Enzyme Classification

- Enzymes are classified according to the type of reaction they catalyse.
- All enzymes have formal ‘EC’ (Enzyme Commission) number and names, and most have trivial names.

Enzymes in this category include :

- Dehydrogenases
- Reductases
- Oxidases
- Peroxidases.

EC-4 Lyases	Cleavage of C-O, C-C, and C-N or other bonds by means other than hydrolysis or oxidation, giving rise to compound with double bonds or catalyze the reverse reaction of the addition of group to a double bond. In cases where addition of groups to double bonds occurs, then synthase (not synthetase of group EC-6) is used in the name	Aldolase Porphobilinogen synthase Fumarase Argininosuccinase Carbonic anhydrase Cysteine desulfurase Decarboxylase
EC-5 Isomerases	Transfer of groups within molecules to yield isomeric forms	Phosphoglucomutase Triphosphate isomerase or mutase Phosphohexose isomerase Glucose 4-epimerase Retinal isomerase

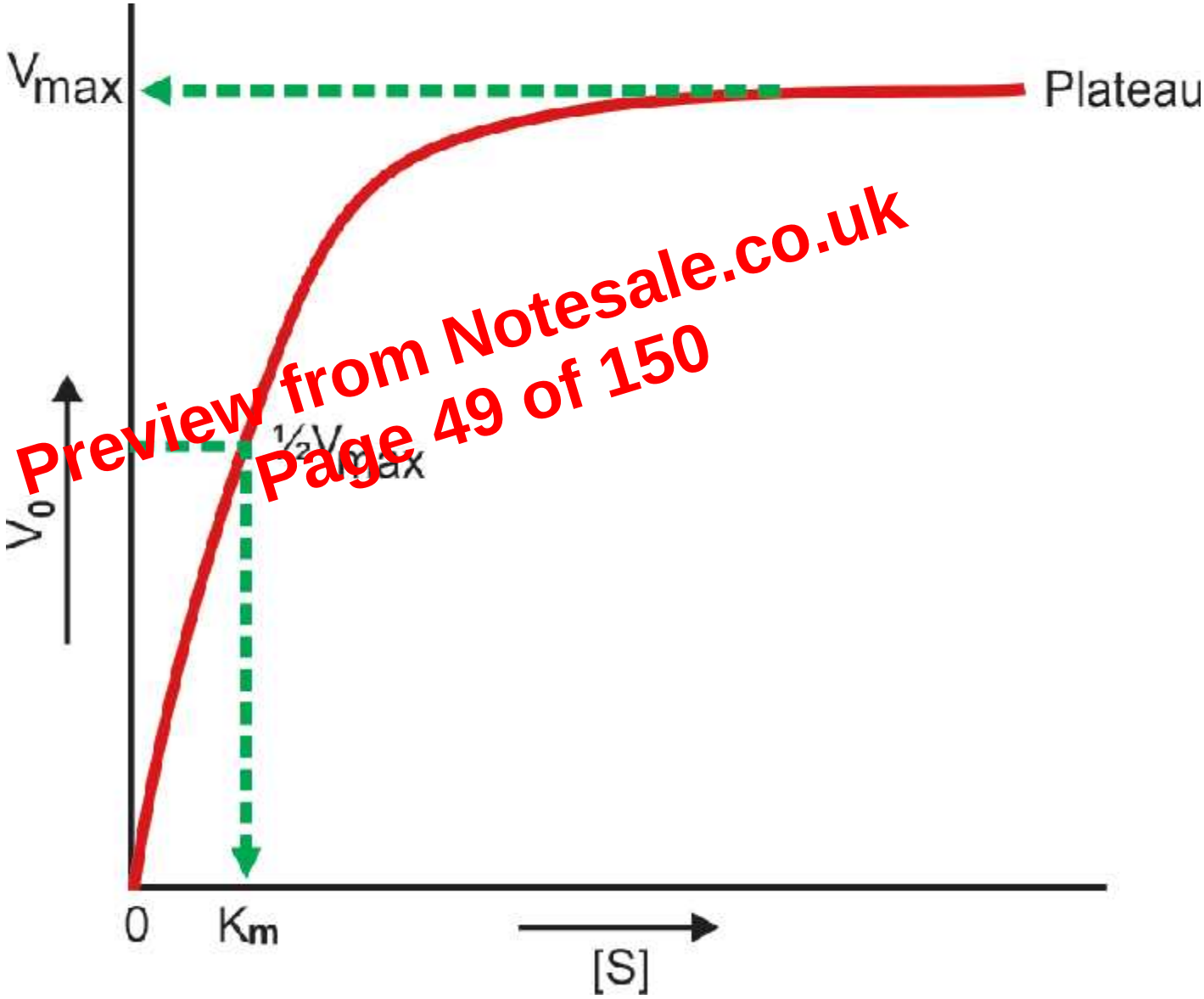
This model explains all mechanisms but do not explain the changes in the enzyme activity in the presence of modulator.

