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Cholesterol and Treatment Effects on Drug Concentration in the Blood Stream and Tissue

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Abstract*: In this study, we investigated the effect of cholesterol on drug distribution in the body. This work also involves mathematical models that represent drug concentration in the blood and in the tissue by introducing a constant cholesterol parameter and treatment in previous works stated in the literature, in an attempt to understand the behavior of a drug administered in the human body over time. In addition, the models help to study and assess the behavior of medication distribution in the body associated with a high or low level of cholesterol. The analytical solutions for the drug concentration in the bloodstream and that of the tissues were obtained using the Laplace's method, and the Wolfram Mathematica software was adopted to simulate the analytical results, where the entering parameters, such as the treatment parameter and the cholesterol parameter, were investigated by varying them, with the results revealed as follows: First, drug diffusion from one compartment to another is hampered by cholesterol ingestion into the circulation. Secondly, over time, the drug concentration in the circulation gradually decreases from the initial injected concentration to virtually nothing in the system. Thirdly, with a lower concentration of treatment, the drug concentration takes longer to reach a peak in the tissue compartment for therapeutic action before fading out of the system. Fourthly, when the treatment control lowers the level of cholesterol present in the system, the drug elimination rate rises. Finally, when the rate of drug transition from the blood compartment to the tissue compartment is reduced, the rate of drug elimination from the body also increases. In conclusion, the increase in the rate at which the drug exits the tissue compartment and the subsequently slightly decreased rate at which the drug leaves the circulation speeds up the drug removal process from the body.*

Keywords: *Mathematical Models, Pharmacokinetics, Cholesterol, Drug Distribution, Ordinary Differential Equations, Lipid*

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I. INTRODUCTION

Lipids are a class of organic compounds that include cholesterol, fats, oils, waxes, sterols, and triglycerides and are insoluble in water. They account for the majority of the fat in the human body.The liver produces about two-thirds of the body's cholesterol needs. Cholesterol is needed to make cell membranes, certain hormones, and vitamin D, among other things in the body. Because cholesterol does not dissolve in water, it is unable to circulate through the bloodstream on its own. The liver produces lipoproteins to help in the circulation of cholesterol. Lipoproteins are particles made up of fat and protein. They carry cholesterol and triglycerides, a kind of fat, through the bloodstream to the tissues and organs. Low-density lipoprotein (LDL) and high-density lipoprotein (HDL) are the two forms of lipoproteins. However, excessive cholesterol in the blood causes deposits to buildup on the inside walls of the blood vessels. This building is called a "plaque." It narrows the blood vessels and can reduce or stop blood circulation. This can result in a heart attack, stroke, or

narrowing of the arteries elsewhere, which prevents drugs for specific ailments from working (Heather, 2021; Bunonyo and Eli, 2020).

The link between mathematics and medicine has given rise to new areas of mathematics in which ideas from both fields are combined and used to solve a variety of problems through mathematical modeling. Mathematical modeling is the process of representing a real-life problem and its relationships with the help of mathematics (Haines and Crouch, 2007). A mathematical model describes the behavior of a real-life system using mathematical language, symbols, and concepts. This research proposes a mathematical model that represents cholesterol as deposited on the tissues that inhibits drug distribution in the human body through an intravenous route.

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Over the years, the most popular method of medication administration in clinical practice has been the oral route. Oral drug delivery mechanisms such as pills have been considered one of the most appropriate methods of drug administration around the world. However, many drugs cannot be taken orally and must be injected into the body using hypodermic needles. As a result, drug diffusion from the source of administration to the target site is a critical factor to consider. This research aims to propose a mathematical model to understand the drug's behavior in the human body over time, and a theoretical study is being carried out to aid in the optimization of medication dose management. We used a mathematical model based on the law of mass action to explore the distribution of medications injected into the body through an intravenous route, similar to the models reported in the works of Khanday *et al.* (2017) and Bunonyo *et al.* (2022). However, in the new proposed model, we evaluated the influence of cholesterol contained in the circulatory system on the movement of the administered medication as the injected medicine travels through the various compartments of the body. Olga *et al.* (2014) used a two-compartment mathematical model to examine cholesterol transport and de novo production in the liver. The work demonstrates the model's relevance to exploring the mechanisms associated with high blood cholesterol, such as reducing cholesterol levels by preventing de novo cholesterol production. Using the analytically derived relationships for the steady state (equilibrium), it also demonstrates how the model could aid in the diagnosis of high blood cholesterol by determining whether the disturbances in cholesterol homeostasis are caused by impaired transport from the liver to the bloodstream or vice versa. Khanday *et al.* (2017) investigated mathematical models for drug diffusion via blood and tissue medium compartments and sought to create mathematical models to explain the distribution of drugs administered into the human body via oral and intravenous routes in their study. According to their findings, mathematical modeling for drug diffusion is an effective prediction technique for gaining a fundamental understanding of bio-transport processes. In Mina *et al.* (2002), a transformation group theoretic technique was used to investigate the diffusion of a drug via a skin-like membrane that partially absorbs the drug. Two cases were considered for the diffusion coefficient.

