# Competitive inhibition

A reversible inhibitor binds temporarily. In competitive inhibition, substrate and inhibitor compete for the active site; the inhibitor often resembles the substrate.

## 1. BINDING MODEL

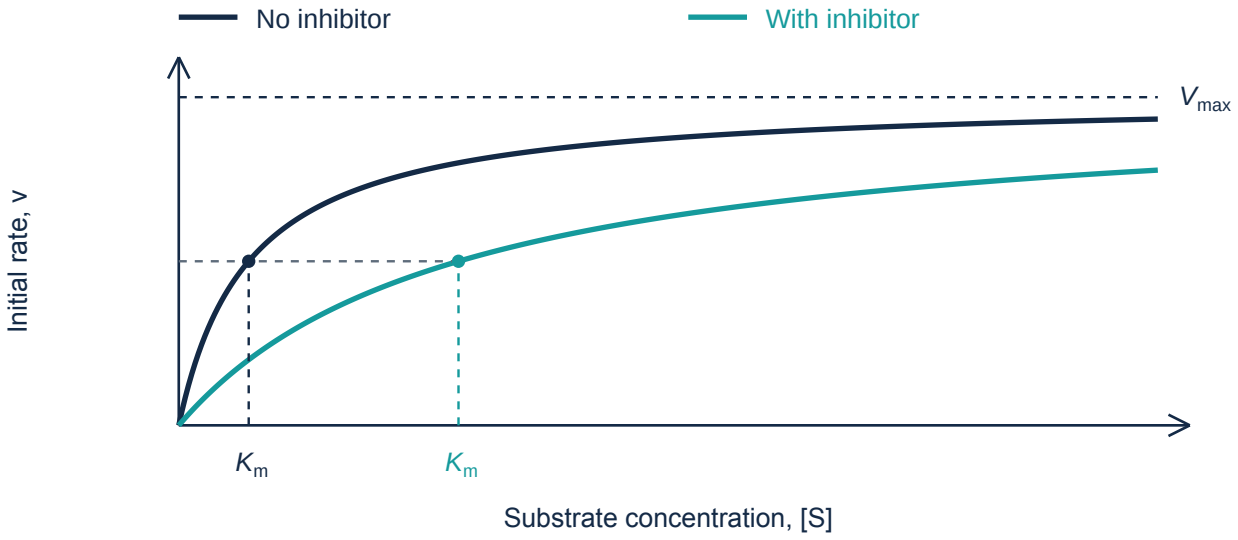
E = enzyme S = substrate I = inhibitor P = product

$$E + S \rightleftharpoons ES \longrightarrow E + P$$

$$E + I \rightleftharpoons EI$$

Active site occupied by I;
S cannot bind at the same time.

## 2. EFFECT ON THE RATE CURVE




## 3. MORE SUBSTRATE CAN OUTCOMPETE THE INHIBITOR

At a fixed inhibitor concentration, increasing [S] makes substrate binding more likely. The same $V_{max}$ can still be approached, but the apparent $K_m$ is higher: more substrate is needed for half-maximum rate. The graph shows two curves approaching the same limiting rate.

Binding model: Worthington Biochemical, Effects of Inhibitors on Enzyme Activity.
Kinetic interpretation: Assay Guidance Manual, Mechanism of Action Assays for Enzymes.

Scope: Cambridge Biology 9700 syllabus, section 3.2, outcome 3, p. 20.

# Non-competitive inhibition

Binding away from the active site alters enzyme function. The pure non-competitive model below reduces catalytic activity without changing substrate binding affinity.

