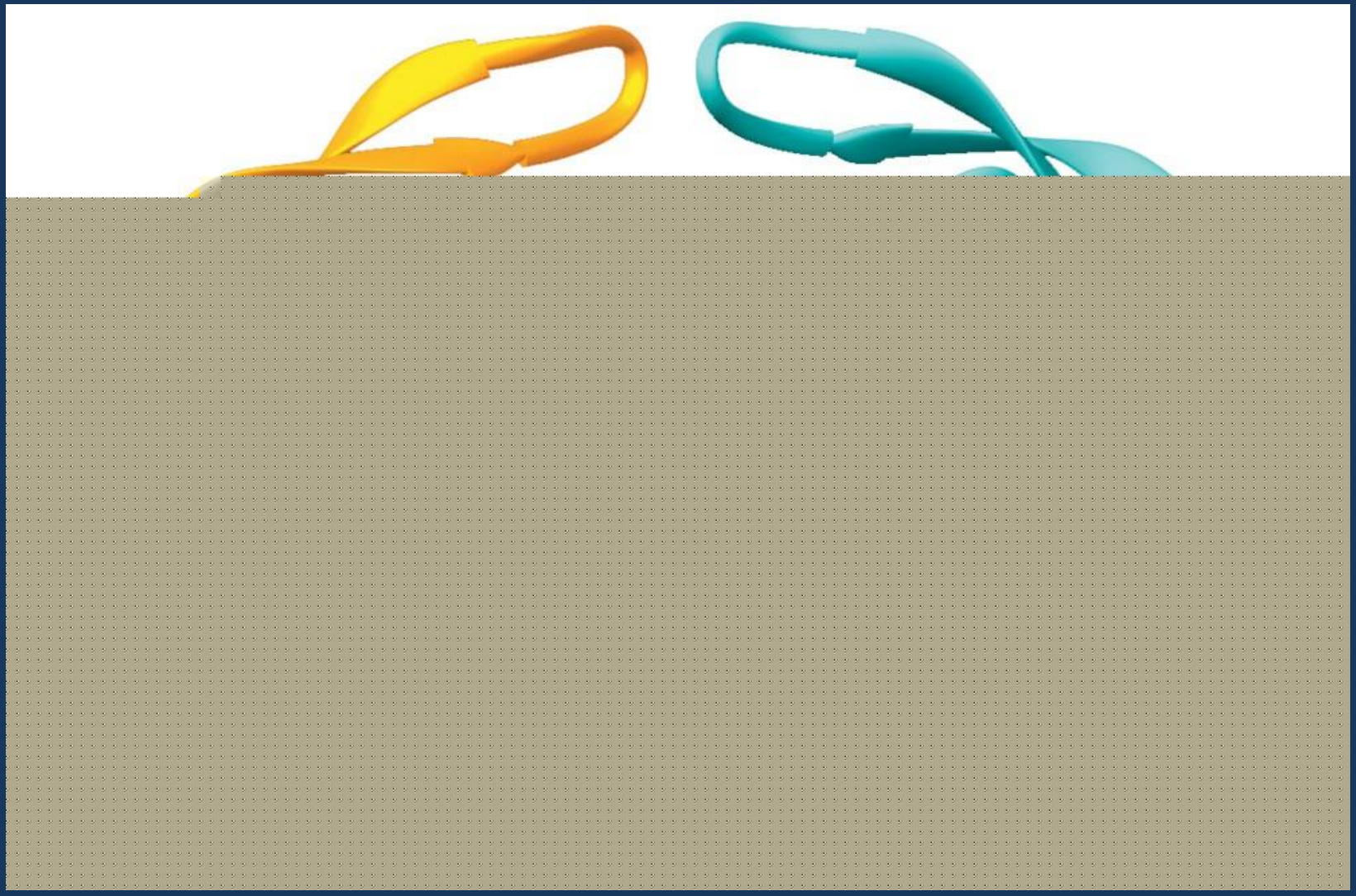
Enzymes and coenzymes II

Dr. Sumbul Fatma
Clinical Chemistry Unit
Department of Pathology

Enzyme inhibition

- Inhibition is a process in which the enzyme activity is regulated or controlled
- To inhibit means to stop the enzyme activity



