Summary of Pharmacokinetic Calculations

The following list was extracted from pharmacology lecture notes provided by Dr. Steven Shafer. It summarizes and embellishes the pharmacokinetic concepts presented:

1. The rate of change (decrease) when drug is injected into a 1 compartment model is

\[
\frac{dX}{dt} = -kX \quad \text{(first order process)}
\]

2. The concentration following that injection is

\[
C(t) = C_0 e^{-kt} \quad \text{where } C_0 \text{ is the initial concentration}
\]

3. The half-life, \( t_{1/2} \) (time required for a 50% decrease), is

\[
t_{1/2} = \frac{0.693}{k}
\]

4. If you know the time required for a 50% decrease, the rate constant, \( k \), is

\[
k = \frac{0.693}{t_{1/2}}
\]

5. The definition of concentration is

\[
C = \frac{X}{V}, \text{ where } X \text{ is amount and } V \text{ is volume}
\]

6. The concentration at time \( t \) following a bolus injection will be

\[
C(t) = \frac{X_0}{V} e^{-kt} \quad \text{where } \frac{X_0}{V} \text{ is the initial concentration}
\]

7. If \( C_{IT} \) is the total clearance (or flow) from a 1 compartment model, the rate at which drug leaves can be calculated

\[
\frac{dX}{dt} = C(C_{IT})
\]

8. Since item 1 and item 7 are the same rate, it follows (after substituting \( X/V \) for \( C \)) that
\[ k = \frac{\text{Cl}_T}{V} \]

Substituting in equation 3, we get this important relationship

\[ t_{\frac{1}{2}} = \frac{0.693(V)}{\text{Cl}_T} \]

So, as clearance (\(\text{Cl}_T\)) increases, \(k\) increases, and the half-life decreases. As volume (\(V\)) increases, \(k\) decreases, and half-life increases.

9. During an infusion at rate \(k_0\), the concentrations are described by the equation

\[ C(t) = C_{ss} (1 - e^{-kt}) \] where \(C_{ss}\) is the concentration at steady-state.

10. The steady-state concentration can be calculated from infusion rate and clearance

\[ C_{ss} = \frac{k_0}{\text{Cl}_T} \]

11. Half-lives describe the time for a 50% decrease in concentration following a bolus, and they also describe the time required to reach 50% of the steady-state concentration during an infusion. Following a bolus, the concentrations will be at 25%, 13%, 6%, and 3% of the initial concentration following 2, 3, 4, and 5 half-lives, respectively. During a constant-rate infusion, the concentration will reach 75%, 88%, 94%, and 97% of the steady-state concentration in 2, 3, 4, and 5 half-lives, respectively.

What do you do with this? Well:

1. If you know the amount of drug injected (\(X_0\)), and the concentration at time 0 (\(C_0\)), you can calculate the volume

\[ V = \frac{X_0}{C_0} \]

2. If you know \(X_0\), \(V\), and \(k\), then you can calculate the concentration at any given time \(t\)

\[ C(t) = \frac{X_0}{V} e^{-kt} \]
3. If you know two concentrations, \( C_1 \) and \( C_2 \), obtained at times \( t_1 \) and \( t_2 \), respectively, you can calculate \( k \) as

\[
k = \frac{\ln(C_1) - \ln(C_2)}{t_2 - t_1}
\]

4. If you want to know the clearance (the flow out of the compartment), you can calculate it as \( k(V) \). If \( k \) and \( V \) are not known, or if there are several values of \( k \) (multicompartment kinetics), you can still calculate

\[
Cl_T = \frac{\text{dose}}{\text{AUC}}
\]

where AUC is the area under the time vs. concentration curve.

5. If you know the initial target concentration you want to achieve, \( C_{\text{target}} \), then you can calculate \( X_{\text{loading}} \), the intravenous dose required to produce that concentration

\[
X_{\text{loading}} = C_{\text{target}}(V)
\]

6. If you want to maintain concentration \( C_{\text{target}} \), then you must continuously infuse drug at the same rate it is leaving. Assuming that you first gave a bolus of \( C_{\text{target}}(V) \), the rate at which drug will leave will be \( C_{\text{target}}(Cl_T) \). Therefore your maintenance infusion \( X_{\text{maintenance}} \) will be

\[
X_{\text{maintenance}} = C_{\text{target}}(Cl_T)
\]
Another exercise from Dr. Shafer:

Dr. Rosow was quite concerned that I wouldn’t explain the basic concepts adequately. He specifically requested that I make sure that if you are going to give a medication to “Joe” (must be a friend of his), you can figure out the dose for Joe. I don’t know Joe, but I do know a few things about a new drug that Carl has started Joe on: cephprololopam, an antibiotic that has beta blocking and anxiolytic properties:

- The clearance of cephprololopam is 0.2 liters/min
- The volume of distribution of cephprololopam is 20 liters
- The therapeutic concentration is 2 µg/ml.

1. Carl forgot to tell me the half-life of cephprololopam. What is it?
   Answer:
   \[
   k = \frac{Cl_T}{V} = \frac{0.2 \text{ liters}}{20 \text{ liters}} = 0.01 \text{ min}^{-1}
   \]
   \[
   t_{1/2} = \frac{0.693}{k} = 69 \text{ min}
   \]

2. What is Joe’s initial dose of cephprololopam?
   Answer:
   \[
   X_{\text{loading}} = C_{\text{target}}(V) = \left(2 \frac{\mu g}{ml}\right)20\text{liters} = 40\text{mg}
   \]

3. How much drug should I give Joe to maintain a cephprololopam concentration of 2 µg/ml?
   Answer:
   \[
   X_{\text{maintenance}} = C_{\text{target}}(Cl_T) = \left(2 \frac{\mu g}{ml}\right)\left(0.2\frac{\text{liters}}{\text{min}}\right) = 0.4 \frac{\text{mg}}{\text{min}}
   \]

4. I want to put Joe on an oral form of cephprololopam, which he will take every 24 hr. How much should I give Joe, assuming the the drug is completely absorbed, and I want Joe’s concentrations, on average, to be at the target?
   Answer: Joe will need the same total amount of drug every 24 hr
   \[
   \left(0.4 \frac{\text{mg}}{\text{min}}\right)1440\text{min} = 576 \frac{\text{mg}}{\text{day}}
   \]


5. How long will it take Joe to reach steady-state dosing with these repeated oral doses? 
Answer: 4-5 half-lives = 276-345 min, i.e., Joe will be at steady state dosing within the time course of the first dose!