ENZYMES

- **Biological catalysts which speed up the rate of reaction without becoming part of the reaction but themselves cannot initiate any chemical reaction**
- **Enzymes : First name is of substrate second, ending in "ASE" indicating type of reaction catalyzed**
- **Clarify the reaction , e.g.**
- **L- Malate + NAD $\rightarrow$ Pyruvate + NADH-H + CO_2**
- **Malate NAD oxidoreductase (Decarboxylating)**
- **IUB Classification and Numbering**
- **Six major classes and 4-13 subclasses**
- **Numbering 1.2.3.4.5.6**

ENZYMES

Nomenclature

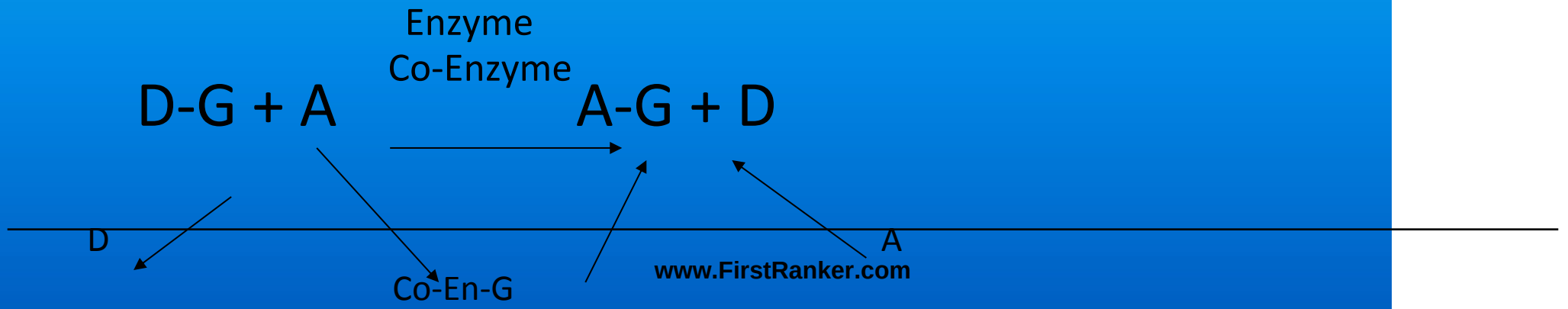
- Oxidoreductases
  - Enzymes acting on CH-OH group
  - Alcohol NAD oxidoreductase [Alcohol dehydrogenase]
  - Alcohol + NAD= Aldehyde or Ketone + NADH.H
  - Glucose+ ATP =Glucose-6 phosphate + ADP
  - ATP.D.Hexose – 6 Phosphotransferase (Hexokinase)

CO-FACTORS OF ENZYMES

ENZYMES	CO FACTORS
Catalase Peroxidase Cytochrome oxidase	Iron Fe^{2+} or Fe^{3+}
Cytochrome oxidase	Copper : Cu^{+2}
Carbonic anhydrase alcohol dehydrogenase	Zinc : Zn^{2+}
Hexokinase Glucose-6-phosphatase Pyruvate kinase	Magnesium Mg^{2+}
Arginase	Manganese Mn^{2+}
Pyruvate kinase	Potassium K^{+}
Urease	Nickel N 2^{+}
Glutathione Peroxidase	Selenium : Se

COENZYMES

- Heat stable, low molecular weight organic compounds non-covalently linked with enzymes & can be separated. APO + CO = Holoenzyme
- If covalently linked to apoenzymes = prosthetic group
- Act as intermediate or ultimate acceptor in group transfer enzyme catalyzed reactions



COENZYMES

CO ENZYMES FOR TRANSFER OF H^+	COENZYMES FOR TRANSFER OF OTHER GROUPS
NAD, NADP	SUGAR PHOSPHATES
FMN, FAD	THIAMINE PYROPHOSPHATE TPP, PYRIDOXAL PHOSPHATE
LIPOIC ACID	FOLATE AND COBAMIDE (VIT B_{12}), BIOTIN
COENZYME, Q	LIPOIC ACID

CO-ENZYMES

REDUCTION OF NAD^+ TO $NADH.H^+$

Lactic acid + NAD $\xrightarrow{\text{LDH}}$ Pyruvic acid + $NADH\text{-}H^+$

Malic acid + NAD $\xrightarrow{\text{Malic dehydrogenase}}$ Oxalo acetic acid + $NADH\ \text{-}H^+$

Glucose-6-phosphate + NADP $\xrightarrow{\text{G-6-P.D}}$ 6-Phosphoglucon-olactone +$NADPH\text{-}H^+$

REDUCTION OF FAD OR FMN TO $FADH_2$ OR $FMNH_2$

FMN is co enzyme for Cytochrome C oxidase, L.Amino acid dehydrogenase

FAD is co-enzyme for xanthene oxidase, acyl-CoA dehydrogenase

CO-ENZYMES

Thiamine Pyrophosphate:

Co-enzyme for oxidative decarboxylation for ketoacids

Pyruvate —(CoA, NAD → NADH-H$^+$; Pyruvate dehydrogenase)→ Acetyl CoA

Pyruvate +TPP —(Pyruvate decarboxylase)→ Acetalaldehyde -TPP complex+Co_2

Alpha ketogluterate+6 CoA-SH —(α-ketogluteratedehydrogenase; NAD → NADH-H$^+$)→ Succinyl CoA + Co_2

Ribose-5 Po_4 + Xylulose-5-Po_4 —(Transketolase)→ Sedoheptulose 7-Po_4 + 3 phosphoglyceraldehyde

CO-ENZYMES

Biotin

- Part of multiunit enzymes causing carboxylation reactions. Acts as carrier of CO_2

$$\text{Acetyl CoA} + HCo_3 + \text{ATP} \xrightarrow[\text{Enz-Biotin-COO}^- \rightarrow \text{Enz-Biotin}]{\text{Acetylcarboxylase}} \text{Malonyl-CoA}$$

$$\text{Pyruvate} + HCo_3 + \text{ATP} \xrightarrow{\text{Pyruvate carboxylase .Biotin}} \text{Oxaloacetate} + \text{ADP} + \text{Pi}$$

$$NH_4 + HCo_3 + 2\text{ATP} \xrightarrow{\text{Carbamoyl Po}_4\text{.Synthetase - Biotin}} \text{CarbamoylPO}_4 + 2\ \text{ADP} + 2\ \text{Pi}$$

CO-ENZYMES

Ascorbic acid (Vitamin C)

- Strong reducing agent
  - Required for hydroxylation of proline into hydroxyproline for synthesis of collagen
  - Conversion of tyrosine into dopamine and into catecholamines (adrenaline and noradrenalin)
  - Bile acid formation
  - Conversion of cholesterol into 7-hydroxylcholesterol
  - Maintain metallic co-factors like Cu^{+} in Monooxygenases and Fe in dioxygenases in reduced form
  - Conversion of cholesterol into steroid hormone in adrenal cortex
  - Absorption of iron by reducing into reduced form which is can be easily absorbed
  - Acts as antioxidant in GIT by preventing formation of nitrosamines during digestion

CO-ENZYMES

- **Folic acid**
  - Active form is tetrahydrofolate which acts as single carbon carrier for synthesis of various compounds like pyrimidines and purines e.g. conversion of dUMP (deoxyuridylate) into dTMP (deoxythymidylate)

- **Vitamin B_{12}**
  - Acts as co-enzyme in groups rearrangements in isomerases e.g. conversion of methyl malonyl CoA into succinyl-CoA by enzyme methylmalonyl-CoA mutase
  - Converts homocystein into methionine
  - Act as maturation factor for RBCs

CLASSIFICATION OF ENZYMES

- Formulated by the enzyme commission of I.U.B six major classes & 4-13 subclasses of each major class, based on the type of reactions catalyzed.

