Modeling the Diffusion of Dichlorvos through Human Stomach Lining

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ABSTRACT

Dichlorvos is the main poison in sniper pesticide which has produced negative effects especially among youths in recent times. The poisonous effects of dichlorvos on humans require urgent studies to combat the damaging impacts among humans. However, the limitations of carrying out experiments on human test subjects request the quest for alternative approach. Such approach can be made through modeling the transport of dichlorvos in the human body and the resulting negative effect. Therefore, this work presents mathematical modeling for the diffusion of dichlorvos through the human stomach lining. The model is set up to determine the amount of dichlorvos that leaves the stomach through diffusion alone and the health effects various concentration of the poison has on humans. Two cases are studied in order to captivate the effects of dichlorvos poisoning for two different scenarios. The initial condition is set to *0.05L* and different driving forces is used to model the scenarios in spherical coordinates. The governing equation is derived from Fick's first law and is solved analytically, a numerical solution is obtained using MATLAB's pdepe solver and graphs are plotted for the two cases. From the results it is observed that about 14.4% of dichlorvos is diffused through the stomach lining in about 60hours for the first case while for the second case, the periodic intake of water along with dichlorvos gradually reduces the dichlorvos concentration in the stomach. These results show consistency with some experimental results from literature. Therefore, the model can be used in addition to the modes of treatment obtained from literature to predict the concentration of dichlorvos in a person and also proffer a life-saving treatment.

Keywords: Dichlorvos, Diffusion, Concentration, Mathematical modeling, Analytical solutions

1. INTRODUCTION

Sniper is an agricultural insecticide made up of Dichlorvos, also known as DDVP (2, 2-dichlorovinyl dimethyl phosphate), a compound of organophosphates. Organophosphate compounds are a varied group of chemicals that are helpful as insecticides, anthelmintic and nerve gases for national and industrial reasons. These chemicals kill pests and cause poisoning in animals by inhibiting the enzyme, acetylcholinesterase (AChE) that metabolizes acetylcholine (ACh) in nerve synapses, leading to accumulation of acetylcholine (ACh) in the blood, belly and muscle.

The toxic effects of DDVP in insects can also be replicated in animals and humans. Acute toxicity may result from inhalation, dermal absorption (skin contact) and ingestion. Numerous research has been done on the effects and treatment of DDVP (dichlorvos) but little work has been done on modelling its flow and diffusion in the stomach, this is largely due to the rapid degradation of DDVP by tissue esterases, particularly in the liver and the serum.

The recommended approach to overcome this limitation is through the use of mathematical models.

Therefore, this work presents a mathematical model for the diffusion of Dichlorvos (the main poison in sniper pesticide), through the human stomach lining in order to determine the amount of Dichlorvos that leaves the stomach through diffusion alone and the health effects various concentration of the poison has on humans. Eddleston et al [1] presented on the how to manage acute organophosphorus pesticide poisoning while Emerson [2] studied the poisoning of organophosphate.

Mathematical modeling for prevention of methanol poisoning was presented by Gosh et al. [3] while Kora et al. [4] submitted sociodemographic profile of the organophosphorus poisoning cases in Southern India. The formulations and impacts of Dichlorvos was explained by Musa et al. [5] and Ezeji [6]. Further studies on the effects of liquid poisoning has been presented in literature [7-21] taking into account the properties of dichlorvos such as diffusivity. In this work, mathematical modeling for the diffusion of dichlorvos through the human stomach lining. Analytical solutions of the problems are presented and the results are discussed.

2. THEORETICAL FRAMEWORK: SITE OF ACTION-STOMACH LINING

Three primary modes of dichlorvos exposure (DDVP) are: inhalation, ingestion, and dermal absorption. This research focuses on ingestion, thus ignoring the other two modes. When most of the poison is first ingested into the stomach, dichlorvos in the stomach may be absorbed into the bloodstream through the stomach lining, or it may proceed into the small intestine where it may be absorbed into the bloodstream again.

Intoxication is caused by the presence of dichlorvos in the blood after absorption into the bloodstream. Although at any stage along the gastrointestinal tract dichlorvos can be consumed, most of it is absorbed either through the lining of the stomach or through the small intestine.

About 50% of the dichlorvos produced is absorbed into the bloodstream. About 20% of this is produced in the stomach and 40% in the small intestine, while the rest of the digestive tract absorbs a negligible quantity (ATSDR, 2000).

