Inhibitors of Enzymes

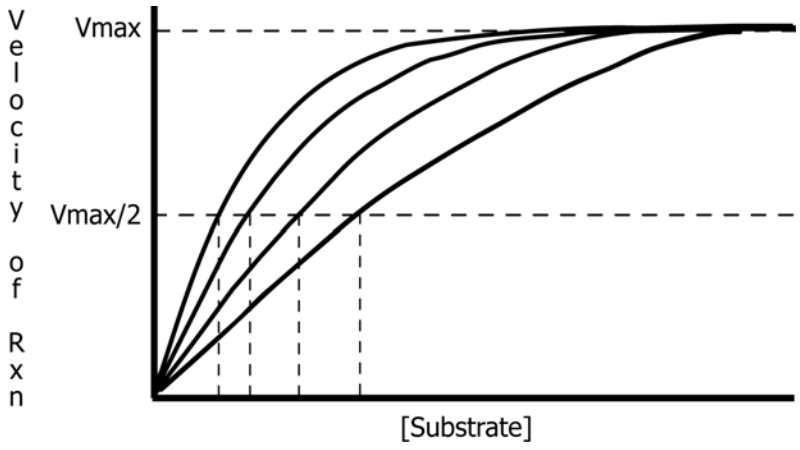
Inhibitors which mimic the transition state bind the most strongly.

There are two classes of inhibitors:

Competitive: These bind to the active site.

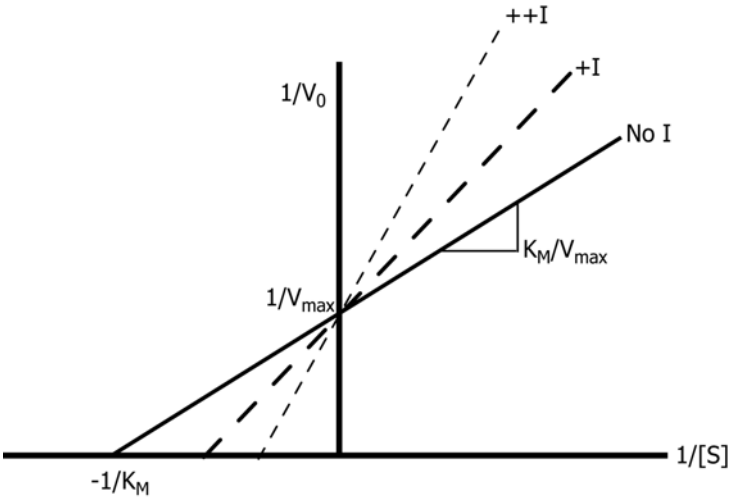
$$E + S \leftrightarrow ES \leftrightarrow E + P$$
$$\updownarrow$$
$$E + I \leftrightarrow EI$$

With enough substrate present, you can displace the inhibitor from the active sites on the enzymes; thus, V_{max} does not change. However, since now you need more substrate to bind the enzyme, the apparent K_m goes up. (Michaelis-Menten plot - Top graph)



$$K_M \rightarrow K_{M_{apparent}} = K_M \left(1 + \frac{[I]}{K_I}\right)$$

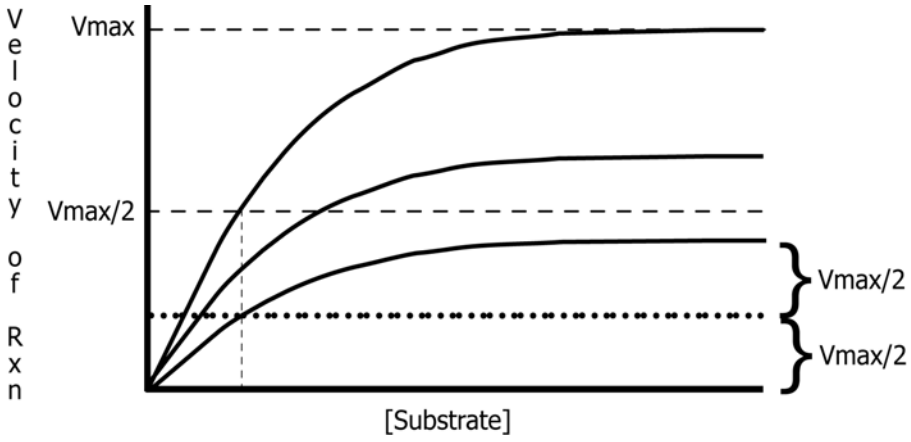
(Lineweaver-Burke plot - Bottom graph)



Inhibitors of Enzymes

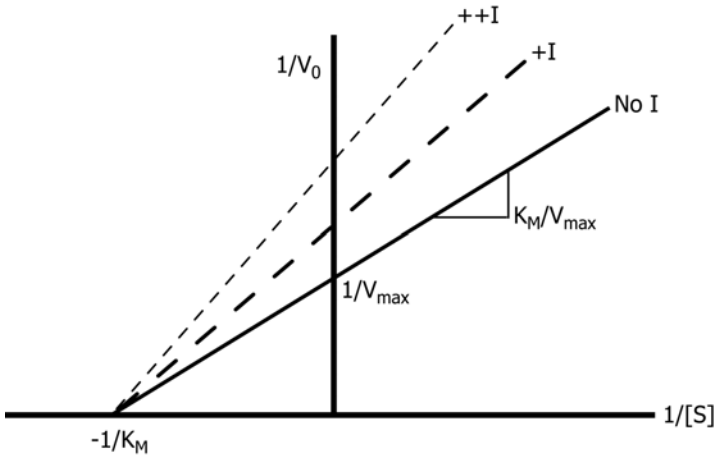
Noncompetitive:
These bind to any site other than the active site.

$$E + S \leftrightarrow ES \leftrightarrow E + P$$
$$\updownarrow$$
$$E + I + S \leftrightarrow EIS$$



No matter how much substrate is present, you can never displace the inhibitor. This effectively lowers the number of active enzymes, which therefore lowers the V_{max}. Since you do not change how well the substrate can bind to the enzyme, the apparent K_M does not change. (Michaelis-Menten - Top graph)

(Lineweaver-Burke - Middle graph)



The other type of noncompetitive inhibition you need to know is **Allostery**.

This follows a sigmoidal binding curve. At low substrate concentrations, the enzyme does not work well, while at high concentrations it works extremely well. There is a non-linear jump in between which is characteristic of the curve. (Bottom graph)