

PHA 5127 Dose Optimization I
Fall 2011
Case Study VI

If you have any questions regarding this case study, do not hesitate to contact Benjamin Weber (benjaminweber@ufl.edu). Please remember that attendance is mandatory. Students whose IPEE coincides with the case study lecture are excused.

Problem 1

A hypertensive patient is going to receive long-term medication of drug A. Drug A can only be administered via IV-bolus injection due to its low oral bioavailability. The volume of distribution and clearance of drug A are 120 L and 10 L/h, respectively. Drug A's plasma protein binding is 30%. Drug A is known to show severe side effects if its free plasma concentration is higher than 5 µg/mL. In order to avoid these side effect and to reach an antihypertensive effect, the Drug A's maximum free drug concentration at steady state should be 20% less than 5 µg/mL. The patient has agreed to come twice a day to hospital for the administration of the drug. The physician asks you as a clinical pharmacist to calculate the dose that should be administered to the patient. Which assumptions did you make to ensure that your calculations are valid?

Problem 2

Another patient receives the same drug (drug A) as a single-dose IV-bolus injection to treat his hypertensive crisis. A metabolite of drug A is known to counteract the effect of another drug that the patient receives. Thus, a physician asks you as a clinical pharmacist to predict the plasma concentration of the metabolite 6 hours after the administration of the drug A. Assume that 500 mg of drug A will be administered and that the elimination rate constant of the metabolite after IV-bolus injection is 5 h⁻¹ ($k_{\text{met}} = 0.04 \text{ h}^{-1}$, $VD_M = VD$).

- Calculate the total amount of metabolite that has been eliminated. Assume the metabolite is solely cleared by the kidney (no further metabolism).
- Sketch a semi-logarithmic plot of the plasma concentration time profile of drug A and its metabolite.
- Would this sketch change tremendously if the elimination rate constant of the metabolite was doubled? If yes, sketch the new semi-logarithmic plot of the plasma-concentration-time-profile.

Problem 3

A company has invented a formulation technique that has increased the oral bioavailability of drug A to 15%. Due to this new possibility two differently formulated tablets have come on the market. The absorption rate constants of formulation FAST and SLOW are 1 h⁻¹ and 0.02 h⁻¹, respectively. Plot the concentration-time-profile from 0-24 h for both formulations. Which formulation shows a “flip-flop”-kinetic?

Problem 4

TRUE (T) or FALSE (F)

For multiple-dosing, the free plasma concentration at steady state is always dependent on the clearance of the drug

T F

It generally takes about five half-lives for a drug to be cleared from the body after steady state has been reached.

T F

For multiple-dosing, the peak-through-fluctuation is independent of the dose only after oral administration of the drug

T F

The average concentration at steady state can be calculated as

$$\frac{Dose}{VD * F}$$

T F

For a one compartment body model and oral administration, K_e cannot be calculated as

$$\frac{C_0}{AUC_{\infty}}$$

T F

After oral administration, T_{max} can always be calculated as

$$\frac{\ln\left(\frac{k_e}{k_a}\right)}{k_e - k_a}$$

T F