3. PROBLEM FORMULATION

Consider a stomach with internal and external layers as shown in **Figs. 1a** and **1b**. In order to develop mathematical model for the transport of dichlorvos in the human stomach, the following assumptions are made
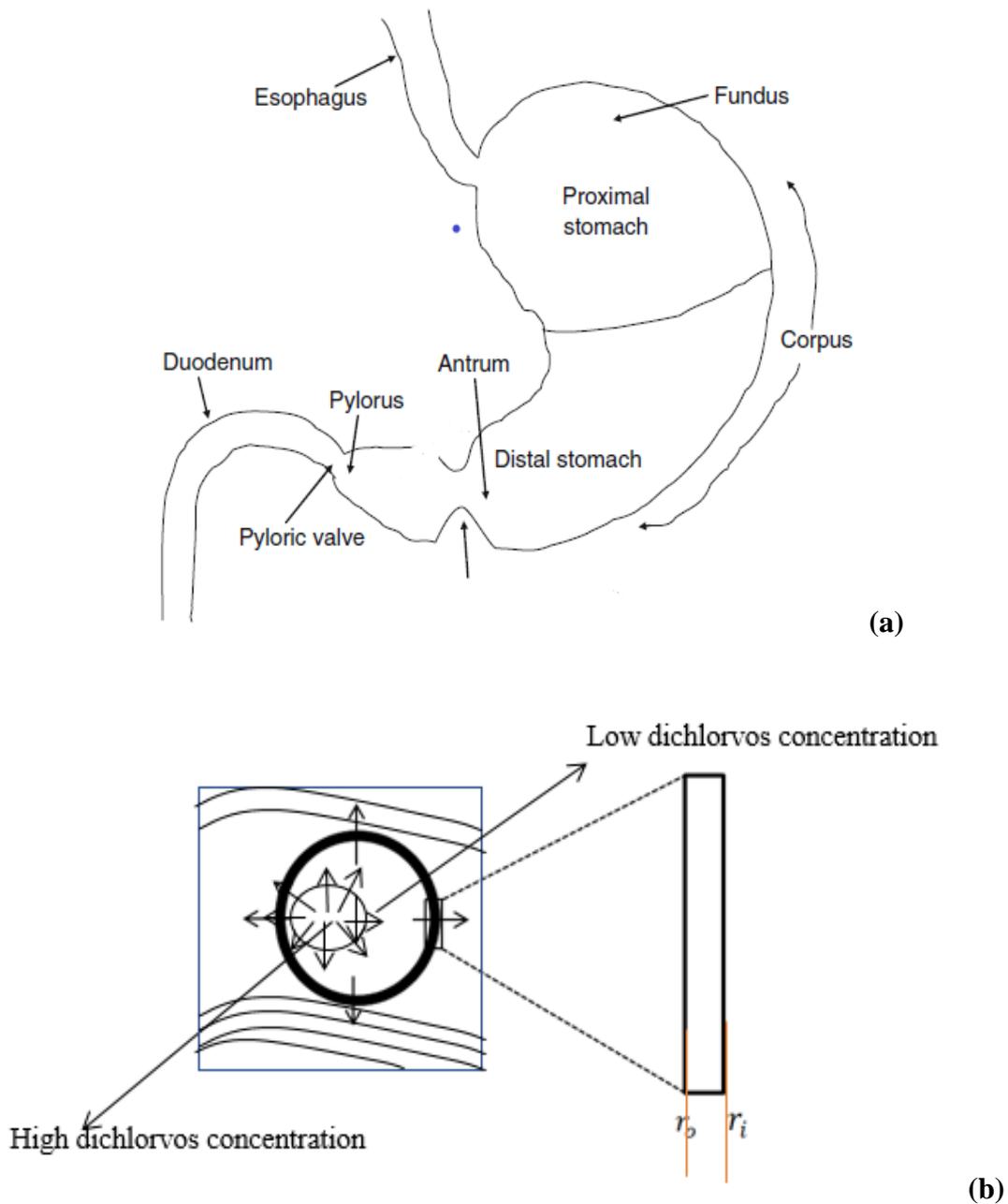
Esophagus

Fundus

Proximal stomach

Corpus

Duodenum

Antrum

Pylorus

Distal stomach

Pyloric valve

(a)

