1. Determine whether the elimination process in the graphs a-d is zero-order or first order. (Cp: Drug concentration in plasma)

Zero-order (straight line)

First-order (straight line after semilogarithmic transformation of the y-axis)
No Elimination

First-order (straight line after semilogarithmic transformation of the plasma concentrations)

2. 200 mg Drug A was administered to a female patient (60 kg) through IV bolus injection. The following plasma concentrations (Cp) were observed.

<table>
<thead>
<tr>
<th>time (h)</th>
<th>Cp (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.260</td>
</tr>
<tr>
<td>4</td>
<td>0.315</td>
</tr>
<tr>
<td>8</td>
<td>0.050</td>
</tr>
<tr>
<td>12</td>
<td>0.008</td>
</tr>
</tbody>
</table>

a) Plot Cp vs. time and determine the order of the elimination process
Plasma concentration vs. time profile is a straight line after semilogarithmic transformation. Thus, the elimination process is a first-order process.

b) Determine $k_e$ and $t_{1/2}$ (half life)

<table>
<thead>
<tr>
<th>time (h)</th>
<th>$C_p$ (µg/mL)</th>
<th>$\ln C_p$ ( )</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2.000</td>
<td>0.6931</td>
</tr>
<tr>
<td>1</td>
<td>1.260</td>
<td>0.2310</td>
</tr>
<tr>
<td>4</td>
<td>0.315</td>
<td>-1.1552</td>
</tr>
<tr>
<td>8</td>
<td>0.050</td>
<td>-3.0036</td>
</tr>
<tr>
<td>12</td>
<td>0.008</td>
<td>-4.8520</td>
</tr>
</tbody>
</table>

\[
Slope = \frac{-1.1552 - 0.2310}{4 - 1 h} = -0.4621 \frac{1}{h}
\]
\[ k_e = 0.4621 \frac{1}{h} \]

\[ t_{1/2} = \frac{\ln (2)}{k_e} = 1.5 \text{ h} \]

c) Estimate the initial concentration \( C_0 \) and the volume of distribution (Vd)

\[ C(t) = C_0 * e^{-k_e*t} \]

\[ \ln C(t) = \ln C_0 - k_e * t \]

\[ \ln C_0 = \ln C(t) + k_e * t \]

\[ \ln C_0 = \ln C(1) + k_e * 1 \]

\[ \ln C_0 = 0.2310 + 0.4621 * 1 = 0.6931 \]

\[ C_0 = e^{0.6931} = 2.00 \frac{\mu g}{mL} \]

\[ C_0 = \frac{\text{Dose}}{Vd} \]

\[ Vd = \frac{200 \text{ mg}}{2.00 \frac{\mu g}{mL}} = 100 \text{ L} \]

d) Calculate AUC_{0-t(last)} and AUC_{0-\infty} (Use trapezoidal rule)

\begin{center}
\begin{tabular}{|c|c|c|}
\hline
\text{time (h)} & \text{Cp (\mu g/mL)} & \text{AUC (\mu g*h/mL)} \\
\hline
0 & 2.000 & 1.63 \\
1 & 1.260 & 2.36 \\
4 & 0.315 & 0.73 \\
8 & 0.050 & 0.11 \\
12 & 0.008 & \\
\hline
\end{tabular}
\end{center}

\[ \text{AUC}_{0-t(last)} = (1.63 + 2.36 + 0.73 + 0.11) \frac{\mu g*h}{mL} = 4.83 \frac{\mu g*h}{mL} \]

\[ AUC_{t(last)} - \infty = \frac{c_{t(last)}}{k_e} = \frac{0.008 \frac{\mu g}{mL}}{0.4621 \frac{1}{h}} = 0.0173 \frac{\mu g*h}{mL} \]

\[ AUC_{0 - \infty} = (4.83 + 0.0173) \frac{\mu g * h}{mL} = 4.847 \frac{\mu g*h}{mL} \]

e) Calculate \( \frac{\text{AUC}_{0-t(last)}}{\text{AUC}_{0-\infty}} \times 100\% \)

\[ \frac{4.83 \frac{\mu g * h}{mL}}{4.847 \frac{\mu g * h}{mL}} \times 100\% = 99.65\% \]

f) Predict the plasma concentration after 6 hours
3. Define LADME and Pharmacokinetics

**LADME: Liberation, Absorption, Distribution, Metabolism, Elimination**

**Pharmacokinetics: The time course of drug and metabolite concentration in the body**

4. TRUE (T) or FALSE (F)

The plasma concentration time profile of a certain drug is dependent on the dosage form

T    F

For a zero-order elimination process, the half-life is dependent on the plasma concentration at time point 0 ($C_0$)

T    F

For a first-order elimination process, the half-life is dependent on the plasma concentration at time point 0 ($C_0$)

T    F

Drugs with a high volume of distribution (Vd) have a narrow therapeutic window

T    F

In the case of perfusion limited distribution, the blood flow determines the rate of uptake

T    F

In the case of permeability limited distribution, the blood flow is not important for the rate of uptake

T    F