Journal of Advanced Research in Applied Sciences and Engineering Technology

Journal homepage:
https://semarakilmu.com.my/journals/index.php/applied_sciences_eng_tech/index
ISSN: 2462-1943

Prediction of Drug Concentration in Human Bloodstream using Adams-Bashforth-Moulton Method

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ARTICLE INFO

Article history:
Received 5 December 2022
Received in revised form 20 December 2022
Accepted 28 December 2022
Available online 5 January 2023

Keywords:
Adams Bashforth method; Adams Moulton method; Drug concentration; Pharmacokinetics

ABSTRACT

Pharmaceutical drugs are chemicals intended to avoid, assess, heal, or cure a disease. It is also commonly referred to as medication. When medicine is taken, it gets absorbed into the bloodstream, spreads throughout the body, and achieves its maximum concentration. Following this, the medication level gradually decreases as it is removed from the body. The drug concentration according to the time can be predicted using mathematical concepts and pharmacokinetic models. The compartmental model is a fundamental type of model used in pharmacokinetics. The number of compartments required to describe the drug's action in the body is one-compartment, two-compartment, and multicompartment. These models can forecast medication concentrations in the body over time. This paper will focus on the one-compartment model and Adams Bashforth-Moulton method. Adams Method is one of the linear multistep techniques applied to solve numerical ordinary differential equations that contain the predictor method (Adams Bashforth) and corrector method (Adams Moulton). The integrated development environment used for the computation and graphing is MATLAB. The expected result of this report is that we can predict the concentration of the chosen drugs over time and how long a particular person needs to wait before donating blood safely.

1. Introduction

The circulation of medications entering, across, and away from the bloodstream are described as pharmacokinetics [1]. The type of reaction a person gets from a medication is defined by the material's essential pharmacological characteristics at the location of the action. The amount and expanse of absorption of the medication after its administration, the amount and expanse of transmission of the drug to different tissues and the rate of drug removal from the area are all factors that affect the beginning, strength, and length of the reaction. Drugs such as Phenobarbitone, Vancomycin, Aminoglycosides, Methotrexate, Carbamazepine, Tacrolimus, Phenytoin, Valproic Acid,

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https://doi.org/10.37934/araset.29.2.5371

Digoxin, and Theophylline are frequently monitored in Malaysia [2]. In this research, we will only look at three different drugs: Aminoglycosides, Vancomycin, and Valproic Acid.

Aminoglycosides are antibiotics mostly used to treat aerobic gram-negative bacilli infections and other bacteria such as Staphylococci and Mycobacterium tuberculosis [3]. Severe infections of the abdomen and urinary tract, bacteremia, and endocarditis are treated using Aminoglycosides. It is also a recognised medication to cure infections caused by aerobic Gram-negative bacilli [4]. Aminoglycosides that are primarily used in Malaysia are Gentamicin and Amikacin. The following drug that we will focus on is Valproic acid. The various types of seizures can be treated with Valproic acid. It can also treat mania in bipolar disorder patients and prevent migraine headaches. Valproic acid belongs to the anticonvulsant medicine class. It raises the concentration of a natural chemical in the brain. Valproic acid is usually used as a prescription for emotional state stabiliser and behavioural and emotional dysregulation [5]. The drug is also used for COVID-19 patients with serious mental illness to help them calm while undergoing therapy [6]. The third type of drug that we will focus on is Vancomycin. The microorganisms *Amycolatopsis orientalis* originated from the Borneo tropical forest and was the source of the first Vancomycin isolation in 1957 [7]. Vancomycin is used to treat intestinal inflammation caused by certain bacteria that can occur after antibiotic therapy and is also movement resistant to enterococcal biofilms [8]. Infections of the urinary system, wounds, the dysbiotic gastrointestinal tract, and endocarditis all exhibit enterococcal biofilms [9].

Medications that can degrade the blood's quality or produce ill effects in the receiver have been discovered in the blood of medication-addicted donors [10]. One of the conditions for becoming a blood donor in Malaysia is not to be on any long-term medications. The majority of drugs do not restrict a person from giving blood. Common drugs, such as blood pressure meds, birth control pills, and over-the-counter pharmaceuticals, do not affect eligibility to give blood. A person that wants to donate platelets must stop taking aspirin or any aspirin-containing medicine at least 48 hours before the appointment. Patients who are on antibiotics should finish them before donating. Regardless of the drug used, the person will usually be requested to wait one week before giving blood. This duration, however, is not always ideal for some people. As a result, donated blood or platelets may include hazardous medicines to the recipient. Unless they utilise teratogenic or platelet aggregation-inhibiting medicines, most blood banks ignore these cases and do not postpone blood donation [11]. The duration for the drug to leave the bloodstream differs depending on the type of drug and the person's health. People taking the same dose of medication can have different lengths to eliminate the medication from the bloodstream. Some factors that affect this are age, height, weight, genetics, and metabolism.

The connection involving medication usage and its concentration at the specified location via different components in biological processes is regarded as a critical topic. The dosage, as well as medication input and output in the working areas, have positive and negative impacts on the human body. Pharmacokinetics researchers explored the activity of a given medicine or chemical in numerous divisions of an individual. It aids in the awareness of the links between medication administration, dispersion, and excretion rates throughout the body and the establishment of the intended therapeutic response. In this research, we want to determine how long certain drugs stay in the bloodstream to know precisely when the potential donor can donate their blood safely for both the blood donor and the blood receiver. This problem is chosen because certain drugs in the blood donated have poor quality and may harm the recipient. Determining the exact concentration of the medicine in the bloodstream before donating blood can raise the safety and quality of the blood as required by regulatory guidelines. Moreover, we can eliminate whoever is unable to donate due to medication effects [11].

Drug diffusion mathematical modelling is a powerful prediction technique for gaining a fundamental grasp of bio-transport processes [12]. Although the mathematical modelling is conceptual, when contrasted and confirmed empirically, the findings are confirmed to lead to realistic outcomes. In the lack of experiments, many analytical modelling and computational methods were performed with high efficiency. Due to regional activities in every area of the section, compartment modelling is important in pharmacokinetics. A compartment model is a mathematical depiction of the body or a portion of the body used to investigate physical or pharmacologic dynamic features. Depending on the method or conveyance of material, the area is depicted as a number of compartments grouped in series or parallel. By using the Adams-Bashforth-Moulton method, we want to check whether the usual duration, which is one week, is enough. In this report, we will only look at three different drugs: Aminoglycosides, Vancomycin, and Valproic Acid. These three medications are chosen because they fit the one-compartment model and are very harmful if they exist in the donated blood.