Low dichlorvos concentration

High dichlorvos concentration

r_o r_i

(b)

Fig. 1(a,b). Stomach diagram **(a),** Schematic representation of the cross section of the stomach, comprising the internal layer $r_o(r = 6cm)$ and the external layer $r_i(r = 6.5cm)$ showing diffusion release pattern of dichlorvos **(b).**

i.   Diffusion alone can account for variations in the substrate concentration at the entrance and exit of the segment being considered.

ii. Diffusion takes place only in the r-direction while diffusion in other directions is negligible.

iii. In the initial condition, the concentration is set to 5% of volume of dichlorvos in the stomach whilst the presence of food and other fluids are neglected in order to avoid a multi-component mixture.

iv. The stomach shape is modeled to be spherical shape and gastric acid entering the small-intestine is negligible.

v.   Absorption of dichlorvos along other parts of the gastro-intestinal tract is neglected.

vi. The dichlorvos is ingested at a rate that achieves the concentration required.

For the purpose of reality, two cases (A and B) of equal dichlorvos poison intake concentration are considered and contrasted for metabolism forecast. Dichlorvos with intent to commit suicide was ingested in both instances. Case A chooses to drink as much as possible but as slowly as possible. Case B drinks dichlorvos then picks up water, then picks up dichlorvos, then drinks water, for a while.

The stomach can be assumed to be roughly spherical (National Research Council, 1999). Fick's second law of diffusion in three dimensional spherical coordinates would be more accurate.

$$\frac{\partial C}{\partial t} = D\left[\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right) + \frac{1}{r^2 sin\theta}\frac{\partial}{\partial \theta}\left(sin\theta\frac{\partial C}{\partial \theta}\right) + \frac{1}{r^2 sin^2\theta}\frac{\partial^2 C}{\partial \emptyset^2}\right] \qquad (1)$$

In order to simplify the problem, constant mixing is assumed in the stomach in order to approximate this as a one-dimensional problem

$$\frac{\partial C}{\partial t} = D\left[\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right)\right] \qquad (2)$$

where:

r, C, t, D represent the radius of stomach (m), concentration of poison in the stomach (ml), t (min), and diffusivity of dichlorvos poison (m^2/s), respectively.

It is presumed for simplicity that the stomach is shaped like a sphere and can be modeled as a sphere. The stomach usually carries about *1* liter of volume. This volume would have a sphere with a radius of about *6.2 cm*, whereas the stomach wall has a thickness of about *0.51 cm ± 0.11 cm* (Rapaccini et al., 1988).

The stomach would therefore be approximated as a sphere with a *6.5 cm* outer radius and a *6.0 cm* inner radius to represent a *0.5 cm* dense wall. In order to keep the concentration, the same throughout the stomach, the diffusivity in the volume of the stomach or in the chamber of the stomach from the center of the stomach to the inner edge of the wall is assumed to be extremely high (i.e $D = 10^{15} cm^2/hr$, if $x < 6cm$). This forces the stomach inside to be well-mixed. Finally, dichlorvos (D) diffusivity is $10^{-5} cm^2/s$ (Groundwater Chemicals Desk Reference).

3. 1. Boundary and initial conditions

The stomach walls of cases A and B all have the same boundary conditions,

$$\frac{dC}{dr}\Big|_{r=0} = 0 \tag{3a}$$

$$C(0, t) = 0 \tag{3b}$$

The first situation makes the concentration profile at the middle of the sphere continuous and distinguishable. The second condition forces the concentration in the stomach to reach zero as the poison leaves the stomach and enters the stream of blood. The volume of the bloodstream is assumed to be much larger than the volume of the stomach. This is a sensible hypothesis as the volume of the stomach is about *1L* and the complete quantity of the blood is about *5L*. The concentration of dichlorvos in the sniper bottle is about 50%.

A dichlorvos bottle has a volume of *100 ml*, therefore the poison by volume concentration is 0.5 in the bottle. Assuming the stomach is only filled with sniper and other fluids whose effects are negligible, the stomach has a total a volume of *1L* then the percentage of sniper in the stomach initially is 5% (i.e $C_0 = 0.05\,L$).