1. **Oxidoreductases**
   - Catalyzing oxidation reduction reactions
2. **Transferases**
   - Catalyzing group transfer
3. **Hydrolases**
   - Catalyzing hydrolytic breakdown

CLASSIFICATION OF ENZYMES

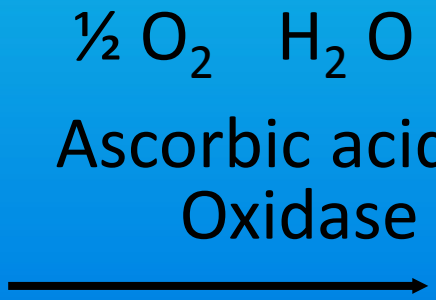
4. **Lyases**
   - Catalyzing removal of groups by mechanism other than hydrolysis and leaving behind double bonds or adding groups to already existing double bonds.
5. **Isomerases**
   - Catalyzing interconversion of isomers
6. **Ligases**
   - Catalyzing formation of bonds and new compounds

1.Oxidoreductases

– Catalyzing oxidation reduction reaction where one substrate is oxidized and other is reduced

CLASSIFICATION OF ENZYMES (OXIDOREDUCTASES)

Oxidases. Catalyzing oxidation of the substrate and atomic oxygen acts as recipient of hydrogen e.g. Ascorbic acid oxidase, Cytochrome oxidase, Tyrosinase



Ascorbic acid → Dehydro ascorbic acid

CLASSIFICATION OF ENZYMES (OXIDOREDUCTASES)

Aerobic Dehydrogenases. Catalyzing oxidation of the substrate and molecular oxygen acts as recipients of hydrogen e.g. Glucose oxidase, L amino acid dehydrogenase, Xanthene dehydrogenase

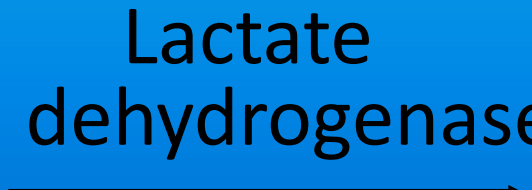
O_2 H_2O_2

glucose Oxidase

Glucose ——— Gluconolactone

CLASSIFICATION OF ENZYMES (OXIDOREDUCTASES)

Anaerobic Dehydrogenases. Catalyzing oxidation of the substrate and coenzymes act as recipients of hydrogen e.g. Lactate Dehydrogenase with NAD and Glucose 6 phosphate dehydrogenase with NADP

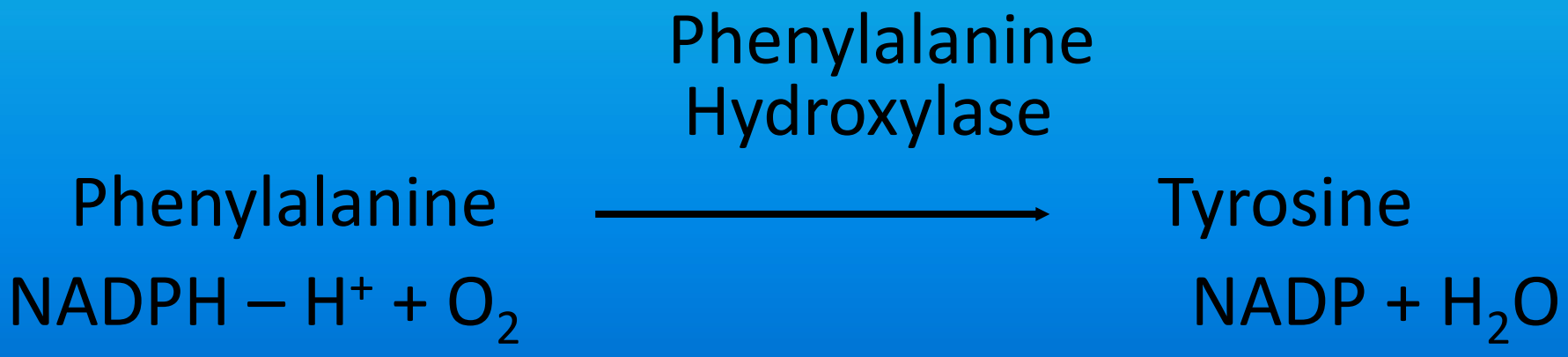


Lactic acid → Pyruvic acid

+ NAD → + NADH – H^+

CLASSIFICATION OF ENZYMES (OXIDOREDUCTASES)

Oxygenases . Catalyzing oxidation of the substrate and oxygen is added to the substrate eg are Homogentisate oxygenase, L Tryptophan dioxygenase



TRANSFERASES

Transaminases. Catalyzing transfer of amino group between an amino acid and a ketoacid e.g. Aspartate Transaminase (AST), Alanine Transaminase (ALT)

Aspartate Transaminase (AST)

Glutamic acid + Oxalo acetic acid → **α Ketoglutaric acid + Aspartic acid**

Alanine Transaminase (ALT)

Glutamic acid + Pyruvic acid → **α ketoglutaric acid + Alanine**

TRANSFERASES

Transmethylases. Catalyzing transfer of methyl group between to substrates e.g. COMT

Catechol O Methyltransferase (COMT)

Noradrenaline + CH_3 → Adrenaline

Transpeptidases. Catalyzing transfer of amino acids to substrates e.g. Benzyl-SCoA transpeptidase

Benzyl-SCoA Transpeptidase

Benzyl - SCoA + Glycine → Hippuric acid

TRANSFERASES

Phosphotransferases. Catalyzing transfer of phosphate group to substrates e.g. Hexokinase, Glucokinase

2.7.1.1 ATP D hexose- 6 Phosphotransferase [Hexokinase]

ATP + Glucose Hexokinase $\rightarrow$ADP + D-Glucose –6-P

Acetyltransferase. Catalyzing transfer of acetyl group to substrates e.g. Choline Acetyltransferase

Acetyl-CoA+ Choline $\rightarrow$ CoA + Acetyl- Choline

HYDROLASES

- **Catalyzing hydrolytic breakdown of different bonds. Most of the GIT enzymes belong to this class**

Enzymes hydrolyzing Carbohydrates

Polysaccharidases

Starch **Amylase** **Maltose, Maltotrios, Dextrins**

Oligosaccharidases

Dextrins **Dextrinase** **Glucose**

Disacharidases

Maltose, Lactose, Sucrose Disacharidases (Maltase, Lactase, Sucrase)

Monosaccharides

Enzymes Hydrolysing Lipids

Triacyl glycerol **Lipase** **Monoacyl glycerol + 2 F.F.A**

Cholesterol ester Cholesterol **Esterase** Free Cholesterol + FFA

HYDROLASES

Phospholipids → Phospholipase → Lysophospholipids

Lecithin → Lysolecithin

Enzymes Acting on Peptide Bonds

Exopeptidases → Carboxypeptidase, Aminopeptidase → Amino acids

Endopeptidase → e.g. Pepsin → Smaller Peptides

HYDROLASES

Tripeptidase : Tripeptide → A.A

Dipeptidase : Dipeptide → AA

Phosphatases

i. Phosphomonoesterases:

Glucose – 6.P. + H_2O G 6. Phosphate → Glucose +Pi

Phosphatase

ii. Phosphodiesterases:

Removal of phosphate Group of diesters

breakdown of 3’-5’ p linkages in cyclic AMP

LYASES

- Catalyzing reactions in which groups are removed without hydrolysis leaving a double bond or add groups to already existing double bonds

$CH_3.CO.COOH$ (Pyruvate) $\xrightarrow[\text{Decarboxylase T.P.P}]{\text{Pyruvate}}$ $CH_3.CHO + CO_2$ (Acetaldehyde)

$COOH.CH = CH.COOH$ (Fumaric acid) $\underset{\text{Fumerase}}{\rightleftharpoons}$ $COOH\text{-}CHOH.CH_2\text{-}COOH$ (Malic Acid)

ISOMERASES

- Involved in inter conversion of pair of isomeric compounds
- Glucose 6. P — Phosphogluco Mutase — glucose I.P
- Glucose 6.P — Phosphohexose Isomerase — Fructose 6.P
- All trans retinene — Retinene Isomerase — 11- CIS retinene
- UDP glucose — UDPG-4 Epimerase — UDP – Galactose

LIGASES

- Catalyze reactions in which linking together of two molecules occur coupled with the breakdown of a high energy phosphate bonds like ATP, GTP

Acetate + CoA +ATP $\xrightarrow[\text{Synthetase}]{\text{Acetyl CoA}}$ Acetyl CoA+AMP+PP

Succinate + CoA + ATP $\xrightarrow[\text{Synthetase}]{\text{Succinyl CoA}}$ Succinyl CoA + ADP+ Pi

Pyruvate + CO_2 + ATP $\xrightarrow[\text{Carboxylase}]{\text{Pyruvate}}$ Oxaloacetate + ADP + Pi

Fatty acid + CoA + ATP $\xrightarrow[\text{Synthetase}]{\text{Acyl CoA}}$ Acyl CoA (Activated fatty acid) + AMP + PiPi

MECHANISM OF ACTION

- S+E ⟶ E-S ⟶ P
- D-G + A $\xrightarrow[ES]{\text{Enzyme (Enzyme}}$ – G) A-G + D

- **Factors affecting enzyme activity**
  - Enzyme concentration
  - Substrate concentration
  - Temperature
  - pH
  - Enzyme inhibitors