Dash *et al.* (2010) examined mathematical models used to predict drug release kinetics from drug delivery devices. According to their findings, using mathematical equations to explain the procedure made quantitative analysis of the values obtained in dissolution and release rates easier. Their findings also suggested that mathematical modeling can aid in optimizing the design of a therapeutic device by providing data on the efficacy of alternative release models.

Feizabadi *et al.* (2009) used the Kozusko and Bajzer (2003) model to expand the two-compartment model by interacting with dynamic anti-mitotic medications that display a diffusion tendency over time after injection.

From many angles, the behavior of pharmaceuticals in the human body, the impact of medications on tumor formation, and the influence of cholesterol in the human body have been mathematically simulated by different researchers. However, this work attempts to extend the previous work carried out by Bunonyo *et al.* (2022) by incorporating the cholesterol and the treatment terms into the system, in an attempt to understand the behaviour of medications delivered in a human body filled with excessive cholesterol.

II. MATHEMATICAL FORMULATION

We considered the concentration of the drug in the bloodstream to be associated with cholesterol produced by the liver and trans fats when developing the mathematical model that represents the distribution of drugs administered via intravenous route into the bloodstream and then to the tissues when developing the mathematical model that represents the distribution of drugs administered via intravenous route into the bloodstream and then to the tissues.now introduced a treatment control to regulate the increase in the level of cholesterol to manage the excessive cholesterol produced by the liver and trans fats. To depict the distribution of drugs delivered into the body through the intravenous route, the model employs a two-compartment structure. The first compartment relates to the blood, into which the medicine is injected, and the second compartment corresponds to the tissues, where the drug exerts its therapeutic effect.In this model, it is assumed that the administered medication is transported to the tissue compartment at a certain rate k_b and that a percentage of it is removed from the body at a different rate k_e, assuming that the rate of drug transportation is hindered by the amount of cholesterol in the system. The system is depicted in the diagram below (*Fig. 1*).

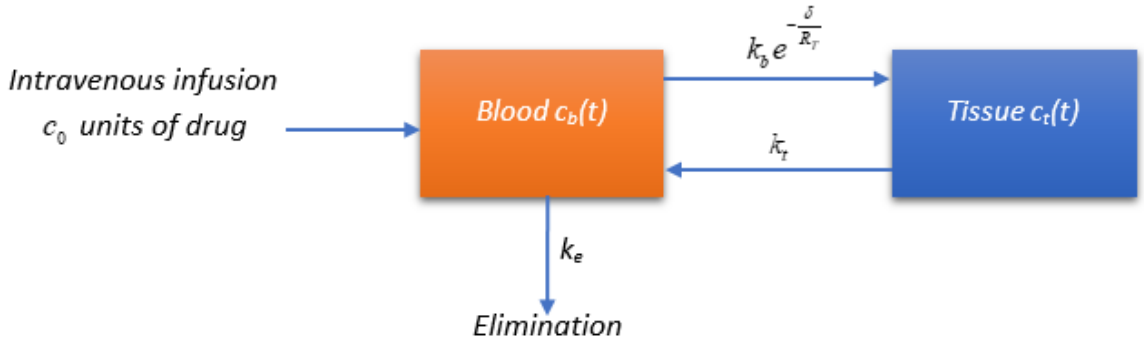

Fig 1 Drug Distribution and Absorption Process from Blood to Tissue

The mathematical representation of the compartment model explaining the intravenous medication delivery process, based on Fig 1, Bunonyo *et al.* (2022) and Kanday *et al.* (2017) as follows:

$$\left.\begin{aligned} \frac{dc_b(t)}{dt} &= -(k_b + k_e)e^{-\frac{\delta}{R_T}} c_b(t) + k_t c_t(t) \qquad \text{at } c_b(0) = c_0 \\ \frac{dc_t(t)}{dt} &= k_b e^{-\frac{\delta}{R_T}} c_b(t) - k_t c_t(t) \qquad \text{at } c_t(0) = 0 \end{aligned}\right\} \tag{1}$$

where $c_b(t)$ and $c_t(t)$ represent drug concentrations in the blood and tissue compartments, respectively, and c_0 represents the initial concentration of drug injected into the body via the intravenous route, and δ and $-R_T$ represent the level of cholesterol found in the system and treatment to control the growth of the cholesterol level, respectively.Let $\dot{c}_b(t)$ represent $\frac{dc_b(t)}{dt}$ and $\dot{c}_t(t)$ represent $\frac{dc_t(t)}{dt}$, then we rewrite Equation(1) as follows:

$$\left.\begin{aligned} \dot{c}_b(t) &= -(k_b + k_e)e^{-\frac{\delta}{R_T}} c_b + k_t c_t \quad \text{at } c_b(0) = c_0 \\ \dot{c}_t(t) &= k_b e^{-\frac{\delta}{R_T}} c_b - k_t c_t \qquad \text{at } c_t(0) = 0 \end{aligned}\right\} \tag{2}$$

