Pharmacokinetics: Determining the function that best represents the decrease in the concentration of two drugs in the body

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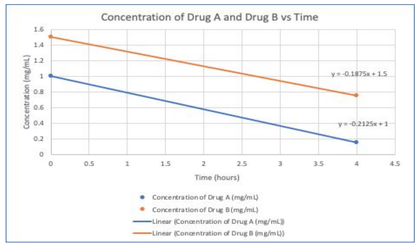
Introduction

Pharmacokinetics is the branch of pharmacology concerned with the absorption and movement of drugs throughout the body. Researchers gather measurements of the concentration of an individual drug at various times after the drug has been administered to try to determine the function that demonstrates the pattern which follows the decrease of the concentration of the drug in the body. In this project, the function that best demonstrates the pattern with which the concentration of Drug A and Drug B decreases in the body will be determined. Assumption: when the drug is administered, it is diffused so rapidly throughout the bloodstream that it reaches its fullest concentration instantly.

Linear Functions

	Drug A	Drug B
Concentration at time t = 0	1.0 *mg/mL*	1.5 *mg/mL*
Concentration after 4 hours	0.15 *mg/mL*	0.75 *mg/mL*

Assumption: the function describing the concentration with respect to time is linear.



Drug A Equation: $f(t) = -0.2125t + 1$

Drug B Equation: $f(t) = -0.1875t + 1.5$

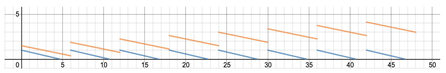
Time until the drug is eliminated:

Drug A	Drug B
$f(t) = -0.2125t + 1$	$f(t) = -0.1875t + 1.5$
$0 = -0.2125t + 1$	$0 = -0.1875t + 1.5$
$t =$ 4.705882353	$t = 8$
4.71 hours	8 hours

Rate at which the drug is eliminated:

Drug A:	Drug B:
0.215 *mg* per hour.	0.1875 *mg* per hour.

Predictions of the drug concentration should the drug be administered every six hours:



1. $f(x) = -0.2125x + 1\ \{0 \le x \le 4.705882353\}$
2. $f(x) = -0.2125(x-6)+1\ \{6 \le x \le 10.706\}$
3. $f(x) = -0.2125(x-12)+1\ \{12 \le x \le 16.706\}$
4. $f(x) = -0.2125(x-18)+1\ \{18 \le x \le 22.706\}$
5. $f(x) = -0.2125(x-24)+1\ \{24 \le x \le 28.706\}$
6. $f(x) = -0.2125(x-30)+1\ \{30 \le x \le 34.706\}$
7. $f(x) = -0.2125(x-36)+1\ \{36 \le x \le 40.706\}$
8. $f(x) = -0.2125(x-42)+1\ \{42 \le x \le 46.706\}$
9. $f(x) = -0.1875x + 1.5\ \{0 \le x \le 6\}$
10. $f(x) = -0.1875(x-6)+1.5+.375\ \{6 \le x \le 12\}$
11. $f(x) = -0.1875(x-12)+1.5+.75\{12 \le x \le 18\}$
12. $f(x) = -0.1875(x-18)+1.5+1.125\{18 \le x \le 24\}$
13. $f(x) = -0.1875(x-24)+1.5+1.5\{24 \le x \le 30\}$
14. $f(x) = -0.1875(x-30)+1.5+1.875\{30 \le x \le 36\}$
15. $f(x) = -0.1875(x-36)+1.5+2.25\{36 \le x \le 42\}$
16. $f(x) = -0.1875(x-42)+1.5+2.625\{42 \le x \le 48\}$

Drug A:

- As the drug is eliminated before six hours, the concentration will never be higher than 1 *mg*.

Drug B:

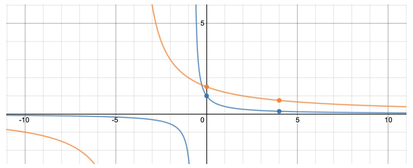
- As the drug is not eliminated by the six hour mark, the concentration will continue to increase indefinitely.

Rational Functions

	Drug A	Drug B
Concentration at time t = 0	1.0 *mg/mL*	1.5 *mg/mL*
Concentration after 4 hours	0.15 *mg/mL*	0.75 *mg/mL*

Assumption: the function describing the concentration with respect to time is a rational function of the form $f(t) = \frac{a}{t-b}$.

Graph: Concentration of Drug A and Drug B vs Time



Drug A: Blue color | Drug B: Orange color

*Only values where $t \ge 0$ are considered as one cannot have a negative amount of time or a negative concentration.

