PHA 5128 Dose Optimization II
Spring 2011
Homework I Solution
10 points

If you any questions regarding this homework assignment, do not hesitate to contact Benjamin Weber (benjaminweber@ufl.edu) or your respective facilitator. Please provide all answers with their **appropriate units** and all graphs with **appropriately labeled axes**. 0.25 points will be deducted for each missing or inappropriate unit or axes label. Please provide all answers on separate sheets (does not apply to TRUE/FALSE questions). **Remember to show how you found your answer**. Answers lacking adequate justification may not receive full credit.

Problem 1 (4 points)

A 37-year-old man is hospitalized. The clinical pharmacists is ask to recommend a dosing regimen for drug A (Dose = 800 mg, CL = 50 L/h, VD = 200 L).The plasma-concentration-time profile of drug A is known to follow a one-compartment body model. For the following scenarios, calculate the peak and trough concentrations (for single dose trough concentration after 12 h).

a) Single Dose, Short-term infusion, T = 45 min

b) Multiple Dose (steady state), IV bolus, τ = 12 h

c) Multiple Dose (steady state), Short-term infusion, T = 30 min, τ = 6 h

d) Multiple Dose (steady state), Short-term infusion, T = 90 min, τ = 8 h

Problem 2 (2 points)

Drug B is administered via multiple short-term infusions. Determine an appropriate dosing regimen of drug B to achieve desired steady state plasma concentrations of 12.5 mg/L for the peak (drawn 2 h after the end of a 2 h infusion) and approximately 3.5 mcg/mL for the trough. Assume that drug B's plasma-concentration-time profile follows a one-compartment body model. (CL = 15 L/h, VD = 100 L)

Problem 3 (0.5 points)

Define high and low extraction drugs (equations are sufficient)

Problem 4 (0.5 points)

List the three different "volumes of distribution" that are defined for a two-compartment body model in increasing order. Explain briefly why the volume of distribution is not constant in a two-compartment body model.

Problem 5 (0.5 points)

Drug C is known to show flip-flop kinetics after oral administration. Sketch a graph (semi-logarithmic plot) of drug C's plasma-concentration-time-profile after IV bolus and oral administration (single dose). You may assume that drug C follows a one-compartment body model.

Problem 6 (1 point)

a) State and explain briefly the three main mechanisms that are involved in renal excretion of drugs

b) Explain briefly why creatinine is used in humans to assess their renal function

c) Explain briefly all parameters (why are they included?) in the Cockcroft-Gault equation.

Problem 7 (1.5 points)

TRUE (T) or FALSE (F)

Poorly water soluble drugs that show a high first-pass effect usually have a low systemic bioavailability after IV bolus administration

T F

For a given drug, at equilibrium, the plasma protein binding is identical to the tissue protein binding

T F

For antibiotics, determination of free drug concentrations at the infection site is important for drug therapy because of their high tissue protein binding

T F

For high extraction drugs, the free plasma concentration at steady state is independent of plasma protein binding

T F

For low extraction drugs, the free plasma concentration at steady state is independent of plasma protein binding

T F

For bioequivalence assessment, statistical tests and decision criteria (i.e. 90% confidence intervals) are applied to C_{max}, AUC, and T_{max}

T F