Now, by applying Laplace transform on equation (2), we get the following:

$$L\{\dot{c}_b(t)\} = -(k_b + k_e)e^{-\frac{\delta}{R_T}} L\{c_b(t)\} + k_t L\{c_t(t)\} \tag{3}$$

$$L\{\dot{c}_t(t)\} = k_b e^{-\frac{\delta}{R_T}} L\{c_b(t)\} - k_t L\{c_t(t)\} \tag{4}$$

Setting $c_b(s) = L\{c_b(t)\}$ and $c_t(s) = L\{c_t(t)\}$ then using the result that $L\{f'\}(s) = sL\{f\}(s) - f(0)$, equation (3) and equation (4) are reduced to the following:

$$sc_b(s) - c_0 = -(k_b + k_e)e^{-\frac{\delta}{R_T}} c_b(s) + k_t c_t(s) \tag{5}$$

$$sc_t(s) = k_b e^{-\frac{\delta}{R_T}} c_b(s) - k_t c_t(s) \tag{6}$$

Rearranging equation(5) and equation(6),we get:

$$\left(s + (k_b + k_e)e^{-\frac{\delta}{R_T}}\right) c_b(s) - k_t c_t(s) = c_0 \tag{7}$$

$$-k_b e^{-\frac{\delta}{R_T}} c_b(s) + (s + k_t)c_t(s) = 0 \tag{8}$$

Now, let ϕ_0 represent $\left(s + (k_b + k_e)e^{-\frac{\delta}{R_T}}\right)$ in equation (7)and ϕ_1 represent $(s + k_t)$ in equation(8), then

$$\phi_0 c_b(s) - k_t c_t(s) = c_0 \tag{9}$$

$$-k_b e^{-\frac{\delta}{R_T}} c_b(s) + \phi_1 c_t(s) = 0 \tag{10}$$

Using Crammer's method to solve for $c_b(s)$ and $c_t(s)$ in equations (9) and (10), we get the following:

$$c_b(s) = \frac{\begin{vmatrix} c_0 & -k_t \\ 0 & \phi_1 \end{vmatrix}}{\begin{vmatrix} \phi_0 & -k_t \\ -k_b e^{-\frac{\delta}{R_T}} & \phi_1 \end{vmatrix}} = \frac{c_0\phi_1}{\phi_0\phi_1 - k_t k_b e^{-\frac{\delta}{R_T}}} \tag{11}$$

$$c_t(s) = \frac{\begin{vmatrix} \phi_0 & c_0 \\ -k_b e^{-\frac{\delta}{R_T}} & 0 \end{vmatrix}}{\begin{vmatrix} \phi_0 & -k_t \\ -k_b e^{-\frac{\delta}{R_T}} & \phi_1 \end{vmatrix}} = \frac{c_0 k_b e^{-\frac{\delta}{R_T}}}{\phi_0\phi_1 - k_t k_b e^{-\frac{\delta}{R_T}}} \tag{12}$$

Rewriting equation (11) and equation(12), we obtain the following two equations respectively:

$$c_b(s) = \frac{c_0(s + k_t)}{\left(s + (k_b + k_e)e^{-\frac{\delta}{R_T}}\right)(s + k_t) - k_t k_b e^{-\frac{\delta}{R_T}}} \tag{13}$$

$$c_t(s) = \frac{c_0 k_b e^{-\frac{\delta}{R_T}}}{\left(s + (k_b + k_e)e^{-\frac{\delta}{R_T}}\right)(s + k_t) - k_t k_b e^{-\frac{\delta}{R_T}}} \tag{14}$$

Now, let $\left(s + (k_b + k_e)e^{-\frac{\delta}{R_T}}\right)(s + k_t) - k_t k_b e^{-\frac{\delta}{R_T}} = 0$ from equation (13)and equation(14) above, then

$$s^2 + sk_b e^{-\frac{\delta}{R_T}} + sk_e e^{-\frac{\delta}{R_T}} + sk_t + k_t k_b e^{-\frac{\delta}{R_T}} + k_t k_e e^{-\frac{\delta}{R_T}} - k_t k_b e^{-\frac{\delta}{R_T}} = 0$$

$$s^2 + \left(k_t + (k_b + k_e)e^{-\frac{\delta}{R_T}}\right)s + k_e k_t = 0 \tag{15}$$

