In Class Exercises (ICE) - 2/14/01

Pharmacokinetics is the study of the introduction, distribution, metabolism and excretion of drugs by the body[1]. Many drugs obey the "linear pharmacokinetic" law. That is, the rate at which the drug is removed from the body is proportional to the concentration of the drug in the body.

- ***Experimental evidence has shown that the drug penicillin-G[2] obeys the linear pharmacokinetic law. Express this as a differential equation involving drug concentration and time.***

In a study[3] designed to examine animal models for testing pharmaceuticals, a researcher injected the drug penicillin-G into a mouse and into a human subject. The researcher took blood samples at regular intervals and measured the concentration of penicillin-G in the blood. The results are presented in Table 1 and Table 2.

Time (minutes)	0	15	30	45	60
Concentration (mg/100ml)	10	1.25	0.15625	0.01953	0.00244

Table 1: Penicillin-G blood plasma concentrations for mouse.

Time (minutes)	0	15	30	45	60
Concentration (mg/100ml)	10	7.07107	5	3.5355	2.5

Table 2: Penicillin-G blood plasma concentrations for human.

- ***Use the data in Tables 1 and 2 to find formulas for concentration as a function of time for the mouse and the human.***

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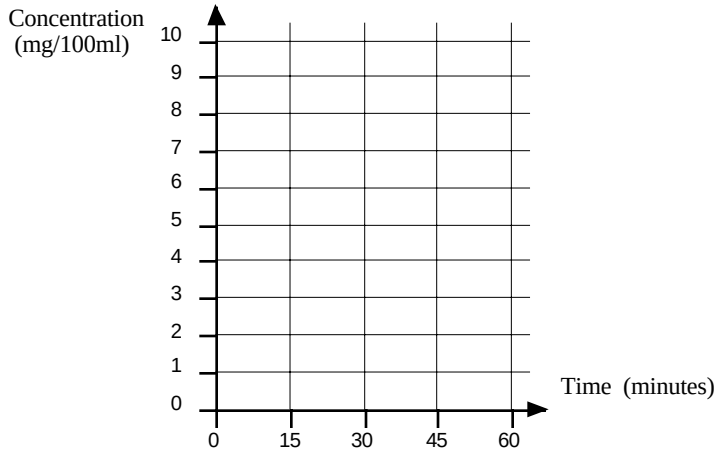
[1] For an introduction to this field, see the course notes for "PHAR 4634: A First Course in Pharmacokinetics and Biopharmaceutics" available on-line at the University of Oklahoma College of Pharmacy.

[2] Marketed under the commercial names Bicillin® and Wycillin® this is an antibiotic used to treat infections of the skin, brain, heart sinuses and ears. (Source: www.healthanswers.com)

[3] W. A. Craig. (2000) "Pharmacokinetics of Antimicrobials: Animal Models." Paper presented at the International Society of Anti-Infective Pharmacology Conference. (Stockholm, Sweden, 5/28/2000)

- ***Do the formulas that you have found obey the linear pharmacokinetic law? Use derivatives and equations to justify your answer. What is the constant of proportionality for humans and mice?***

- ***Use the axes provided below to sketch a graph of concentration as a function of time for the human. Can you explain why your graph has the shape that it does (increasing/decreasing, concavity) from the linear pharmacokinetic law?***



- ***In the same study, another mouse was injected with the antibiotic minocycline[4]. When the mouse had a blood plasma concentration of 5 mg/100ml, the concentration of minocycline in its blood was decreasing at a rate of 0.00578 mg/100ml per minute. Express this statement using mathematical symbols, and then find a formula for the concentration of minocycline as a function of time. If you are told that the mouse initially had 10 mg/100ml of minocycline in it's blood, how can you modify your answer?***

[4] Minocycline is a tetracycline antibiotic that is sometimes used to treat extreme cases of acne. The drug is controversial, as it has been linked to the onset of autoimmune disease in some patients. (Source: Medical Sciences Bulletin, 1996, **18**(8): 4.)