# Pharmecokinetic Model of Drug Dosage and Concentrations

In order to be effective, the concentration of a drug in the bloodstream needs to reach a medicinal level. Below this level, the drug will be ineffective. For some drugs, there is also the limitation that above some concentration level they become toxic. Thus, it is critical to vary the dosage such that the steady state concentration is between the effective and toxic dose.

Models of this system can take account of a number of related factors as illustrated below.
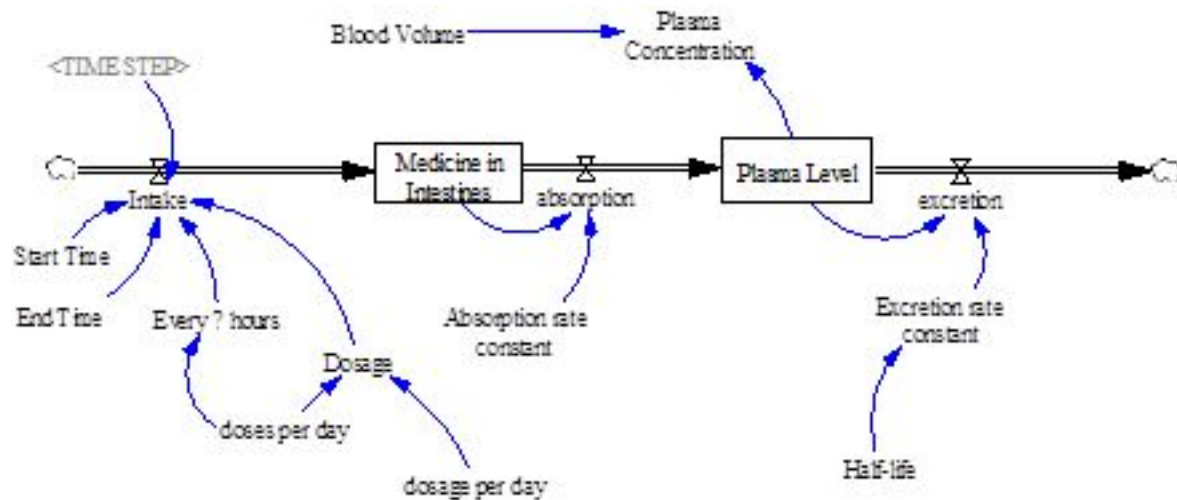
Medicine is ingested as oral doses one or more times per day with each pill containing a particular dosage. Those doses are given at discrete times. Assuming a 16 hour day during which medicine could be taken, the doses can be assumed to be distributed evenly over that time period.

Once a dose is taken, that amount is resident is the intestines. For each increment of time, part of that dose is absorbed into the bloodstream at an adsorption rate, adds to the amount in the blood plasma and reduces the amount in the intestines. Once absorbed, the medicine also leaves the body at each increment of time depending on the half-life of the drug and the excretion rate.

At any of the time periods, the plasma concentration is a function of the plasma level divided by the blood volume of the person who took the drug. That is the level to be simulated over time to make sure it gets to the effective dose and is below the toxic dose.

There are two articles to read that discuss the underlying science, variations on related models, and evidence based models based on testing of patients. You should review these articles and may look for other materials on pharmacokinetic models on the Internet.

We have prepared a partial script to get you started on the project:

Drug_dosage_model.sws

The first part of the model defines the parameters that you are to use for the various constants in the model, the therapeutic and toxic levels of the drug, and a routine to calculate the intake of the drug into the patient's system.

