We have now laid enough foundation to move from an IV bolus to oral delivery. Oral delivery is more complicated because the drug must be absorbed from the gastrointestinal tract and withstand the metabolic effects of the liver before reaching general circulation. A typical $C_p$-time curve for an oral drug is shown below. The curve demonstrates the rise in concentration as the drug is absorbed followed by the eventual drop in concentration as the drug is cleared. The peak in concentration, $C_p^{\text{max}}$, occurs at $t_{\text{max}}$, which is a standard pharmacokinetic parameter that is listed with oral drugs.

\[ C_p \text{ vs. time - oral dose} \]

The formula for $C_p$ is more complicated for an oral drug and requires two new variables – bioavailability ($F$) and the absorption rate constant ($k_{ab}$). We have already talked about bioavailability, the fraction of an administered dose that actually reaches general circulation. $k_{ab}$, with units of inverse time, is a rate constant and almost always larger than $k_{el}$.

\[ C_p = \frac{FD_0}{V_d} \cdot \frac{k_{ab}}{k_{ab} - k_{el}} \cdot (e^{-k_{el}t} - e^{-k_{ab}t}) \]

Before a drug is tested in an oral form, it will have already been dosed as an IV bolus. That means the variables $k_{el}$ and $V_d$ will already be known. That leaves $F$ and $k_{ab}$ to be determined. $k_{ab}$ can be calculated from $t_{\text{max}}$, which can be estimated from the oral $C_p$-time curve. The calculation of $k_{ab}$ is not exact, but it can be estimated by trial-and-error. Keep in mind that $k_{ab}$ is almost always larger than $k_{el}$.

\[ t_{\text{max}} = \frac{\ln k_{el} - \ln k_{ab}}{k_{el} - k_{ab}} \]

Calculating $F$ requires more work. It is possible that $F$ might be known from the IV bolus. If renal clearance is zero, then total clearance can be used to determine the hepatic extraction...
ratio \( (E_i) \) and then bioavailability \( (F) \). If \( F \) is not known, then it will need to be estimated from \( AUC \) data and the trapezoidal rule.

The trapezoidal rule is actually easier to apply to oral drug data because one does not need to estimate \( C_p^0 \). \( C_p^0 \) for an oral drug is 0. For a specific drug, the \( AUC \) of the oral form can be compared to the \( AUC \) of the IV bolus to determine \( F \). If the two formulations are administered in different doses, then the dose amounts can be used to normalize the data in the calculation.

\[
F_{\text{oral}} = \frac{\frac{AUC_{\text{oral}}}{D_{\text{oral}}}}{\frac{AUC_{\text{IV}}}{D_0}}
\]

The calculated \( F \) is specific to oral administration and is often reported as oral bioavailability \( (F_{\text{oral}}) \). Other non-IV routes of administration (e.g., intramuscular injection, nasal, transdermal, or inhalation) have their own distinct bioavailability. Each is calculated by comparing the \( AUC \) of a dose from one administrative route to \( AUC_{\text{IV}} \).