## 1. BINDING MODEL

E = enzyme  S = substrate  I = inhibitor  P = product

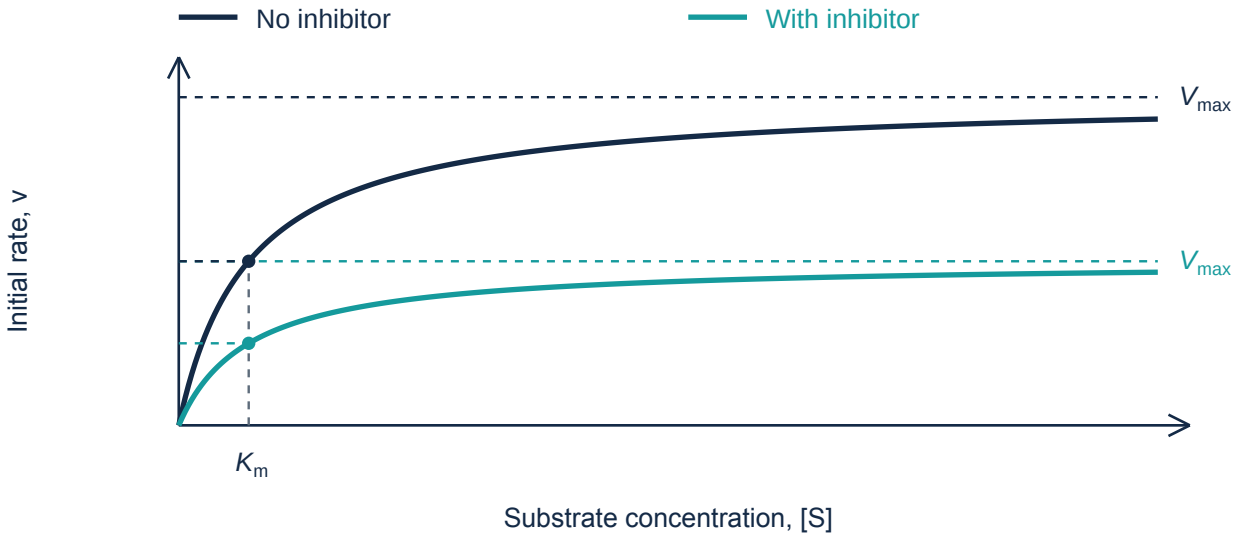
$$E + I \rightleftharpoons EI$$

I binds at a separate site, with equal affinity for E and ES.

$$ES + I \rightleftharpoons ESI$$

I-bound enzyme does not produce product in this model.

## 2. EFFECT ON THE RATE CURVE




## 3. MORE SUBSTRATE DOES NOT RESTORE THE MAXIMUM

$V_{max}$ decreases, while $K_m$ is unchanged in this pure model. The dots mark half of each curve's own maximum; both give the same [S]. Adding substrate cannot displace an inhibitor from its separate site, so the uninhibited maximum is not recovered.

Enzyme regulation: OpenStax Biology 2e, section 6.5, Enzymes.
Pure non-competitive model: Assay Guidance Manual, Mechanism of Action Assays.

Scope: Cambridge Biology 9700 syllabus, section 3.2, outcome 3, p. 20.

# Compare, then interpret

Use matched conditions: the same enzyme concentration, temperature and pH. Vary substrate concentration while keeping inhibitor concentration fixed within each curve.

## 1. TWO REVERSIBLE MODELS

| Feature | Competitive | Pure non-competitive |
|---|---|---|
| Binding site | Active site | Separate site |
| Maximum rate | Unchanged | Decreased |
| Apparent $K_m$ | Increased | Unchanged |
| Very high [S] | Restores limiting rate | Cannot restore maximum |

## 2. WORKED COMPARISON: ILLUSTRATIVE FITTED VALUES

Control: $V_{max}$ = 100 rate units; $K_m$ = 2 concentration units.
With inhibitor A: $V_{max}$ = 100; apparent $K_m$ = 6.
With inhibitor B: $V_{max}$ = 50; $K_m$ = 2.

A fits competitive inhibition. B fits pure non-competitive inhibition. For B, half-maximum is 25 rate units, not the control's value of 50.

## 3. REVERSIBLE DOES NOT MEAN PERMANENT DAMAGE

The inhibitor can dissociate from the enzyme. Removing free inhibitor shifts binding toward unbound enzyme and permits recovery of activity. Do not describe temporary inhibition as automatic denaturation or irreversible destruction.

Model boundary: binding outside the active site alone does not prove pure non-competitive kinetics. Unequal binding to E and ES gives mixed inhibition, in which $K_m$ can also change. Compare the measured rate curves, not just the binding-site location.

Reversible regulation: OpenStax Biology 2e, section 6.5, Enzymes.
Model definitions: Assay Guidance Manual, Mechanism of Action Assays for Enzymes.

Scope: Cambridge Biology 9700 syllabus, section 3.2, outcome 3, p. 20.