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Mathematical Modeling of Time-Dependent Concentration of Alcohol in the Human Bloodstream Using the Eigenvalue Method

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Abstract
We have been able to mimic the time-dependent concentration of alcohol in the human blood stream and body. We started by proposing a two-compartmental mathematical model to describe and understand the alcohol dynamics in the body and bloodstream. We went further to solve the proposed model analytically using the eigenvalue method. Through numerical study of the solutions, we carried out sensitivity analysis of the model parameters k_{12} and k_{21} to the alcohol blood concentration as a function of time and the maximum blood alcohol concentration as a function of initial concentration for 40 hours and found out that the bloodstream attains its maximum alcohol concentration at 2 hours, 20 minutes. Lastly, we found out that while the magnitude of the maximum blood alcohol concentration increases as k_{12} increases, it decreases as k_{21} increases. The novelty of the project is the fact that we have been able to mimic alcohol concentration in the bloodstream and in the body using mathematical models.

Keywords
Blood alcohol concentration, Alcoholism, Alcohol, Time-dependent, Eigenvalue method

INTRODUCTION

Alcohol use was considered to be the second-leading risk factor for the attributable burden of disease among those between the ages of 10 and 24, and the ninth-leading risk factor across all age groups, per the 2017 National Survey on Drug Use and Health [12]. Worldwide, alcohol use contributed to 2.07 million male fatalities and 374,000 female fatalities in 2019 [1].

Alcohol has physiological effects on the body in addition to mental ones. Proof suggests that even light drinking may raise a person's risk of dying from a number of ailments, including several types of cancer and some types of heart disease [5]. Every drop of alcohol creates an imminent threat to the well-being and health of an individual, and the danger starts the moment the initial sip is taken. According to reports, more than half of the projected 95,000 yearly deaths from alcohol-related causes (about 68,000 men and 27,000 women) are linked to long-term health impacts such as heart or liver disease brought on by excessive drinking [11]. Drinking too much alcohol does not just make you feel bad in the moment. It can also cause problems with your blood and your body's health. One issue is anemia, which often happens when people drink too much. This shows how the things you eat and drink affect your blood. The liver, a part of your body that helps with digestion, can also be damaged by alcohol, and this can make blood problems worse. Intense drinking, or consuming large amounts of alcohol quickly, puts more strain on your body and internal organs (and may leave you feeling hungover afterward). Headaches, severe dehydration, nausea, vomiting, diarrhea, and indigestion can all be brought on by drinking too much alcohol [9]. According to [19], these health hazards include those for the liver, pancreas, brain, and cardiovascular systems. Alcohol does not digest after consumption; instead, it enters the bloodstream quickly and goes to all areas of the body. Alcohol affects the body in many ways, depending on age, gender, weight, and the type of alcohol consumed. The brain is the organ that is most negatively impacted by alcohol, followed by the kidneys, lungs, and liver [4].

Apart from its social aspects, alcohol affects our entire body through different physical pathways. Important researchers like [17] have done ground-breaking studies to understand how alcohol influences our metabolism and the body's ability to keep things in balance. Their diligent work has shown that alcohol does more than only cause intoxication; it also sets off intricate chemical processes that have an impact on various organ systems.

Human-based compartment models that result in differential equation systems are typical mathematical models for blood alcohol content [14]. 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 [18] to more complex multi-compartment models that use fractional methods with three compartments or more. Additionally, models that use fractional methods have been used [15]. Models range in complexity from simple single-compartment models [18] to more complex multi-compartment models [13, 16] with three compartments or more. Additionally, models that use fractional methods have been used [15].

The use of mathematical compartmental models in the analysis, study, and control of negative effects has made them crucial instruments for predicting the body's alcohol content. Using a mathematical model, [7] 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.[10] forecast blood ethanol concentration levels over time for a variety of drinking and eating scenarios by including the process of food digestion in the model. In order to analyze the concentration of alcohol in the GI tract and bloodstream, [2] produced a mathematical model. The model was analytically solved, and some useful entry parameters were derived. According to their findings, the alcohol content in a compartment rises as the pace of alcohol movement in that compartment increases. [8] used Fick's principle and the law of mass action to create three models 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 eigenvalue methods were applied. According to the findings, the drug concentration gradually rises in the other compartments while falling in the first. [6] used the Widmark formula to calculate the blood alcohol concentration (BAC) after consuming alcoholic drinks and came to the conclusion that BAC must be understood as the total amount of alcohol consumed.