In order to account for the rate of degradation of the poison through the stomach lining, a driving force Q (ml/s) is included in the equation.

$$\frac{\partial C}{\partial t} = D\left[\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right)\right] + Q \tag{4}$$

3. 2. Case A

Case A started off with no dichlorvos in his stomach. This sets the concentration (C_o) to 0 everywhere. He then starts drinking the poison at a slow constant rate. The driving force (Q) is modeled as a constant function applied to inside of the stomach volume only $(0 < r < 6cm)$.

Case A (Spherical Coordinates):

Table 1. Spherical Coordinates for Case A Diffusion equation initial and boundary conditions.

$\frac{\partial C}{\partial t} = D\left[\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial C}{\partial r}\right)\right] + Q$ $Q(r < 6cm) = 0.0187$ $Q(r > 6cm) = 0$	$C(r < 6cm, t = 0) = 0$ $C(r > 6cm, t = 0) = 0$	$\frac{\partial C}{\partial r}(r = 0, t) = 0$ $C(r = 6.5cm, t) = 0$

3. 3. Case B

Case B also drank consistently until he felt he had enough to kill himself at time t = 0. The initial conditions for this problem set the concentration to 0.05 poison by volume inside the stomach volume $(0 < r < 6\ cm)$ and to 0 in the stomach wall$(6cm < r < 6.5\ cm)$. In addition, this person consistently had a drink of dichlorvos, then water, then a drink of dichlorvos and so on. The driving force can be modeled by a sine squared function applied to the inside of the stomach volume only$(0 < r < 6\ cm)$. Each time he drinks dichlorvos he is increasing on the part of the function; each time he drinks water he is decreasing on the part of the function. The driving force was obtained from Olufemi and Olayebi, 2017).

Case B (Spherical Coordinate):

Table 2. Spherical Coordinates for Case B Diffusion equation initial and boundary conditions.

$\dfrac{\partial C}{\partial t} = D\left[\dfrac{1}{r^2}\dfrac{\partial}{\partial r}\left(r^2\dfrac{\partial C}{\partial r}\right)\right] + Q$ $Q(r < 6cm) = 0.01sin^2(\pi t)$ $Q(r > 6cm) = 0$	$C(r < 6cm, t = 0) = 0.05$ $C(r > 6cm, t = 0) = 0$	$\dfrac{\partial C}{\partial r}(r = 0, t) = 0$ $C(r = 6.5cm, t) = 0$

4. THE METHOD OF SOLUTION: ANALYTICAL SOLUTION USING SEPARATION OF VARIABLES

The developed models are solved analytically using method of separation of variables. The analysis is presented as follows. Considering Eq. (2),

$$\frac{\partial C}{\partial t} = D\frac{1}{r^2}\frac{\partial}{\partial r}r^2\frac{\partial C}{\partial r} \tag{5}$$

The independent variable is separated as

$$C(r,t) = B(r)T(t) \tag{6}$$

Substitution of Eq. (6) into Eq. (5),

$$B\frac{\partial T}{\partial t} = DT\frac{1}{r^2}\frac{\partial}{\partial r}r^2\frac{\partial B}{\partial r} \tag{7}$$

After rearrangement;

$$\frac{1}{DT}\frac{\partial T}{\partial t} = \frac{1}{Br^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial B}{\partial r}\right) \tag{8}$$

Equating Eq. (8) to $-\lambda^2$,

$$\frac{1}{DT}\frac{\partial T}{\partial t} = \frac{1}{Br^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial B}{\partial r}\right) = -\lambda^2 \tag{9}$$

Both sides of the above equation are independent. Thus, for them to be equal, they must both be equal to a constant. Solving both sides separately:

$$\frac{\partial T}{\partial t} = -\lambda^2 DT = T(t) = Ae^{-\lambda^2 Dt} \tag{10}$$

$$\frac{\partial}{\partial r}\left(r^2\frac{\partial B}{\partial r}\right) = -\lambda^2 r^2 B \tag{11}$$

Substitution with x:

$$x = \lambda r => dx = \lambda dr \tag{12}$$

Eq. (11) becomes:

$$\lambda\frac{\partial}{\partial x}\left(\frac{x^2}{\lambda^2}\lambda\frac{\partial B}{\partial r}\right) = -x^2 B \tag{13}$$