Using the quadratic formula on equation (15), we have the following:

$$\beta_i = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a} \quad \text{for } i = 1, 2. \tag{16}$$

where $a = 1$, $b = \left(k_t + (k_b + k_e)e^{-\frac{\delta}{R_T}}\right)$ and $c = k_e k_t$. Such that

$$\beta_i = \frac{1}{2}\left[-\left(k_b + (k_t + k_e)e^{-\frac{\delta}{R_T}}\right) \pm \sqrt{\left(k_b + (k_t + k_e)e^{-\frac{\delta}{R_T}}\right)^2 - 4k_e k_t}\right] \quad \text{for } i = 1, 2. \tag{17}$$

$$-\beta_i = \frac{1}{2}\left[\left(k_b + (k_t + k_e)e^{-\frac{\delta}{R_T}}\right) \mp \sqrt{\left(k_b + (k_t + k_e)e^{-\frac{\delta}{R_T}}\right)^2 - 4k_e k_t}\right] \quad \text{for } i = 1, 2. \tag{18}$$

Which implies,

$$-\beta_1 = \frac{1}{2}\left[\left(k_b + (k_t + k_e)e^{-\frac{\delta}{R_T}}\right) - \sqrt{\left(k_b + (k_t + k_e)e^{-\frac{\delta}{R_T}}\right)^2 - 4k_e k_t}\right] \tag{19}$$

$$-\beta_2 = \frac{1}{2}\left[\left(k_b + (k_t + k_e)e^{-\frac{\delta}{R_T}}\right) + \sqrt{\left(k_b + (k_t + k_e)e^{-\frac{\delta}{R_T}}\right)^2 - 4k_e k_t}\right] \tag{20}$$

Thus, $-\beta_1$ and $-\beta_2$ are the roots of the equation in equation(15), and we have the following equations:

$$c_b(s) = \frac{c_0(s + k_t)}{(s + \beta_1)(s + \beta_2)} \tag{21}$$

$$c_t(s) = \frac{c_0 k_b e^{-\frac{\delta}{R_T}}}{(s + \beta_1)(s + \beta_2)} \tag{22}$$

Using inverse Laplace transform on equations(21)and (22), we get the following:

$$L_s^{-1}\{c_b(s)\}(t) = L_s^{-1}\left\{\frac{c_0(s + k_t)}{(s + \beta_1)(s + \beta_2)}\right\}(t) \tag{23}$$

Then,

$$c_b(t) = \frac{c_0}{\beta_1 - \beta_2}\left(e^{-\beta_1 t}(-k_t + \beta_1) + e^{-\beta_2 t}(k_t - \beta_2)\right) \tag{24}$$

Also,

$$L_s^{-1}\{c_t(s)\}(t) = L_s^{-1}\left\{\frac{c_0 k_b e^{-\frac{\delta}{R_T}}}{(s + \beta_1)(s + \beta_2)}\right\}(t) \tag{25}$$

Then,

$$c_t(t) = e^{-\frac{\delta}{R_T}} c_0 k_b \left(\frac{e^{-t\beta_2}}{\beta_1 - \beta_2} + \frac{e^{-t\beta_1}}{-\beta_1 + \beta_2}\right) \tag{26}$$

The solutions in equations (25) and(26) correspond to the exponential decay of a drug delivered intravenously into the system as it is absorbed by the body into the tissue compartment.

III. RESULTS AND DISCUSSION

The mathematical model was solved analytically using Laplace's technique, and the results in equations (25) and (26) were simulated using Wolfram Mathematica to demonstrate the influence of the biophysical parameters. Within the time span $(t = 0 \text{ to } 20)$, the graphical and numerical findings are shown in Fig. 1 to Fig. 3 and Table 1 to Table 2, respectively. The following specify the initial conditions and values of some of the parameters utilised in the plots. $c_0 = 500,\ R_T = 5,\ t_0 = 0,\ t_f = 20$ for different levels of cholesterol in the body, $\delta_1 = 5,\ \delta_2 = 4,\ \delta_3 = 3$ and $\delta_4 = 2$.

