta^2+3k_\gamma\right)}{3\times 2^{2/3}\left(-2k_\beta^3+9k_\beta k_\gamma-27k_\phi+\sqrt{-4\left(k_\beta^2-3k_\gamma\right)^3+\left(2k_\beta^3-9k_\beta k_\gamma+27k_\phi\right)^2}\right)^{1/3}}+\frac{\left(-1+\sqrt[i]{3}\right)\left(-2k_\beta^3+9k_\beta k_\gamma-27k_\phi+\sqrt{-4\left(k_\beta^2-3k_\gamma\right)^3+\left(2k_\beta^3-9k_\beta k_\gamma+27k_\phi\right)^2}\right)^{1/3}}{6\times 2^{1/3}} \quad (52)$$

$$r_3=\ s+\frac{k_\beta}{3}+\frac{\left(1+\sqrt[i]{3}\right)\left(-2k_\beta^3+9k_\beta k_\gamma-27k_\phi+\sqrt{-4\left(k_\beta^2-3k_\gamma\right)^3+\left(2k_\beta^3-9k_\beta k_\gamma+27k_\phi\right)^2}\right)^{1/3}}{6\times 2^{1/3}}+\frac{\left(1-\sqrt[i]{3}\right)\left(-k_\beta^2+3k_\gamma\right)}{3\times 2^{2/3}\left(-2k_\beta^3+9k_\beta k_\gamma-27k_\phi+\sqrt{-4\left(k_\beta^2-3k_\gamma\right)^3+\left(2k_\beta^3-9k_\beta k_\gamma+27k_\phi\right)^2}\right)^{1/3}} \quad (53)$$

where A, B, C and D are constants and can be obtained by solving equation (49)

Simplifying equation (40), we obtained:

$$c_1(t)=L^{-1}\left\{c_1(s)\right\}=\beta_0 AL^{-1}\left\{\frac{1}{(s+k_a)}\right\}+\beta_0 BL^{-1}\left\{\frac{1}{s-r_1}\right\}+\beta_0 CL^{-1}\left\{\frac{1}{s-r_2}\right\}+\beta_0 DL^{-1}\left\{\frac{1}{s-r_3}\right\} \quad (54)$$

Finally, upon adopting the basic Laplace technique, equation can be simplified as:

$$c_1(t)=L^{-1}\left\{c_1(s)\right\}=\beta_0 Ae^{-k_a t}+\beta_0 Be^{r_1 t}+\beta_0 Ce^{r_2 t}+\beta_0 De^{r_3 t} \quad (55)$$

RESULTS

The numerical simulation of the analytical solutions of the system of mathematical models formulated in our previous sections was done using Wolfram Mathematica, version 12, and the graphical results are presented as follows:

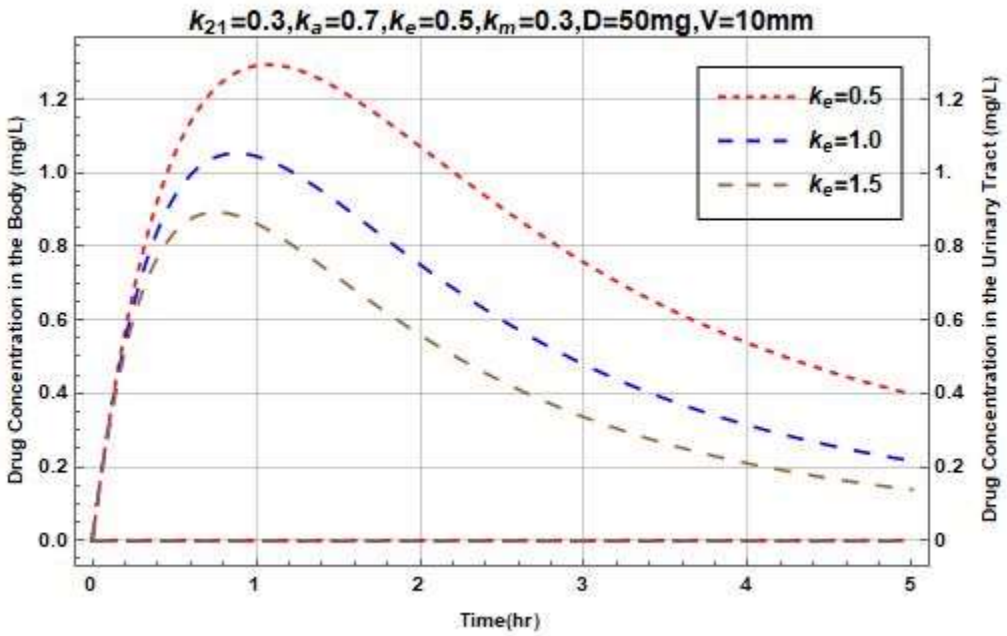

Figure 2 Effect of elimination rate on drug concentration in the body and the urinary tract compartments