MICHEALIS – MENTON EQUATION

$$V_i = \frac{V_{max}[S]}{Km + \{S\}}$$

V_i = Measured initial velocity

V max = Maximum velocity

S = Substrate

Km = Michaelis constant

Variations

A. **When (S) is much less than Km**

$$Vi = \frac{V_{max}[S]}{Km + \{S\}} \quad \text{OR} \quad \frac{V_{max}}{Km}[S] \quad K[S]$$

So Vi depends upon substrate concentration

ENZYME KINETICS

B. When substrate concentration is much greater than Km

$$Vi = \frac{Vmax\,[S]}{Km + [S]} \quad \text{or} \quad Vi = \frac{Vmax\,[S]}{[S]}$$

Or $Vmax = Vi$

C. When substrate concentration is equal to Km

$$Vi = \frac{Vmax\,[S]}{Km + [S]} \quad \text{or} \quad Vi = \frac{Vmax\,[S]}{[S] + [S]}$$

$$\text{Or} \quad Vi = \frac{Vmax\,[S]}{2\,[S]} \quad \text{or} \quad Vi = \frac{Vmax}{2}$$

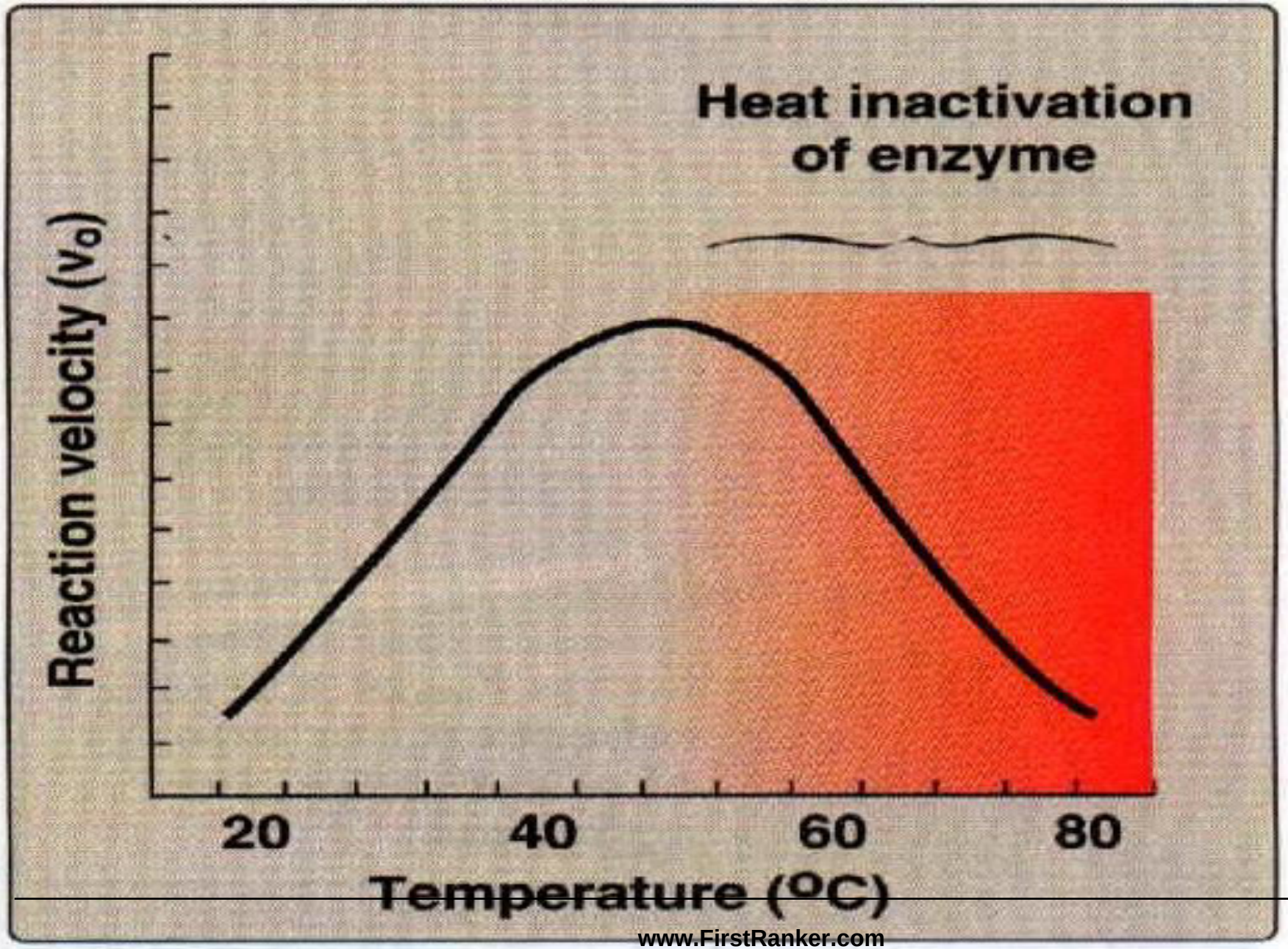
So Vi = half of maximum velocity

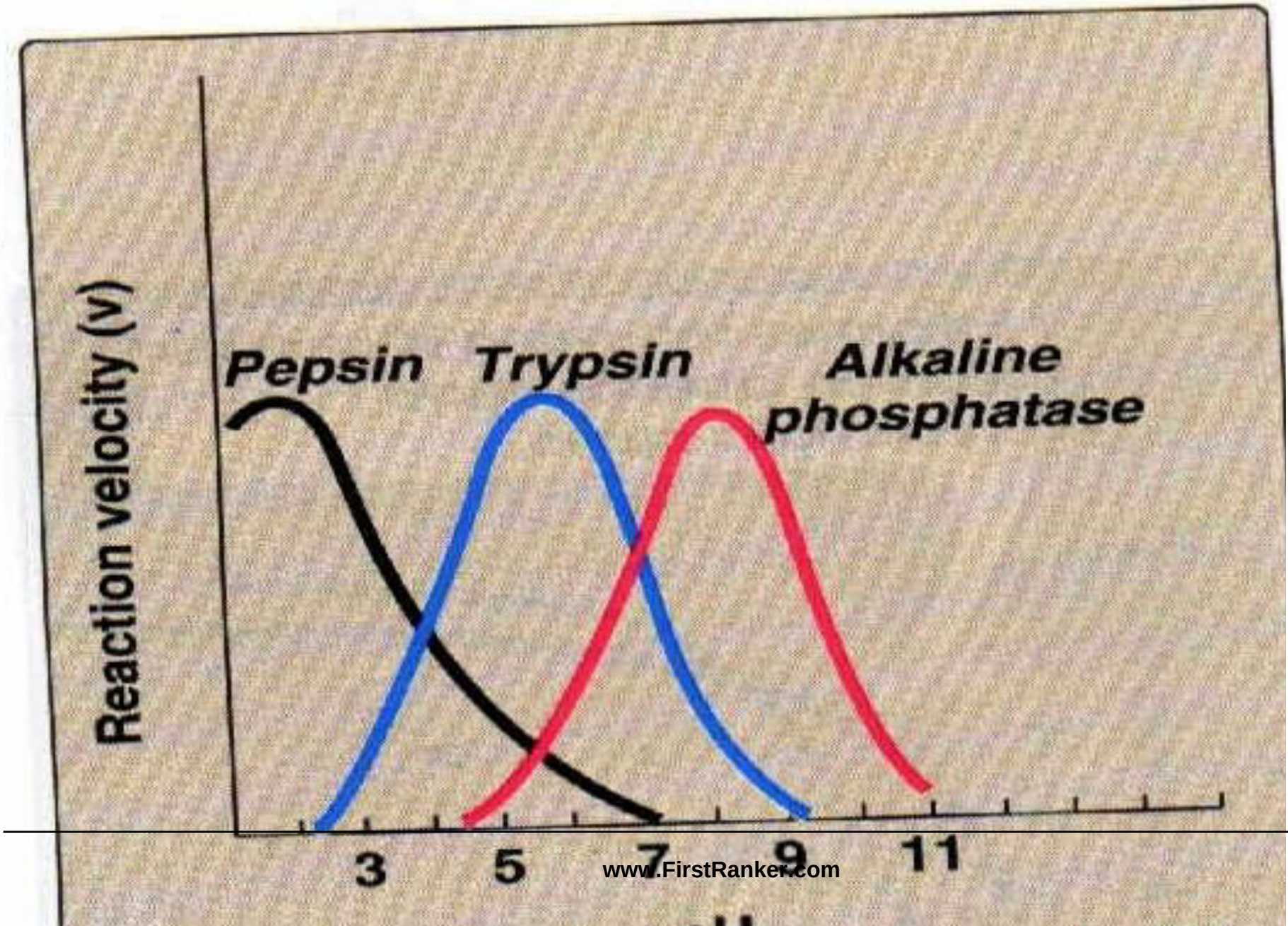
Enzyme Catalysis

- Catalysis by Proximity : Higher conc of "S" will increase their proximity to each other thereby promoting enhanced binding to enzyme resulting in increased catalysis
- Acid-Base Catalysis : Ionizable functional gps of aminoacyl side chains & prosthetic gps can act as acids or bases. In "specific acid or base catalysis" rate of reaction is sensitive to changes in protons , but is independent of conc of other acids or bases present in the solution or at active site. In "general acid or base catalysis" reaction rates are sensitive to all acids & bases present .