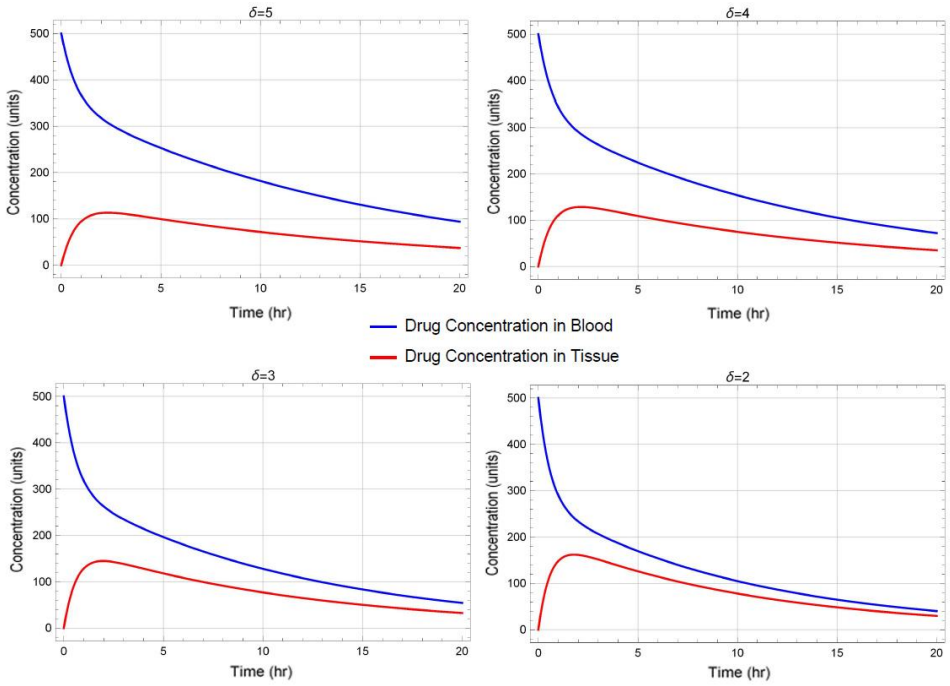

Fig. 1 Effect of Cholesterol on Drug Concentration in Blood and Tissue Compartments with $k_b = 0.9776,\ k_e = 0.25$ and $k_t = 0.9776$

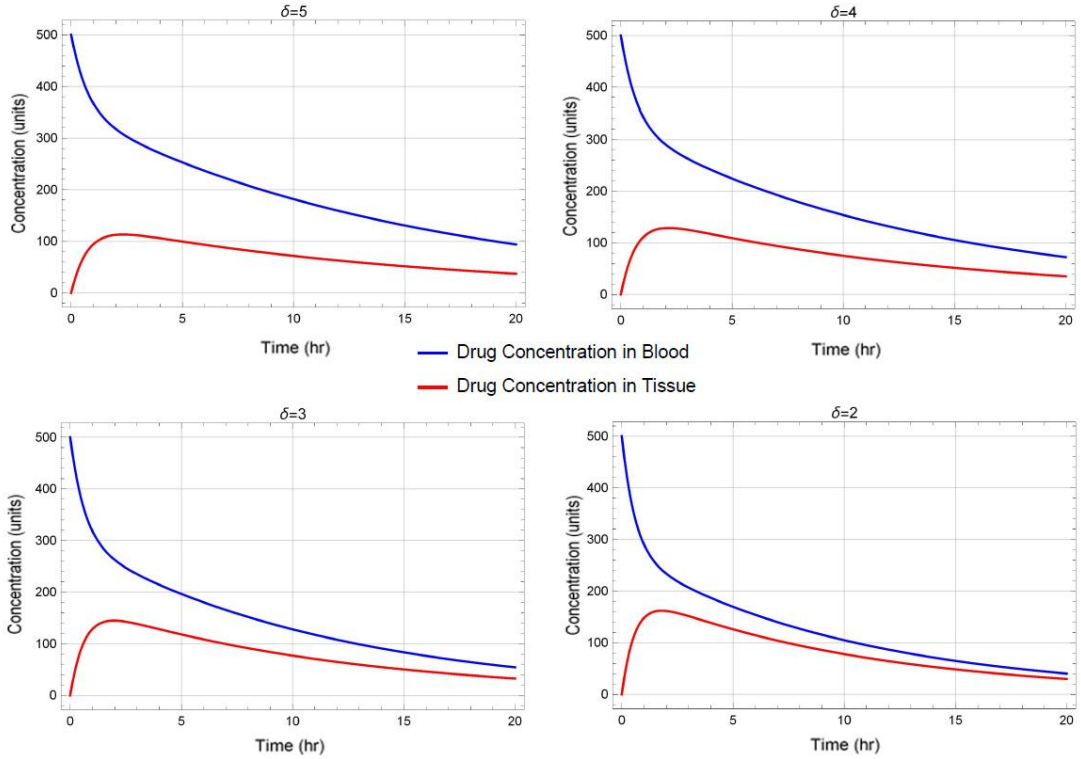

Fig. 2 Effect of Cholesterol on Drug Concentration in Blood and Tissue Compartments with $k_b = 0.2213$, $k_e = 0.2213$ and $k_t = 0.3293$

