

This behavior is consistent with a kinetic scheme in which the inhibitor competes with the substrate for the formation of an enzyme complex as follows

By forming a complex with the enzyme, I reduces [E] thereby decreasing the formation of an ES complex and thus the rate.

At “high” [S], the ES complex will be strongly favored so that the maximum rate can be obtained.

The rate equation can be derived in a manner similar to that for the reaction in the absence of inhibitor as follows

Note that if  $[S]$  is  $\gg K_M$  and  $K_M[I]/K_I$ ,  $v = V_{\max}$  consistent with observed rates.

Also note that if  $[I]$  is zero, the rate equation reduces to the M-M equation.

$K_I$  can be determined from the  $1/[S]$  intercept of a double reciprocal plot of the rate equation and the value of  $K_M$  determined in the absence of inhibitor as follows

The above equation also has the form of a straight line with a slope of

$$K_M(1+[I]/K_I)/V_{\max}$$

Consider what the intercepts will be. Observe from the reciprocal equation that if  $1/[S] = 0$ ,  $1/v = 1/V_{\max}$ .

Also if  $1/v = 0$ , we can show that  $1/[S] = -1/K_M(1+[I]/K_I)$ .

The double reciprocal plot will then appear as follows

To determine  $K_I$  from the  $1/[S]$  intercept one must know the value of  $K_M$ .  $K_M$  is determined from the double reciprocal plot in the absence of inhibitor that may be added to the above plot.

Note that the  $1/v$  intercept for a competitive inhibitor is the same as that in the absence of inhibitor.

Inhibitors of this kind generally have structures similar to the substrate.

This observation suggests that competitive inhibitors bind to the enzyme at the same site as the substrate.

In order to obtain information about the substrate binding-site, one can test a variety of molecules as competitive inhibitors to determine what groups are required to form a complex with the enzyme.

Consider possible competitive inhibitors of succinic dehydrogenase

The requirement for two carboxylate groups would suggest that binding occurs through electrostatic interactions such as with lysine or arginine residues