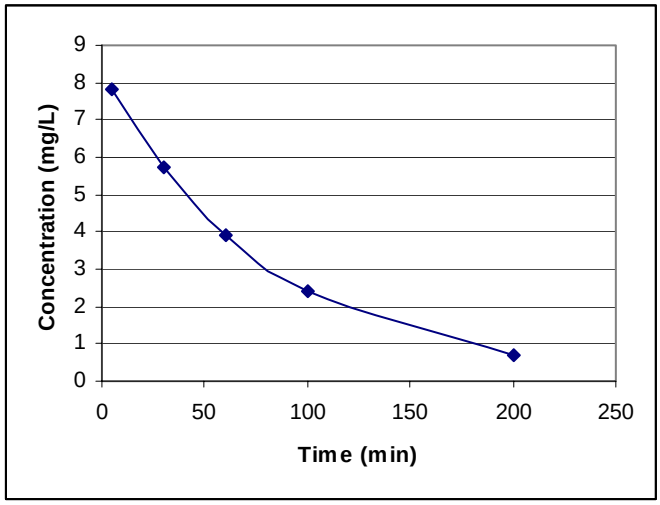
Case Study 1 answers

1. A 50 year old male suffering from pneumonia was given a 1000mg IV bolus dose of the antibiotic Baqilmycin. The following table contains his plasma concentrations.

Time (min)	Concentration (mg/L)
5	7.8
30	5.7
60	3.9
100	2.4
200	0.7

Calculate the $AUC_{0-\infty}$ and the volume of distribution.

Let's first plot the data:



Obviously the amount of drug eliminated is dependent on concentration indicating first-order elimination. Knowing this, let's use 2 time points to determine ke.

$$\frac{\ln(7.8) - \ln(0.7)}{(200-5)} = 0.0124/\text{min}$$

Now we can determine the half life

$t_{1/2} = 0.693 / 0.0124 = \sim 56$ min

Now let's determine the initial concentration.

$C_0 = 0.7/e^{-0.0124*200} = 8.35$mg/L

Now we can determine the Volume of distribution

Vd = 1000 mg/ 8.35 mg/L = 120L

Now let's use the trapezoidal method to determine the AUC for the time points we know.

AUC_{0-5} = (8.35 + 7.8) * 5/2 = 40.38 mg*min/L
AUC_{5-30} = (7.8 + 5.7) * 25/2 = 168.75 mg*min/L
AUC_{30-60} = (5.7 + 3.9) * 30/2 = 144 mg*min/L
AUC_{60-100} = (3.9 + 2.4) * 40/2 = 126 mg*min/L
$AUC_{100-200}$ = (2.7 + 0.7) * 100/2 = 170 mg*min/L

The sum of these values will give you AUC_{0-200} = 649.13 mg*min/L
Now $AUC_{200-\infty}$ = 0.7/0.0124 = 56.5 mg*min/L adding this to AUC_{0-200} will give you
$AUC_{0-\infty}$ = 705.6 mg*min/L

2. The same patient was also given a 500mg IV bolus dose of Grebohol. His initial plasma concentration is 10mg/L. If protein binding in the tissue is equal for both drugs, what is the difference in plasma protein binding between the two? (use a plasma volume of 3L and a tissue volume of 38L)

First we need to calculate Vd for Grebohol.
Vd = 500/10 = 50 L

Knowing that tissue protein binding is the same for both drugs solve for this with both drugs using the Vd equation.

$Vd = Vp + Vt * f_u/f_{ut}$

And we get for Grebohol
$f_{ut} = f_{uG} * 38/47$

And for Baqilmycin

$f_{ut} = f_{uB} * 38/117$

Set these equations equal to each other and solve for either f_{uG} or f_{uB}

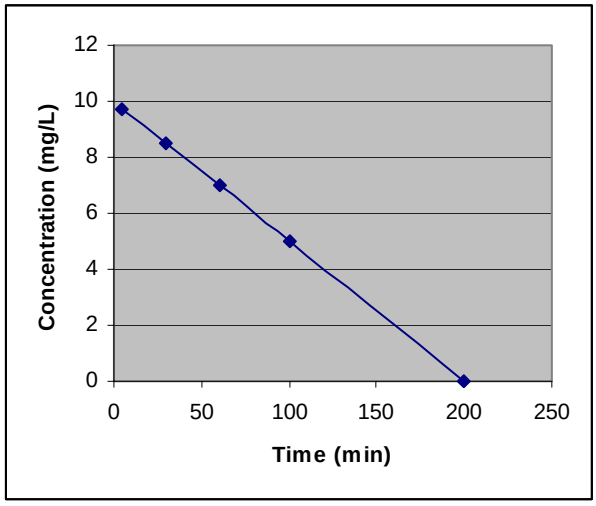
$f_{uB} = 2.5\ f_{uG}$ or $f_{uG} = 0.4\ f_{uB}$

3. The following table contains the patient's plasma concentrations for Grebohol.

Time(min)	Concentration (mg/L)
5	9.75
30	8.5
60	7
100	5
200	0

What is the difference between Baqilmycin's and Grebohol's elimination? What would cause a drug to be eliminated in such a way?

Let's first make a graph of the data



We can see that the same amount of drug is eliminated all the time indicating zero order elimination. That is the difference Baqilmycin has first order elimination and Grebohol has zero order elimination. You would expect zero order elimination when the enzymes involved in the drugs elimination are saturated.