Absolute substrate specificity

Certain enzymes will act on only one substrate and catalyze one reaction, e.g. Glucokinase, lactase, urease, etc.

Broad substrate specificity

- Enzyme acts on more than one structurally related substrates.
- hexokinase catalyzes the phosphorylation of more than one kind of hexoses such as glucose, fructose and mannose.



Effect of Substrate Concentration

Effect of Temperature

- Enzyme catalyzed reactions show an increase in rate with increasing temperature only within a relatively small and low temperature range.
- Each enzyme shows the highest activity at a particular temperature called *optimum temperature*.
- The activity progressively declines both above and below this temperature.

Effect of Activators and Co-enzymes

In absence of activators and coenzymes, enzymes become functionally inactive.

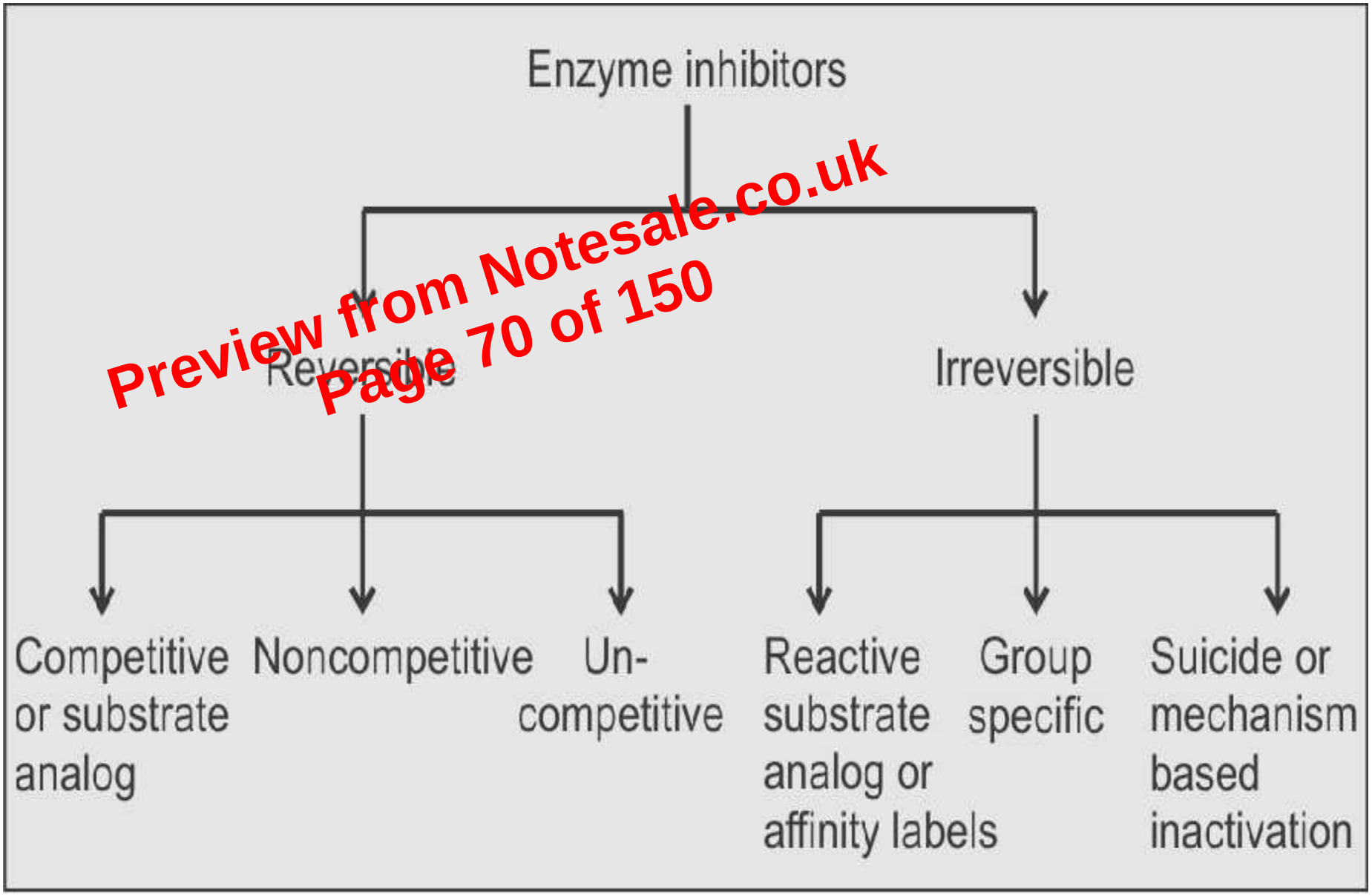
ENZYME INHIBITION

- Any substance that can diminish the velocity of an enzyme reaction is called inhibitor.

- Two general classes of inhibitors are:

1. Reversible inhibitor

2. Irreversible inhibitor.



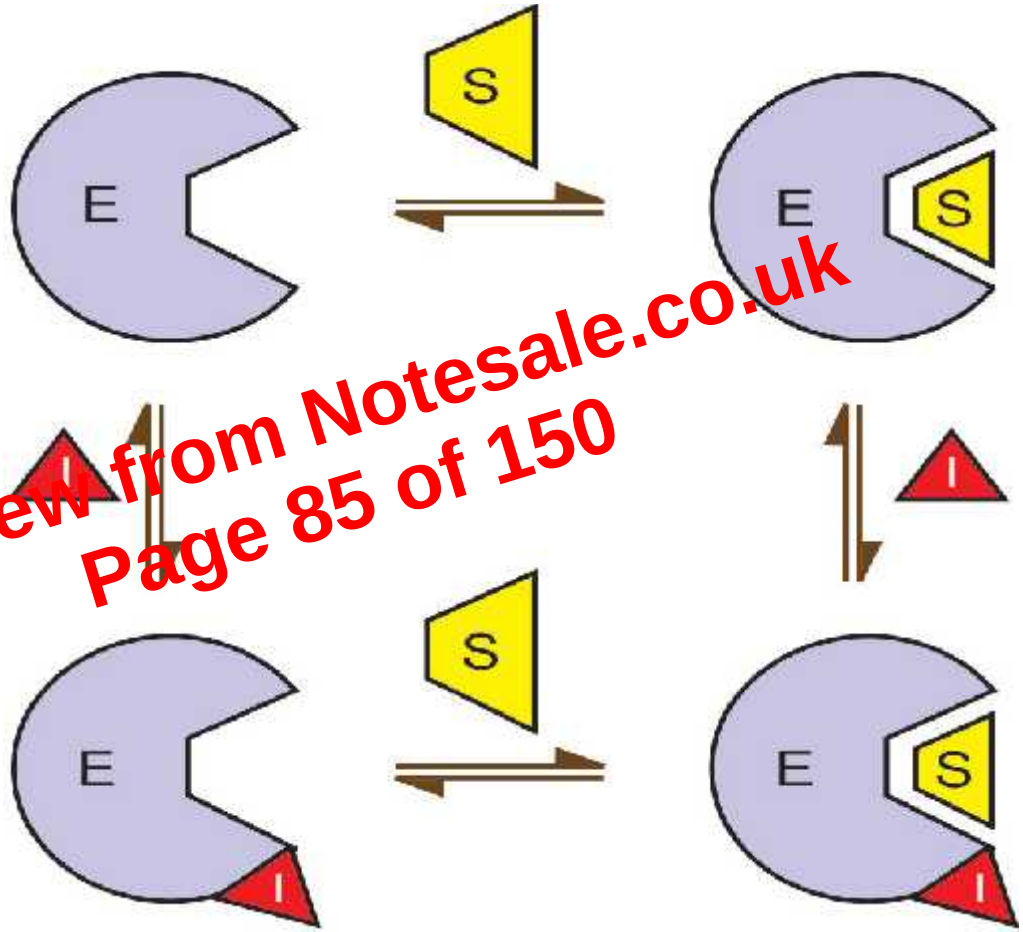
➢ Sulphonamide

Analogue of P- aminobenzoic acid (PABA) and inhibits the synthesis of folic acid in microorganisms.