Substituting Eqs. (12) in (13):

$$x^2\ddot{B} + 2x\dot{B} + x^2 B = 0 \tag{14}$$

The solutions are Bessel functions with k = 0. Thus

$$x^2\ddot{B} + 2x\dot{B} + [x^2 + k(k+1)]B = 0 \tag{15}$$

Then, we have

$$B(x) = P_1\frac{sinx}{x} + P_2\frac{cosx}{x} \tag{16}$$

$$B(r) = P_1\frac{sin\lambda r}{r} + P_2\frac{cos\lambda r}{r} \tag{17}$$

Therefore, substituting Eqs. (11) and (17) in Eq. (6):

$$C(r,t) = \left(C_1\frac{sin\lambda r}{r} + C_2\frac{cos\lambda r}{r}\right) \cdot e^{-\lambda^2 Dt} \tag{18}$$

Applying the boundary conditions:

$$\frac{cos\lambda r}{\lambda r} (r = 0) \text{ is discontinuous} \quad \therefore C_2 = 0 \tag{19}$$

At $r = R$;

$$C(R,t) = 0 = C_1 \frac{sin\lambda R}{R} e^{-\lambda^2 Dt} \tag{20}$$

where:

$$\lambda R = n\pi \implies \lambda_n = \frac{n\pi}{R} \text{ for } n = 1,2,3 \ldots$$

Also,

$$C(r,0) = \begin{cases} C_0, & r < R - w \\ 0, & r > R - w \end{cases} \tag{21}$$

$\therefore$ For $r < R - w$:

$$C_0 = \sum_{n=1}^{\infty} C_n \frac{sin\frac{n\pi r}{R}}{\frac{n\pi r}{R}} e^0 \tag{22}$$

The general solution for $C(r,t)$ is written as follows:

$$C(r,t) = \sum_{n=1}^{\infty} C_n e^{-\lambda_n^2 Dt} \frac{\sin(\lambda_n r)}{r} \tag{23}$$

where:

$$\lambda_n = \frac{n\pi}{R}$$

Also, the MATLAB built in pdepe solver was used to numerically approximate the solutions modeling cases A and B. Code and plots are attached for the two cases. The simulations were carried out using the following parameters in **Table 3**.

Table 3. Simulation parameters.

S/N	Parameter Description	Symbol	Value	Source
1	Diffusion Coefficient for dichlorvos	D	$10^{-5} cm^2/s$	Groundwater chemicals Desk Reference
2	Radius at the center of the stomach	r_0	0	Rapaccini et al (1988)
3	Radius of stomach at inner lining	r_1	6cm	Rapaccini et al (1988)
4	Radius of stomach at outer lining	r_2	6.5cm	Rapaccini et al (1988)

5	Driving force for Case A	v	0.0187L/s	Olufemi and Olayebi (2017)
6	Driving force for Case B	v	$0.01sin^2(\pi t)$ L/s	Olufemi and Olayebi (2017)
7	Initial Concentration for Case A	C_0	0	ATSDR
8	Initial Concentration for Case B	C_0	0.05L	ATSDR

5. RESULTS AND DISCUSSION

The results of the analytical and numerical simulations for the two cases considered are presented in this section. For the Case A, **Fig. 2** is the case where the concentration inside the center of the stomach is initially 0 and the concentration in the stomach lining is initially 0. A constant driving force is applied to the system in order to simulate Case's A constant drinking.