Drug A and Drug B equations:

Drug A	Drug B
$f(t) = \frac{a}{t-b}$	$f(t) = \frac{a}{t-b}$
$f(0) = 1$	$f(0) = 1.5$
$f(4) = 0.15$	$f(4) = 0.75$
$1 = \frac{a}{-b}$	$1.5 = \frac{a}{-b}$
$-b = a$	$-1.5b = a$
$0.15 = \frac{a}{4-b}$	$0.75 = \frac{a}{4-b}$
$0.6 - 0.15b = a$	$3 - 0.75b = a$
$0.6 - 0.15b = -b$	$3 - 0.75b = -1.5b$
$0.6 = -0.85b$	$3 = -0.75b$
$b = -0.70588235294$	$b = -4$
$-b = a$	$-1.5b = a$
$a = 0.70588235294$	$a = 6$
$f(t) = \frac{0.70588235294}{t+0.70588235294}$	$f(t) = \frac{6}{t+4}$

Time until the drug is eliminated:

Drug A and Drug B

- Despite no further doses being administered, the functions for Drug A and Drug B have horizontal asymptotes at $x = 0$ and were found to be divergent so the drug, while of an increasingly miniscule concentration, never completely leaves the blood.

Rate at which the drug is eliminated:

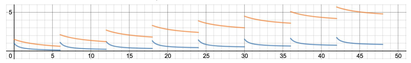
Drug A

- The rate at which the drug is eliminated is the derivative of the original function such that $f(t) = \frac{-0.70588235294}{(t+0.70588235294)^2}$. The rate at which the drug is eliminated is $\frac{0.70588235294}{(t+0.70588235294)^2}$ *mg* per hour.

Drug B

- The rate at which the drug is eliminated is $\frac{-6}{(t+4)^2}$ *mg* per hour.

Predictions of the drug concentration should the drug be administered every six hours:



Drug A: Blue color | Drug B: Orange color

Drug A and Drug B

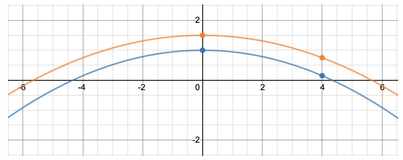
- As the drugs aren't eliminated by the six hour mark, the concentrations will continue to increase indefinitely.

Polynomial Functions

	Drug A	Drug B
Concentration at time t = 0	1.0 *mg/mL*	1.5 *mg/mL*
Concentration after 4 hours	0.15 *mg/mL*	0.75 *mg/mL*

Assumption: the rate at which the concentration is decreasing at time t is modeled by the equation in the form of $dy/dt = -kt$ where y is the concentration of the drug in the blood at time t, and k is a constant.

Graph: Concentration of Drug A and Drug B vs Time



Drug A: Blue color | Drug B: Orange color

*Only values where $t \ge 0$ are considered as one cannot have a negative amount of time or a negative concentration.

Drug A and Drug B equations:

Drug A	Drug B
$\frac{dy}{dt} = -kt$	$\frac{dy}{dt} = -kt$
$y = \int -ktdt$	$y = \int -ktdt$
$y = \frac{-k}{2}t^2 + c$	$y = \frac{-k}{2}t^2 + c$
$c = 1$ (concentration at $t = 0$)	$c = 1.5$ (concentration at $t = 0$)
$y = \frac{-k}{2}t^2 + 1$	$y = \frac{-k}{2}t^2 + 1.5$
$0.15 = \frac{-k}{2}(4^2) + 1$	$0.75 = \frac{-k}{2}(4^2) + 1.5$
$0.15 = \frac{-k}{2}(16) + 1$	$0.75 = \frac{-k}{2}(16) + 1.5$
$-0.85 = -8k$	$-0.75 = -8k$
$k = 0.10625$	$k = 0.0.09375$
$k = \frac{17}{160}$	$k = \frac{3}{32}$
$y = \frac{-17}{320}t^2 + 1$	$y = \frac{-3}{64}t^2 + 1.5$

Time until the drug is eliminated:

Drug A	Drug B
$y = \frac{-17}{320}t^2 + 1$	$y = \frac{-3}{64}t^2 + 1.5$
$0 = \frac{-17}{320}t^2 + 1$	$0 = \frac{-3}{64}t^2 + 1.5$
$\frac{320}{17} = t^2$	$\frac{96}{3} = t^2$
$t = \frac{8\sqrt{85}}{17}$	$t = \sqrt{32}$
$t = 4.338609156$	$t = 5.656854249$

Rate at which the drug is eliminated:

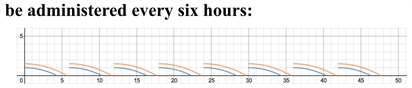
Drug A

- The rate at which the drug is eliminated is the derivative of the original function such that $f'(t) = -0.10625t$. The rate at which the drug is eliminated is $0.10625t$ *mg* per hour.

Drug B

- The rate at which the drug is eliminated is $0.09375t$ *mg* per hour.