Enzyme Catalysis

- Catalysis by Strain : Binding of Enzyme to substrates whose covalent bond are to be cleaved in an unfavorable configuration thereby exerting strain on the bonds ,stretching or distorting bonds.
- Covalent Catalysis: Formation of transient covalent bond between enzyme & substrate(s) makes it more reactant & introduces a new faster pathway of catalysis with much lowered energy of activation. On completion of reaction, enzyme returns to its original state. Cysteine, serine or histidine residues on enzyme participate in covalent catalysis



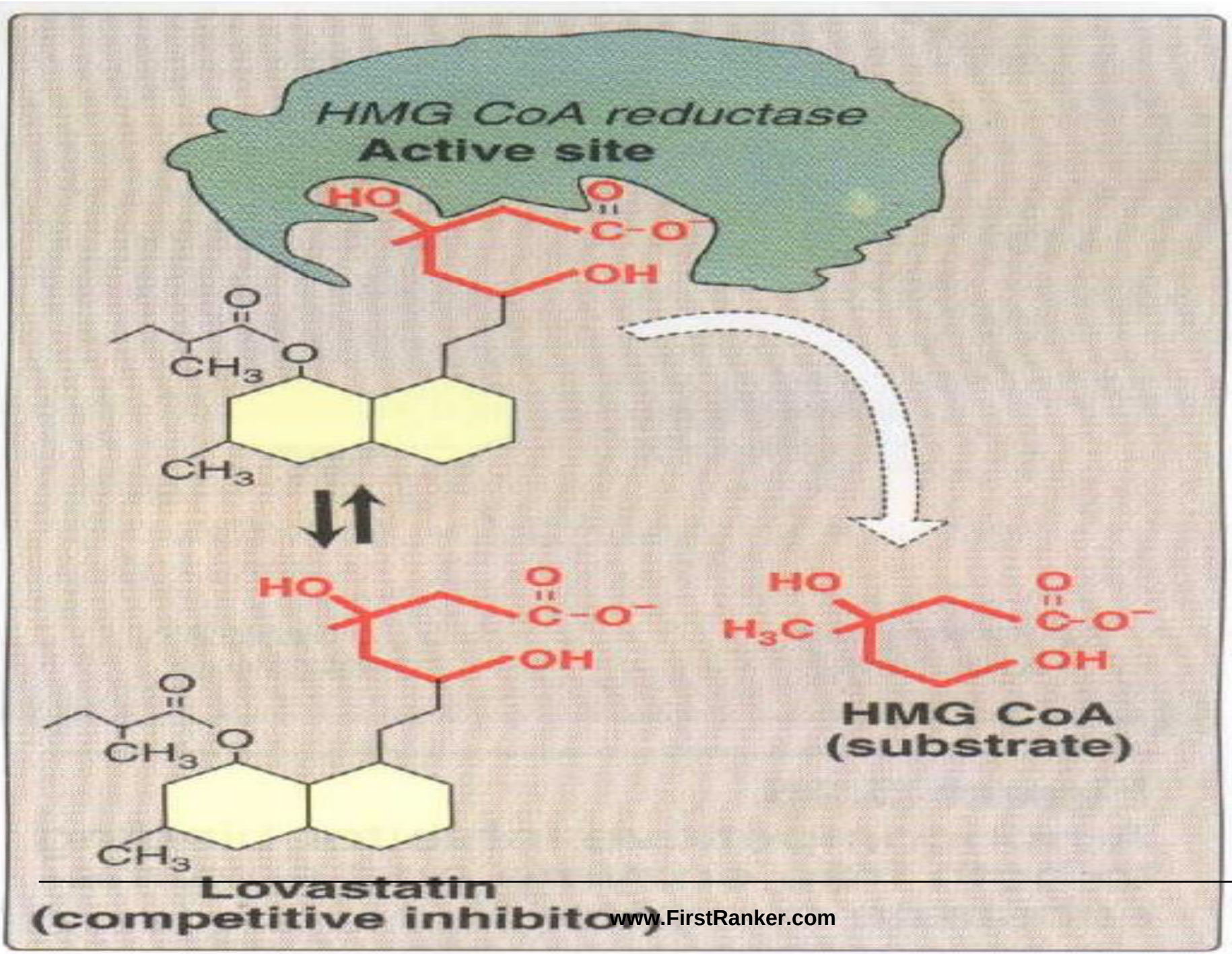


ENZYME INHIBITION

- Competitive inhibition
- Non competitive inhibition
- Irreversible inhibition

Competitive inhibition

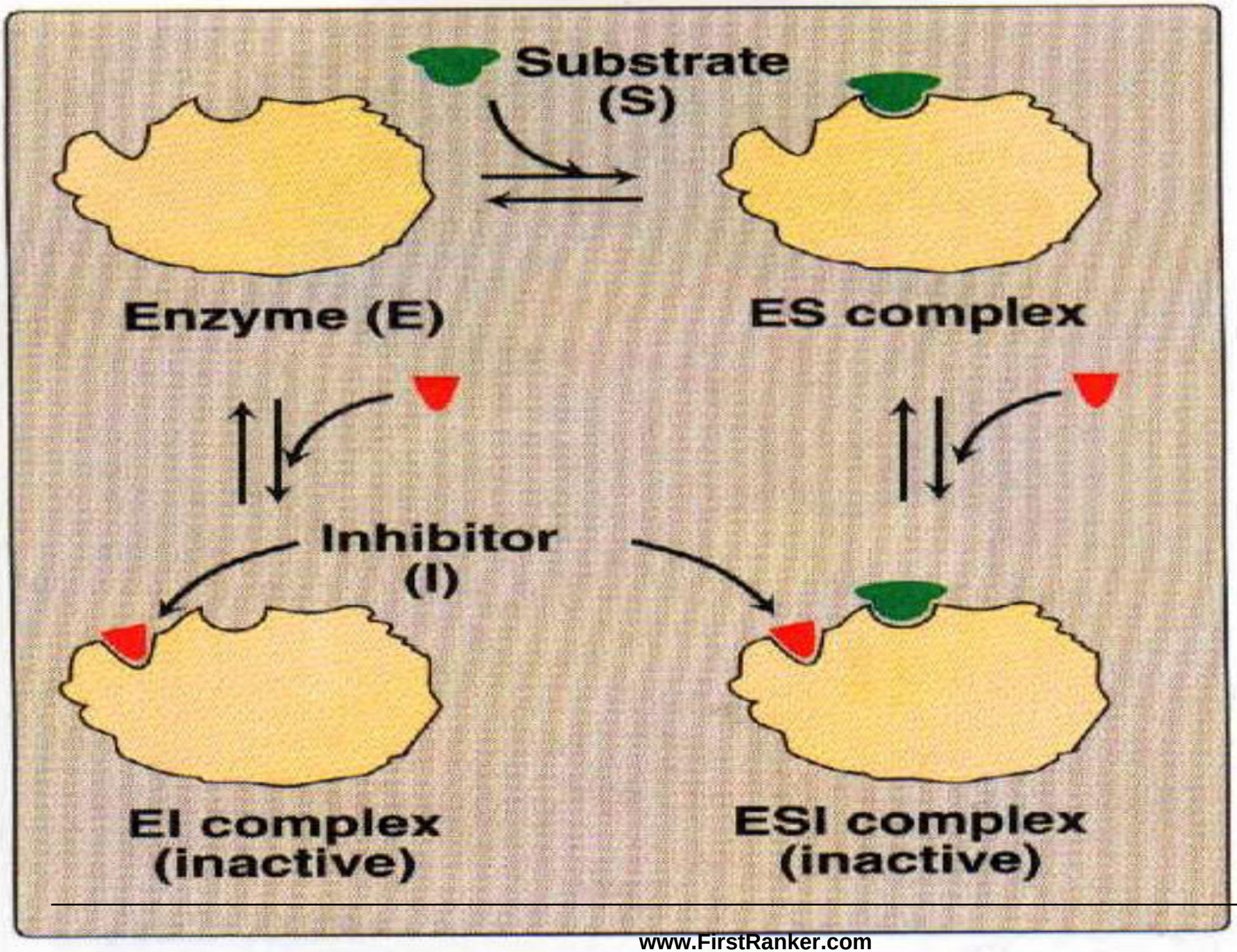
- Inhibitors resemble substrate, Km is increased no change in Vmax
- Succinate ——Enz——→ Fumarate
- Malonate (structural analog of Succinate) Enz – inhibition ——→ no product
- Drug Allopurinol, structural analog of Xanthene is used for treatment of gout /hyperuricemia as it is a competitive inhibitor of enzyme Xanthene oxidase which normally converts Xanthene into Uric acid
- Addition of excess of normal [S] will reverse this inhibition