The concentration inside the stomach increases everywhere and eventually reaches a steady state, the steady state concentration is dependent on the position within the stomach lining. It can be observed that the constant intake of dichlorvos results in the increase of the concentration to about *0.45 L*, *0.2 L* and *0.08 L* at the center of the stomach, entrance and exit of stomach lining respectively. This is expected since the dichlorvos is not diluted with water or any other substance. **Figure 3.1b** shows the concentration profile at *t = 30 hours* and this verifies the concentration profile in **Fig. 2**.
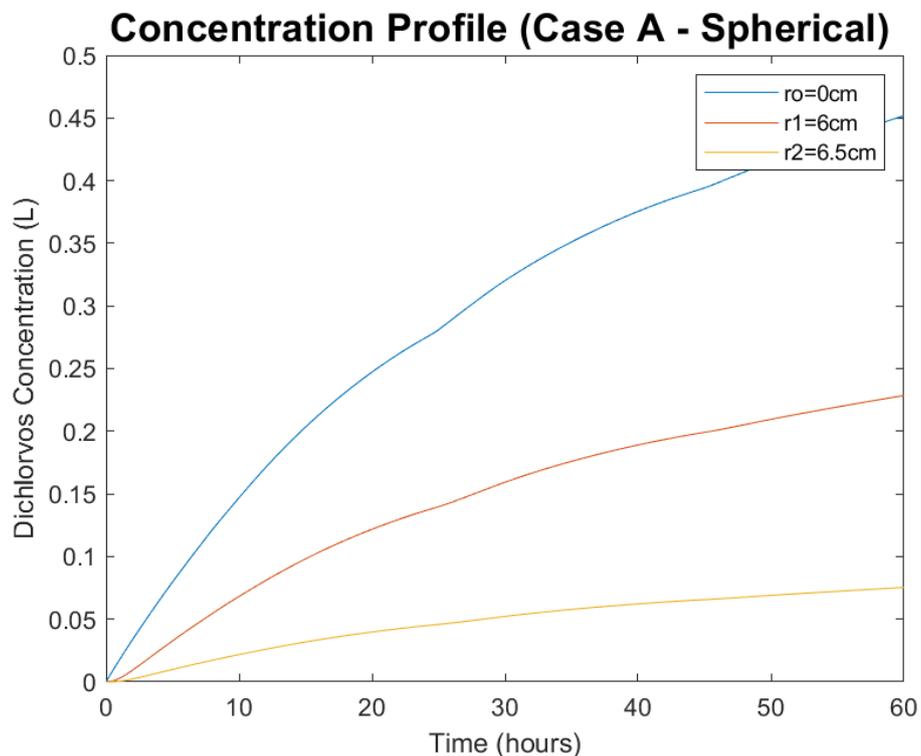

Figure 2. Concentration profile for CASE A in spherical coordinate

Fig. 3 is the case where the concentration was initially 0L at the center of the stomach. It then increases to *0.45 L* after *60 hours*, but only about *0.065 L* was present at the exit of the stomach lining after *60 hours*. Therefore, only about *14.4%* of dichlorvos was diffused through the stomach lining, this is consistent with literature. From literature with *0.065 L* diffused through the stomach lining the person should already be experiencing nausea, anxiety and restlessness. At this point if the person is taken to the hospital and given small doses of atropine, gastric lavage is conducted such a person will survive as long as there are no further complications. If this concentration increases further, then more severe effects such as respiratory failure and coma may occur. The person will require large doses of atropine at a dose of 0.*03-0.05 mg/kg*, this should be provided intravenously every 10-20 minutes or, then every *1-4 hours* for at least *24 hours* until indications of atropinization (hot dry washed skin, dilated pupil, increased *HR > 80 b/min*, systolic *BP > 80 mmHg*, and fast inversion of bronchospasm and bronchorrhea).
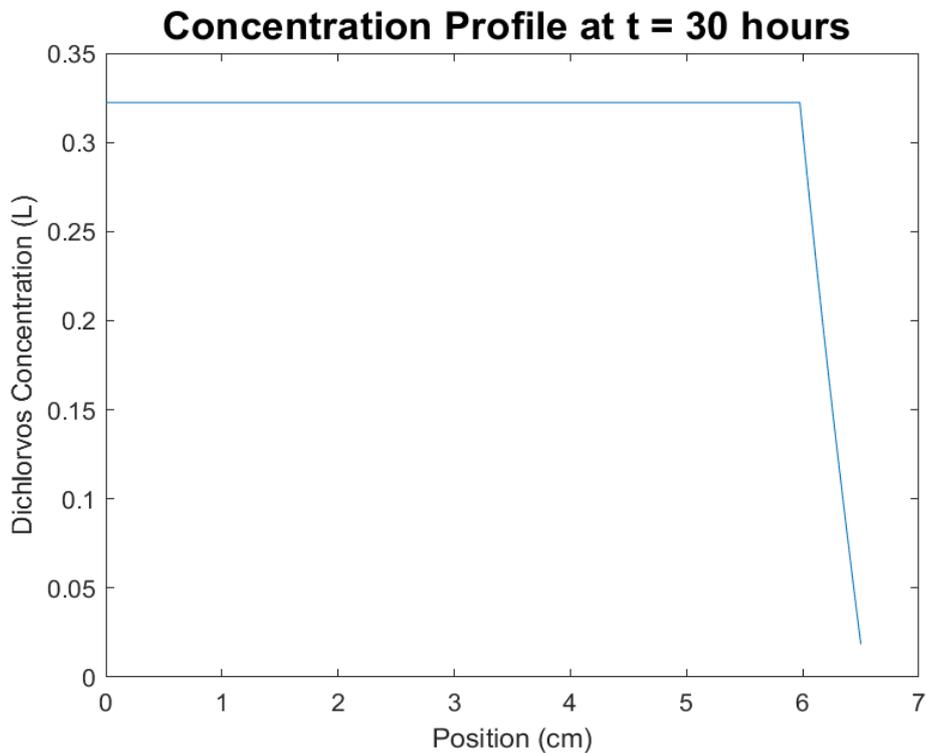