Alcohol metabolism does not follow a simple, linear pattern. It can be affected by factors like binge drinking, where alcohol concentration levels may rise rapidly, leading to nonlinear behavior that is hard to predict and therefore affecting one's health negatively. Likewise, alcohol absorption and elimination rates change with time, as well as with factors like food intake, hydration, and the type of alcoholic beverage consumed. Hence, there is a lack of detailed insight about this mechanism and no mathematical model that accurately predicts alcohol concentration levels in the body. To address these challenges, we will develop a mathematical model following [2] to mimic alcohol concentration and diffusion from one compartment to another using a mathematical model and offer exact analytical solutions using eigenvalue.

Mathematical Model Formulation

This research is a theoretical study that involves the representation of alcohol concentration in the body and bloodstream compartments using mathematical models. Proffering exact analytical solutions to the models using the eigenvalue method and performing numerical simulation using Matlab software, where the pertinent parameters are varied for the purpose of studying their importance to alcohol concentration in a particular compartment.

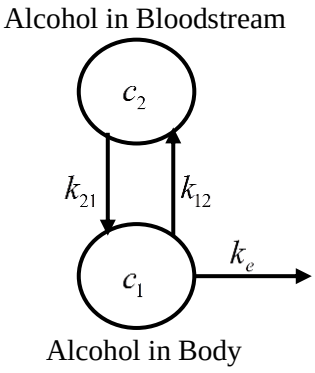

Fig. 1 Diagram showing concentration in bloodstream and body compartments

Following [2] and [3], we shall present the modeled system of mathematical models are:

$$\frac{dc_1}{dt} = k_{21}c_2 - k_{12}c_1 - k_e c_1 \qquad (1)$$

$$\frac{dc_2}{dt} = k_{12}c_1 - k_{21}c_2 \tag{2}$$

The initial conditions are:

$$\left.\begin{aligned} c_1(0) &= \frac{D}{V} \\ c_2(0) &= 0 \end{aligned}\right\} \tag{3}$$

MATHEMATICAL MODEL SOLUTION

We will represent equation 1 and equation 2 in matrix form as;

$$\vec{C}\,'(t) = A\vec{C}(t) \tag{4}$$

where

$$\vec{C}\,'(t) = \begin{Bmatrix} c_1\,'(t) \\ c_2\,'(t) \end{Bmatrix}, \quad A = \begin{bmatrix} -(k_{12}+k_e) & k_{21} \\ k_{12} & -k_{21} \end{bmatrix} \text{ and } \vec{C}(t) = \begin{Bmatrix} c_1(t) \\ c_2(t) \end{Bmatrix} \tag{5}$$

and the initial conditions are

$$\vec{C}(0) = \begin{Bmatrix} \frac{D}{V} \\ 0 \end{Bmatrix} \tag{6}$$

The first thing we need to do is find the eigenvalues of the matrix A.

$$\det(A - \lambda I) = \begin{vmatrix} -(k_{12}+k_e) - \lambda & k_{21} \\ k_{12} & -k_{21} - \lambda \end{vmatrix} = 0$$

$$\left(-(k_{12}+k_e) - \lambda\right)\left(-k_{21} - \lambda\right) - k_{12}k_{21} = 0$$

Expand and collect in terms of λ:

$$k_e k_{21} + \lambda\left(k_{12} + k_e + k_{21}\right) + \lambda^2 = 0 \tag{7}$$

Subtract $k_e k_{21}$ to both sides of equation 7:

$$\lambda\left(k_{12} + k_e + k_{21}\right) + \lambda^2 = -k_e k_{21} \tag{8}$$

Add $\frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2$ to both sides of equation 8:

$$\lambda\left(k_{12} + k_e + k_{21}\right) + \lambda^2 + \frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2 = -k_e k_{21} + \frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2 \tag{9}$$

Write the left hand side equation 9 as a square:

$$\left(\lambda + \frac{1}{2}\left(k_{12} + k_e + k_{21}\right)\right)^2 = -k_e k_{21} + \frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2 \tag{10}$$

Take the square root of both sides of equation 10:

$$\lambda + \frac{1}{2}\left(k_{12} + k_e + k_{21}\right) = \pm\sqrt{-k_e k_{21} + \frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2} \tag{11}$$

Subtract $\frac{1}{2}\left(k_{12} + k_e + k_{21}\right)$ from both sides of equation 11:

$$\lambda = \pm\sqrt{-k_e k_{21} + \frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2} - \frac{1}{2}\left(k_{12} + k_e + k_{21}\right)$$

where

$$\lambda_1 = \sqrt{-k_e k_{21} + \frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2} - \frac{1}{2}\left(k_{12} + k_e + k_{21}\right) \tag{12}$$

and

$$\lambda_2 = -\sqrt{-k_e k_{21} + \frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2} - \frac{1}{2}\left(k_{12} + k_e + k_{21}\right) \tag{13}$$

