

PHA 5127 Dose Optimization I, Fall 2012, Homework IV Solution
Total Points: 10

Problem 1 (4 points)

TRUE (T) or FALSE (F)

For a low extraction drug, the oral bioavailability is approximately 100%

T **F**

For a high extraction drug, the oral bioavailability increases with decreasing plasma protein binding

T **F**

The oral bioavailability is always higher than 20%.

T **F**

If, for a given drug, $Q_H \lll f_u * CL_{int}$, the drug is considered to be a high extraction drug

T **F**

Enzyme induction affects the hepatic clearance of low extraction drug

T **F**

For a high extraction drug, the hepatic clearance increases with an increase in renal blood flow

T **F**

For a low extraction drug, the hepatic clearance decreases with an increase in liver blood flow

T **F**

The oral bioavailability of low extraction drugs is not significantly affected by enzyme induction

T **F**

Problem 2 (6 points)

Assume an intrinsic clearance of I) 80000 L/h and II) 0.08 L/h and a liver blood flow of 80 L/h.

- a) Calculate the hepatic clearance and oral bioavailability for both situations assuming a plasma protein binding of 50%.

I. High extraction drug

$$CL_H \approx Q_H = 80 \frac{L}{h}$$

$$F \approx \frac{Q_H}{f_U * CL_{int}} = \frac{80 \frac{L}{h}}{0.5 * 80000 \frac{L}{h}} = 0.002 = 0.2\%$$

II. Low extraction drug

$$CL_H \approx f_U * CL_{int} = 0.5 * 0.08 \frac{L}{h} = 0.04 \frac{L}{h}$$

$$F \approx 1$$

- b) Calculate the hepatic clearance and oral bioavailability for both situations assuming a plasma protein binding of 99%.

III. High extraction drug

$$CL_H \approx Q_H = 80 \frac{L}{h}$$

$$F \approx \frac{Q_H}{f_U * CL_{int}} = \frac{80 \frac{L}{h}}{0.01 * 80000 \frac{L}{h}} = 0.1 = 10\%$$

IV. Low extraction drug

$$CL_H \approx f_U * CL_{int} = 0.01 * 0.08 \frac{L}{h} = 0.0008 \frac{L}{h}$$

$$F \approx 1$$