Figure 3. Concentration profile for CASE A at time t = 30 hours, in spherical coordinate

Fig. 4 shows the case B where the concentration inside the center of the stomach is initially *0.05* and the concentration in the stomach lining is initially 0L. The concentration inside the stomach decreases over time. The rate at which the concentration decreases does not depend on position within the stomach volume inside the inner wall. The concentration in the stomach wall initially increases, and then eventually decreases over time. Also, multiple impulses are applied to the system in order to simulate the person's periodic drinking behavior or drinking pattern. This is modeled by using a driving force that is a squared sine function.
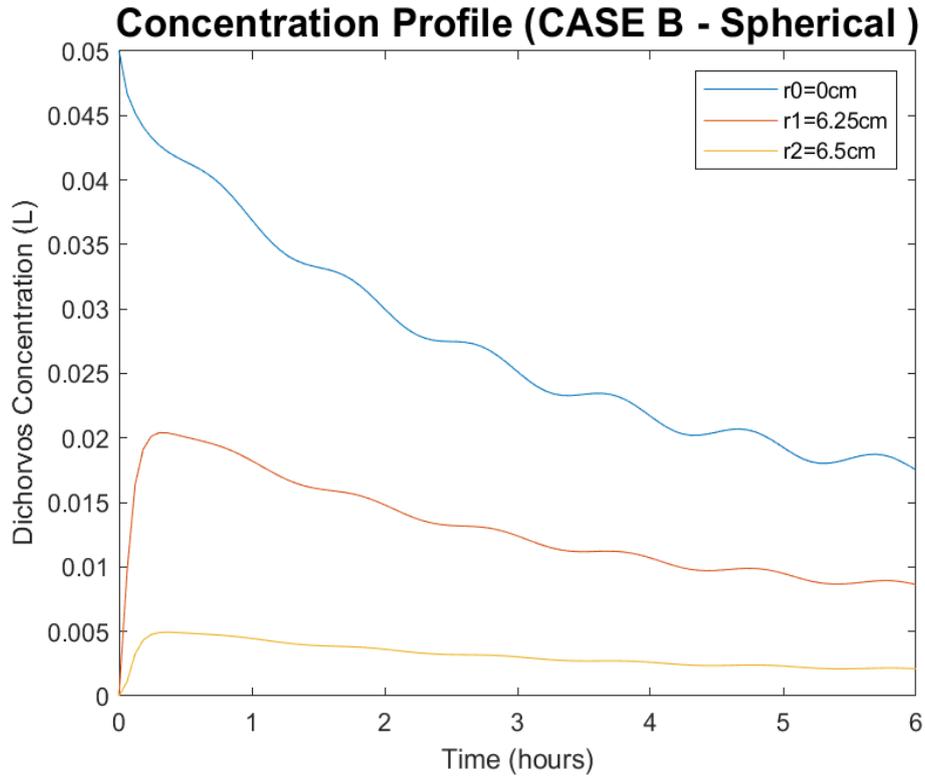
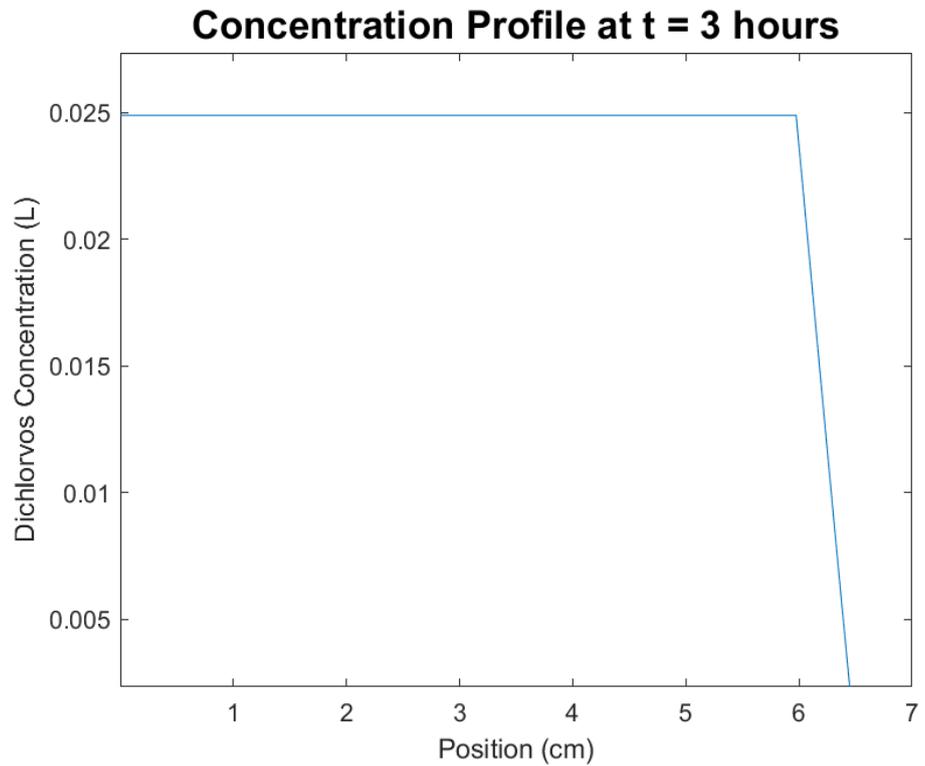**Figure 4.** Concentration profile for CASE B in spherical coordinate.