The Adams-Bashforth-Moulton is a technique for solving differential equations numerically. It is also called the Adams-Predictor-Corrector method, in which the Adams-Bashforth technique is a predictor; meanwhile, the Adams-Moulton process is the corrector [13]. In the prediction step, a predictor-corrector technique calculates a rough approximation overtly, then simplifies the first estimation indirectly in the corrector step. As a result, it is more precise in anticipating solutions and provides greater stability. To generate the four beginning requirements for the Adams-Bashforth-Moulton method, we will use the fourth-order Runge-Kutta (RK4) process. Other numerical approaches, including the Euler method, yield less accurate findings and are numerically unstable; hence the RK4 method is preferred. The Runge-Kutta method is used in many fields, such as numerical modelling, numerical analysis and fluid dynamics [14-16]. This research aims to investigate what kind of drugs (medicine) are frequently monitored in Malaysia. Secondly, to create a differential equation based on the mixing problem, which is a drug (substance) dissolved in the human body and finally to estimate the concentration of drug in the bloodstream by an arbitrary time by using the Adams-Bashforth-Moulton technique and creating a code by MATLAB. This article is written out as follows. The first section is an introduction, followed by a description of the technique in Section 2. The outcomes are discussed in the next section. The fourth section is devoted to discussions. The conclusion is found in Section 5.

2. Methodology

2.1 Differential Equation for Drugs

We use the simplest pharmacokinetics model to generate a differential equation for the rate of drug concentration. Figure 1 depicts a compartment model describing a material's transport in and out of the compartment [17]. The rate of change in the amount of the substance in the compartment equals the difference between the rates at which it enters and exits the compartment. The Balance Law states that '*we cannot generate or destroy any stuff within the compartment*'. Expressing the mathematical relationship in words, we get

Change in amount of substance in compartment = Transfer in - Transfer Out (1)

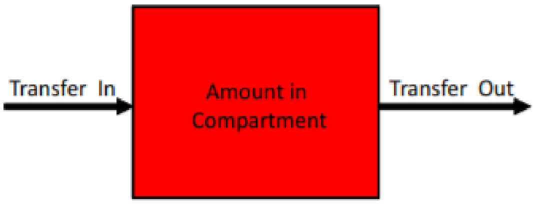


Fig. 1. One compartment model

From Figure 2, we look at the single injection model, which assumes that just one injection is provided. The injection is represented by the model's initial conditions. Let $b(t)$ be the quantity of medication in the bloodstream at any time t, measured in hours. Let α be the rate of metabolisation of the medication. The amount of medication in the bloodstream determines the rate at which it leaves the bloodstream.

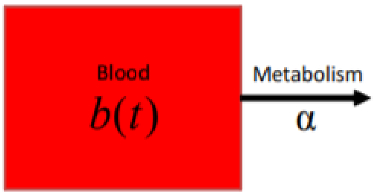


Fig. 2. Single injection model

Thus, by Eq. (1), it implies

$$\frac{db}{dt} = -\alpha b(t) \tag{2}$$

2.2 Aminoglycosides

Next, to get the value of α for aminoglycosides, we have to find the estimated creatinine clearance (CrCl) and estimate aminoglycoside clearance (CLamg) [2].

$$CrCL(ml/min) = \frac{(140-age)\times Body\ Weight(kg)\times 1.04(Female)@1.23(Male)}{Serum\ creatinine\ level(\mu mol/ml)} \tag{3}$$

$$CLamg(l/hr) = 0.06 \times CrCL(ml/min) \tag{4}$$

Substituting Eq. (3) into Eq. (4), we obtain,

$$CLamg(l/hr) = \frac{0.06\times(140-age)\times Body\ Weight(kg)\times 1.04(Female)@1.23(Male)}{Serum\ creatinine\ level(\mu mol/ml)} \tag{5}$$

We calculate for

$$\alpha(hr^{-1}) = \frac{CLamg}{Vd} \tag{6}$$

where the volume distribution (Vd) for Aminoglycosides:

$$Vd\ (l) = 0.26 \times Body\ Weight\ (kg) \tag{7}$$

Hence, we get

$$\alpha(hr^{-1}) = \frac{0.06\times(140-age)\times1.04(Female)@1.23(Male)}{0.26\times Serum\ creatinine\ level(\mu mol/ml)} \tag{8}$$

2.3 Valproic Acid

Next, the formula for Clearance (CL) of Valproic Acid is

$$CL(l/hr) = \frac{CL\big((ml/kg)/hr\big)\times BodyWeight(kg)}{1000ml} \tag{9}$$

where the value for CL(ml/kg/hr) is shown below in Table 1 [2].

Table 1
The clearance value for Valproic Acid

	Monotherapy	Polytherapy
Children	10 – 20ml/kg/hr	20 -30ml/kg/hr
Adult	Adult 7 – 12ml/kg/hr	15 -18ml/kg/hr

The value of α is obtained by using the formula

$$\alpha(hr^{-1}) = \frac{CL(l/hr)}{Vd(l)} \tag{10}$$

where the volume distribution (Vd) for Valproic Acid:

$$Vd\ (l) = Vd(l/kg) \times Body\ Weight\ (kg) \tag{11}$$

Note that, Vd(l/kg) for adults is 0.15 L/kg for adults and 0.2 L/kg for children under 12 years of age. Then,

$$Vd\ (l) = 0.15(Adults)@0.2(Children) \times Body\ Weight\ (kg) \tag{12}$$

Substituting the Eq. (9) and Eq. (12) into Eq. (10), we get,

$$\alpha(hr^{-1}) = \frac{CL\big((ml/kg)/hr\big)}{1000ml\times0.15(Adults)@0.2(Children)} \tag{13}$$

where we assume the CL(ml/kg/hr) value is the median for monotherapy based on Table 1. Therefore, for adults, $\alpha(hr^{-1}) = \frac{19}{300}$whereas $\alpha(hr^{-1}) = \frac{3}{40}$ for children.