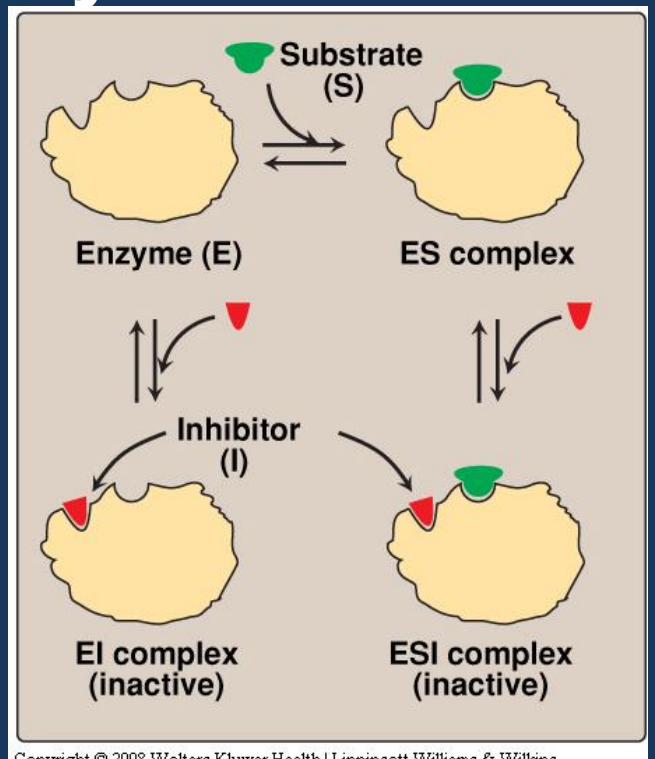
An enzyme without inhibitor

Voet *Biochemistry* 3e
© 2004 John Wiley & Sons, Inc.

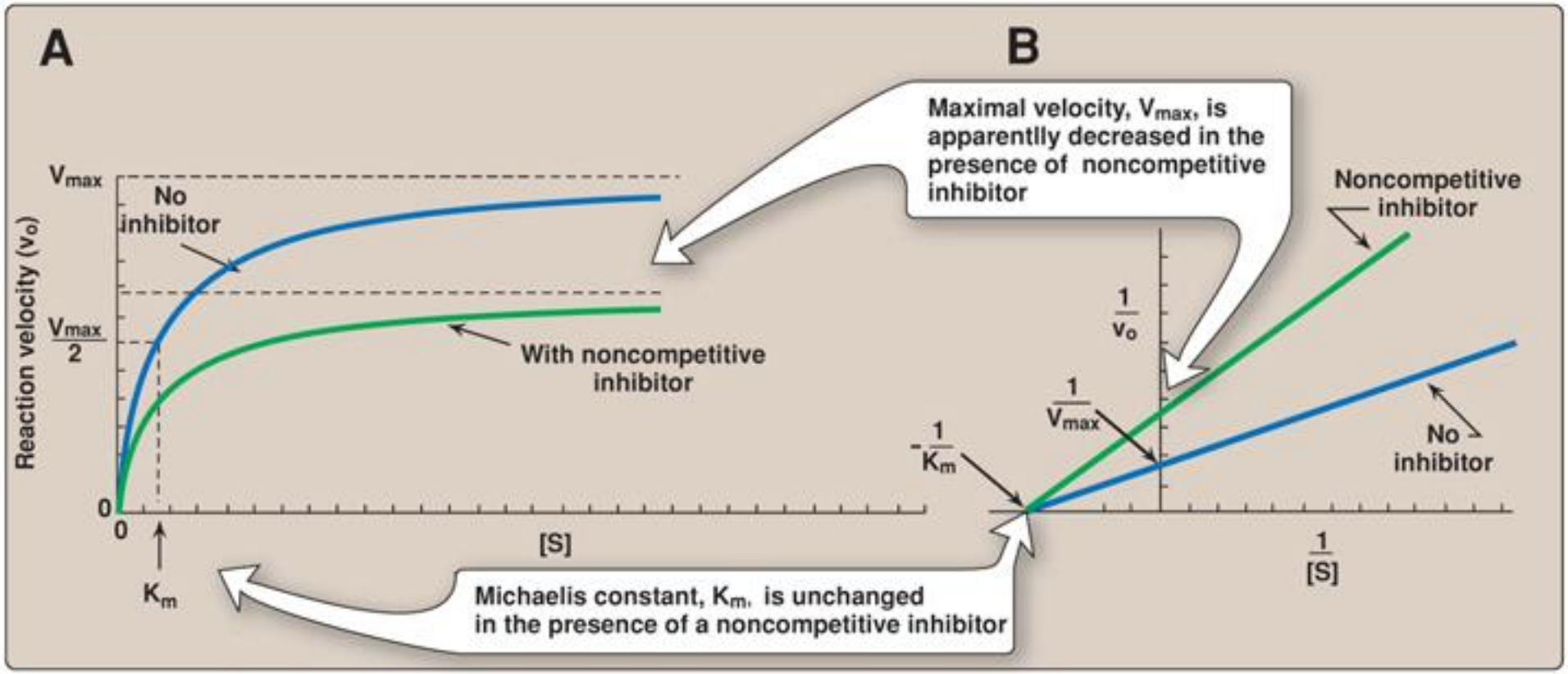
ES + I ⏐ ESI (inactive)