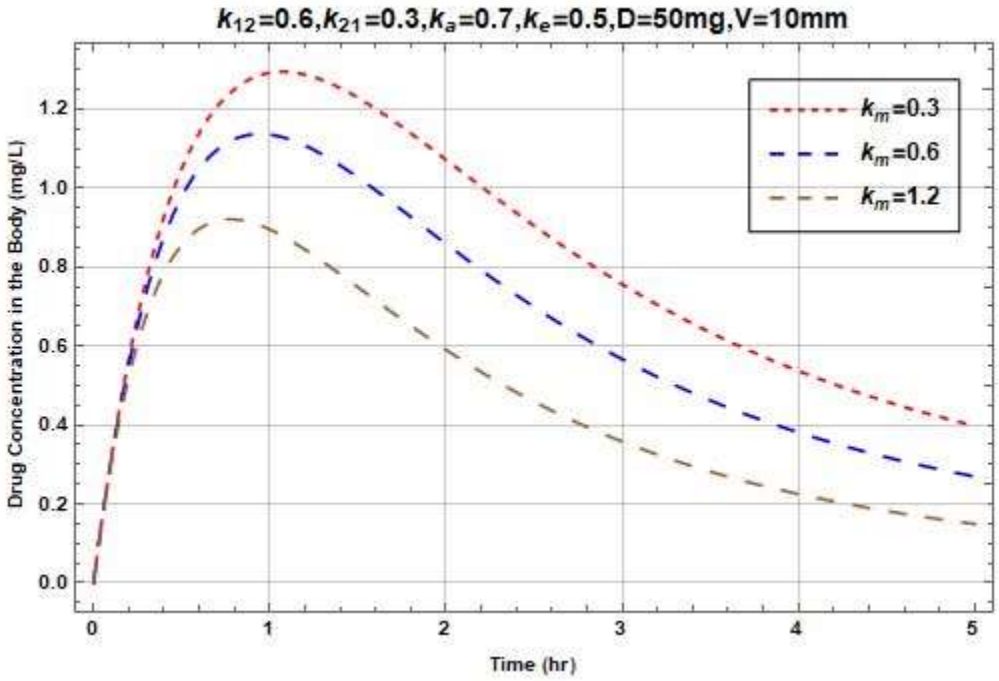

Figure 3 Effect of metabolic rate on drug concentration in the body compartment

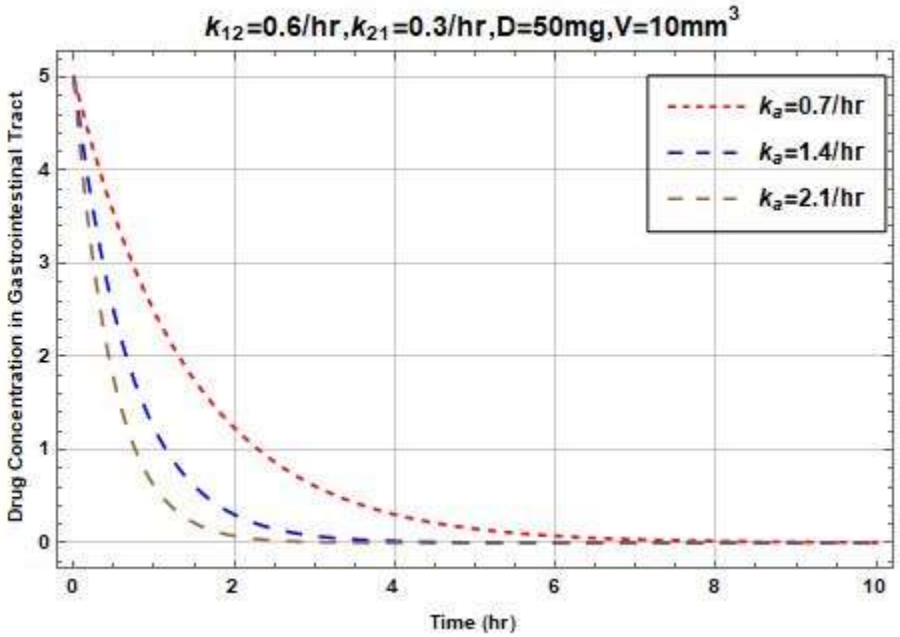

Figure 4 Effect of first order rate constant on drug concentration in the gastrointestinal tract compartment