2.4 Vancomycin

The formula of α for aminoglycosides and Vancomycin are the same but have different values of Vd [2]. The volume distribution for Vancomycin is calculated by

$$Vd\ (l) = 0.7 \times Body\ Weight\ (kg) \tag{14}$$

Hence,

$$\alpha(hr^{-1}) = \frac{0.06\times(140-age)\times1.04(Female)@1.23(Male)}{0.7\times Serumcreatininelevel(\mu mol/ml)} \tag{15}$$

2.5 Calculate Initial Concentration for Drugs

The equation for the initial concentration of the drug is

$$b_0\ (mg/l) = \frac{Dose\ Administered\ (mg)}{Vd\ (l)} \tag{16}$$

Then, the equation for Dose Administered is

$$Dose\ Administered\ (mg)\ =\ Dosage\ (mg/kg)\ \times Body\ Weight\ (kg) \tag{17}$$

Substituting Eq. (17) into Eq. (16), we get,

$$b_0(mg/l) = \frac{Dosage(mg/kg)\times BodyWeight(kg)}{Vd\ (l)} \tag{18}$$

2.6 Safe Level of Drug Concentration to Donate Blood

Aminoglycoside and Vancomycin are antibiotics. The person that took any antibiotic has to wait at least seven days after their last tablet. This is to make sure the person is free from any bacterial infection that could be transmitted through blood. The same conditions are valid for Valproic acid. Hence, the concentration for all three drugs must be zero (less than 0.002 is enough) before the donation of blood is allowed.

2.7 The Adams-Bashforth-Moulton Method

The Adams-Bashforth-Moulton method is chosen to solve this problem. An algorithm that operates in two phases is known as a predictor-corrector approach [18]. Runge Kutta Forth Order formula is used to find the initial values. The prediction process is done by using the Adams Bashforth formula to calculate a rough approximation of the target quantity. Then, the corrector part is done by using the Adams Moulton formula that refines the initial estimate using a different method. It employs both an explicit and an implicit strategy for the predictor and corrector steps, respectively.

Runge Kutta Forth Order Formula

$$\begin{aligned} K_1 &= hf(t_i, b_i) \\ K_2 &= hf\left(t_i + \frac{h}{2}, b_i + \frac{K_1}{2}\right) \\ K_3 &= hf\left(t_i + \frac{h}{2}, b_i + \frac{K_2}{2}\right) \\ K_4 &= hf(t_i + h, b_i + K_3) \end{aligned} \tag{19}$$

$$b_{i+1} = b_i + \frac{1}{6}(K_1 + 2K_2 + 2K_3 + K_4) \tag{20}$$

Forth Order Adams Bashforth Formula

$$y_{i+1} = y_i + \frac{h}{24} 5(5f_i - 59f_{i-1} + 37f_{i-2} - 9f_{i-3}) \quad (21)$$

Forth Order Adams Moulton Formula

$$y_{i+1} = y_i + \frac{h}{24} (9f_{i+1} - 19f_i - 5f_{i-1} + f_{i-2}) \quad (22)$$

3. Implementation

By the proposed solution in the previous section, we can generate script files with MATLAB to make the computation easier and generate a graph for the rate of drug concentration. The main script file is drug_interface.m, and the computational part is by Adam_Bashforth.m. We are using MATLAB as the programming IDE to generate the solution in this project. Table 2 explains each script file and its description.

Table 2
Description for each script file

Script File	Description
drug_interface.m	This is the main file that runs the whole program. It gives instructions/choices to the user and takes the input. Therefore, it acts as a user interface for the system.
Adam_Bashforth.m	This is the computational function that calculates the initial values by Runge-Kutta Fourth Order and then proceeds with Adam-Bashforth Predictor-Corrector. It will display two tables based on each method and generate a graph 'drug concentration vs time'.
Drug_A.m	This is a function type of script file, and it generates a differential equation and initial value condition for the Aminoglycosides. Then, it calls the computational function to generate the solution.
Drug_B.m	This is a function type of script file, and it generates a differential equation and initial value condition for the Valproic Acid. Then, it calls the computational function to generate the solution.
Drug_C.m	This is a function type of script file, and it generates a differential equation and initial value condition for the Vancomycin. Then, it calls the computational function to generate the solution.

3.1 Flowcharts
3.1.1 Flow chart for the main script file: drug_interface.m

Figure 3 below shows the flowchart for the main script file, acting as the interface for the coding system. At first, it will display the list of drugs and ask the user to select a drug to check its concentration. Then, the script file will check whether the choice for the drug exists. If the drug input is not in the system, the user will choose whether to try again or stop the system. Next, assume the drug input is in the list, and then it will ask for a few inputs based on the selected drug. It will ask for body weight in kg, age, the dose of the drug in mg and the value for a time interval that we want to investigate the concentration for all types of drugs. In addition, if the drug is Aminoglycosides or Vancomycin, it will ask for more information which is the gender. Based on gender, it will set the constant value and serum creatinine level. Note that the serum creatinine level range for males is 60–110 micromoles per litre and for females is 45–90 mcmol/l. Therefore, in this coding, we take 90 mcmol/l for females and 65 mcmol/l. Lastly, this program will call the drug function based on the selected drug.

