

PHA 5127 Dose Optimization I Case Study IV

Problem 1

A female patient (6'0" tall, 65.5 kg, 35 years old) shows a serum creatinine level of 1.1 mg/dL.

- a) Use the Cockcroft-Gault-Equation to calculate her creatinine clearance and glomerular filtration rate (GFR).
- b) Why do we use the creatinine clearance to estimate the GFR?
- c) Drug A shows a plasma protein binding and tissue protein binding of 20% and 30%, respectively. Drug A is eliminated by hepatic (20%) and renal processes (80%). Calculate the total systemic clearance of drug A (in L/h) when administered to the patient. Assume that the drug is neither actively secreted nor reabsorbed.
- d) Graph the plasma-concentration time profile for the first 48 hours when 200mg of drug A are administered to the patient via IV bolus injection. A blood sample taken at the time of injection showed a plasma concentration of 2mg/L. Assume that the drug is immediately distributed throughout the body and that all elimination processes are first-order processes.

Problem 2

Which properties does a drug need to have in order to demonstrate the following? Explain briefly.

- a) Active tubular secretion
- b) Glomerular secretion
- c) Passive tubular reabsorption

Problem 3

Sketch the relationship between the following PK metrics and Dose for linear and non-linear pharmacokinetics.

- a) CL vs. Dose
- b) Vd vs. Dose
- c) AUC vs. Dose
- d) K_e vs. Dose