Predictions of the drug concentration should the drug be administered every six hours:



Drug A: Blue color | Drug B: Orange color

Drug A and Drug B

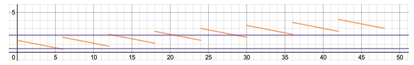
- As the drugs are eliminated before six hours, the concentrations will never be higher than the concentrations at $t = 0$ (1 *mg* for Drug A and 1.5 *mg* for Drug B).

Drug B Dosage

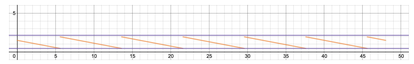
***For the dosage questions, only Drug B is considered as the equations for Drug A and Drug B share share the same form for each considered function.**

In terms of the linear function:

- If the dose is given every six hours, the appropriate concentrations will not be maintained
- This is because from 5.6 - 6 hours, the dosage concentration will be too low and from hour 12 to infinity, the dosage added will go over into the danger zone until eventually, the dosage is in the danger zone for the entire six hours.
- Unless the administration of the dosages are stopped, will remain the case indefinitely.



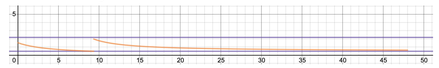
- For Drug B, the linear function representing the decrease in concentration will only maintain the appropriate concentrations if the drug if administered when t= 5.6 and not re-administered until hour 13.6 where it would then be re-administered every eight hours.



In terms of the rational function:

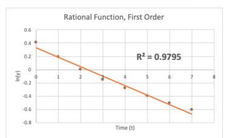
- If the dose is given every six hours, the appropriate concentrations will not be maintained indefinitely or even for 48 hours because at hour 12, the dosage added will start to go over into the danger zone.
- This will continue to occur at each re-administration of the drug until eventually the dosage is in the danger zone for the entire six hours.
- This will remain the case indefinitely, or, at least, until the dosage administrations are halted.

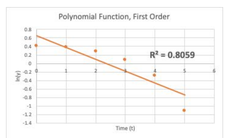
- Adjusting the time interval at which the drug is administered as was done for Part A would not result in a satisfactory long run level.
- As the function is a divergent function, when the dosage is first re-administered at 9.333 hours, the properties of the function itself prohibits the dosage from decreasing below the minimum effective level of the drug (0.45 *mg/mL*).
- Not only would the drug never be entirely metabolized by the body, but it will remain effective in the body indefinitely.

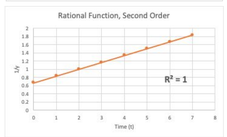


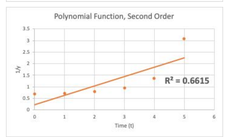
In determining if the rational or polynomial functions represent first or second order reactions:

Only the trendline in the Rational Function, Second Order graph has a linear slope (R^2=1), which means that the decrease in the concentration of Drug B matches that of a second order reaction if the decrease is represented by a rational function. The concentration values for the polynomial function matches neither those for a first order nor a second order reaction.





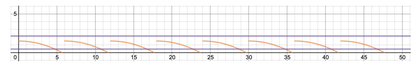




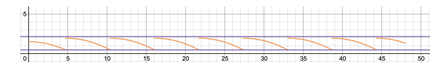
Dosage Cont.

In terms of the polynomial function:

- If the dose is given every six hours, the appropriate concentrations will not be maintained.
- For the last 1.267 hours in each six hour interval, the dosage concentration will be too low to be effective. This remains constant indefinitely.



- If the time period was altered so that the first new dose was administered at 4.733 hours, and each subsequent dose was administered every 5.657 hours, the appropriate concentrations will be maintained indefinitely.



Other Factors in the Rate of Elimination

In terms of the linear function:

- Drug A and Drug B are eliminated by zero order kinetics (in zero order kinetics, a constant amount is eliminated per unit time).
- For the linear function, the drug elimination is independent of the drug concentration.

In terms of the rational and polynomial functions:

- The rational and polynomial functions are nonlinear functions and so the drug elimination is not independent of the drug concentration.
- Some other factors would include the type of mechanism the reaction follows as well as possible side reactions that may occur.

Conclusion

The model that I believe most accurately portrays the concentration of Drug A and Drug B in the body is the model for the linear functions. This is the case because while the drug concentration values for the rational functions match those for a second order reaction, the function is divergent and so draws the conclusion that if the dosage was readministered at or above the minimum effective level for the drug, the drug will remain effective indefinitely as it will never cross that minimum effective level due to its horizontal asymptote.

While the polynomial function did not present any glaring inconsistencies as the rational function did, my research into pharmacokinetics revealed that most functions for the elimination of a drug are first order, second order, or zero order functions. As the polynomial functions aren't first order, second order, or zero order and the linear functions are zero order, it seems more likely that the model that most accurately portrays the concentration of Drug A and Drug B in the body is the model for the linear functions.

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