

STUDENT VERSION

Drug Model for Caffeine Elimination

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STATEMENT

How does the human body eliminate some drugs, particularly caffeine? That is the question for this activity.

CAFFEINE ELIMINATION

Activity 1: First Thoughts

(1.1) Typically when a drug is administered to an individual, the concentration of the drug $C(t)$ in the body changes over time. The drug is gradually eliminated from the body. The concentration is amount per unit volume. Although this can be a very complicated process, we will apply a very simple model. Write an equation in which the rate is **proportional to** the concentration of the drug in the body.

$$\frac{dC}{dt} = \quad (1)$$

(1.2) Identify the following for your equation, or write “none”: independent variable(s) independent variable(s); dependent variable(s); constant(s); parameter(s).

(1.3) For a drug that is eliminated from the body at a proportional rate, would you expect the concentration of drug in the body to increase, stay the same, or decrease for awhile? What value would you expect for the initial concentration of drug in the body?

Activity 2: A General Model

(2.1) Drugs might be administered to people or other animals in a variety of ways, including, but not limited to, tablet form, gum, and in food or beverages. Caffeine is rapidly and almost completely absorbed in humans. A general simple model of concentration of an eliminated drug is given by

$$\frac{dC}{dt} = -k C(t) \quad (2)$$

Use your mathematical background to complete the sentence:

$\frac{dC}{dt}$ represents the _____ of the concentration of drug in the body over time.

(2.2) A “first-order reaction” in pharmacokinetics is exemplified by (2). Classify this equation using mathematical terms and calculate a general solution.

(2.3) We make a simplifying assumption. Let us assume that our initial time ($t = 0$) occurs when the body has gained the maximum concentration of the drug and that this occurs immediately. Let C_0 be the initial concentration; that is, $C(0) = C_0$. Solve the initial value problem.

Activity 3: Caffeine Model

Background: Caffeine is a drug that can be used to enhance safety and performance in military situations, among other uses. It can be administered to people and other animals in a variety of ways, including in tablet form, gum, and in food or beverages. Caffeine is rapidly and almost completely absorbed in humans. The concentration of a single dose of caffeine in the body is modeled by a First-Order Reaction.

Specific Situation

A healthy adult male soldier is administered a form of caffeine that is estimated to yield an initial concentration of 4 mg/kg, meaning four milligrams of caffeine per kilogram of body weight.

Assume volume and body weight are constant over the timeframe of the model.

These are somewhat “interchangeable” quantities, so mass per kg of body weight is an equivalent and often more convenient way to represent concentration.

A note about quantities and units: “Concentration” is generally defined as “mass of a substance per unit volume.” In a pharmacokinetic model of drug elimination, “volume” is more specifically the “apparent volume of distribution”, representing the space that the drug occupies in the body, and generally equivalently described as a percent of body weight. For instance, “caffeine binds reversibly to plasma proteins, and protein-bound caffeine accounts for about 10 to 30 percent

of the total plasma pool.” [2] Plasma generally accounts for 4.5% of a person’s body weight. [3] “The distribution volume [of caffeine] within the body is 0.7 L/kg.” [2] From these, if we were so inclined, we could express concentration in terms of mg/L and then make further conversions based upon the person’s weight and volume of plasma. Instead, we can use mg substance per kg of body weight.

(3.1) State as much as you can of the initial First-Order Reaction model for this Situation using the given information. Give the differential equation with initial condition and its solution $C(t) = C_0 e^{-k t}$ where $C(t)$ is measured in units of _____.

(3.2) The half-life of a drug, $t_{1/2}$, is the time it takes for one half of the amount of the drug to be eliminated. A reasonable half life in our situation is 3.0 hours [2].

State a general equation that relates $C(t_{1/2})$ and C_0 . Calculate any remaining parameter(s) for caffeine in this situation.

(3.3) Give the full model, both in the form of an initial value problem and its solution.

(3.4) Graph the resulting $C(t)$ against t on the left side of this space.

(3.5) To the right of your graph above, create a “phase plane” for our situation. A phase plane in this context is a graph with $C(t)$ on the horizontal axis and the rate of change of the drug amount $\frac{dC}{dt}$ on the vertical axis.

Activity 4: Zero-Order Reaction Characteristics

A very general form of a differential equation is $\frac{dg}{dt} = f(t, g(t))$. In this case, f is a “rate function” that may or may not depend upon the independent variable t and/or the dependent variable $g(t)$. In other words, most generally speaking, f might be a constant, only directly depend upon t , only directly depend upon g , or depend directly upon both t and $g(t)$.

(4.1) State the rate function for (2).

In what way might we say this rate function is “First-Order”?

(4.2) In which Activity did you graph the rate function for caffeine?

Does the rate function modeled by a First-Order Reaction change with respect to time as the concentration changes? or is it constant with respect to time?

(4.3) In which Activity did you graph the concentration of caffeine over time?

Does a drug concentration modeled by a First-Order Reaction change linearly with respect to time with this model? or nonlinearly?

REFERENCES

- [1] Institute for Scientific Information on Coffee. <http://www.coffeeandhealth.org/topic-overview/all-about-caffeine-2/>. Accessed 15 Aug 2018.
- [2] Institute of Medicine (US) Committee on Military Nutrition Research. 2001. “Caffeine for the Sustainment of Mental Task Performance: Formulations for Military Operations.” Washington DC: National Academies Press. Guest access <http://www.nap.edu/download/10219>. Accessed 11 Aug 2016.

- [3] Shargel, L. and A. Yu 2016. *Applied Biopharmaceutics and Pharmacokinetics. 7th ed.* New York: McGraw Hill.