1: Predict the changes in Cl\textsubscript{h} given the following scenarios:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Direction of change</th>
<th>effect on Cl\textsubscript{h} for a low Extraction drug</th>
<th>effect on Cl\textsubscript{h} for a high Extraction drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>fraction of unbound drug</td>
<td>Increases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>intrinsic clearance</td>
<td>Decreases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>hepatic blood flow</td>
<td>Increases</td>
<td></td>
<td></td>
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</tbody>
</table>

2: True or False Questions

T F Total clearance is dependent on the half-life of the drug.

T F Volume of distribution and clearance are two major pharmacokinetic parameters, and they are dependent on each other based on equation:

\[ CL = V_d \cdot k_e \]

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

T F According to the equation: 

\[ AUC_\infty = \frac{Dose}{CL} = \frac{Dose}{V_d \cdot k_e} \]

the change of volume of distribution does affect \( AUC_\infty \).

T F Intrinsic clearance is not dependent on blood flow, and it represents the activities of enzyme system when we talk about liver metabolism.

T F Liver blood flow affects high extraction drug much more than low extraction drug when drug major elimination pathway is hepatic elimination.

3: Gamma-hydroxybutyric Acid (GHB) is an abused drug and also an endogenous compound. Recently, a study in rats was carried out to understand pharmacokinetics of GHB. A couple of rats were given a dose at 100mg intravenously in this study. Blood samples were taken at several time points. A graduate student in this lab plotted concentration-time data. He found that drug concentration-time profile can be best described by a one-compartmental linear model. He also determined that total clearance is 150 mL/hr, and \( t_{1/2} \) is 0.5 hr.
A: Calculate Volume of Distribution of GHB, GHB concentration at time zero, and $AUC_\infty$.

B: If liver metabolism is the major elimination pathway for GHB in rat, blood flow rate in rat is 1.5 L/hr, what is the extraction ratio for GHB in liver?

C: According to the Question B, is GHB a high or low extraction drug? If the free fraction of GHB in plasma is 0.3, what is the intrinsic clearance?

D: If liver blood flow in rat reduces to 1.0 L/hr after 2 hrs due to an anesthesia procedure, what is the intrinsic clearance and total clearance (still based on information from question B and C)? Compared to the values before anesthesia, do they change or not? Why?