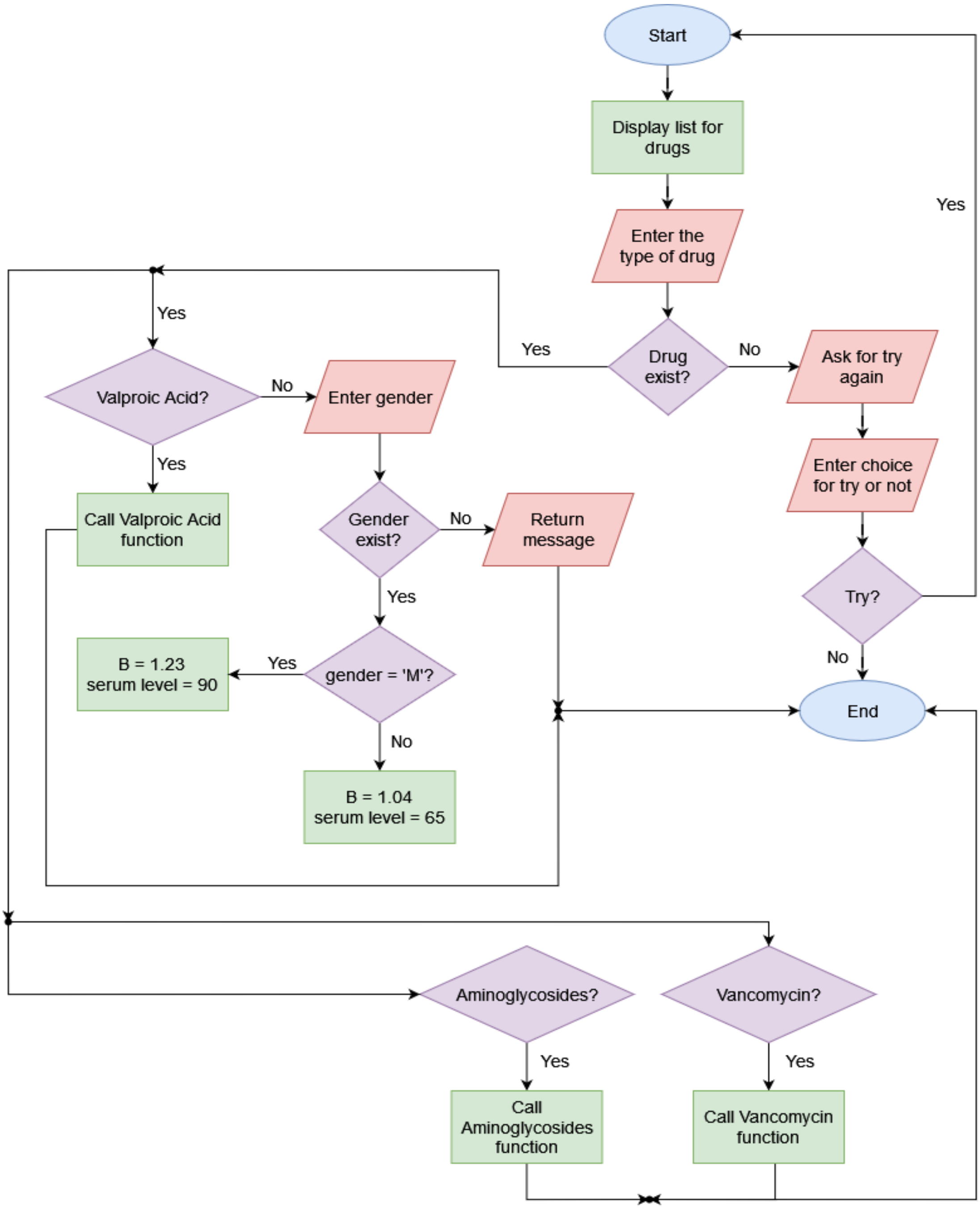


Fig. 3. Flow chart for the drug_interface.m

3.1.2 Flowchart for the computational script file: Adam_Bashforth.m

Adam_Bashforth.m is the computational script file for the coding, as shown in Figure 4 below. It returns the values for the rate of drug concentration by the Adams-Bashforth-Moulton method and displays the graph for the drug concentration vs time. In order to investigate further, the script file will get the values for a differential equation, initial condition, and duration. Then, it will proceed with the Runge-Kutta Fourth Order iteration will find three more initial values for the rate of drug concentration. Since it stated that i = 1:3, its means i = 1, 2, 3. Thus, it will find values for t(2), t(3), t(4), b(2), b(3), and b(4). Each iteration will display the value and plot the graph based on the calculated values. Next, it will proceed with Adams-Bashforth Predictor-Corrector Method for i = 4 and continue until the last subinterval. b0 give the value for the predictor, and b1 gives the value for the corrector, based on Adams-Bashforth Predictor-Corrector formulas. Each iteration will display the value and plot the graph based on the calculated values. After all calculations and plotting have been done, it will display a graph for 'Drug Concentration vs Time by Adams-Bashforth Method'.