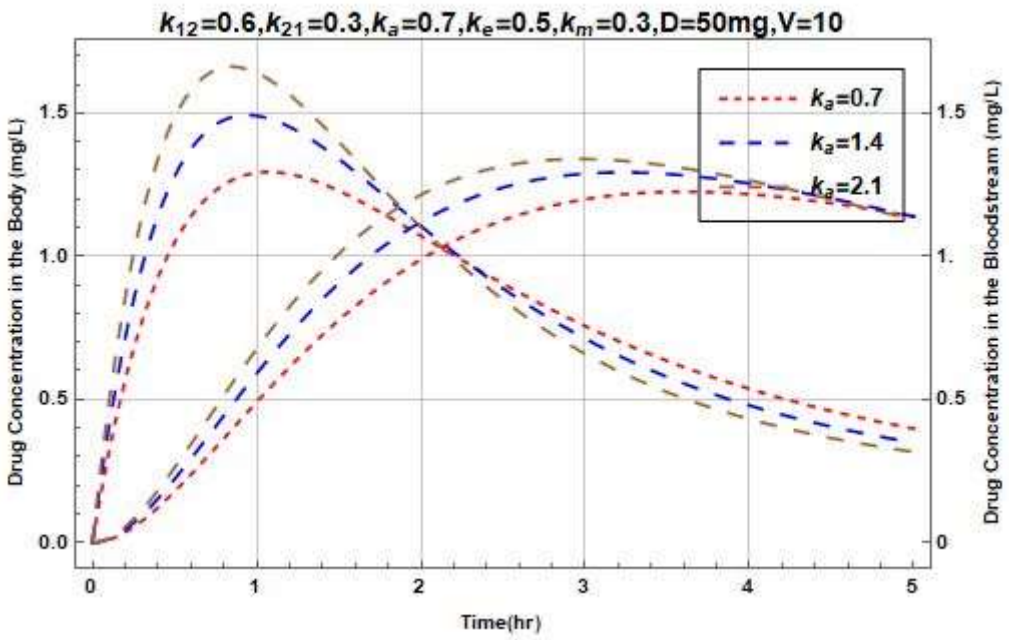

Figure 5 Effect of first order rate constant on drug concentration in the body and bloodstream compartments

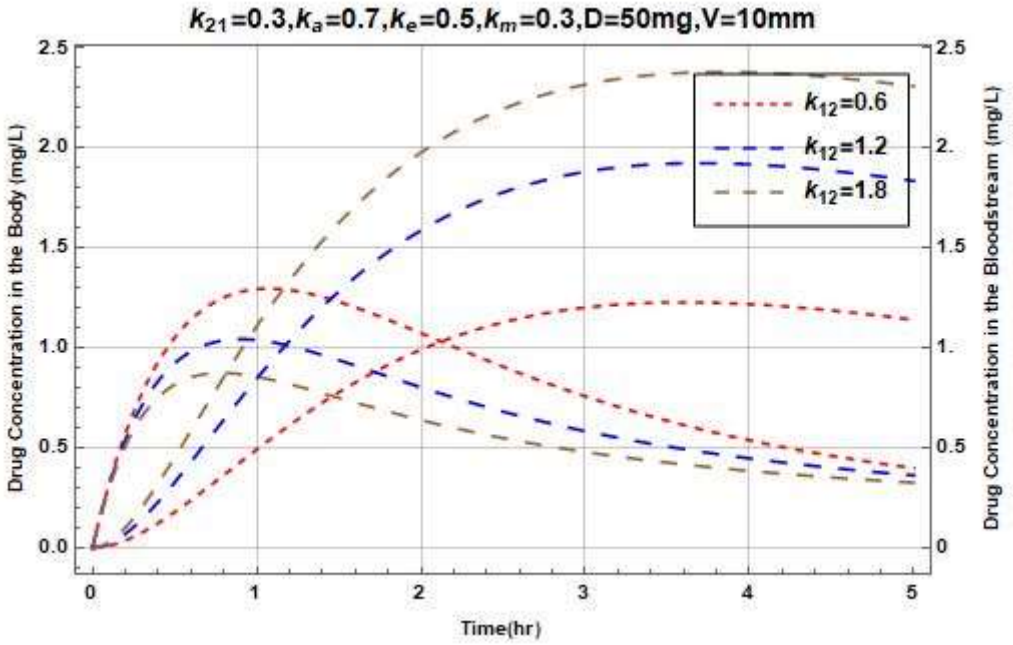

Figure 6 Effect of the inter-compartment distribution rate on drug concentration in the body and bloodstream compartments

