One-Compartment Model of Single Dose — Aspirin —

Metabolism of a drug in the human body is a complex system to represent in a model. Thus, in Step 2 of the modeling process, particularly for our first attempt, we should make simplifying assumptions about the drug and the body. A **one-compartment model** is a simplified representation of how a body processes a drug. In this model, we consider the body to be one homogeneous compartment, where distribution is instantaneous, the **concentration** of the drug in the system (amount of drug/volume of blood) is proportional to the drug dosage, and the rate of elimination is proportional to the amount of drug in the system. The concentration of a drug instead of the absolute quantity is important because a quantity that might be appropriate for a small child might be ineffective for a large adult. A drug has a **minimum effective concentration** (MEC), which is the least amount of drug that is helpful, and a **maximum therapeutic concentration** or **minimum toxic concentration** (MTC), which is the largest amount that is helpful without having dangerous or intolerable side effects. The **therapeutic range** for a drug consists of concentrations between the MEC and MTC. A drug's **half-life**, or the amount of time for half the drug to be eliminated from the system, is useful for modeling as well as patient treatment. Often concentrations and half-life are expressed in relationship to the drug in the plasma or blood serum. The total amount of blood in an adult's body is approximately 5 liters; while the amount of **plasma**, or fluid that contains the blood cells, is about 3 liters. Blood **serum** is the clear fluid that separates from blood when it clots, and an adult human has about 3 liters of blood serum.

Example 1 One-Compartment

We begin by modeling the concentration in the body of aspirin (acetylsalicylic acid). For adults and children over the age of 12, the dosage for a headache is one or two 325 mg tablets every four hours as necessary up to 12 tablets/day. Analgesic effectiveness occurs at plasma levels of about 150 to 300 μg/ml, while toxicity may occur at plasma concentrations of 350 μg/ml. The plasma half-life of a dose from 300 to 650 mg is 3.1 to 3.2 hr, with a larger dose having a longer half-life.

For simplicity, we assume a one-compartment model with the aspirin immediately available in the plasma. A stock (box variable), *aspirin_in_plasma*, represents the mass of aspirin in the compartment, which is the person's system, and has an initial value of the mass of two aspirin, (2)(325 mg)(1000 μg/mg), where 1 milligram (mg) is equivalent to 1000 micrograms (μg).

The flow from *aspirin_in_plasma* (*elimination*) is proportional to the amount present in the system, *aspirin_in_plasma*. Thus, the rate of change of the drug leaving the system is proportional to the quantity of drug in the system (*aspirin_in_plasma*, or Q in the following equation):

$$dQ/dt = -KQ$$

Vensim

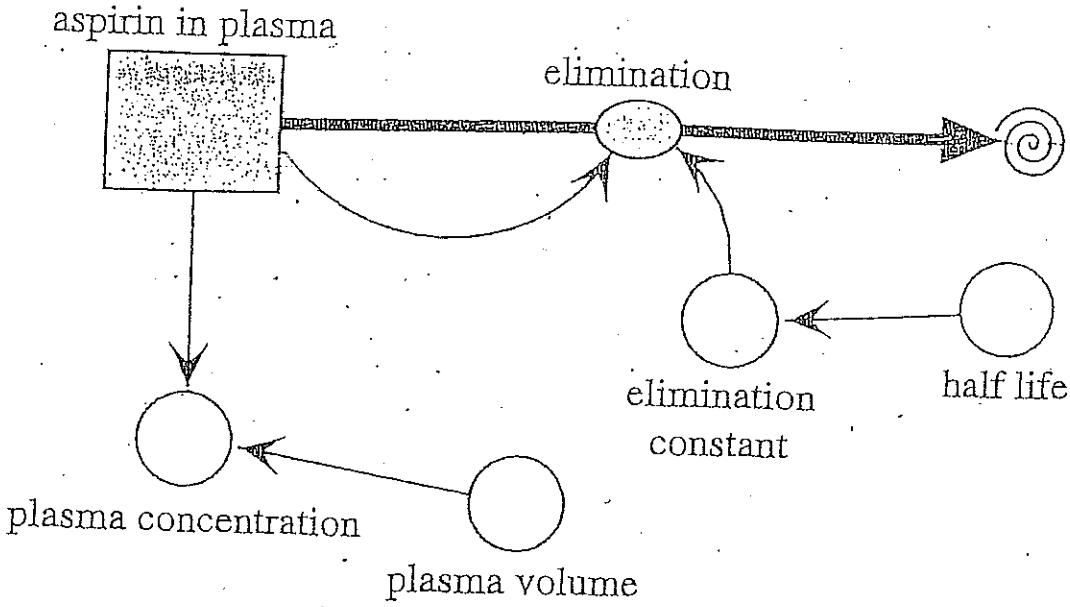

Figure 3.5.1 One-compartment model of aspirin

As Module 3.2 on "Unconstrained Growth" shows, the solution to this differential equation is as follows:

$$Q = Q_0 e^{-Kt}$$

Using this solution, as Exercise 1 shows, the constant of proportionality K above and *elimination_constant* in the system dynamics software model has the following relationship to the drug's half-life ($t_{1/2}$):

$$K = -\ln(0.5)/t_{1/2}$$

Pharmaceutical sources widely report a drug's half-life.

