PHA 5127 Dose Optimization I

Homework III (Due on Sep. 23)

1. Drug A with oral bioavailability of 90% was given to a patient. Due to a change in the physiological conditions, the plasma protein binding was changed from 60% to 80%, and tissue binding was changed from 80% to 20%. Please determine the change in half life. (Assuming there is only hepatic clearance and other conditions remain the same, Q_H=80L/h, Vp=3L, V_T=38L) **(4 points)**

2. A patient was given 200mg of a drug as an IV bolus injection and plasma concentration dropped from a peak concentration of 0.5mg/L with a rate constant of 0.15 h^{-1}. **(3 points)**

(1) Estimate the hepatic clearance and AUC_{∞}. (Assume there are only hepatic and renal clearance, and renal clearance of this patient is 4L/h)

(2) If the fraction unbound in plasma increases two fold, please determine the oral bioavailability of this drug. (Assume the liver blood flow of this patient is 65L/h and there is no other physiological change.)

3. Please predict how the following parameters will change when the liver blood flow is increased in a patient by choosing from options below: (3 points)

(A) About the same (B) Increase significantly (C) Decrease significantly

(1) when taking a high extraction drug (1.5 points, 0.5 each)

the extraction ratio (E) _____

the clearance (Cl) _____

oral bioavailability (F) _____

(2) when taking a low extraction drug (1.5 points, 0.5 each)

the extraction ratio (E) _____

the clearance (Cl) _____

oral bioavailability (F) _____