ENZYME INHIBITION

NON COMPETITIVE INHIBITION

- Inhibitor binds on separate site on enzyme therefore no competition with substrate. Vmax is reduced and no change in Km
- Inhibitor can bind with either free enzyme or enzyme – substrate complex and in both cases render these inactive
- **Lead poisoning** is an example of this inhibition and it inhibits enzyme Ferrochelatase which adds iron molecule to the centre of porphyrin ring in the synthesis of Hemoglobin



IRREVERSIBLE INHIBITION

Permanent covalent linkage with enzyme rendering it irreversibly inhibited

- Diisopropyl phospho fluoride (DIPF)
- Iodoacetamide
- Heavy metal [Ag^{+} Hg^{+2}], Silver, Mercury
- Oxidizing agents
- Covalent linkage with enzyme: inactivation of enzyme
- Kinetics are same as of non competitive inhibition, therefore difficult to distinguish between the two
- Examples are insecticides which act as enzyme poisons for the insects & disinfectants used for micro-organisms

REGULATION OF ENZYME ACTIVITY

- **3 main mechanism in regulation**

A. Rate of synthesis and degradation determine enzyme quantity

synthesis

Amino acids Enzyme

REGULATION OF ENZYME ACTIVITY

B. **INDUCTION OF ENZYME SYNTHESIS**

In bacteria → glucose → no Beta galactosidase

lactose → induction of B-galactosidase

In animals → Enzymes of Urea Cycle

→ HMG CoA reductase in Cholesterol synthesis

→ Sucrase or invertase for Sucrose

REGULATION OF ENZYME ACTIVITY

C. REPRESSION OF ENZYME SYNTHESIS

- In bacteria → glucose → repression of B- Galactosidase
- S typhimurium → Histidine → Repression of enzyme for histidine : product feed back repression

  HMG CoA Reductase: Induction or stimulation of synthesis = fed state or insulin effect

  Repression of synthesis = fasting or starvation
- Hormone sensitive Lipoprotein lipase :