E + I ⏐ EI (inactive)

- The value of V_{max} is decreased by the inhibitor, but K_m is unchanged because the affinity of S for E is unchanged



Copyright © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins



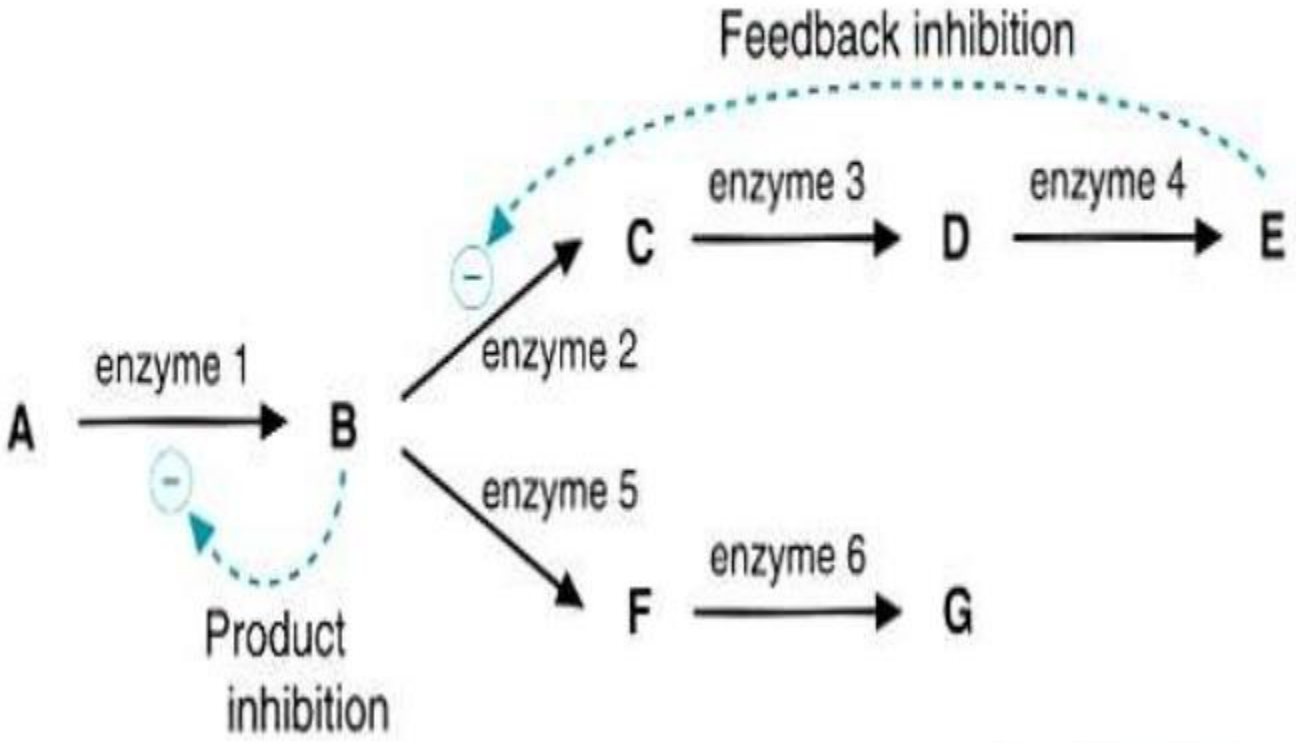
Copyright © 2008 Wolters Kluwer Health | Lippincott Williams & Wilkins

Regulation of enzyme activity

- Regulatory enzymes usually catalyze the first or an early reaction in a metabolic pathway
- They catalyze a rate limiting reaction that controls the overall pathway
- They may also catalyze a reaction unique to that pathway known as committed step

- **Feedback inhibition:**
  - **When the end product of a metabolic pathway exceeds its concentration limit, it inhibits the regulatory enzyme to normalize the pathway (feedback inhibition)**
- **Feed positive activation:**
  - **When the end product of a metabolic pathway is below its concentration limit, it activates the regulatory enzyme to normalize the pathway**

