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Mathematical Modelling of the Oral Administration of Drugs into the Stomach and the Treatment Effect with the Influence of Temperature

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Abstract

This research deals with the mathematical formulation that mimics the oral administration of drug intake into the stomach and the therapeutic effect of temperature increases. We solved the formulated ordinary differential equations (ODEs) using the Laplace method, and the numerical simulation was carried out using Wolfram Mathematica by varying the thermal conductivity and the treatment terms and studying the significant role they play in eliminating the drug from the human body. The study showed that the pertinent parameters influence the drug concentration in the stomach compartment under the influence of temperature. In conclusion, with the help of this simple model, researchers should be able to better understand oral drug administration and provide reliable and appropriate care to patients.

Keyword: Treatment; Drug; Temperature; Application; Modelling; Administration; Stomach

1. Introduction

Drinking excessively in a short period of time or binge drinking increases stress on your body and internal organs and can lead to a hangover after a drinking session. High alcohol levels in the body can lead to headaches, severe dehydration, nausea, vomiting, diarrhea, and indigestion (Maher, 1997). When alcohol is consumed excessively and over long periods of time, its long-term effects can damage many of your body's vital organ systems. Among these health risks are cardiovascular health risks, brain health risks, pancreatic health risks, and liver health risks (Wang et al. 2010). When alcohol is consumed, it is not digested; it quickly enters the bloodstream and spreads to every part of the body.

The brain is affected first by alcohol, followed by the kidneys, lungs, and liver; the impact on the body depends on age, gender, weight, and type of alcohol (Cohen, 2022). Studies on ethanol metabolism have mainly relied on single-dose experimental studies that address road safety aspects or monitor ethanol elimination over time (Saha et al. 2015). A study by Shirley (2007) used Markov or hidden Markov models to describe subjects' drinking behavior. These models are better suited to describe processes that lead to sudden changes rather than gradual changes over time. Ghadirinejad *et al*. (2016) proposed a stochastic model for the ethanol removal process. The main features of their model were that it took into account multiple doses as well as zero rejection and first-order rejection. Their results may explain differences in drinking schedules as well as the amount of alcohol consumed. Bunonyo and Amadi (2023) presented a mathematical model to study alcohol concentrations in the gastrointestinal tract and blood circulation. The model was solved analytically, and some relevant input parameters were obtained. Samanta (2015) developed a mathematical model of alcohol abuse consisting of 4 groups corresponding to 4 population groups: moderate and occasional drinkers, heavy drinkers, drinkers in treatment, and transient groups. Pieters et al. (1990) described the pharmacokinetics of alcohol after oral administration using a three-compartment model assuming concentration-dependent absorption and excretion.

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Compartment mathematical models have become important tools for predicting alcohol concentrations in the body and providing effective measures for analysis, research, and control of adverse effects.

2. Formula models

We postulated that drug concentrations in the stomach may be affected by treatment and temperature increases in order to develop a mathematical model system that represents the absorption and distribution of oral drugs in the body through the stomach. To idealize the system, we use the diagram below (Fig. 1).

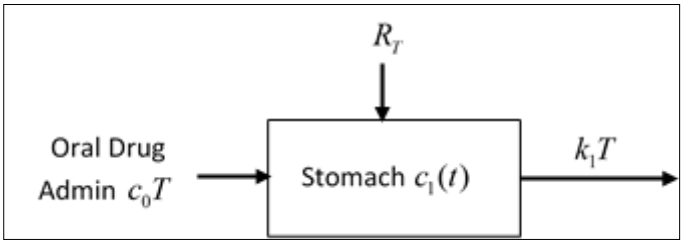

Figure 1 Diagram showing the intake of drug with initial concentration and treatment into the stomach

2.1. Assumption

Before formulating the mathematical model to investigate the effect of treatment and rise in temperature on drug concentration in the stomach. The assumptions are as follows:

- The drug is consumed under specific temperature T
- The concentration of the drug in the stomach compartment be denoted as c_1
- The treatment is directly applied to the stomach compartment as R_T
- The drug can be eliminated with a rate k_1

The Fig.1, is a diagram showing the intake of drug into the stomach where treatment is applied for the purpose of treatment and control of drug abuse. Where $c_1(t)$ and $T(t)$ denote the concentrations of drug in the stomach and the temperature level respectively. The initial concentration of the drug is the stomach is denoted as c_0 and the basic was derived from Bunonyo *et al*. (2023) and Bunonyo *et al*. (2023):

