Do not forget the units of the results. 0.1 points will be deducted for each time an answer is provided without the appropriate unit.

1. 500 mg Drug A was administered to a male patient (80 kg, 35 years old) 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>0.794</td>
</tr>
<tr>
<td>3</td>
<td>0.500</td>
</tr>
<tr>
<td>6</td>
<td>0.250</td>
</tr>
<tr>
<td>11</td>
<td>0.079</td>
</tr>
</tbody>
</table>

a) Plot Cp vs. time and determine the order of the elimination process (0.75 points, 0.25 for each plot, and 0.25 for the conclusion that is first-order elimination)
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) (1 point, 0.5 for each correct answer)

<table>
<thead>
<tr>
<th>time (h)</th>
<th>$C_p$ (µg/mL)</th>
<th>ln $C_p$ (µg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.000</td>
<td>0.0000</td>
</tr>
<tr>
<td>1</td>
<td>0.794</td>
<td>-0.2310</td>
</tr>
<tr>
<td>3</td>
<td>0.500</td>
<td>-0.6931</td>
</tr>
<tr>
<td>6</td>
<td>0.250</td>
<td>-1.3863</td>
</tr>
<tr>
<td>11</td>
<td>0.079</td>
<td>-2.5415</td>
</tr>
</tbody>
</table>

\[
\text{Slope} = \frac{-0.6931 - (-0.2310)}{3 - 1} h = -0.231 \frac{1}{h}
\]

\[
k_e = 0.231 \frac{1}{h}
\]

\[
t_{1/2} = \frac{\ln (2)}{k_e} = 3.0 \text{ h}
\]

c) Estimate the initial concentration $C_0$ and the volume of distribution ($V_d$) (1 point, 0.5 for each correct answer)

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

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

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

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

\[
\ln C_0 = -0.2310 + 0.231 * 1 = 0
\]

\[
C_0 = e^0 = 1 \frac{µg}{mL}
\]

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

\[
V_d = \frac{500 \text{ mg}}{1.00 \frac{µg}{mL}} = 500 \text{ L}
\]

d) Calculate $\text{AUC}_{0-\text{t(last)}}$ and $\text{AUC}_{0-\infty}$ (Use trapezoidal rule) (1 point, 0.5 for each correct answer)

<table>
<thead>
<tr>
<th>time (h)</th>
<th>$C_p$ (µg/mL)</th>
<th>AUC (µg*h/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1.000</td>
<td>0.90</td>
</tr>
</tbody>
</table>
AUC₀-t(last) = (0.9 + 1.29 + 1.13 + 0.82) μg*h/mL = 4.14 μg*h/mL

\[ AUC_t(\text{last}) - \infty = \frac{C_t(\text{last})}{k_e} = \frac{0.079 \text{ μg/mL}}{0.231 \text{ h}^{-1}} = 0.342 \text{ μg} * \text{h/mL} \]

\[ AUC_0 - \infty = (4.14 + 0.342) \mu g * h/mL = 4.482 \mu g*h/mL \]

c) Calculate \( \frac{AUC_0 - t(\text{last})}{AUC_0 - \infty} \times 100\% \) (0.5 points)

\[ \frac{4.14 \mu g * h/mL}{4.482 \mu g * h/mL} \times 100\% = 92.36\% \]

d) Predict the plasma concentration after 9 hours (0.5 points)

\[ C(9) = 1.00 \frac{\mu g}{mL} \times e^{-0.231 \frac{1}{h}}^{9 \text{h}} = 0.125 \frac{\mu g}{mL} \]

2. For first-order elimination process, derive that the half-life \( (t_{1/2}) \) is independent of \( C_0 \) (1 point)

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

\[ C(t_{1/2}) = C_0 \times e^{-k_e*t_{1/2}} \]

\[ C(t_{1/2}) = \frac{1}{2} \times C_0 \]

\[ \frac{1}{2} \times C_0 = C_0 \times e^{-k_e*t_{1/2}} \]

\[ \ln \left( \frac{1}{2} \times C_0 \right) = \ln C_0 - k_e \times t_{1/2} \]

\[ \ln(1) - \ln(2) + \ln C_0 = \ln C_0 - k_e \times t_{1/2} \]

\[ 0 - \ln(2) = -k_e \times t_{1/2} \]

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

Equation for half-life does not contain \( C_0 \). Hence, it is independent of \( C_0 \).

3. Describe the fate of a drug after its administration (assume that a tablet has been administered orally). Hint: LADME (1.25 point)
Liberation: Disintegration of tablet (0.25 points)
Absorption: Drug absorption into the systemic circulation (0.25 points)
Distribution: Distribution of the drug throughout the body (0.25 points)
Metabolism: Transformation of the parent drug into its metabolites (0.25 points)
Elimination: Excretion of the drug from the body (0.25 points)

4. TRUE (T) or FALSE (F) (3 points, 0.5 points for each question)

The plasma concentration time profile of a certain drug is not 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 (C₀)

T F

Therapeutic drug level monitoring (TDM) can be useful to optimize the dosage regimen for an individual patient

T F

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

T F

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

T F

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

T F