Feedback Inhibition



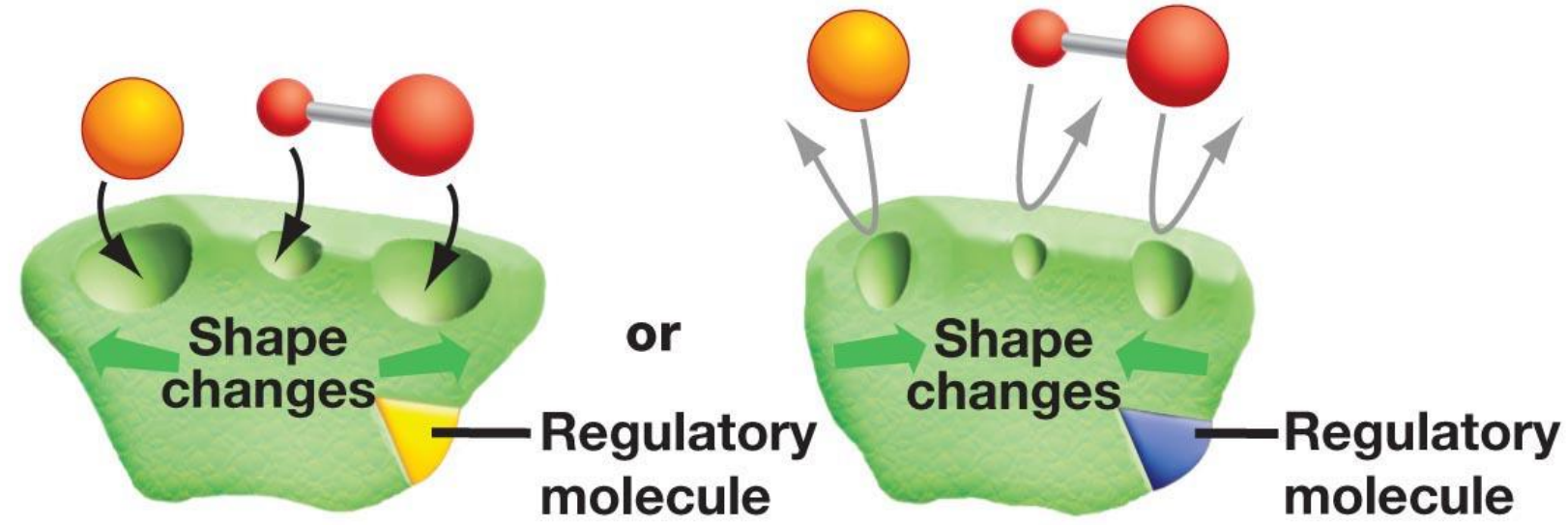
Types of regulation

- **Allosteric enzyme regulation**
  - **The enzymes in metabolic pathways whose activities can be regulated by certain compounds that bind to enzyme other than the catalytic site are known as allosteric enzymes**
  - **The term “allosteric” came from Greek word “ allos ” meaning “other”**

- **Cooperative binding**
  - **The process by which binding of a ligand to a regulatory site affects binding of the same or of another ligand to the enzyme is known as cooperative binding**

- **Binding of an allosteric modulator causes a change in the conformation of the enzyme**
- **This causes a change in the binding affinity of enzyme for the substrate**

(b) Allosteric regulation



Allosteric activation

The active site becomes available to the substrates when a regulatory molecule binds to a different site on the enzyme.

Allosteric deactivation

The active site becomes unavailable to the substrates when a regulatory molecule binds to a different site on the enzyme.

© 2011 Pearson Education, Inc.

- The effect of a modulator may be positive (activation) or negative (inhibition)
  - Positive: increased E, S affinity
  - Negative decreased E, S affinity
- Most allosteric enzymes are oligomers (two or more polypeptide chains or subunits)
- The subunits are known as protomers

- Two types of interactions occur in allosteric enzymes:
  - Homotropic
  - Heterotropic
- Homotropic: Effect of one ligand on the binding of the same ligand (a regulatory enzyme modulated by its own substrate)
- Heterotropic: Effect of one ligand on the binding of a different ligand

Enzymatic diagnosis and prognosis of diseases

- Enzymes are used clinically in three ways:
  - As indicators of enzyme activity or conc. in body fluids (serum, urine) in the diagnosis/prognosis of diseases
  - As analytical reagents in measuring activity of other enzymes or compounds in body fluids
  - As therapeutic agents

- The most commonly used body fluids for measuring enzyme activity are serum and plasma
- There are:
  - Plasma-specific enzymes
  - Nonplasma-specific enzymes

Serum markers in the diagnosis of diseases

- Heart disease
- Pancreatic diseases
- Liver diseases

Reference

- Lippincott- Illustrated Reviews in Biochemistry, 4th Edition