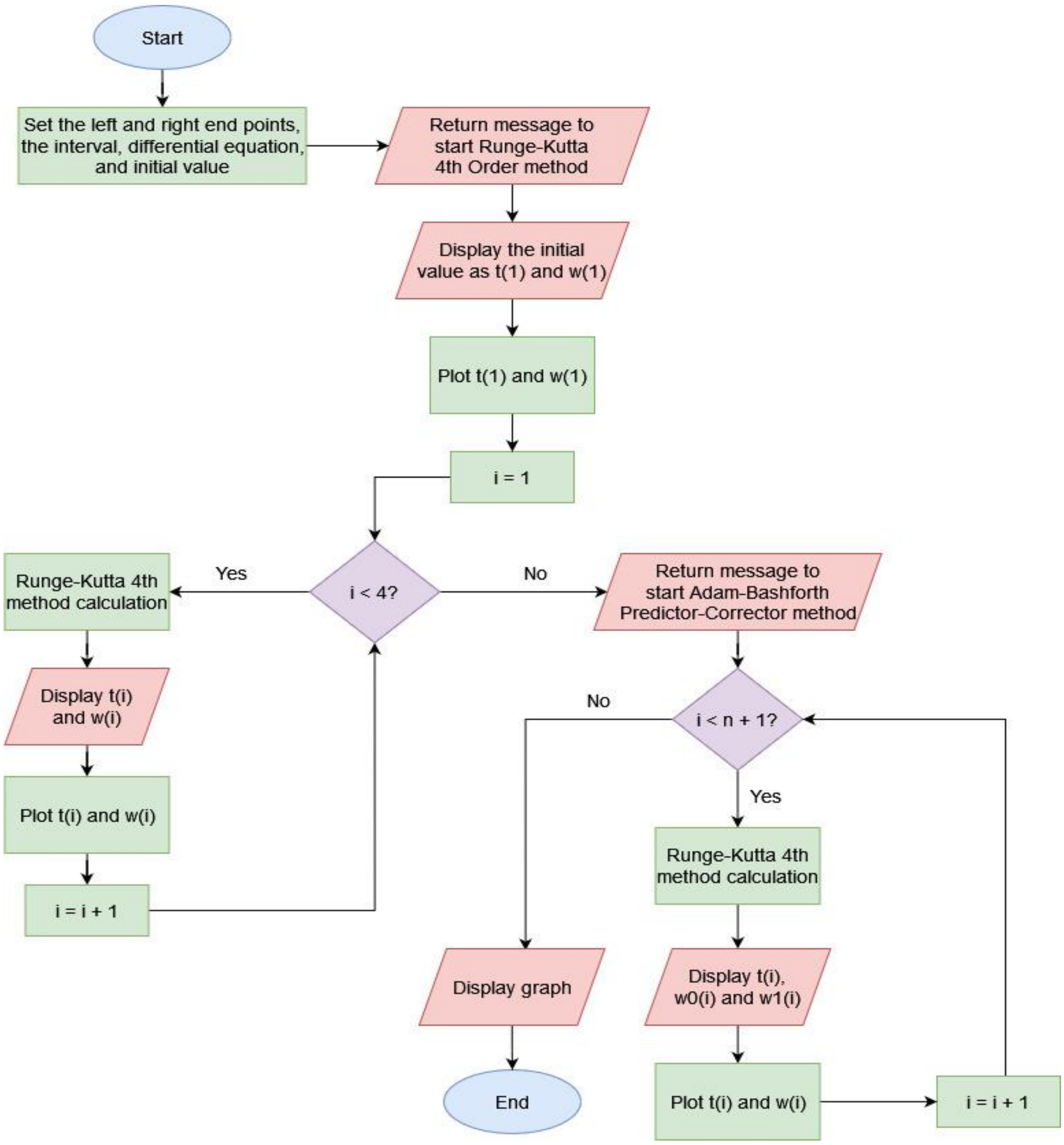


Fig. 4. Flow chart for the Adam_Bashforth.m

3.1.3 Flowchart for the function script file Aminoglycosides

Drug_A.m will generate the differential equation and initial value/condition for Aminoglycosides based on user input in the drug_interface.m, as shown in Figure 5. The function Aminoglycosides will take the values of body weight in kg, age, drug dose in mg, duration in hours, constant B based on gender, and Serum Creatinine level from the drug_interface.m. Then, it calculates the value for Vd, Cl, and alpha for Aminoglycoside's drug. Based on these, it will generate a differential equation and initial condition. Lastly, it will call the Adam_Bashforth function to generate the solution.

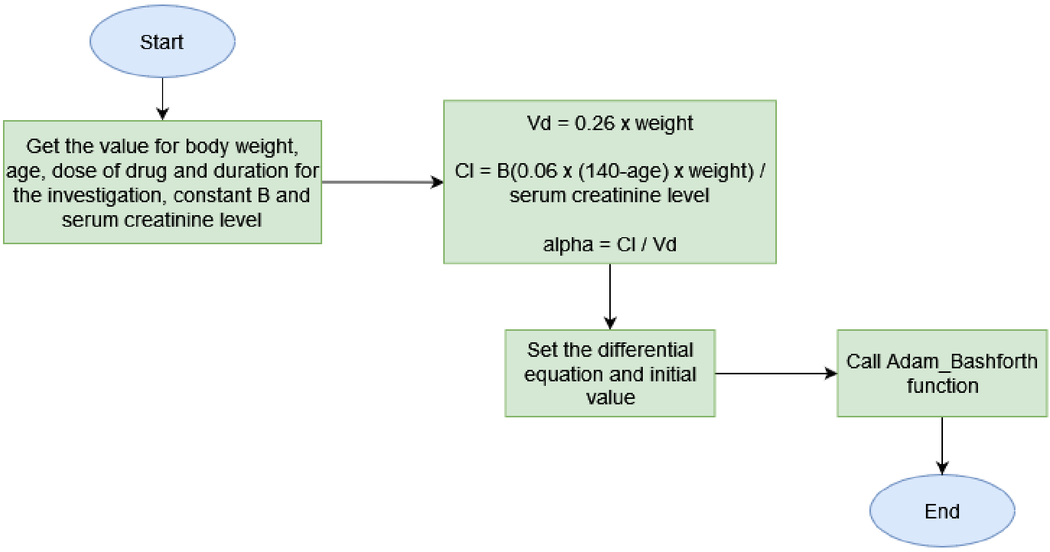


Fig. 5. Flow chart for the Drug_A.m

3.1.4 Flowchart for the function script file for Valproic Acid

Figure 6 shows the flowchart for Drug_B.m that will generate the differential equation and initial value/condition for Valproic Acid based on user input in the drug_interface.m. This function script will take all necessary values from the drug_interface.m, such as body weight in kg, age, drug dose in mg, and duration in hours. Then, based on age, it will classify whether the person is a child or an adult. If he/she is an adult, we will set the value for volume distribution (Vd) as 0.15 times body weight, and the alpha is 19/300. Otherwise, the value for Vd is 0.2 times body weight, and the alpha is 3/40. The alpha value is used to generate the differential equation for the problem, and Vd is used to find the initial value for the drug concentration for t=0. The differential equation and the initial value are for Valproic Acid only.

