

9.5: Enzyme Inhibition

Enzymes can be regulated in ways that either promote or reduce their activity. There are many different kinds of molecules that inhibit or promote enzyme function, and various mechanisms exist for doing so. In some cases of enzyme inhibition, for example, an inhibitor molecule is similar enough to a substrate that it can bind to the active site and simply block the substrate from binding. When this happens, the enzyme is inhibited through **competitive inhibition**, because an inhibitor molecule competes with the substrate for active site binding. On the other hand, in **noncompetitive inhibition**, an inhibitor molecule binds to the enzyme in a location other than an allosteric site and still manages to block substrate binding to the active site.

Elucidating Mechanisms for the Inhibition of Enzyme Catalysis

When an **inhibitor** interacts with an enzyme it decreases the enzyme's catalytic efficiency. An irreversible inhibitor covalently binds to the enzyme's active site, producing a permanent loss in catalytic efficiency even if we decrease the inhibitor's concentration. A reversible inhibitor forms a noncovalent complex with the enzyme, resulting in a temporary decrease in catalytic efficiency. If we remove the inhibitor, the enzyme's catalytic efficiency returns to its normal level.

There are several pathways for the reversible binding of an inhibitor to an enzyme, as shown in Figure 9.5.1. In **competitive inhibition** the substrate and the inhibitor compete for the same active site on the enzyme. Because the substrate cannot bind to an enzyme–inhibitor complex, EI, the enzyme's catalytic efficiency for the substrate decreases. With **noncompetitive inhibition** the substrate and the inhibitor bind to different active sites on the enzyme, forming an enzyme–substrate–inhibitor, or ESI complex. The formation of an ESI complex decreases catalytic efficiency because only the enzyme–substrate complex reacts to form the product. Finally, in **uncompetitive inhibition** the inhibitor binds to the enzyme–substrate complex, forming an inactive ESI complex.

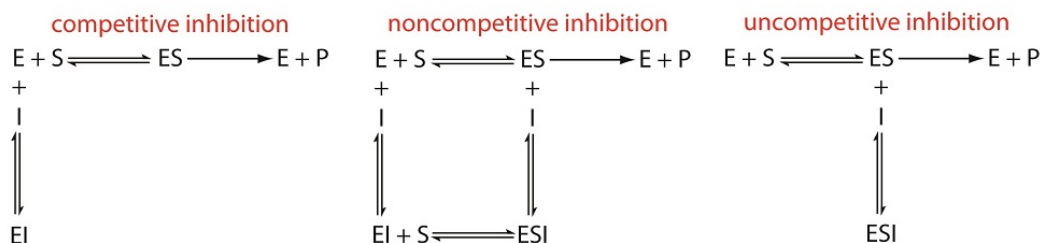


Figure 9.5.1: Mechanisms for the reversible inhibition of enzyme catalysis. E: enzyme, S: substrate, P: product, I: inhibitor, ES: enzyme–substrate complex, EI: enzyme–inhibitor complex, ESI: enzyme–substrate–inhibitor complex.

We can identify the type of reversible inhibition by observing how a change in the inhibitor's concentration affects the relationship between the rate of reaction and the substrate's concentration. As shown in Figure 13.14, when we display kinetic data using as a **Lineweaver-Burk** plot it is easy to determine which mechanism is in effect. For example, an increase in slope, a decrease in the x-intercept, and no change in the y-intercept indicates competitive inhibition. Because the inhibitor's binding is reversible, we can still obtain the same maximum velocity—thus the constant value for the y-intercept—by adding enough substrate to completely displace the inhibitor. Because it takes more substrate, the value of K_m increases, which explains the increase in the slope and the decrease in the x-intercept's value.

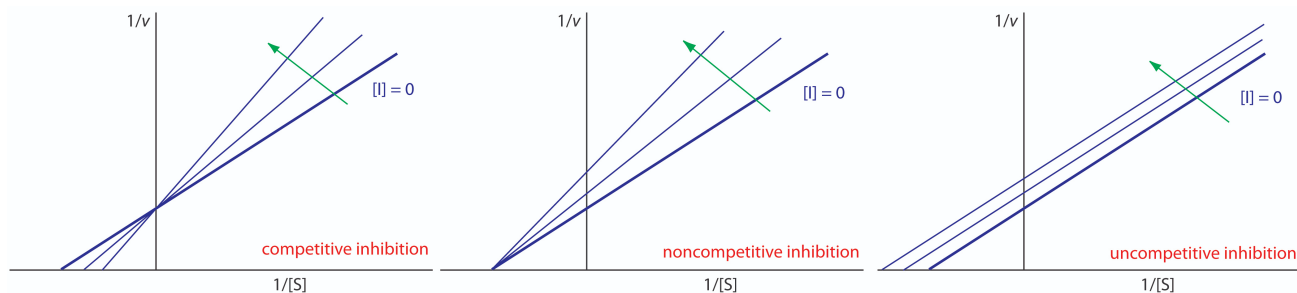


Figure 9.5.2: Lineweaver–Burk plots for competitive inhibition, noncompetitive inhibition, and uncompetitive inhibition. The thick blue line in each plot shows the kinetic behavior in the absence of inhibitor, and the thin blue lines in each plot show the change in behavior for increasing concentrations of the inhibitor. In each plot, the inhibitor's concentration increases in the direction of the green arrow.

✓ Example 9.5.1

Practice Exercise 13.3 provides kinetic data for the oxidation of catechol (the substrate) to *o*-quinone by the enzyme *o*-diphenyl oxidase in the absence of an inhibitor. The following additional data are available when the reaction is run in the presence of *p*-hydroxybenzoic acid, PBHA. Is PBHA an inhibitor for this reaction and, if so, what type of inhibitor is it?

[catechol] (mM)	0.3	0.6	1.2	4.8
rate ($\Delta\text{AU}/\text{min}$)	0.011	0.019	0.022	0.060

Solution

Figure 9.5.3 shows the resulting Lineweaver–Burk plot for the data in Practice Exercise 13.3 and Example 13.7. Although the *y*-intercepts are not identical in value—the result of uncertainty in measuring the rates—the plot suggests that PBHA is a competitive inhibitor for the enzyme’s reaction with catechol.

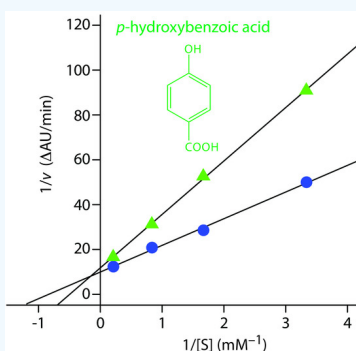


Figure 9.5.3: Lineweaver–Burk plots for the data in Practice Exercise 13.3 and Example 13.7.

? Exercise 9.5.1

Practice Exercise 13.3 provides kinetic data for the oxidation of catechol (the substrate) to *o*-quinone by the enzyme *o*-diphenyl oxidase in the absence of an inhibitor. The following additional data are available when the reaction is run in the presence of phenylthiourea. Is phenylthiourea an inhibitor for this reaction and, if so, what type of inhibitor is it? The data in this exercise are adapted from jkimball.

[catechol] (mM)	0.3	0.6	1.2	4.8
rate ($\Delta\text{AU}/\text{min}$)	0.010	0.016	0.024	0.040

Click [here](#) to review your answer to this exercise.

Contributors

- David Harvey (DePauw University)

9.5: Enzyme Inhibition is shared under a [not declared](#) license and was authored, remixed, and/or curated by LibreTexts.