You will first need to alter the model to create a complete estimate of the plasma level drug concentration and plot it on a graph with both the therapeutic and toxic drug levels, given a particular number of doses and dosage amount. The relevant underlying equations that express the relationships in the diagram are of this form:

Absorption (i) = time_step * absorption_rate *medicine_in_intestines(i)

 Where i is the time that is iterated from 0 to 48 hours by the time step

Then

Excretion (i) = (time_step * excretion rate * plasma level(i)

Medicine_in_intestines (i+1) = medicine in intestines (i) – absorption(i) + intake(i)

Plasma_level (i+1) = plasma _level(i) - excretion(i) +absorption(i)

Plasma_concentration (i+1) = plasma_level(I + 1) /blood volume

If your model is working correctly, the results for one dose at a dosage level of 6000 should look like this:
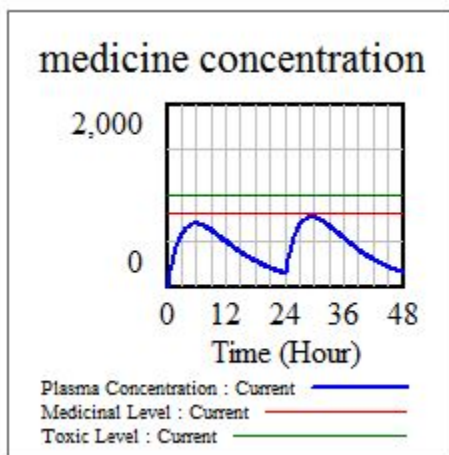
Once you have a working model, you need to change the number of doses and dosage level so that the steady state concentration in the plasma stays between the medicinal and toxic levels.

For the person with the given "average" blood volume, use the model results to illustrate the combinations of dosage and number of doses that build the concentration to target levels. Test the impact of reasonable changes in the excretion constant on the results. For example, if the person drinks a lot of coffee, they are likely to excrete more of the drug as the coffee acts as a diuretic. Include in your final submission a description of your code, the underlying model assumptions, the sensitivity testing, and the results with the given parameters as described below.

Prepare a final submission package to be given to the contest judges for scoring. The package should include the following:

1. All relevant versions of the code you used to test the range of circumstances you analyzed. Each version should be internally documented to indicate which of the circumstances was tested and what parameters were changed. For sensitivity runs, you need not present multiple versions of the code with each parameter change but should indicate in the internal documentation the range of runs that were made and the range of values used in those test.
2. Prepare a summary report of the project that contains the following:
    a. A title, list of team members, and date of the contest
    b. A summary of the project results including the following sections:
        i. Description of the final main code along with a code listing
        ii. A summary of the model assumptions and how the model simplifies the systems that it represents
        iii. A summary of the model runs made to derive the values of the parameters that met the objective of the modeling exercise. The summary should embed graphs and/or table to illustrate the model results.
        iv. A summary of the sensitivity testing that was completed along with their results using appropriate graphs and/or tables.
3. If you undertake any of the bonus projects below, provide a report appendix that provides the relevant summary, code changes, graphs, and tables as appropriate as a separated section for each of the bonus projects.

Bonus Projects

1. Dosage directions tend not to be followed when the number of doses in a day is more than two. Drugs can be manufactured to time release the medicine over a 12 hour period to reduce the total number of pills one needs to take. Rework the model to provide two doses of time released capsules and figure out what the hourly dosage needs to be to maintain the correct drug levels in the plasma.

2. People vary in size and thus in plasma volume. Change the model to simulate the changes in dosage that would be required for people ranging from 20% smaller (and proportionally less plasma volume) up to 20% larger than the volume given in this model.

3. Doctors could use a model such as this to alter their prescription so that the dosage and response was set correctly for each person's relative size. Find a reasonable estimate of the relationship between body weight and blood plasma. Alter the model so that it interactively asks for the patient's weight as an input and then searches a set of solutions that include the dosage appropriate for that person's weight.

4. Find a specific drug and look up its published pharmacokinetics. You can use a website such as webmd.com or http://www.nlm.nih.gov/medlineplus/ to search for the drug or do a search for a brand name. Once there, find the link to the manufacturer's site and look up the **full prescribing information**. Alternatively, use the brand name and search for the name and prescribing information. It should have a section on the pharmacokinetics. Use that information to change the model parameters to match the published rates for absorption and excretion. What does the altered model predict about the steady state concentration of the drug? Some possible candidates: mesalamine (Apriso), Celebrex, Lotensin HCT, synthroid.