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, $Q_H << f_u * CL_{int}$, 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

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

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

II. Low extraction drug

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

$$F \approx 1$$

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

III. High extraction drug

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

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

IV. Low extraction drug

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

$$F \approx 1$$