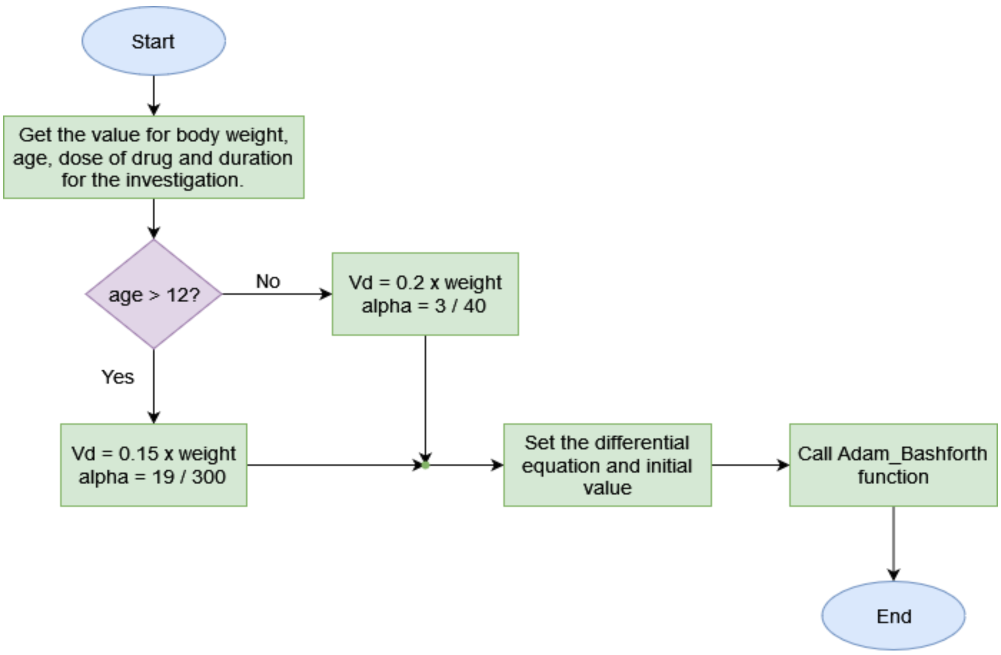


Fig. 6. Flow chart for the Drug_B.m

3.1.5 Flow chart for the function script file for Vancomycin

Drug_C.m will generate the differential equation and initial value/condition for Vancomycin based on user input in the drug_interface.m, as shown in Figure 7. This script files a function to generate a differential equation and the initial value for the Vancomycin drug. Everything is the same as the Drug_A.m script file. The only difference is the formula for Vd.

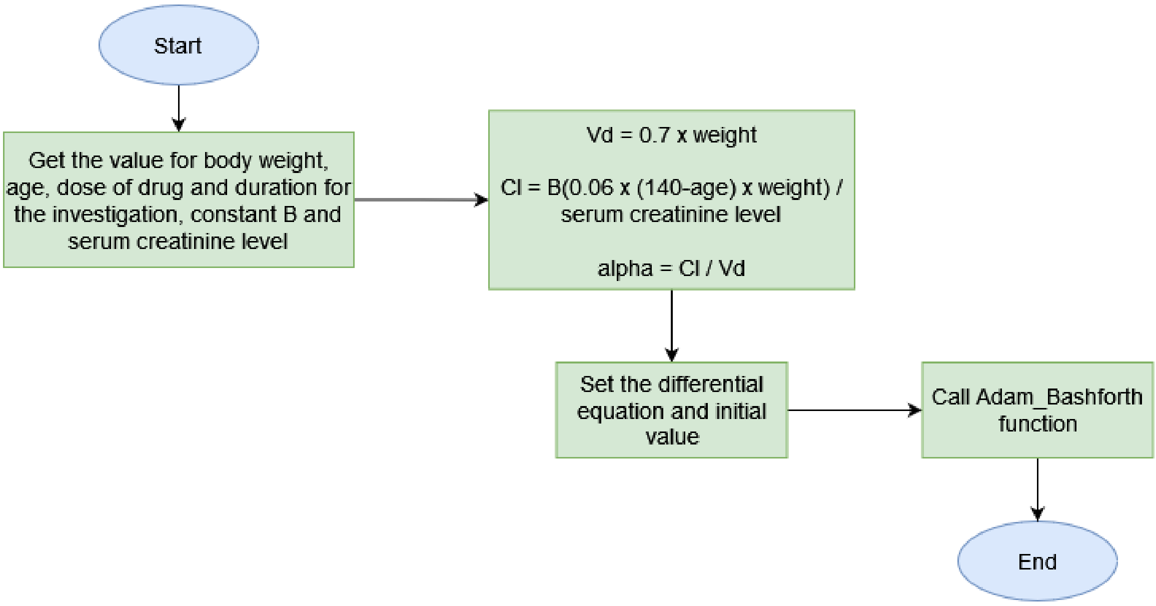


Fig. 7. Flow chart for the Drug_C.m

4. Results

In order to generate the result and compare these three drugs, we have to fix an assumption. Let the person be a female with 60kg, and she is 30 years old. Assume she consumes the maximum dose for the drug. We want to see the estimated value and the graph for the next 18 hours after she consumes the drug.

4.1 Output for Aminoglycosides (Drug A)

There are two types of Aminoglycosides, and they have different doses based on weight,

I. Amikacin: 5.0–7.5 mg/kg
II. Gentamicin Tobramycin: 1.5–2.0 mg/kg

Since Amikacin has a higher dose than Gentamicin Tobramycin, we chose Amikacin as the consumed drug. Therefore, the dose is 7.5 x 60 = 450mg. The result for Amikacin (Aminoglycosides) are shown in Figure 8 to 10.

```
Command Window
Type of drug (medicine)
A: Aminoglycosides
B: Valproic Acid
C: Vancomycin

Enter type of drug: A
Enter body weight (in kg): 60
Enter age: 30
Enter drug dose (in mg): 450
Enter duration (in hours): 12
Enter M for male and F for female.
Enter gender: F


By Runge-Kutta Forth Order, the initial values are:

   t          b
--------------------
0.0000  28.84615385
1.0000  19.22001572
2.0000  12.80617881
3.0000   8.53267854
```

Fig. 8. The input and the initial values for Aminoglycosides

```
Hence, by Adam-Bashforth Predictor-Corrector Method, we have:

   t      Predictor     Corrector
--------------------------------
4.0000   5.73600526   5.67379443
5.0000   3.82107062   3.77274878
6.0000   2.53396587   2.50941357
7.0000   1.68759755   1.66872103
8.0000   1.12292115   1.10962198
9.0000   0.74631345   0.73789903
10.0000   0.49632709   0.49069288
11.0000   0.33009982   0.32629889
12.0000   0.21949353   0.21698334
13.0000   0.14595729   0.14429031
14.0000   0.09706184   0.09595031
15.0000   0.06454391   0.06380521
16.0000   0.04292028   0.04242933
17.0000   0.02854134   0.02821473
18.0000   0.01897947   0.01876228
```

