STUDY MATERIAL

VIVEKANANDA COLLEGE
THAKURPUKUR

NAAC ACCREDITED GRADE—'A'

Enzyme Inhibition

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Enzyme Inhibition

- Any chemical entity or compound which either retards or blocks enzyme catalysis.
- Enzyme inhibitors are compounds that reduce enzyme catalysed reaction.
- The inhibitor may interact reversibly or irreversibly with the enzyme.

Importance of enzyme inhibition

- Regulation of enzyme activity.
- Catalytic groups at the active site.
- Substrate specificity of enzyme.
- Kinetic mechanism of an enzyme in a multi-substrate reaction.

Types of inhibitors

1. Reversible Inhibitor :

- Interacts with enzyme through non-covalent association/dissociation reaction.

2. Irreversible Inhibitor :

- It forms covalent bonds with side change or prosthetic groups in the enzyme .

Reversible Inhibitors

- It falls into three major categories :

  a) Competitive

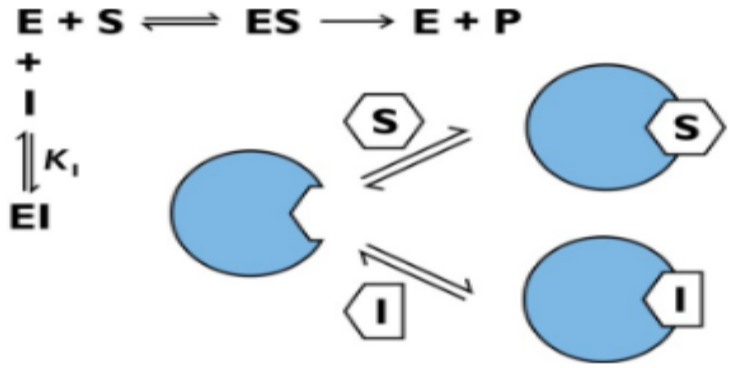
  b) Uncompetitive

  c) Mixed

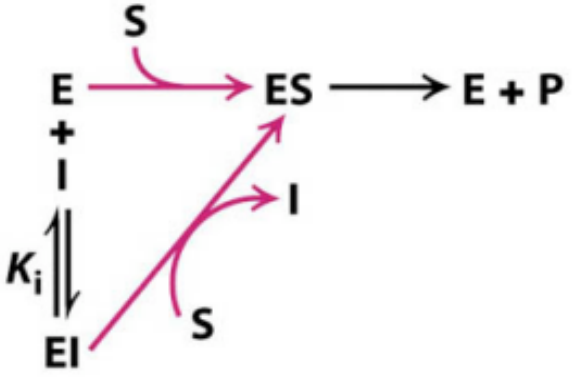
Competitive Inhibitor

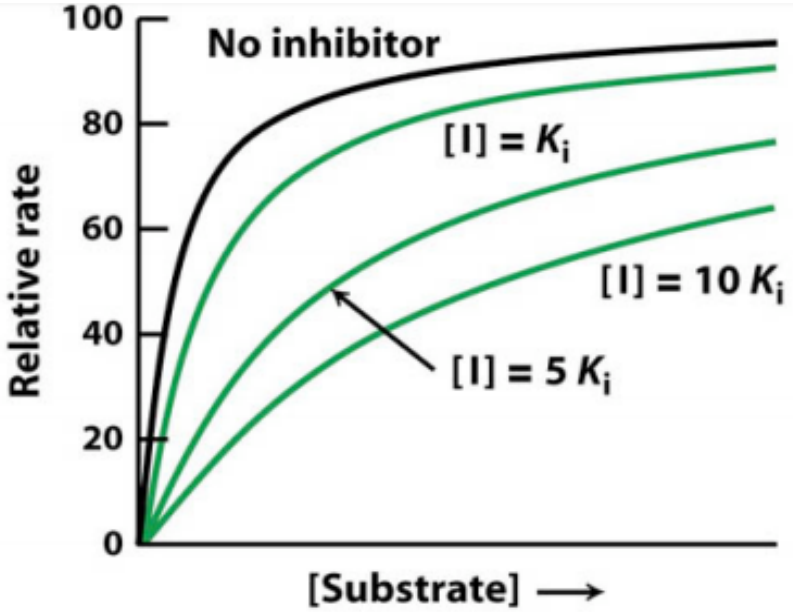
A competitive Inhibitor often has structural similarity to those of the substrate whose reaction they inhibit. e.g. succinate dehydrogenase..

- Increases Km but does not affect Vmax.