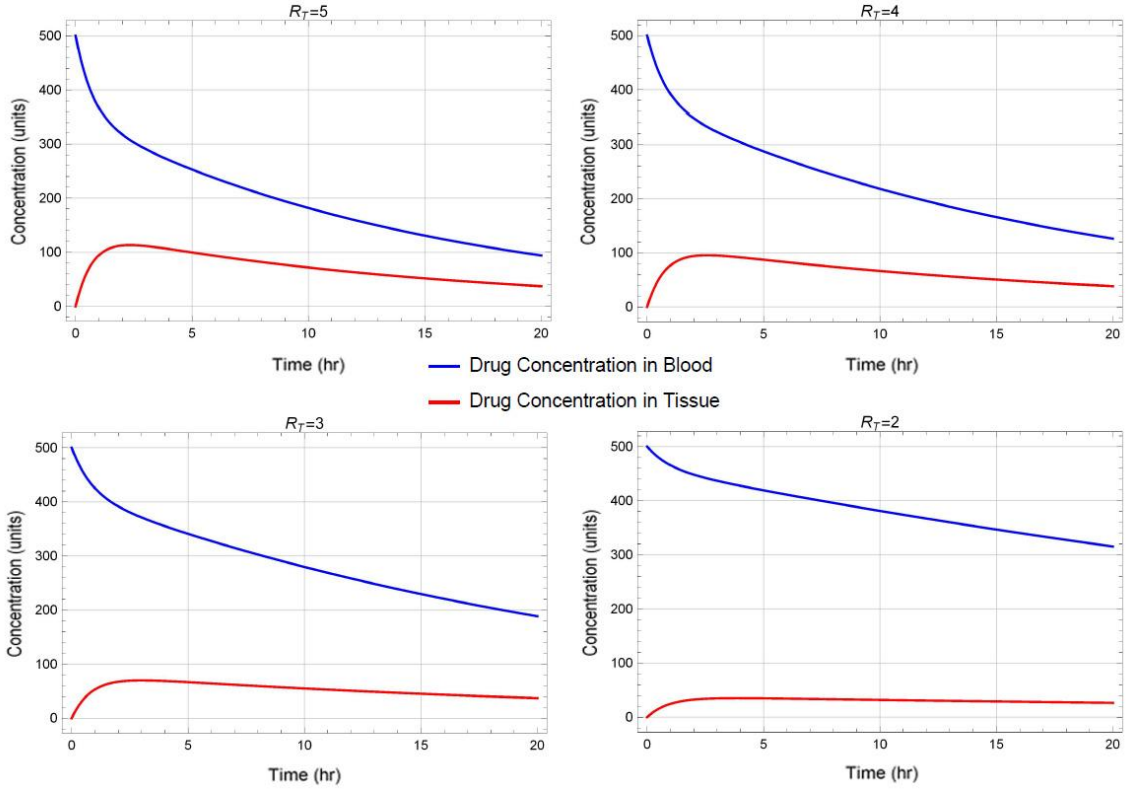

Fig. 3 Effect of Treatment on Drug Concentration in Blood and Tissue Compartments with $k_b = 0.9776$, $k_e = 0.25$ and $k_t = 0.9776$

Table 1 Drug Conconcentration in Blood and Tissue Compartments with Cholesterol at $k_b = 0.9776$, $k_e = 0.25$ and $k_t = 0.9776$

Time (hr)	$\delta = 5$		$\delta = 4$		$\delta = 3$		$\delta = 2$	
	c_b	c_t	c_b	c_t	c_b	c_t	c_b	c_t
0	500.	0.	500.	0.	500.	0.	500.	0.
1	366.962	94.3033	343.834	110.528	318.103	128.502	290.032	148.005
2	317.671	112.410	290.821	128.318	262.556	144.803	233.596	161.361
3	290.777	111.407	263.117	125.019	234.85	138.524	206.757	151.47
4	270.525	105.876	242.443	117.333	214.283	128.324	186.821	138.479
5	252.826	99.522	224.445	109.126	196.422	118.033	169.52	125.95
6	236.579	93.2734	208.03	101.263	180.239	108.393	153.951	114.436
7	221.451	87.3467	192.874	93.9125	165.429	99.5044	139.836	103.954
8	207.31	81.7787	178.836	87.0835	151.844	91.337	127.02	94.4279
9	194.076	76.5609	165.822	80.7481	139.377	83.8384	115.378	85.7741
10	181.689	71.6749	153.756	74.8729	127.933	76.9551	104.804	77.9132
11	170.093	67.1004	142.569	69.4251	117.43	70.6369	95.1994	70.7727
12	159.237	62.8178	132.195	64.3736	107.788	64.8374	86.4747	64.2867
13	149.074	58.8085	122.576	59.6897	98.9386	59.514	78.5496	58.395
14	139.559	55.0551	113.657	55.3465	90.8154	54.6278	71.3508	53.0433
15	130.652	51.5412	105.387	51.3194	83.3592	50.1426	64.8118	48.1821
16	122.313	48.2516	97.7193	47.5853	76.5151	46.0258	58.872	43.7664
17	114.506	45.172	90.609	44.1229	70.233	42.2469	53.4766	39.7553
18	107.198	42.2889	84.0162	40.9124	64.4667	38.7783	48.5756	36.1119
19	100.356	39.5899	77.903	37.9356	59.1738	35.5945	44.1238	32.8024
20	93.9511	37.0631	72.2346	35.1753	54.3154	32.6721	40.08	29.7961

