

Q1) Say true or false

T F Clearance defines the amount of drug eliminated from body per unit time

T F For any drug, the AUC is affected by its dose and volume of distribution

T F As intrinsic clearance describes the liver's innate ability to clear unbound drug from intracellular water via metabolism or biliary excretion, the higher the liver blood flow, the higher will be a drug's clearance

T F For a high extraction drug that has predominant hepatic metabolism, the liver blood flow is a rate limiting step in its clearance

T F For a low extraction drug, the higher the protein binding the higher will be the clearance

Q2) Predict the changes in Hepatic Clearance ( $CL_H$ ) for the following scenarios

| Parameter | Change occurring | Effect on low extraction drug | Effect on High extraction drug |
|-----------|------------------|-------------------------------|--------------------------------|
| $f_u$     | ↓                |                               |                                |
| $CL_i$    | ↑                |                               |                                |
| $Q_h$     | ↑                |                               |                                |

Q3) Predict changes in Oral bioavailability for the following scenarios

| Parameter | Change occurring | Effect on low extraction drug | Effect on High extraction drug |
|-----------|------------------|-------------------------------|--------------------------------|
| $f_u$     | ↓                |                               |                                |
| $CL_i$    | ↑                |                               |                                |
| $Q_h$     | ↑                |                               |                                |

Q4) A patient is to be started on two medications (A and B) administered by IV bolus injections. Blood samples were taken at 1 and 4 hours following the first injections of drug A or B alone in order to determine whether concentrations were in an appropriate range for each drug. See table below for these levels and additional information.

| <b>Drug</b> | <b>Dose (mg)</b> | <b>Cp at 1h (mg/L)</b> | <b>Cp at 4h (mg/L)</b> | <b>E<sub>H</sub></b> | <b>f<sub>u</sub></b> |
|-------------|------------------|------------------------|------------------------|----------------------|----------------------|
| <b>A</b>    | 400              | 1.22                   | 0.76                   | 0.1                  | 0.3                  |
| <b>B</b>    | 1200             | 0.92                   | 0.51                   | 0.8                  | 0.1                  |

Assume liver blood flow of 90 L/h, where E<sub>H</sub> is the extraction ratio and f<sub>u</sub> is the fraction unbound. Renal elimination and hepatic metabolism are the only clearance pathways for both of these drugs.

- Calculate the CL(hepatic) for Drug B and CL (renal) for Drug B
- Also calculate the AUC<sub>0-∞</sub> Drug B