Fig. 9. The predictor and corrector value for Aminoglycosides 450mg for 18 hours

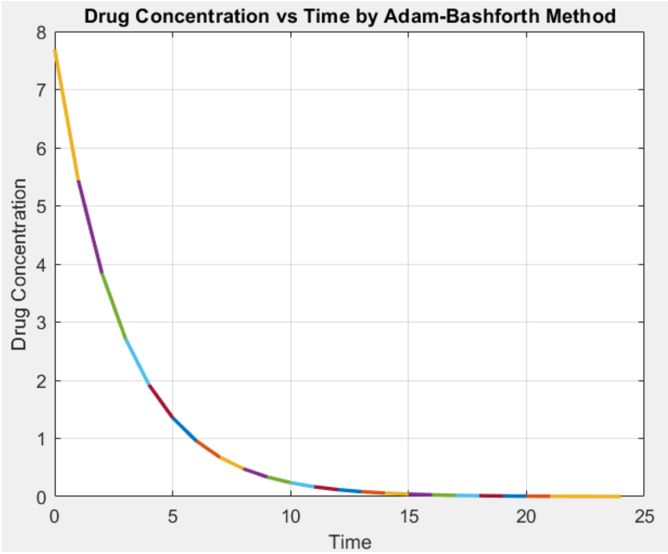
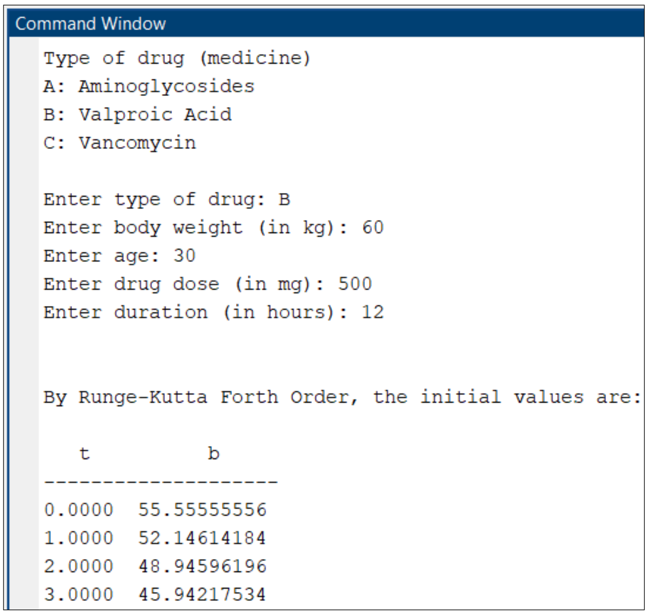


Fig. 10. Drug concentration vs time for Aminoglycosides (18 hours)

Figure 8 is the input and the initial values for Aminoglycosides. Based on Figure 9 and Figure 10, we can see that the concentration of the drug is flushed out from the body before 18 hours.

4.2 Output for Valproic Acid (Drug B)

The starting dose for Valproic Acid is 250mg, and a person can take at most 500mg of Valproic Acid. By assuming the dose taken is 500mg, we can generate the following result as shown in Figure 11 to 13.



```
Command Window
Type of drug (medicine)
A: Aminoglycosides
B: Valproic Acid
C: Vancomycin

Enter type of drug: B
Enter body weight (in kg): 60
Enter age: 30
Enter drug dose (in mg): 500
Enter duration (in hours): 12


By Runge-Kutta Forth Order, the initial values are:

   t          b
--------------------
0.0000  55.55555556
1.0000  52.14614184
2.0000  48.94596196
3.0000  45.94217534
```

Fig. 11. The input and the initial values for Valproic Acid

```
Hence, by Adam-Bashforth Predictor-Corrector Method, we have:

   t      Predictor    Corrector
--------------------------------
4.0000  43.12274651  43.12272739
5.0000  40.47632564  40.47630754
6.0000  37.99231397  37.99229713
7.0000  35.66074503  35.66072918
8.0000  33.47226325  33.47224837
9.0000  31.41808747  31.41807351
10.0000  29.48997542  29.48996231
11.0000  27.68019063  27.68017832
12.0000  25.98147141  25.98145986
13.0000  24.38700172  24.38699088
14.0000  22.89038383  22.89037365
15.0000  21.48561261  21.48560306
16.0000  20.16705149  20.16704253
17.0000  18.92940980  18.92940138
18.0000  17.76772154  17.76771365
```

Fig. 12. The predictor and corrector value for Valproic Acid 500mg for 18 hours

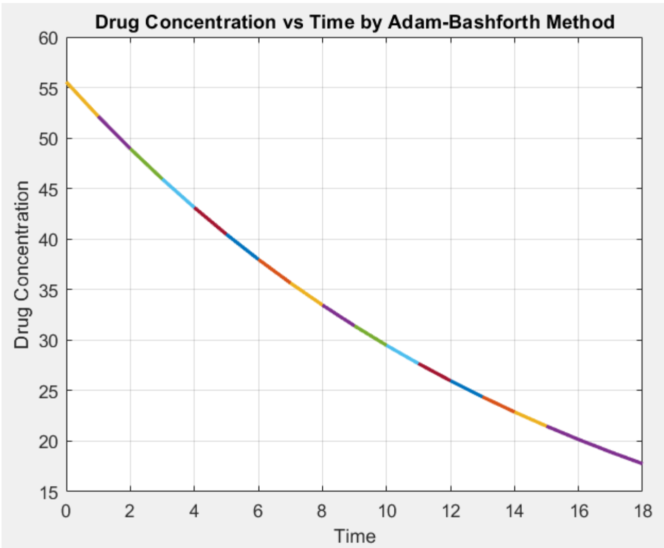


Fig. 13. Drug concentration vs time for Valproic Acid (18 hours)

Figure 11 is the input and the initial values for Valproic Acid. Based on Figure 12 and Figure 13, we can see that the drug concentration remains high in the body even after 18 hours.

4.3 Output for Vancomycin (Drug C)

The dose of Vancomycin for an adult is 15 to 20 mg/kg. Therefore, the dose chosen for Vancomycin is 1200mg.