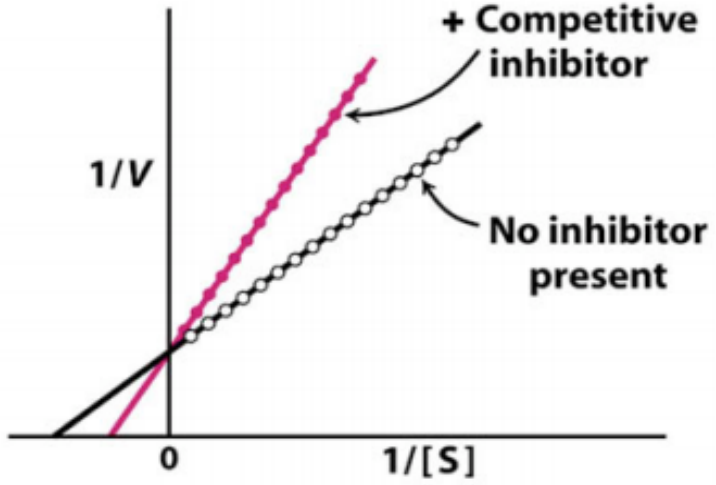


Berg, Tymoczko & Stryer, 6th ed. Fig. 8.17:
V_o vs. [S], competitive inhibition





Berg, Tymoczko & Stryer, 6th ed. Fig. 8.20:
$1/V_o$ vs. 1/[S], competitive inhibition

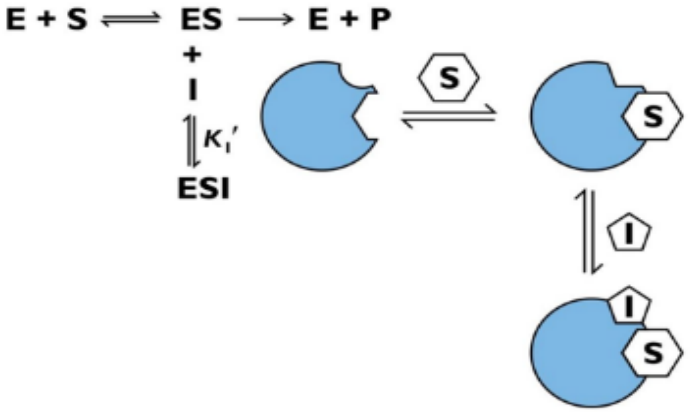


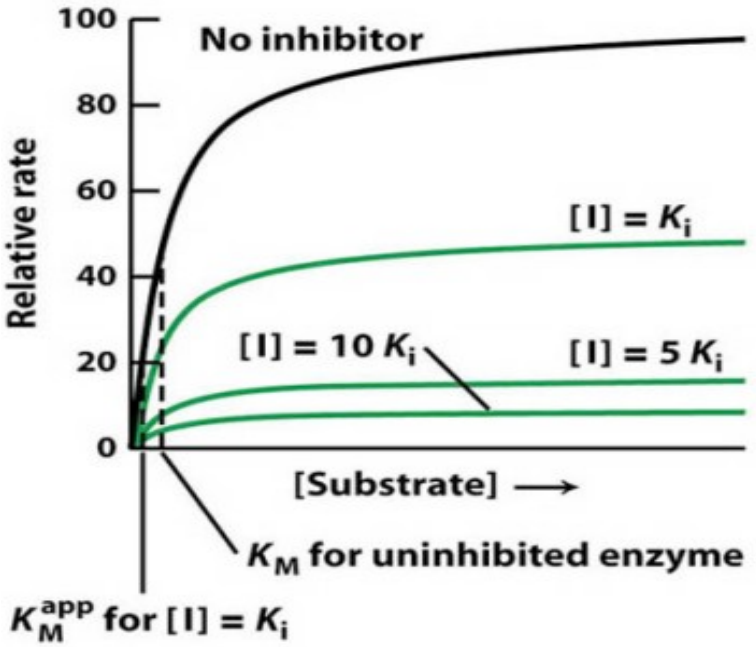
Double reciprocal Lineweaver-Burk analysis of competitive inhibition

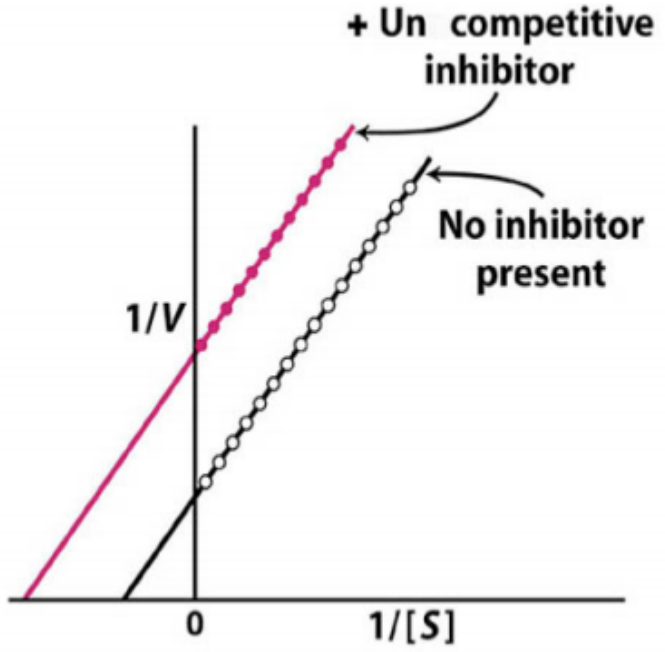
Uncompetitive Inhibitor

It does not bind to free enzyme but to enzyme-substrate complex to yield an in active ESI complex e.g. 3-enolpyruvylshikimate-5-P-synthase.