  Induction or stimulation =adrenalin, cortisol, fasting, stress

  Repression = insulin, fed state

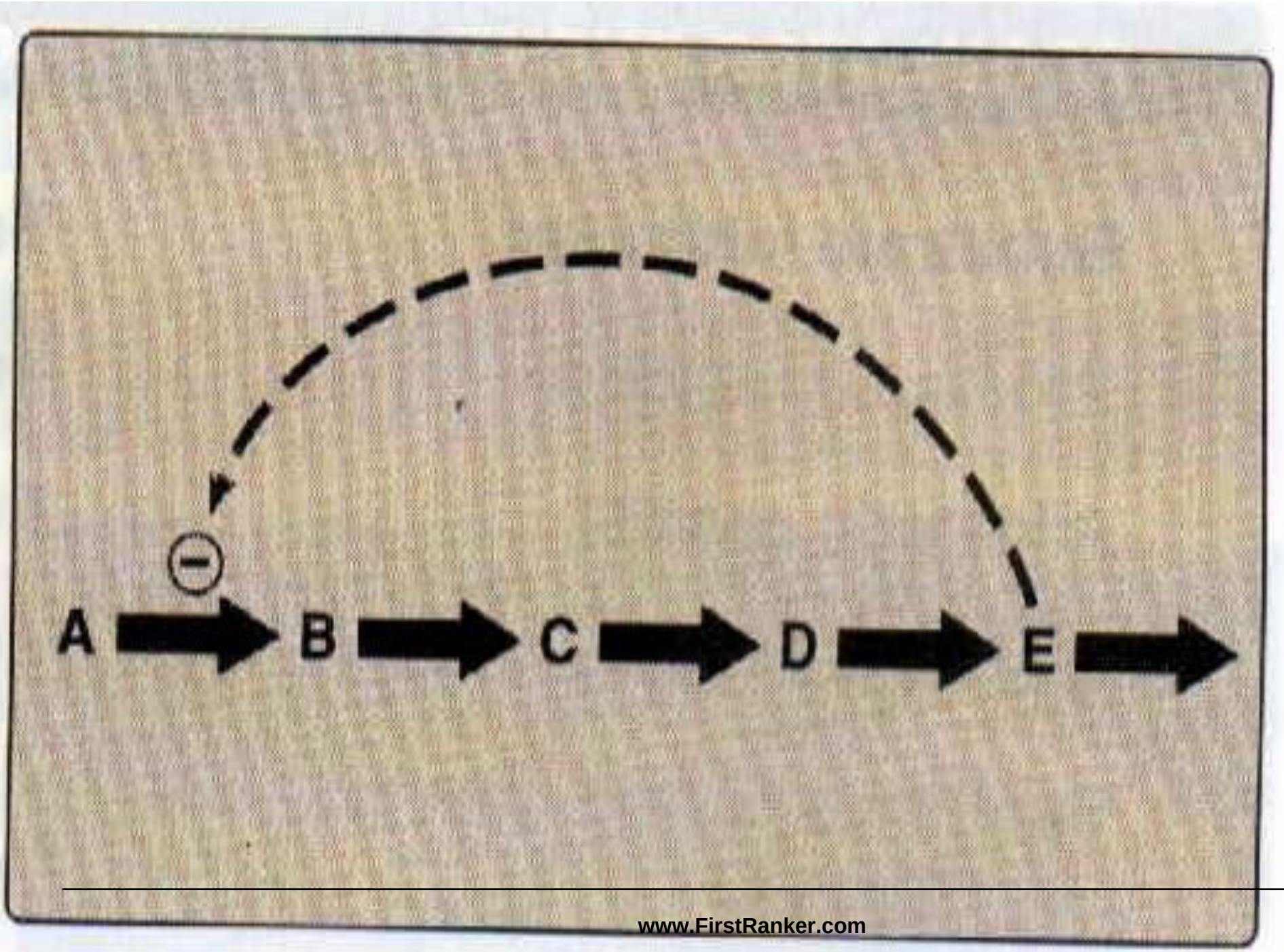
ALLOSTERIC REGULATION

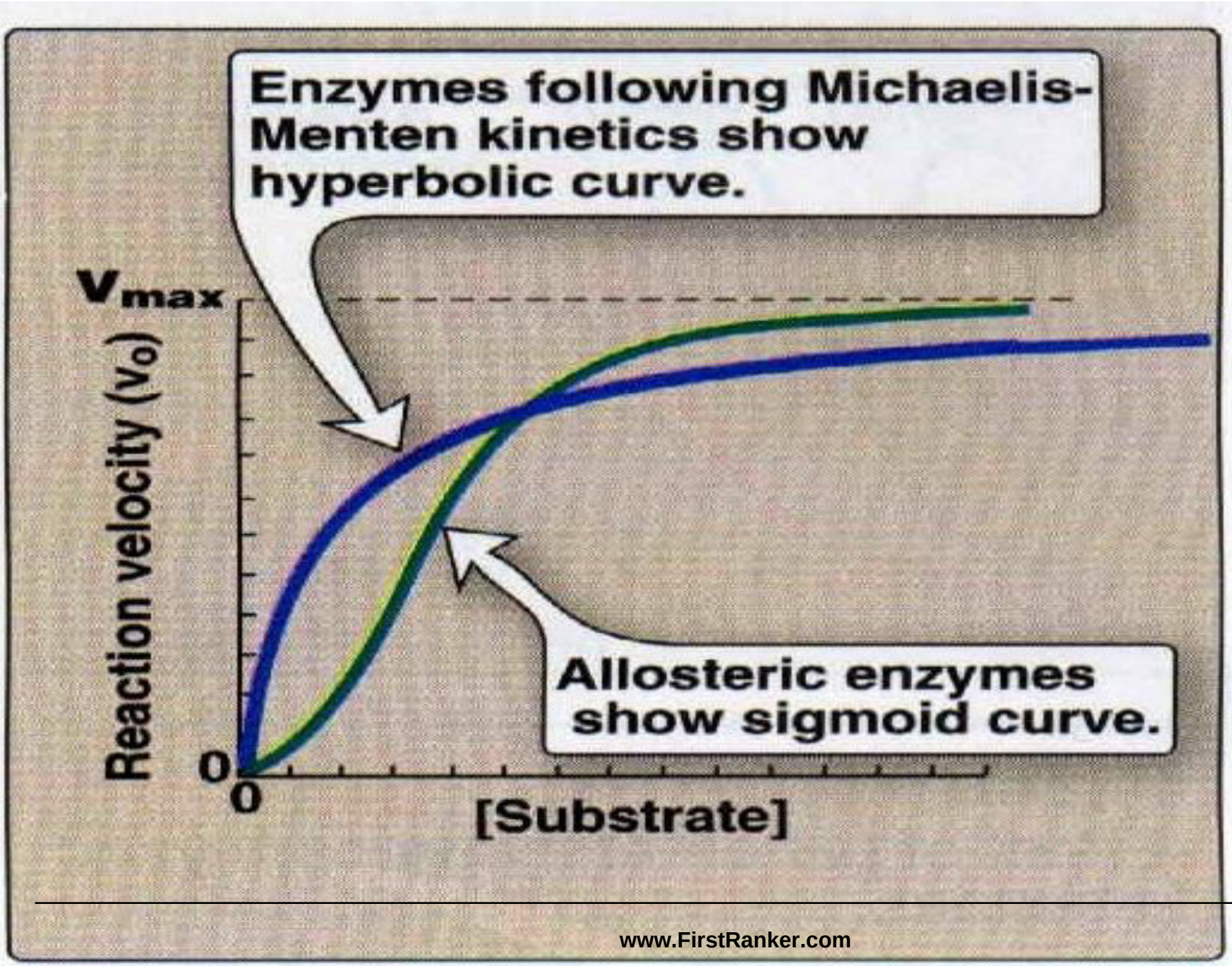
- Low molecular wt allosteric effectors structurally not similar to substrate

$$A \xrightarrow{E_1} \quad B \xrightarrow{E_2} \quad C \xrightarrow{E_3} D$$

Bind at sites other than active site leading to feed back inhibition

Usually product or last small molecule before macromolecules in biosynthesis



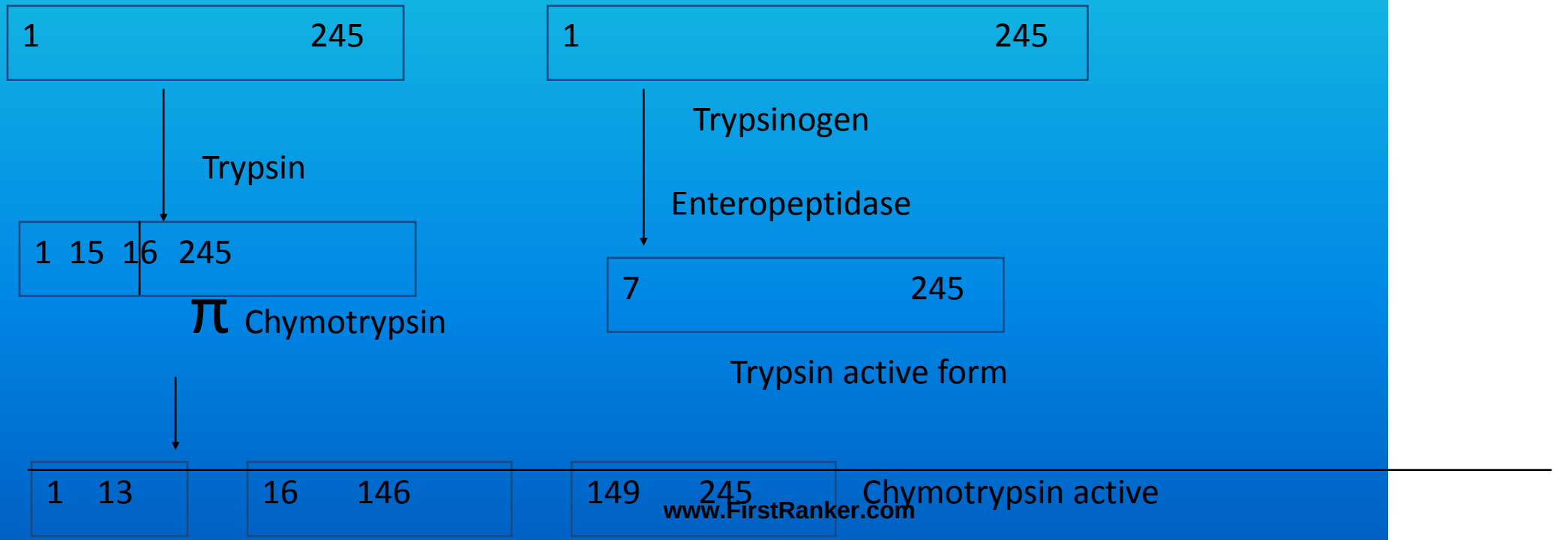


PROENZYMES

- Inactive enzymes initially secreted as large molecules, active site not exposed

Pepsinogen —HCl→ Pepsin

Prochyomotrypsin —Proteolysis→ Chymotrypsin



PROENZYMES

- Required for control of catalytic activity of enzymes so that catalytic activities only occur when required
- Pancreatic enzymes if all the time active = auto digestion of pancreas
- Blood clot lysis enzymes only active when blood clot is formed