➢ Isoniazide [Isonicotinic acid hydrazine (INH)]

It is an anti-tuberculosis drug, inhibits the biosynthesis of NAD and restrict the growth of the organisms that cause tuberculosis.

Drugs such an **ibuprofen** (anti-inflammatory drug), **statin** (cholesterol lowing drug) are competitive inhibitors of enzymes, that involved in the prostaglandins and cholesterol synthesis respectively.



Diagrammatic representation of noncompetitive inhibition.

(E = Enzyme; S = Substrate; I = Non-competitive inhibitor; P = Product)

Examples of non-competitive inhibitors are:

- Ethanol or certain narcotic drugs are non-com- petitive inhibitor of acid phosphatase.

- Trypsin inhibitors occur in soybean and raw egg white, inhibit activity of trypsin.

- *Ascaris* parasites (worm) contain pepsin and trypsin inhibitors, inhibit action of pepsin and trypsin.

Irreversible inhibitors can be divided into three categories:

- Substrate analogue inhibitor or affinity labels
- Group specific inhibitors
- Suicide inhibitor or mechanism based inactivation.

- DIPF can inhibit an enzyme acetylcholine esterase by covalently reacting with hydroxyl group of a serine residue present at the active site of the enzyme

- DIPF has also been found to inhibit trypsin, chymotrypsin, elastase and phosphoglucomutase

- Iodoacetamide and heavy metals like, Pb^{2+}, Ag^{+}, Hg^{2+}, etc. which react with sulfhydryl (-SH) group of cysteine residues present at the active site of the enzyme and makes them inactive.

- LDH has five isoenzymes:
  - LDH_1
  - LDH_2
  - LDH_3
  - LDH_4
  - LDH_5.

Clinical Applications of LDH

1. Significant elevation of LDH1 and LDH2 occurs within 24 to 48 hours after myocardial infarction.
2. Predominant elevation of LDH2 and LDH3 occur in leukaemia.
3. LDH3 elevated in malignancy of many tissues.
4. Elevation of LDH5 occurs after damage to the liver or skeletal muscle.

CLINICAL SIGNIFICANCE OF ENZYMES

Certain enzymes are used:

- For the diagnosis of the disease
- As therapeutic agents
- As analytical reagents.

Diagnostic Use of Enzymes

The enzymes that are found in plasma can be categorized into two major groups:

- Plasma specific enzyme
- Plasma nonspecific enzyme.

Acid phosphatase (ACP)

- It hydrolyzes phosphoric acid ester at pH 5 to 6.

- Normal serum value for ACP is 0.5 to 4 KA units/dL.

- Acid phosphatase enzyme is useful for the diagnosis and prognosis of prostate cancer. ACP is therefore an important tumor marker.

Enzymes as tumor markers and their associated types of cancer.

Enzymes	*Types of cancer*
Aldolase	Liver
Alkaline phosphatase	Bone, liver, leukemia, and sarcoma
Placental alkaline phosphatase	Ovarian, lung, gastrointestinal, and Hodgkin's disease
Amylase	Pancreatic
Creatine kinase	Prostate, lung, breast, colon, and ovarian
γ-glutamyl transferase (GGT)	Liver
Lactate dehydrogenase (LDH)	Liver, lymphomas, and leukemia
5′-nucleotidase	Liver
Prostate-specific antigen	Prostate
Prostatic acid phosphatase	Prostate

Some important therapeutic enzymes.	
Enzymes	***Uses***
Asparaginase	Leukemia
Chymotrypsin	Inflammation and edema
Collagenase	Skin ulcers
Fibrinolysin	Blood clot
Glutaminase	Leukemia
Hyaluronidase	Heart attack
Lysozyme	Antibiotic
Rhodanase	Cyanide poisoning
Ribonuclease	Antiviral
β-lactamase	Penicillin allergy
Streptokinase	Blood clots
Trypsin	To dissolve the blood clot
Uricase	Gout
Urokinase	Blood clots