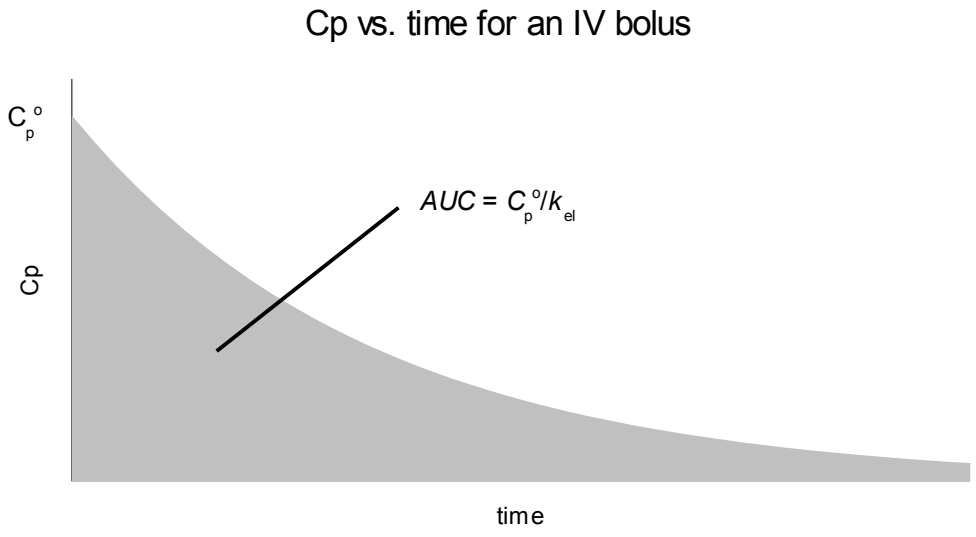
DavidsonX – D001x – Medicinal Chemistry
Chapter 7 – Pharmacokinetics
Part 3 – Clearance II
Video Clip – Area Under Curve

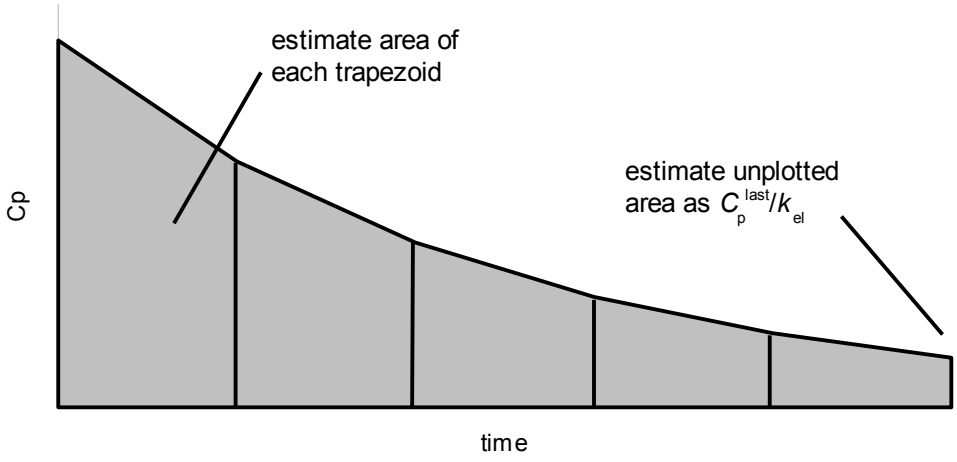
Drug's with a lower clearance persist for a longer time in the body. Drug's with a higher clearance persist for a shorter time in the body. The longer a drug resides in the body, then the greater the exposure a patient has to a drug. A measure of drug exposure is the **area under curve (*AUC*)**. *AUC* is the area beneath the C_p-time curve. The units on *AUC* are a very non-intuitive concentration·time. (As with any area, the units are simply the units for the *x*-axis multiplied by the units of the *y*-axis.) For this discussion, concentration is specifically mass/vol and not molarity. Molarity is convenient for the coverage of in vitro results and binding studies, but pharmacokinetic data originate from living systems – either animals or humans. C_p data in animals and humans are normally in mass/vol. *AUC* and clearance are intimately related. In fact, it is through *AUC* that clearance can be calculated. So, how can one determine *AUC* for a drug?

AUC can be determined in two ways. Method one involves integrating the C_p-time plot of a drug. An idealized C_p-time plot for an IV bolus is shown below. The *AUC* for this plot, when evaluated from t=0 to t=∞, is C_p^o/k_{el}. Of course, one would first need to know both C_p^o and k_{el}. These values could be determined from a ln C_p-time plot from the same data.



Method two for determining *AUC* for a drug is to crudely estimate the value with the *trapezoid rule*. Each data point defines a trapezoid-shaped region in the curve. The sum of the areas created by each data point gives an approximate *AUC*. While crude, this method is fairly effective and simple. Because C_p-time data points do not stretch to infinity, one needs a method to estimate the *AUC* from the last C_p data point to infinite time. The remaining area can be estimated as the value of the final C_p point divided by the k_{el} value of the drug.

Cp vs. time for an IV bolus



Regardless of how *AUC* is estimated, dividing the amount of drug that the animal or human was dosed by *AUC* gives *CL*. This calculation is the most common method for determining *CL* for a drug.

$$CL = \frac{D_o}{AUC}$$

Note the units on *CL*. If dose is a drug mass and *AUC* uses mass instead of moles, then the mass units cancel and *CL* comes out with the correct units of volume/time.

$$\frac{\text{volume}}{\text{time}} = \frac{\cancel{\text{mass}}}{\frac{\cancel{\text{mass}} \times \text{time}}{\text{volume}}}$$