Figure 5. Concentration profile for CASE B at time t = 3hours, in spherical coordinate.

Also, it can be observed that the concentration profile for Case B oscillates due to the sine term, this causes the concentration to slightly increase at each point in time and then decrease. This is accurate as the person is repeatedly drinking dichlorvos, then diluting the concentration of dichlorvos in his stomach with water. It can be observed that the periodic intake of dichlorvos in addition with water results in the decrease of the concentration at the center but a slight increase from *0* in the first 1hr to about *0.02 L* at the entrance of the stomach lining. The slight increase is a result of the initial concentration of *0.05 L* and the eventual decrease is as a result of the periodic intake of water in addition to dichlorvos.

Fig. 5 is for case B where the concentration was initially *0.05 L* at the center of the stomach. It then decreases to *0.023 L* after *6 hours*, but about *0.0025 L* was present at the exit of the stomach lining after *6 hours*. Therefore, the periodic intake of water along with dichlorvos gradually reduces the dichlorvos concentration in the stomach. This case presents less severe poisoning and small doses of Atropine and gastric lavage should be conducted; such a person will survive as long as there are no further complications.

5. CONCLUSIONS

In this work, mathematical model for the diffusion of dichlorvos through the stomach lining was developed and analytical solution using separation of variable was presented. The developed mathematical model was also solved using Matlab's pdepe solver. The concentration of dichlorvos in the stomach was computed as a function of time for two Cases A and B in spherical coordinates. From Case A, it was observed that about *14.4%* of dichlorvos was diffused in *60 hours*, at a constant rate of ingestion. The results confirmed the results observed in literature, that only about 20% of dichlorvos is absorbed through the stomach lining. This means that diffusion alone is not sufficient to transfer all the available dichlorvos through the stomach lining in the amount of time observed from literature. For the Case B, it was clearly showed that the intake of water which was modeled using a sine squared function as a driving force, rapidly reduced the concentration in the stomach. Therefore, diluting the dichlorvos with water can slow down its poisonous effects. From the analysis, it could be concluded that the best mode of treatment is application of the drug Atropine, because it reverses the impacts of muscarinia, in large doses of *0.03-0.05 mg/kg*. This should be provided intravenously every *10-20 minutes* or, then every *1-4 hours* for at least *24 hours* until indications of atropinization (hot dry washed skin, dilated pupil, increased *HR > 80b/min*, systolic *BP > 80 mmHg*, and fast inversion of bronchospasm and bronchorrhea) appear. Also, it was observed from literature that local remedies such as activated charcoal, palm oil, coconut water, milk and so on only tend to dilute the poison. They do not in fact stop the poison from spreading.

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