Table 2 Drug Concentration in Blood and Tissue Compartments with Cholesterol at $k_b = 0.2213$, $k_e = 0.2213$ and $k_t = 0.3293$

Time (hr)	$\delta = 5$		$\delta = 4$		$\delta = 3$		$\delta = 2$	
	c_b	c_t	c_b	c_t	c_b	c_t	c_b	c_t
0	500.	0.	500.	0.	500.	0.	500.	0
1	430.274	32.0061	416.272	38.4149	399.82	45.9354	380.655	54.683
2	378.559	50.8962	356.338	60.0928	331.154	70.4616	303.073	81.9465
3	338.947	61.3689	311.957	71.3514	282.356	82.1625	250.627	93.5621
4	307.57	66.4747	277.872	76.1803	246.249	86.2711	213.52	96.3901
5	281.891	68.1916	250.723	77.0952	218.4	85.9709	185.957	94.4168
6	260.237	67.8006	228.354	75.6789	196.057	83.1919	164.493	89.9474
7	241.501	66.1292	209.37	72.9238	177.497	79.0986	147.068	84.3049
8	224.946	63.7103	192.864	69.4492	161.637	74.3879	132.432	78.2392
9	210.073	60.8856	178.238	65.6384	147.781	69.4718	119.816	72.1665
10	196.543	57.8726	165.091	61.7261	135.477	64.589	108.738	66.3096
11	184.119	54.808	153.151	57.8531	124.421	59.8732	98.8819	60.7799
12	172.634	51.7766	142.224	54.1016	114.406	55.3948	90.0359	55.6251
13	161.966	48.8296	132.173	50.517	105.282	51.1863	82.0499	50.8573
14	152.023	45.9964	122.893	47.1216	96.9383	47.2578	74.8125	46.4687
15	142.733	43.2927	114.303	43.924	89.2874	43.6066	68.2371	42.4416
16	134.038	40.7252	106.338	40.9241	82.26	40.2226	62.2536	38.7535
17	125.891	38.2953	98.9437	38.1169	75.7976	37.0922	56.8028	35.38
18	118.25	36.0008	92.0731	35.4946	69.8503	34.1999	51.8341	32.2967
19	111.082	33.8375	85.6859	33.0478	64.3741	31.5298	47.3028	29.4801
20	104.352	31.8002	79.7457	30.7666	59.33	29.066	43.1693	26.9079

Table 3 Drug Concentration in Blood and Tissue Compartments with Treatment at $k_s = 0.9776$, $k_e = 0.25$ and $k_t = 0.9776$

Time (hr)	$R_T = 5$		$R_T = 4$		$R_T = 3$		$R_T = 2$	
	c_b	c_t	c_b	c_t	c_b	c_t	c_b	c_t
0	500.	0.	500.	0.	500.	0.	500.	0.
1	366.962	94.3033	392.114	76.5929	425.264	53.1573	465.667	24.4708
2	317.671	112.41	348.458	93.9139	391.621	67.599	448.281	32.4946
3	290.777	111.407	323.484	94.881	371.135	70.1043	436.874	34.8257
4	270.525	105.876	304.415	91.4826	355.122	68.9815	427.64	35.1918
5	252.826	99.522	287.644	87.0597	340.869	66.8061	419.258	34.885
6	236.579	93.2734	272.126	82.536	327.523	64.3748	411.268	34.3531
7	221.451	87.3467	257.539	78.1599	314.803	61.9319	403.51	33.7512
8	207.31	81.7787	243.759	73.9914	302.61	59.5508	395.926	33.1328
9	194.076	76.5609	230.723	70.0384	290.898	57.2516	388.494	32.5164
10	181.689	71.6749	218.387	66.2947	279.643	55.0382	381.205	31.9083
11	170.093	67.1004	206.711	62.7505	268.825	52.9095	374.054	31.3103
12	159.237	62.8178	195.659	59.3957	258.425	50.8628	367.037	30.7232
13	149.074	58.8085	185.199	56.2202	248.428	48.8952	360.152	30.147
14	139.559	55.0551	175.297	53.2144	238.817	47.0037	353.396	29.5815
15	130.652	51.5412	165.925	50.3693	229.578	45.1853	346.767	29.0266
16	122.313	48.2516	157.054	47.6764	220.697	43.4373	340.263	28.4822
17	114.506	45.172	148.657	45.1274	212.159	41.7569	333.88	27.9479
18	107.198	42.2889	140.709	42.7147	203.952	40.1415	327.617	27.4236
19	100.356	39.5899	133.187	40.431	196.062	38.5886	321.472	26.9092
20	93.9511	37.0631	126.066	38.2694	188.477	37.0958	315.441	26.4045