2.2. Mathematical Models

$$\frac{dc_1}{dt} = R_T - k_1 c_1 T \tag{1}$$

$$\frac{dT}{dt} = -k_T\left(T - T_s\right) \tag{2}$$

Equations (1)-(3) are subject to the following initial conditions:

$$\left.\begin{aligned} c_1(0) &= c_0 \\ T(0) &= T_0 \end{aligned}\right\} \tag{3}$$

3. Method of Solution

In order to investigate the effect of temperature rise or lose on the drug administered in stomach, we first solve equation (2), then substitute the result into equation (1) and solve it, then:

3.1. Laplace Method

We simply recall the basic Laplace formula which we shall be using to solve the formulated models in section 2. They are stated as follows:

$$L\{T(t)\} = T(s) = \int_0^\infty e^{-st} T(t) dt \tag{4}$$

$$L\{c_1(t)\} = c_1(s) = \int_0^\infty e^{-st} c_1(t) dt \tag{5}$$

Applying equation (4) to solve equation (2), we have the following:

$$sT(s) - T(0) + k_T T(s) = k_T T_s \int_0^\infty e^{-st} dt \tag{6}$$

Simplifying equation (6), we have:

$$T(s) = -\frac{k_T T_s}{s(s + k_T)} \tag{7}$$

Applying equations (4) and (5) to solve equations (1)), we have:

$$sc_1(s) - c_1(0) = -\frac{R_T}{s} - k_1 c_1(s) T(s) \tag{8}$$

Simplifying equation (8), we have

$$(s + k_1 T(s)) c_1(s) = c_0 - \frac{R_T}{s} \tag{9}$$

Substitute equation (7) into equation (9), we have:

$$\left(s - \frac{k_1 k_T T_s}{s(s + k_T)}\right) c_1(s) = c_0 - \frac{R_T}{s} \tag{10}$$

Simplifying equation (10), we have:

$$c_1(s) = \left(\frac{c_0 s - R_T}{s}\right) \frac{s(s + k_T)}{s^2(s + k_T) - k_1 k_T T_s} \tag{11}$$

Simplifying equation (11), we have:

$$c_1(s) = \frac{c_0 s^2 + (c_0 k_T - R_T) s - R_T k_T}{s^3 + s^2 k_T - k_1 k_T T_s} \tag{12}$$

Equation (12) can be represented as follows:

$$c_1(s) = \frac{c_0 s^2 + (c_0 k_T - R_T)s - R_T k_T}{s^3 + s^2 k_T - k_1 k_T T_s} = \frac{A}{(s-\lambda_1)} + \frac{B}{(s-\lambda_2)} + \frac{C}{(s-\lambda_3)} \qquad (13)$$

Taking the inverse of equation (13), we have:

$$c_1(t) = L^{-1}\{c_1(s)\} = AL^{-1}\left\{\frac{1}{(s-\lambda_1)}\right\} + BL^{-1}\left\{\frac{1}{(s-\lambda_2)}\right\} + CL^{-1}\left\{\frac{1}{(s-\lambda_3)}\right\} \quad (14)$$

Simplifying the equation (14), we have:

$$c_1(t) = L^{-1}\{c_1(s)\} = Ae^{\lambda_1 t} + Be^{\lambda_2 t} + Ce^{\lambda_3 t} \qquad (15)$$