Quick Review Question 1

Determine the elimination constant with units for aspirin assuming a half-life of 3.2 hr.

To compute aspirin's plasma concentration (*plasma_concentration*) in a converter (variable), we have another converter for the volume of the system (*plasma_volume*) with a value of 3000 ml and appropriate connectors and equation. Figure 3.5.1 contains a one-compartment model for one dose of a drug, where the initial value of *plasma_concentration* is the dosage; and Equation Set 3.5.1 gives the corresponding equations and values explicitly entered for the model of aspirin.

Quick Review Question 2

In terms of the variables in the model of Figure 3.5.1, give the equation for *plasma_concentration*.

Equation Set 3.5.1

Explicitly entered equations and values for one-compartment model of aspirin

$half\_life = 3.2$ hr
$plasma\_volume = 3000$ ml

$aspirin\_in\_plasma(0) = 2 * 325 * 1000$ μg
$elimination\_constant = -\ln(0.5)/half\_life$
$elimination = elimination\_constant * aspirin\_in\_plasma$
$plasma\_concentration = aspirin\_in\_plasma/plasma\_volume$

Running the simulation for 8 hr and plotting *plasma_concentration*, the resulting graph in Figure 3.5.2 indicates that the concentration of the drug in the plasma is initially approximately 217 μg/ml, which is a safe, therapeutic dose. Subsequently, the concentration decreases exponentially.

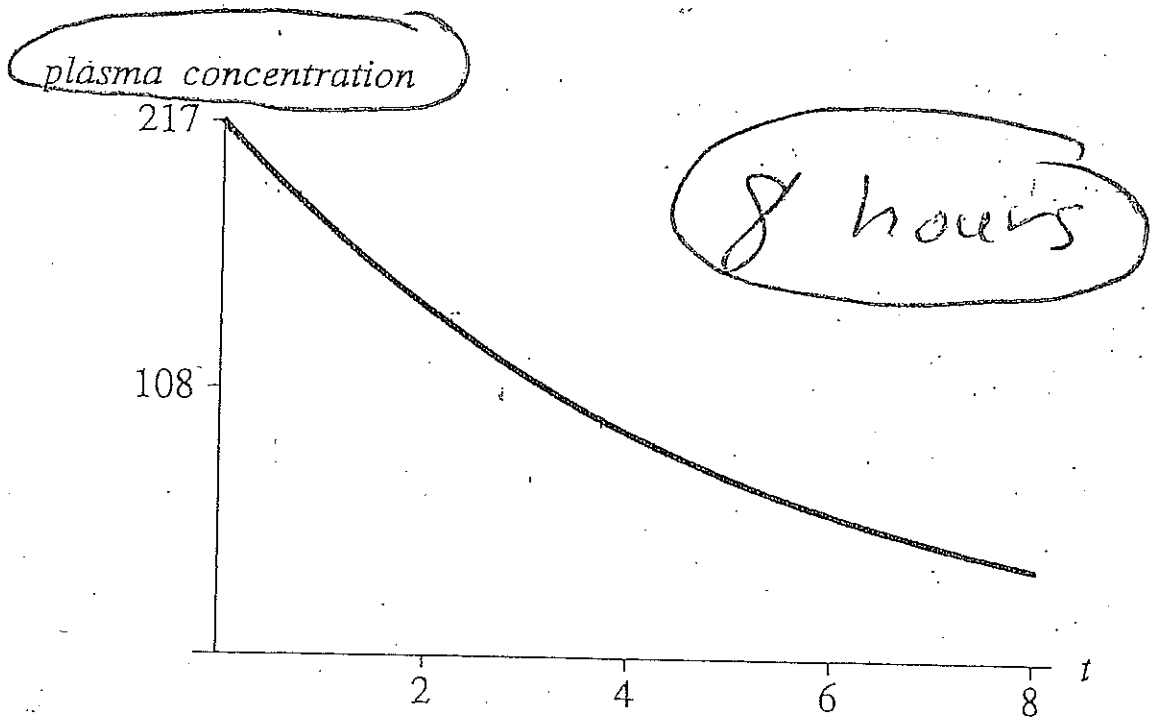

Figure 3.5.2 Graph of *plasma_concentration* (μg/ml) versus *t*(hr) for aspirin