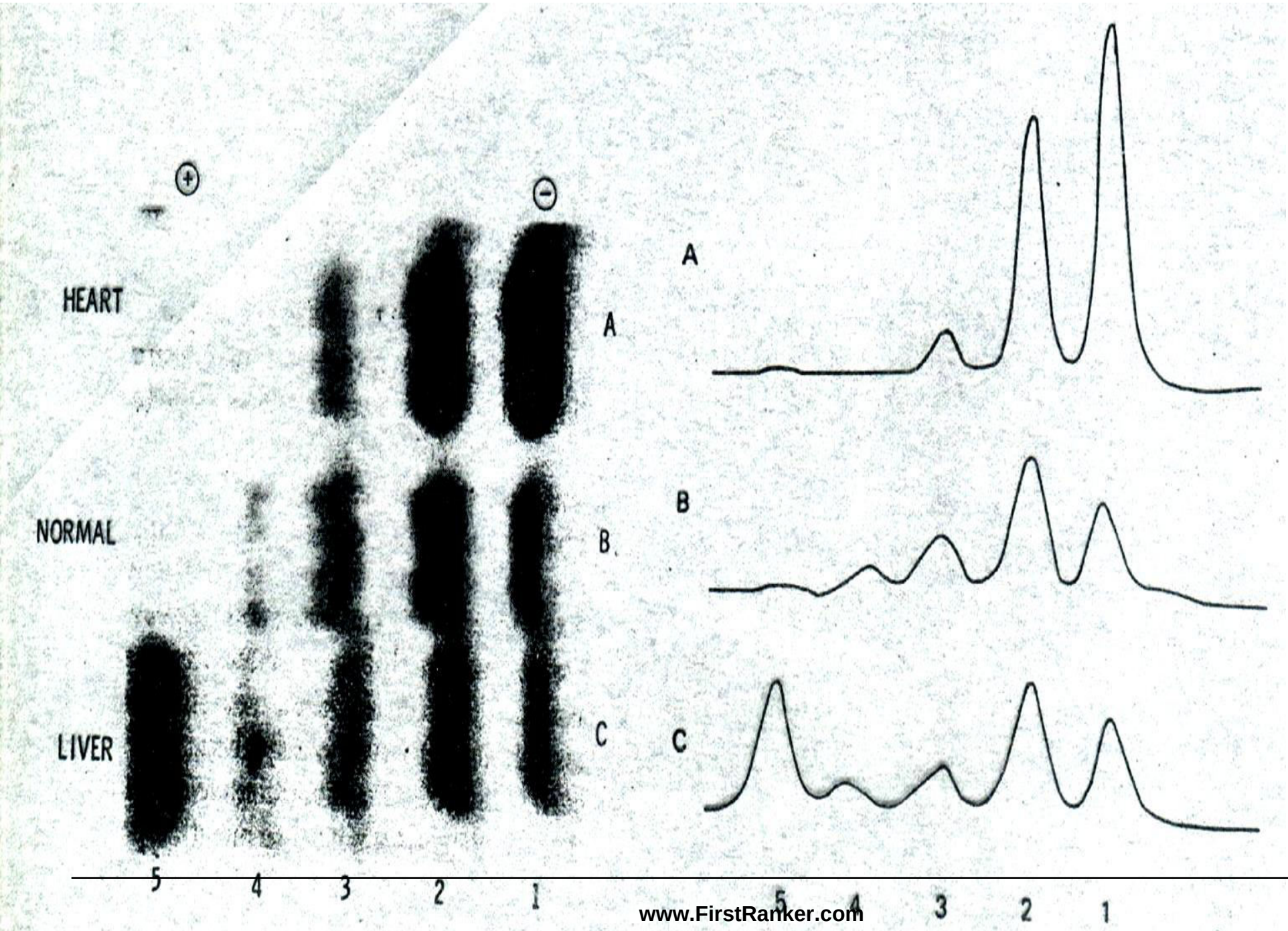
Examples of Pro enzymes

- Pepsinogen
- Trypsinogen
- Profibrolysin

ISOENZYMES

- Physically distinct forms or protomers of an oligmeric enzyme which can occur in different tissues of same organs, in different cell types, or in sub cellular compartments catalyzing same reaction. these can be separated by electrophoresis.

- Lactate dehydrogenase on electrophoresis gives 5 different bands and has 4 protomers



CREATININE KINASE (CK): 3 ISOENZYMES

CK1	BB	OCCURS IN BRAIN,SMOOTH MUSCLES of GIT AND URINARY TRACT
CK2	MB	MYOCARDIUM (35 %), SK MUSCLE (5%) ↑ IN ACUTE MI
CK3	MM	OCCURS IN SK MUSCLES ↑ IN MUSCLE DYSTROPHIES

LACTATE DEHYDROGENASE: 5 ISOENZYMES

LDH 1	HHHH	Occurs in myocardium(aerobic tissues) ↑in Acute Myocardial Infarction
LDH 2	HHHM	↑ In Acute Leukemia
LDH 3	HHMM	↑ In Acute Leukemia
LDH 4	HMMM	Occurs in muscle and liver (anaerobic tissues)
LDH 5	MMMM	Occurs in muscle and liver (anaerobic tissues) ↑ in Liver Diseases

CLINICAL ENZYMOLOGY

- **CLASSIFICATION OF ENZYMES IN BLOOD**
  - PLASMA SPECIFIC ENZYMES: PROCOAGULANTS, FIBRINOALYTIC ENZYMES
  - SECRETED ENZYMES: LIPASE, α-AMYLASE, ACID PHOSPHATASE
  - TRUE CELLULAR ENZYMES: LDH, ALT, AST, ALP

CLINICAL ENZYMOLOGY

STUDY OF PLASMA ENZYME LEVELS IN THE DIAGNOSIS OF VARIOUS DISEASES

- **PLASMA ENZYME LEVEL DEPENDS ON**
  - **RATE OF RELEASE FROM DAMAGED CELL**
  - **EXTENT OF CELL DAMAGE**
- **IN THE ABSENCE OF CELL DAMAGE, IT DEPENDS ON**
  - **RATE OF CELL PROLIFERATION**
  - **DEGREE OF INDUCTION OF ENZYME SYNTHESIS**
  - **RATE OF ENZYME CLEARANCE FROM CIRCULATION**

CLINICAL ENZYMOLOGY

PHYSIOLOGICAL FACTORS/VARIATIONS

- PLASMA AST IS INCREASED IN NEONATES
- ALKALINE PHOSPHATASE IS INCREASED IN CHILDREN AND IN LAST TRIMESTER OF PREGNANCY
- TRANSAMINASES AND CREATINE KINASE INCREASED AFTER LABOUR

CLINICAL ENZYMOLOGY
MYOCARDIAL DISEASES

- **CREATINE PHOSPHOKINASE(CK,CPK)**
  - PRESENT IN HEART, SKELETAL MUSCLES
  - NORMAL LEVEL TOTAL: LESS THAN 195 U/L
  - MODERATE INCREASE
    - MUSCLE INJURY
    - AFTER EXERTION
    - AFTER SURGERY

CLINICAL ENZYMOLOGY
MYOCARDIAL DISEASES

–SIGNIFICANT INCREASE

- MYOCARDIAL INFARCTION
- 4-8 HRS AFTER THE ATTACK
- PEAK 24-48 HRS
- NORMALIZES WITHIN 3-5 DAYS(IF NO FRESH ATTACK HAS OCCURRED)