Now let us find the eigenvectors for each eigenvalue:

$$\lambda = \lambda_1 :$$

We need to solve,

$$\begin{bmatrix} -\left(k_{12} + k_e\right) - \left(R - P\right) & k_{21} \\ k_{12} & -k_{21} - \left(R - P\right) \end{bmatrix} \begin{bmatrix} \eta_1 \\ \eta_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix} \tag{14}$$

where

$$P = \frac{1}{2}\left(k_{12} + k_e + k_{21}\right) \text{ and}$$

$$R = \sqrt{-k_e k_{21} + \frac{1}{4}\left(k_{12} + k_e + k_{21}\right)^2}$$

We consider the second row of equation (14):

$$\eta_1 k_{12} - \left(k_{21} + R - P\right)\eta_2 = 0$$

$$\eta_1 k_{12} = \left(k_{21} + R - P\right)\eta_2$$

$$\eta_1 = \frac{\left(k_{21} + R - P\right)}{k_{12}}\eta_2$$

$$\vec{\eta} = \begin{bmatrix} \eta_1 \\ \eta_2 \end{bmatrix} = \begin{bmatrix} \frac{k_{21} + R - P}{k_{12}}\eta_2 \\ \eta_2 \end{bmatrix} = \eta_2 \begin{bmatrix} \frac{k_{21} + R - P}{k_{12}} \\ 1 \end{bmatrix}$$

Let $\eta_2 = k_{12}$, then,

$$\vec{\eta} = \begin{bmatrix} k_{21} + R - P \\ k_{12} \end{bmatrix} \tag{15}$$

$\lambda = \lambda_2 :$

We need to solve,

$$\begin{bmatrix} -\left(k_{12} + k_e\right) - \left(-R - P\right) & k_{21} \\ k_{12} & -k_{21} - \left(-R - P\right) \end{bmatrix} \begin{bmatrix} \eta_1 \\ \eta_2 \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix} \tag{16}$$

We consider the second row of equation 16:

$$\eta_1 k_{12} - \left(k_{21} - R - P\right)\eta_2 = 0$$

$$\eta_1 k_{12} = \left(k_{21} - R - P\right)\eta_2$$

$$\eta_1 = \frac{\left(k_{21} - R - P\right)}{k_{12}}\eta_2$$

$$\vec{\eta} = \begin{bmatrix} \eta_1 \\ \eta_2 \end{bmatrix} = \begin{bmatrix} \frac{k_{21} - R - P}{k_{12}}\eta_2 \\ \eta_2 \end{bmatrix} = \eta_2 \begin{bmatrix} \frac{k_{21} - R - P}{k_{12}} \\ 1 \end{bmatrix}$$

Let $\eta_2 = k_{12}$, then,

$$\vec{\eta} = \begin{bmatrix} k_{21} - R - P \\ k_{12} \end{bmatrix} \tag{17}$$

Then, the general solution to equation 1 and equation 2 is given as:

$$\vec{C}(t) = A_0 e^{(R-P)t} \begin{bmatrix} k_{21} + R - P \\ k_{12} \end{bmatrix} + A_1 e^{-(R+P)t} \begin{bmatrix} k_{21} - R - P \\ k_{12} \end{bmatrix}. \tag{18}$$

Now, we can find the constants. To do this we simply need to apply the initial conditions in equation (3).

$$\vec{C}(0)=\begin{bmatrix}\frac{D}{V}\\0\end{bmatrix}=A_0\begin{bmatrix}k_{21}+R-P\\k_{12}\end{bmatrix}+A_1\begin{bmatrix}k_{21}-R-P\\k_{12}\end{bmatrix} \tag{19}$$