IV. DISCUSSION AND CONCLUSION

The plots in Fig. 1 and the results in Table 1reveal an increase in drug concentration in the tissue compartment from 94.3033 to 148.005 units in the first hour after the drug is delivered into the bloodstream for reducing cholesterol levels (which interprets that as the amount of cholesterol present in the system reduces, so also the rate at which the drug gets into the tissue compartment becomes faster), and this increase is also seen within the time span $(t = 0 \text{ to } 11)$ hours, as shown in Table 1. This shift in concentration, however, exhibits a variable tendency during the following hour, ranging from 62.8178 to 64.3736, 64.8374, and 64.2867 unitsbefore fading out of the system. The findings in Table 1also reveal that as the cholesterol level rises, the drug concentration in the blood compartment also falls slowly with time. This means that when the quantity of cholesterol in the system rises, the pace at which the drug injected into the bloodstream travels into the tissue compartment for therapeutic action slows down.However, the drug concentration in the tissue compartment reaches a peak by the second hour after the medicine is injected into the bloodstream and then steadily declines over the next hours.

The plots in Fig. 2 and the results in Table 2 show an increase in drug concentration in the tissue compartment from 32.0061 to 54.683 units for lowering cholesterol levels within the first hour the drug is administered into the bloodstream (which translates that as the amount of cholesterol in the system decreases, so does the rate at which the drug gets into the tissue compartment), and this increase is seen within the time span $(t = 0 \text{ to } 12)$ hours, as shown in Table 2. However, this movement in concentration has a varied tendency throughout the next four hours, between time $(t = 13 \text{ to } 15)$ before fizzling out of the system steadily. The data in Table 2also show that when cholesterol level rises, the drug concentration in the blood compartment gradually decreases over time rather than faster. This implies that as the amount of cholesterol in the system increases, the rate at which the medicine injected into the circulation goes into the tissue compartment for therapeutic effect becomes slower. The drug concentration in the tissue compartment, on the other hand, reaches its peak by the fourth hour in $\delta = 2 \text{ or } 3$ and by the fifth hour in $\delta = 4 \text{ or } 5$ after the medicine is injected into the circulation and then gradually drops over the next hours.

The plots in Fig. 3 and data in Table 3 show a drop in drug concentration in the tissue compartment from 94.3033 to 24.4708 units in the first hour after the medication was delivered into the bloodstream for lowering cholesterol treatment levels.The results in Table 3further show that when the amount of cholesterol in the system is lowered by the treatment parameter, the pace at which the drug performs its therapeutic function and subsequently returns to the bloodstream for elimination accelerates. Table 3 illustrates that the drug concentration increases with increasing treatment values in the tissue compartment, but decreases in the bloodstream. Similarly, as illustrated by the red oval shapes in Table 3, the drug concentration reaches distinct maxima at different periods before diminishing its action. This peak, however, is reached faster when the cholesterol level is reduced by increasing the degree of treatment.Furthermore, after reaching distinct concentration maxima, the varied concentration levels began to fall to their lowest levels as the concentration in the circulatory compartment continued to fall as it diffused from one compartment to the next.

V. CONCLUSION

The research employed a mathematical model to study and assess the behavior of medication distribution in the body linked with high or low cholesterol levels. The Wolfram Mathematica software was adopted to simulate the analytical results, where the entering parameters, such as the treatment parameter and the cholesterol parameter, were investigated. Based on the findings reported, we infer that (1) cholesterol ingestion into the circulation hinders drug diffusion from one compartment to another. (2) Between 0 and 20 hours, the drug concentration in the circulation steadily decreases from the initial injected concentration of 500 to 93.9511 units (inTable 1), and then to basically nothing in the system in the following hours. (3) With a lower concentration of treatment, the concentration takes longer to reach a peak in the tissue compartment for therapeutic action before fading out of the system. (4) When the treatment control lowers the level of cholesterol present in the system, the drug elimination rate rises. (5) When the rate constant k_b of drug transit from the blood compartment to the tissue compartment is reduced, the rate of drug elimination from the body increases. Thus, increasing the value of the rate constant k_t at which the drug exits the tissue compartment and subsequently slightly decreasing the rate at which the drug leaves the circulation speeds up the drug removal process (from the body).

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DEFINITION OF VARIABLES AND PARAMETERS

c_b Concentration of drug in the blood.

c_t Concentration of drug in the tissue.

c_0 Initial drug concentration administered into the body (through oral or intravenous route).

k_b The rate at which drug is taken from the blood compartment to the tissue compartment.

k_t The rate at which drug is taken from the tissue compartment back to the blood compartment for elimination.

k_e The rate of drug elimination (clearance) from the body.

δ The level of cholesterol found in the system.

$-R_T$ Treatment parameter (control) to inhibit or proliferate the level of cholesterol found in the system.

t_0 Initial time. The moment the drug is administered into the body.

t_f Final time under consideration in the observation.

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