where $A = \dfrac{\begin{Bmatrix} \left[-R_T k_T(\lambda_1+\lambda_3) - (R_T - c_0 k_T)\lambda_1\lambda_3\right] \\ -\left[-R_T k_T(\lambda_2+\lambda_3) - \lambda_2\lambda_3(R_T - c_0 k_T)\right] \\ +c_0\left[\lambda_1\lambda_3(\lambda_2+\lambda_3) - \lambda_2\lambda_3(\lambda_1+\lambda_3)\right] \end{Bmatrix}}{\begin{Bmatrix} \left[(\lambda_1+\lambda_3)\lambda_1\lambda_2 - (\lambda_1+\lambda_2)\lambda_1\lambda_3\right] \\ -\left[\lambda_1\lambda_2(\lambda_2+\lambda_3) - \lambda_2\lambda_3(\lambda_1+\lambda_2)\right] \\ +\left[\lambda_1\lambda_3(\lambda_2+\lambda_3) - \lambda_2\lambda_3(\lambda_1+\lambda_3)\right] \end{Bmatrix}}$, $B = \dfrac{\begin{Bmatrix} \left[\lambda_1\lambda_2(R_T - c_0 k_T) - R_T k_T(\lambda_1+\lambda_2)\right] \\ -c_0\left[\lambda_1\lambda_2(\lambda_2+\lambda_3) - \lambda_2\lambda_3(\lambda_1+\lambda_2)\right] \\ -\left[R_T k_T(\lambda_2+\lambda_3) + \lambda_2\lambda_3(R_T - c_0 k_T)\right] \end{Bmatrix}}{\begin{Bmatrix} \left[(\lambda_1+\lambda_3)\lambda_1\lambda_2 - (\lambda_1+\lambda_2)\lambda_1\lambda_3\right] \\ -\left[\lambda_1\lambda_2(\lambda_2+\lambda_3) - \lambda_2\lambda_3(\lambda_1+\lambda_2)\right] \\ +\left[\lambda_1\lambda_3(\lambda_2+\lambda_3) - \lambda_2\lambda_3(\lambda_1+\lambda_3)\right] \end{Bmatrix}}$,

$C = \dfrac{\begin{Bmatrix} c_0\left[\lambda_1\lambda_2(\lambda_1+\lambda_3) - (\lambda_1+\lambda_2)\lambda_1\lambda_3\right] \\ -\left[\lambda_1\lambda_2(R_T - c_0 k_T) - R_T k_T(\lambda_1+\lambda_2)\right] \\ +\left[\lambda_1\lambda_3(R_T - c_0 k_T) - R_T k_T(\lambda_1+\lambda_3)\right] \end{Bmatrix}}{\begin{Bmatrix} \left[(\lambda_1+\lambda_3)\lambda_1\lambda_2 - (\lambda_1+\lambda_2)\lambda_1\lambda_3\right] \\ -\left[\lambda_1\lambda_2(\lambda_2+\lambda_3) - \lambda_2\lambda_3(\lambda_1+\lambda_2)\right] \\ +\left[\lambda_1\lambda_3(\lambda_2+\lambda_3) - \lambda_2\lambda_3(\lambda_1+\lambda_3)\right] \end{Bmatrix}}$, $\lambda_1 = \sqrt{k_1 k_T}$, $\lambda_2 = -\sqrt{k_1 k_T}$, and $\lambda_3 = T_s - k_T$

4. Results

In this section, we performed numerical simulation of the analytical results for the drug concentration in the stomach and that of change in temperature in the stomach using Wolfram Mathematica, version 12, and produced the graphical results as follows:

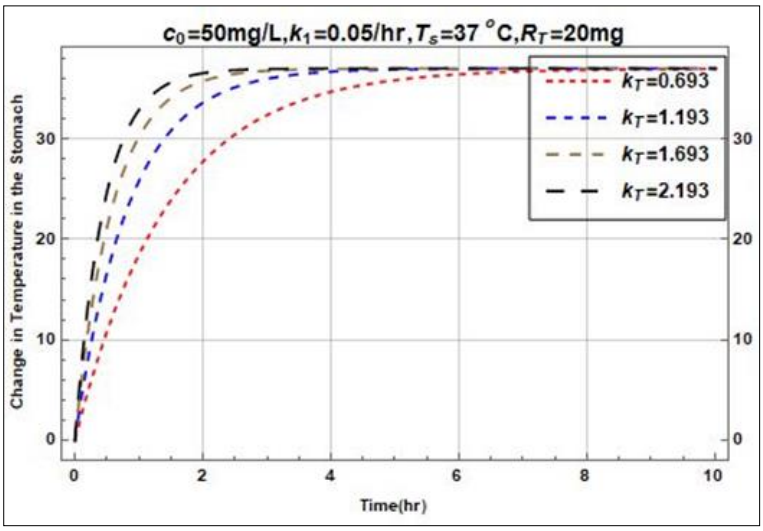

Figure 2 Effect of conductive term on the temperature profile

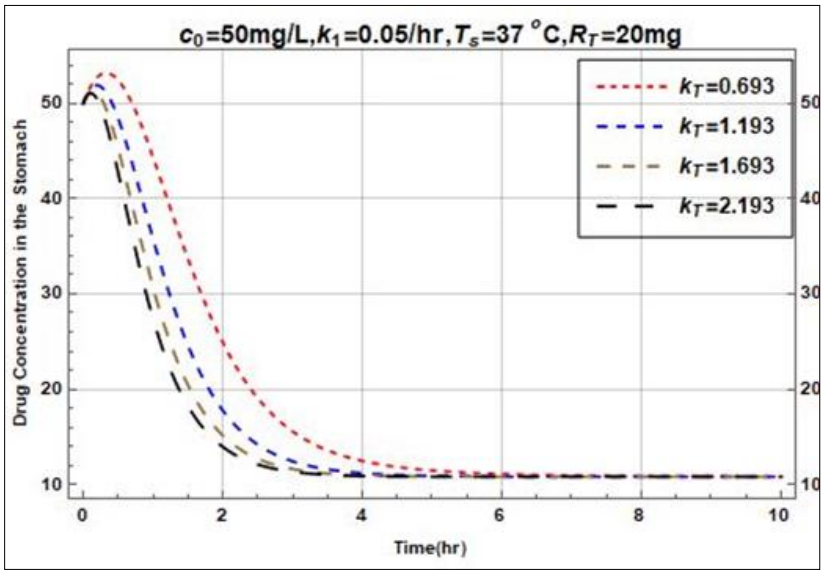

Figure 3 Effect of conductive term on the Drug concentration

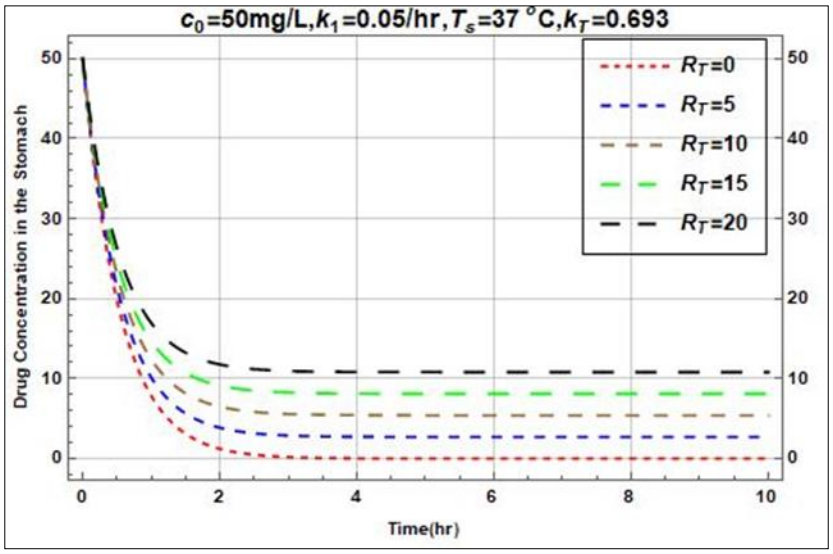

Figure 4 Effect of Treatment on the Drug concentration

5. Discussion

Fig. 2 illustrates that the temperature in the stomach rises with an increase in conductivity. The result is that the temperature in the stomach remained zero for the conductivity at 0.693. With an incremental value of 0.5, the temperature started to increase and then stabilized. Fig. 3 shows that an increase in conductivity creates a mild increase in drug concentration in the stomach before decreasing stability after 10 hours. In addition, it was observed that after the sharp drop, the drug concentration in the body began to decrease as it dropped to stability. The result in the above Fig. 4 showed that the drug concentration was at a peak of 50 mg/L, then dropped sharply to near zero, and maintained stability at zero for a long time. Furthermore, it is seen that concentration sharply drops with an increase in treatment from 0, 5, 10, 15, and 20 mg. And the results obtained are in consistent with previous studies by Bunonyo et al. (2023)

6. Conclusion

We have been able to formulate a system of mathematical models that involved treatment by introducing the treatment term on the model representing drug concentration in the stomach, solving the problem, and concluding that the thermal conductivity increase affects the drug concentration in the stomach as well as changes the temperature in the stomach. Finally, the drug concentration also changes by increasing the treatment level.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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