All we need to do now is multiply the constants though and then get two equations (one for each row) that we can solve for the constants. This gives,

$$\left(k_{21}+R-P\right)A_0+\left(k_{21}-R-P\right)A_1=\frac{D}{V} \tag{20}$$

$$k_{12}\left(A_0+A_1\right)=0 \tag{21}$$

From equation 21,

$k_{12}\neq 0$

So,

$$A_0+A_1=0 \text{ and } A_0=-A_1$$

Equation 20 becomes

$$-\left(k_{21}+R-P\right)A_1+\left(k_{21}-R-P\right)A_1=\frac{D}{V}$$

$$-\left(k_{21}+R-P\right)A_1+\left(k_{21}-R-P\right)A_1=\frac{D}{V}$$

$$A_1=-\frac{D}{2RV}$$

$$A_0=\frac{D}{2RV}$$

Equation 18 becomes

$$\vec{C}(t)=\frac{D}{2RV}e^{(R-P)t}\begin{bmatrix}k_{21}+R-P\\k_{12}\end{bmatrix}-\frac{D}{2RV}e^{-(R+P)t}\begin{bmatrix}k_{21}-R-P\\k_{12}\end{bmatrix}. \tag{22}$$

NUMERICAL SIMULATION

To determine the alcohol content for 40 hours, we ran a numerical simulation in Matlab. Fig. 2 shows the outcomes of the simulation for the alcohol concentration in the body and bloodstream. Further, we demonstrated how, for various rate constants, the beginning alcohol concentration in the bodily compartment affects the maximum alcohol concentration in the bloodstream. Fig. 3 shows these findings. Finally, we compared the blood alcohol content for various rate constant values in the range of 40 hours. Fig. 4 presents these findings.

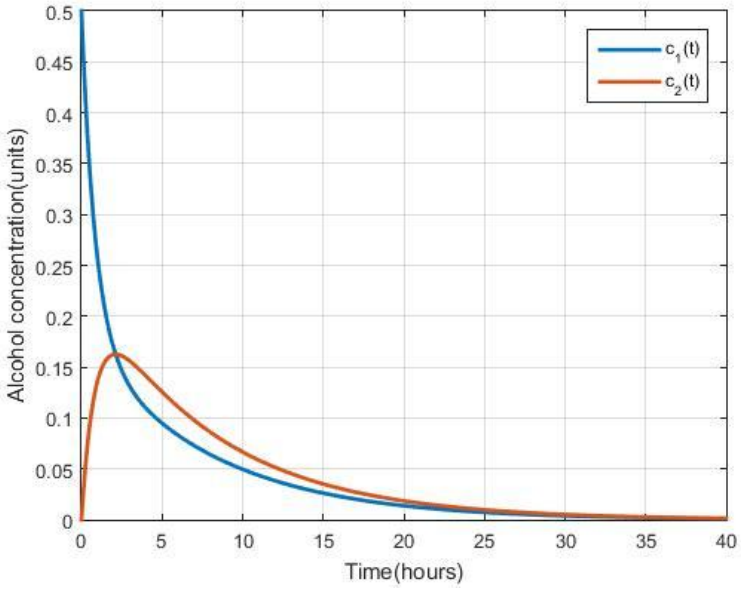

Fig. 2 Alcohol concentration in body and bloodstream

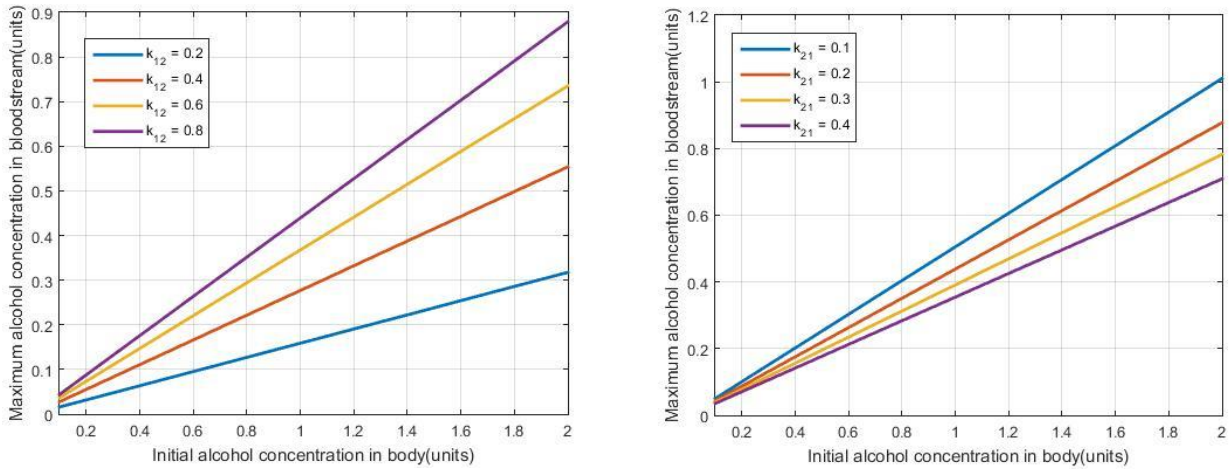

Fig. 3 (a & b) Maximum blood alcohol concentration and initial alcohol intake impacts for different (a) k_{12} (b) k_{21}.