The input and starting values for Vancomycin are shown in Figure 14. Figure 15 and Figure 16 show that even after 18 hours, the drug concentration is still present in the body.

```
Command Window
Type of drug (medicine)
A: Aminoglycosides
B: Valproic Acid
C: Vancomycin

Enter type of drug: C
Enter body weight (in kg): 60
Enter age: 30
Enter drug dose (in mg): 1200
Enter duration (in hours): 12
Enter M for male and F for female.
Enter gender: F


By Runge-Kutta Forth Order, the initial values are:

   t          b
--------------------
0.0000  28.57142857
1.0000  24.57060508
2.0000  21.13001219
3.0000  18.17120148
```

Fig. 14. The input and the initial values for Vancomycin

```
Hence, by Adam-Bashforth Predictor-Corrector Method, we have:

   t     Predictor    Corrector
--------------------------------
4.0000  15.62727929  15.62662562
5.0000  13.43895488  13.43837686
6.0000  11.55703642  11.55655618
7.0000   9.93867184   9.93825281
8.0000   8.54692628   8.54656590
9.0000   7.35007141   7.34976158
10.0000   6.32081625   6.32054979
11.0000   5.43569113   5.43546198
12.0000   4.67451305   4.67431599
13.0000   4.01992529   4.01975582
14.0000   3.45700166   3.45685592
15.0000   2.97290611   2.97278078
16.0000   2.55660008   2.55649230
17.0000   2.19859079   2.19849810
18.0000   1.89071474   1.89063503
```

Fig. 15. The predictor and corrector value for Vancomycin 1200mg for 18 hours

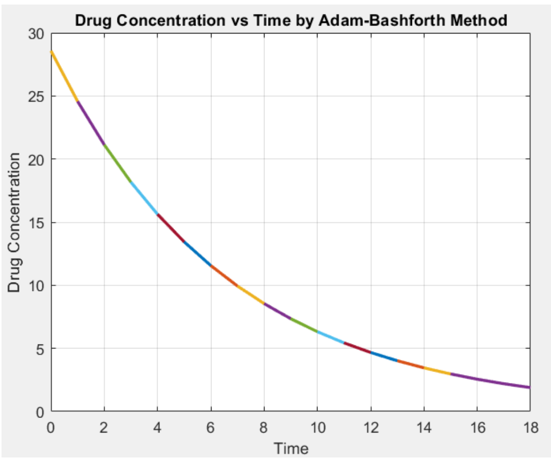


Fig. 16. Drug concentration vs time for Valproic Acid (18 hours)

4.4 Output If Error Occur

The error will occur when the user enters an input that does not allow the system to proceed or an irrational value. For instance, the system already gives a list of drugs for the user to select, but the user enters a value out of the list. Therefore, based on Figure 17, the system will give the user another chance to try the system again.

```
Command Window
Type of drug (medicine)
A: Aminoglycosides
B: Valproic Acid
C: Vancomycin

Enter type of drug: F
The type of drug is not in the list! Please choose A/B/C only
Do you want to try again?
fx Type Y if yes:
```

Fig. 17. The drug type is not exists

Next, from Figure 18, the user also may enter a different value for the gender even though it is already stated that M is for males and F for females. Then, the system will stop running.

```
Command Window
Type of drug (medicine)
A: Aminoglycosides
B: Valproic Acid
C: Vancomycin

Enter type of drug: C
Enter body weight (in kg): 50
Enter age: 25
Enter drug dose (in mg): 2
Enter duration (in hours): 24
Enter M for male and F for female.
Enter gender: K
Wrong input!!!
fx >>
```

Fig. 18. User enters other values for gender

Other than that, the user also may

I. Enter a negative value for body weight
II. Enter a body weight in other units such as g or lbs.
III. Enter a negative value for age
IV. Enter a negative duration
V. Enter the duration in other units, such as minutes

Even though the error occurs because the value is irrational/illogical, the system will still calculate and generate a solution for the problem.

5. Discussions

We realised that combining all these outputs into one table and a graph would be more accessible. However, it is more readable if we separate them into their function and only show the values for the drug we want. Also, we can add more drugs easily to investigate them without changing the whole code. Moreover, each drug type will have different doses based on the consumer, and the consumer also has a different body type and gender. Hence, having the output in one table/graph is impossible. However, we gather all information that we achieve in this section. Refer to Table 3 for comparing these drugs for the same assumption.

Table 3
Comparison of these drugs

Drug	Aminoglycosides	Valproic Acid	Vancomycin
Dose range (for adult)	Amikacin: 5.0–7.5 mg/kg Gentamicin Tobramycin: 1.5–2.0 mg/kg	250mg to 500mg	15 to 20 mg/kg
Assumption	A woman who is 30 years old and her weight is 60kg. She consumes the maximum dose of the drug.		
Dose	Amikacin: 450mg	500mg	1200mg
Initial drug concentration	28.84615	55.55556	28.57143
Drug concentration at time = 18 hours	0.01876	17.76771	1.89064
Drug concentration at time = 48 hours	0.00000009	2.65748933	0.02046708
Drug concentration at time = 168 hours	0	0.00132994	0

Since aspirin interferes with platelet function, it should be stopped before platelet donation. However, after 48 hours, the drug concentration level is already too low for all these three drugs. So it is safe to donate blood. Note that a week has 168 hours, and all these drugs take less than that to achieve a concentration of less than 0.002. Therefore, we can conclude that the drug will completely flush from our bodies in less than a week.

Based on this report, we know that every type of drug has a different differential equation. Thus, we need to generate the differential equation based on the assumption. MATLAB makes it easier to generate the differential equation and the solution. Without MATLAB, it is time-killing to calculate each iteration for the Adams-Bashforth Predictor Corrector method.

Table 3 shows that Valproic acid has the highest initial drug concentration. Note that bipolar disorder, epilepsy, and migraine are treated with valproic acid. Hence, it needs long-term effects on the human body to cure/assess the pain. At the same time, Aminoglycosides and Vancomycin have a lower initial concentration and are easy to eliminate from the human body.

6. Conclusions

The report was designed to estimate the concentration of drugs over time for three particular drugs: Aminoglycosides, Valproic Acid and Vancomycin, and determine how long each person has to wait before donating blood. The drug concentration duration to zero in the bloodstream for each person is different. However, the differences are minimal, and we can conclude that the maximum duration for all three drugs will be eliminated from the bloodstream is one week. This method can also be applied to drugs that fit the one-compartment model, like Theophylline, Ethosuximide and Procainamide. The only distinction will be in the computation for Vd and α. Moreover, the coding created can also be used to detect rare cases where the drug concentration for a particular person is not zero by a week. Then, we can use this finding to temporarily defer that person from donating. It will assist blood banks in determining whether a blood donor on medication should be rejected. Hence, the safety of the donor and the receiver can be ensured and prevent things like transmission of the drug during the donation process can cause very harmful effects on the health of the person receiving the blood.

Acknowledgement
This research is supported by Research University Grant (RUI) (1001/PMATHS/8011131) by Universiti Sains Malaysia.

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