- Both Km and Vmax decreased by same factor.



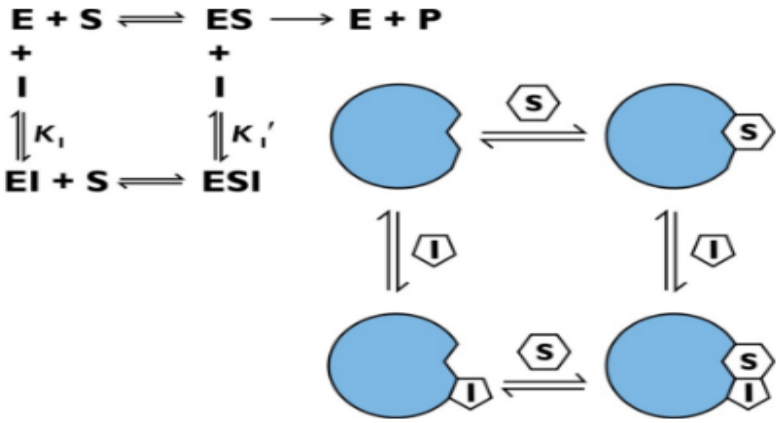


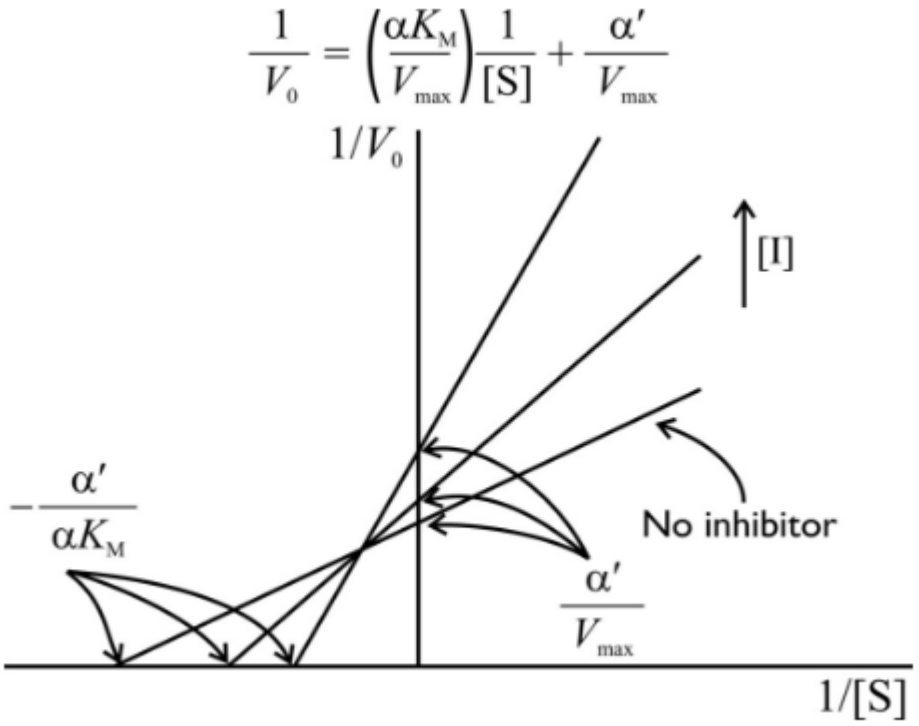


Double reciprocal Lineweaver-Burk analysis of uncompetitive inhibition

Mixed Inhibition

- It can bind to the free enzymes as well as to the enzyme-substrate complex.
- When a=a',non-competitive inhibition occurs.





Double reciprocal Lineweaver-Burk analysis of mixed inhibition

Irreversible Inhibition

- Transition state analog:structural similarity to transition state,which binds even more tightly to enzyme than substrate,very high affinity for active site.
- Suicide Inhibitor:structural similarity to substrate 'guides' reagent to active site.
- e.g.Penicillin (for both transition-state analog and suicide inhibitor

Questions

- What type of enzyme inhibitor is Diisopropylflourophosphate?
- What is the difference between competitive and uncompetitive inhibitor ?
- What is the need for studying enzyme inhibition?
- Three inhibitors with their Ki values provided below,which inhibitor binds with a higher affinity to the free enzyme?
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Inhibitor	Ki(uM)
A	5
B	1
C	0.2

References

- Lehninger-Principles of Biochemistry
- Biochemistry-Jeremy M. Berg,Tymoczko & Lubert Stryer
- Google