

Enzyme Kinetics III

Enzyme inhibitors

Competitive inhibition

- Inhibitor is similar to substrate and both bind to or near active site. compete' for binding
- inhibitor is unreactive - EI state
- Lineweaver Burke intersect at the Y axis

noncompetitive inhibitor

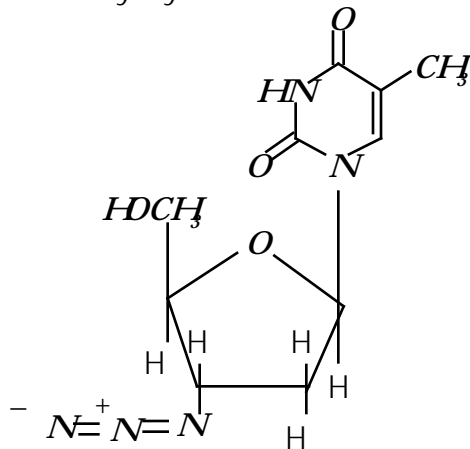
- inhibitor binds distal to active site
- effects enzyme rate not affinity
- binds E in E S or E
- reversible
- Lineweaver Burke intersect at the Y axis

Uncompetitive inhibitor

- binds covalently in the transition state
- suicide inhibitor
- binds to the ES complex
- lowers affinity and velocity
- lineweaver Burke plots are parallel

most drug treatments are examples

- AZT - 3' azido-2', 3' - dideoxythymidine



methotrexate - dihydrofolate reductase inhibitor. Reduces the production of Thymidine monophosphate (TMP) - used in cancer treatment

kinetics of allosteric enzymes

- do not follow Michaelis-Menten kinetics - instead use a hill plot for both + and - effects
similar to O₂ dissociation of hemoglobin

Penicillin as a suicide substrate

- suicide substrates are often un competitive inhibitors that decrease the energy of the transition state and allow the ES to have lower energy than that of the EP.

Bacterial cell wall - extensive cross linking of sugars and peptides

Penicillin (and ampicillin) have a highly reactive β lactam ring which makes a peptide bond very reactive.

Penicillin mimics the peptide ala ala and forms a low energy intermediate by covalently reacting with a serine

In molecular biology, we use this as a tool. Ampicillin will stop E. coli growth. Bacteria that have a gene (plasmid) inserted into the bacteria have β lactamase. An enzyme that hydrolyses the reactive peptide bond found in ampicillin and penicillin

Competitive	Noncompetitive	Uncompetitive
Binds active site	binds to other than binding site	Transition analog
inhibition reversed by increasing [S]	not reversed by increasing [S]	binds covalently to ES not E_{free}
K_{mapp} increases with inhibitor (x axis intercept changes)	no effect on S binding (K_{m}) only slows down rate (V)	changes both x and y axis (K_{m} and V_{max})
no change in $1/V_{\text{max}}$	decreased V_{maxapp} (Y axis intercept)	
Usually analogs of substrate	inhibitor binds both E_{free} and ES complex	