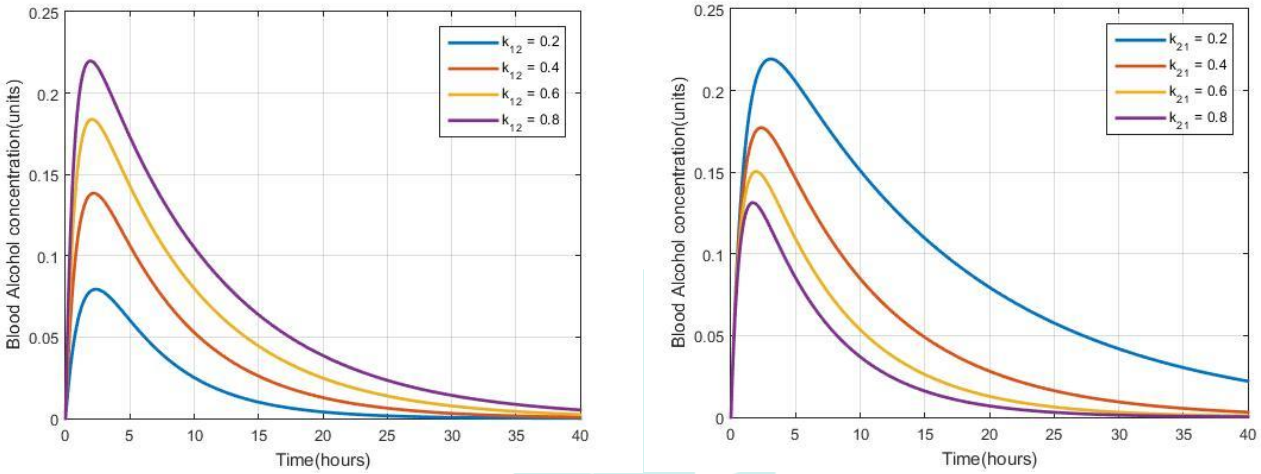

Fig. 4 (a & b) Numerical simulation result of alcohol concentration in bloodstream for different values (a) k_{12} (b) k_{21}.

DISCUSSION

Numerical simulation results in Fig. 2 showed that while the alcohol concentration in the body reduced from a maximum value of 0.5 to 0, the blood alcohol concentration increased to a maximum at 2hrs 20mins before reducing to zero.

In Fig. 3, a high value of k_{12} produces a high value of maximum alcohol concentration in bloodstream and vice versa, i.e., increasing the value of k_{12} increases the maximum concentration of alcohol in the bloodstream. The same cannot be said for k_{21}, which shows an inverse relationship with k_{12}.

In Fig. 4, we have altered the values of k_{12} and k_{21} and simulated it for 40 hours. As stated above, the maximum concentration in the bloodstream occurred at 2hrs 20mins. While the magnitude of this maximum increases as k_{12} increases it decreases as k_{21} increases.

CONCLUSION

In order to comprehend how blood alcohol concentration moves throughout the human body, we have suggested a compartmental mathematical model in this study. The body compartment and the circulatory compartment were taken into consideration when we created a system of ordinary differential equations. The eigenvalue approach was then used to solve this problem and produce an analytical solution. To get numerical data, we used MATLAB software to conduct a 40-day numerical investigation of the model equation. Based on the results obtained, numerical results agreed with analytical results, and the maximum alcohol concentration in the bloodstream was observed within the first three hours of introduction.

Likewise, the blood alcohol concentration decreases to a minimum as the rate of flow out of the bloodstream increases, and vice versa. There is a linear relationship between the maximum blood alcohol concentration and the starting blood alcohol concentration, meaning that the blood alcohol concentration rises as the initial blood alcohol concentration rises.

RECOMMENDATIONS

Since a higher rate constant increases the blood alcohol concentration, we recommend that individuals consume less alcohol so as to maintain a low initial alcohol concentration, which in turn maintains a low rate constant value.

Even with a low rate constant, k_{21}, it is never an assurance that the alcohol concentration in the body will be low. It also depends on the elimination rate constant, which is affected by the liver. To this effect, we recommend that individuals with poor liver performance consume less alcohol so that the concentration in the body will be lower.

Since the proposed model equations are all linear, we recommend that the Laplace transform method also be used to obtain the analytical solution, as the method is very efficient and simpler than the eigenvalue method used in this research.

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