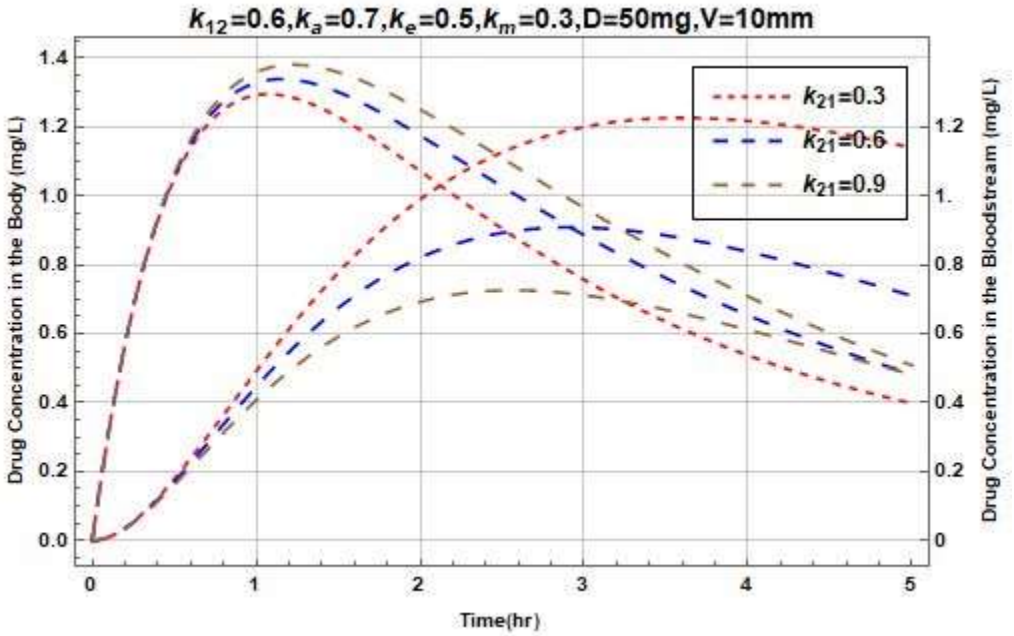

Figure 7 Effect of the inter-compartment distribution rate on drug concentration in the body and bloodstream compartments

DISCUSSION

In Figure 2, we noticed that the drug concentration in the body increases for the elimination rate at 0.5 unit furthermore, the drug concentration in the body keeps decreases for an increase in the elimination rate from 0.5 to 1.5 units. The result also showed that the drug concentration decreases for time for as fast as the rate become. The rate of metabolism effect on drug concentration in the body was also investigated and found out that for the metabolic rate at 0.3 unit, the drug concentration in the body decrease after attaining different maximum height as seen in Figure 3.

Figure 4 depicts the effect of the first rate constant on drug concentration in gastrointestinal tract compartment. It can be seen that the rate constant of 0.7 per hour, the drug concentration in the gastrointestinal tract decreases, for an increase in rate constant, furtherance of the investigation, we can see that the gastrointestinal drug concentration continuously decreased to zero stability level at the different first order rate constant. Figure 5 illustrates the influence of the first rate constant on drug concentration in the body and in the bloodstream compartments for different rate constants. It can be seen that the rate constant of 0.7 unit per hour, the drug concentration in the body and in the bloodstream compartment increases, however, the investigation revealed that the drug concentration in both compartments increased to a maximum before decreasing to steady sate over time.

Figures 6 and 7 illustrate the influence of the inter-compartmental rates of the drug concentration in the bloodstream and body compartments. The results indicated that as the inter-compartmental rate k_{12} term increases the drug concentration levels in the body compartment decrease, however, it has been observed that the increase k_{12} term the drug concentration in the bloodstream compartment increases.

CONCLUSION

In conclusion, we have been able to formulate a system of mathematical models to mimic the diffusion of drug and the concentration of drug from one compartment to another where the first compartment denotes the gastrointestinal, the second the body, the fourth is the bloodstream, and finally, the urinary tract compartments respectively. In a similar vein, we developed computational codes using Wolfram Mathematica to simulate the effect of the various rates on the drug concentration in the body and bloodstream compartments as part of the research objectives, and based on research investigation, we conclude as follows:

- The drug concentration in the body keeps decreases for an increase in the elimination rate from 0.5 to 1.5 units. This showed that for one to quickly elimination the drug concentration in the body system, we must accelerate the elimination rate.
- The rate of metabolism affects the drug concentration in the body with a little increase in metabolic rate.
- To decrease the drug concentration in the gastrointestinal tract, there should be an increase in rate constant.
- In order to reduce the drug concentration in the body and the bloodstream compartments, one has to increase the rate constant.
- The inter-compartmental rates increase influenced the drug concentration in the bloodstream and body compartments.

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