– CIRCULATORY FAILURE

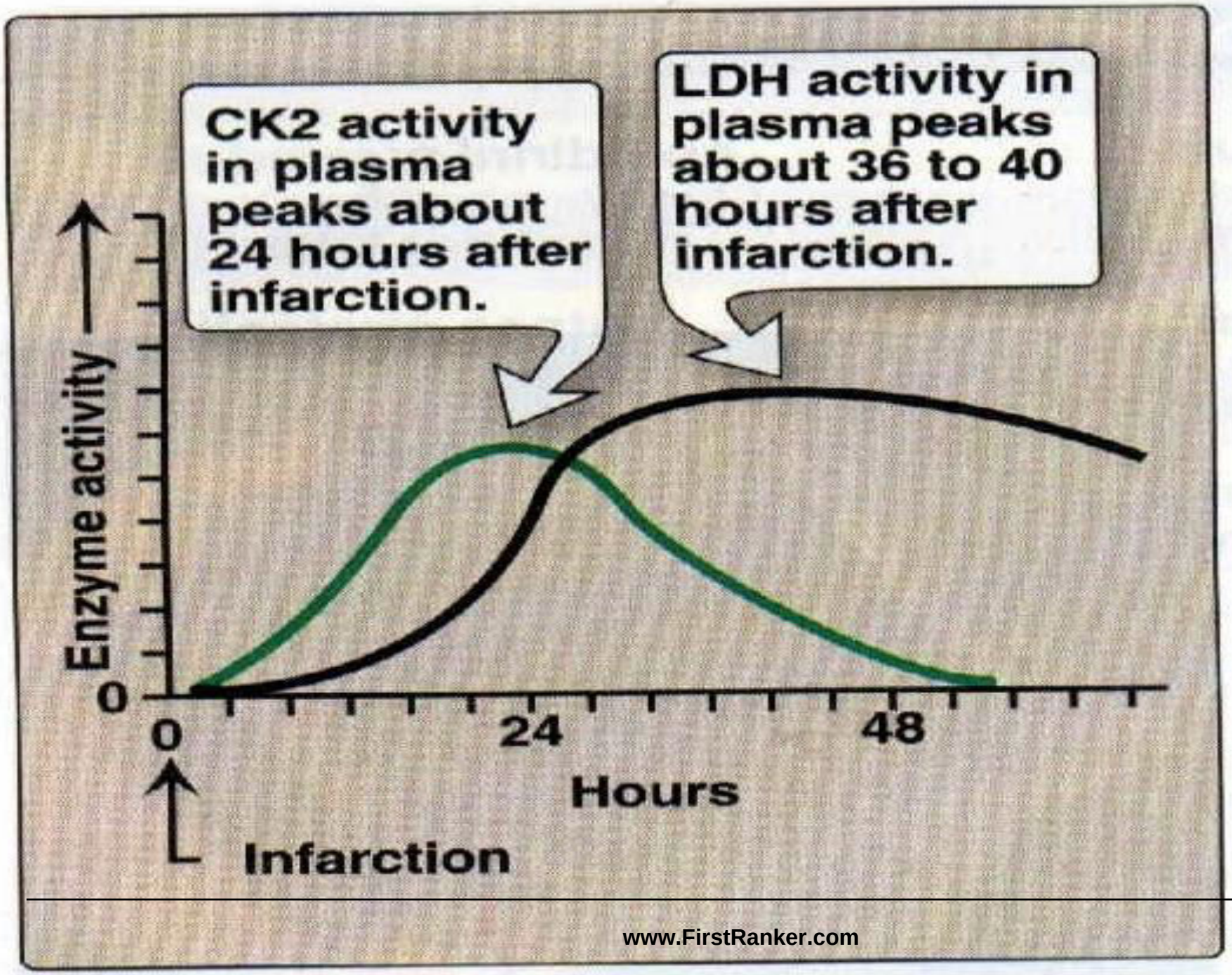
– MUSCLE DYSTROPHIES

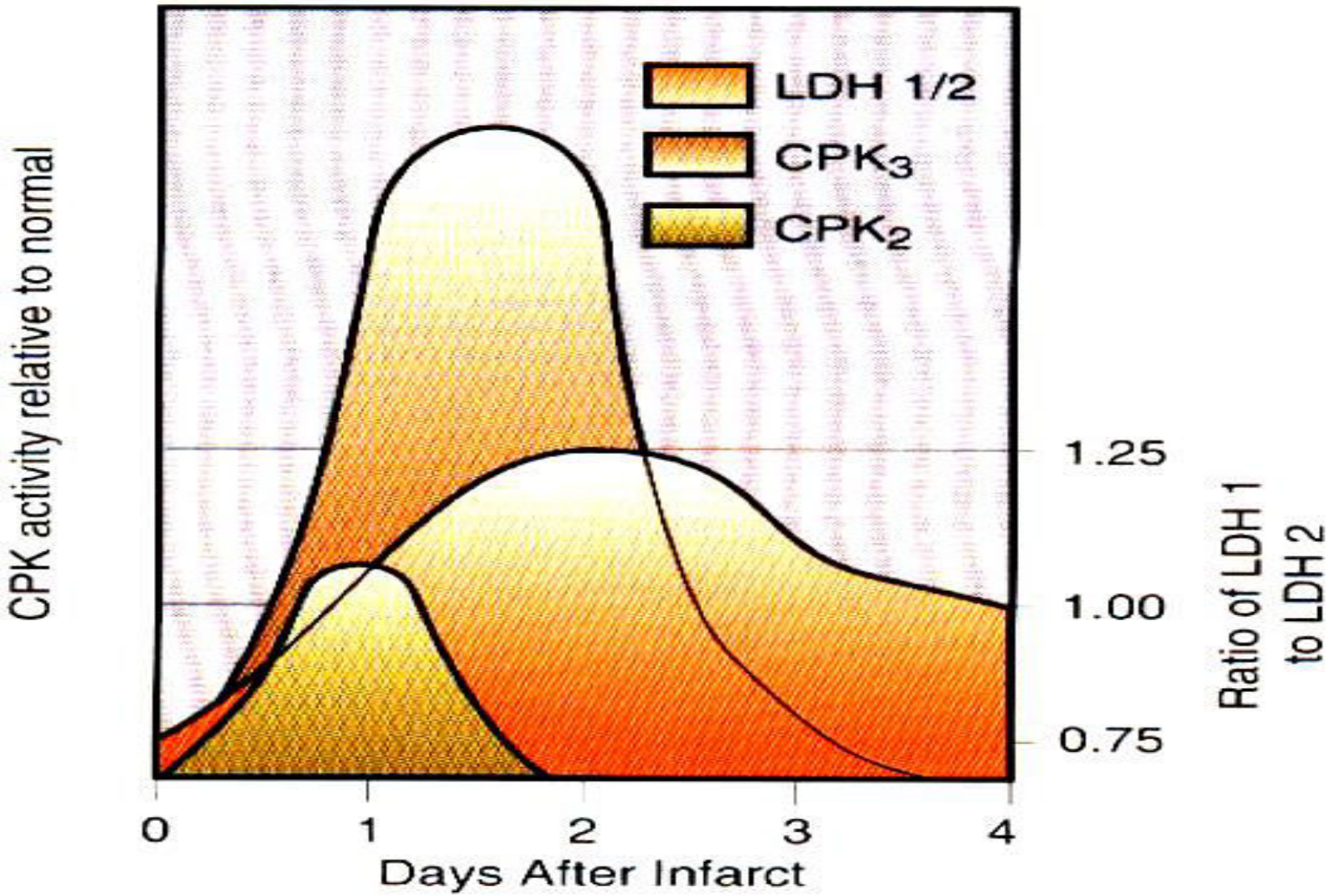
CLINICAL ENZYMOLOGY

MYOCARDIAL DISEASES

LACTATE DEHYDROGENASE (LDH,LD)

- PRESENT IN HEART SKELETAL MUSCLE, LIVER AND KIDNEYS
- NORMAL SERUM LEVEL 125-220 U/L
- **MODERATE INCREASE**
  - VIRAL HEPATITIS
  - SKELETAL MUSCLE DISEASE
  - MALIGNANCY OF ANY TISSUE
- **SIGNIFICANT INCREASE**
  - MYOCARDIAL INFARCTION
  - 24-48 HRS AFTER THE ATTACK
  - PEAK = 2-3 DAYS
  - NORMALIZES 7-12 DAYS(IF NO FRESH ATTACK HAS OCCURRED)





Characteristic changes in serum CPK and LDH isozymes following a myocardial infarction.

CLINICAL ENZYMOLOGY

TRANSAMINASES

NORMAL LEVELS	AST (U/L)	ALT(U/L)
MALES 20-60 YRS:	LESS THAN 40	LESS THAN 45
OVER 60 YRS:	35	40
FEMALES:	35	40
PREGNANCY	40	40
3RD TRIMESTER:		

CLINICAL ENZYMOLOGY

ASPARTATE TRANSAMINASE (AST OR SGOT)

- PRESENT IN HEART, LIVER, MUSCLES, KIDNEYS, RBCs, MITOCHONDRIAL AND CYTOSOLIC ENZYME
- MODERATE INCREASE
  - CIRRHOSIS OF LIVER
  - SKELETAL MUSCLE DISEASE
  - AFTER TRAUMA OR SURGERY
- SIGNIFICANT INCREASE
  - MYOCARDIAL INFARCTION
  - 8-12 HRS AFTER THE ATTACK
  - PEAK = 24 HRS
  - NORMALIZES 5-6 DAYS

CLINICAL ENZYMOLOGY

LIVER DISEASES

ALANINE TRANSAMINASE (ALT OR SGPT)

- PRESENT IN LIVER, SKELETAL MUSCLE, KIDNEYS & HEART, CYTOSOLIC ENZYME
- MODERATE INCREASE
  - CIRRHOSIS OF LIVER
  - LIVER CONGESTION
  - CONGESTIVE CARDIAC FAILURE
  - JAUNDICE
  - CIRCULATORY FAILURE
- SIGNIFICANT INCREASE
  - ACUTE VIRAL OR TOXIC HEPATITIS

CLINICAL ENZYMOLOGY
LIVER DISEASES

- **ALKALINE PHOSPHATASE (ALP)**

- **PRESENT IN BONE, HEPATOBILIARY, INTESTINAL TRACT, RENAL TUBULES & PLACENTA**

- **NORMAL SERUM LEVELS**
- **MALES: 40-258 U/L**
- **FEMALES: 35-258 U/L**

CLINICAL ENZYMOLOGY

LIVER DISEASES

ALKALINE PHOSPHATASE (ALP)

- SIGNIFICANT INCREASE
  - BONE DISEASES LIKE OSTEOMALACIA, RICKETS, PAGET'S OSTEOGENIC CARCINOMA & SECONDARY DEPOSITS IN BONE.
  - LIVER DISEASES LIKE CHOLESTATIC JAUNDICE, TUMOR OR DRUG INTOXICATION
  - TUMOR: BONE OR LIVER, DIRECT OR SECONDARY DEPOSITS

CLINICAL ENZYMOLOGY

LIVER DISEASES

ALKALINE PHOSPHATASE (ALP)

- SIGNIFICANT INCREASE
  - BONE DISEASES LIKE OSTEOMALACIA, RICKETS, PAGET'S OSTEOGENIC CARCINOMA & SECONDARY DEPOSITS IN BONE.
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  - TUMOR: BONE OR LIVER, DIRECT OR SECONDARY DEPOSITS

CLINICAL ENZYMOLOGY

LIVER DISEASES

- **GAMA GLUTAMYL TRANSFERASE (γGT)**
- **PRESENT IN LIVER, KIDNEYS, PANCREAS AND PROSTATE**
- **NORMAL SERUM LEVELS: MALES 30 U/L**
  FEMALES < 25 U/L

- **SIGNIFICANT INCREASE**
- **INDUCTION BY ALCOHALS AND DRUGS LIKE PHENOBARBITONE**
- **CHRONIC ALCOHALIC HEPATITIS**
- **CHOLESTATIC LIVER DISEASE**

CLINICAL ENZYMOLOGY
LIVER DISEASES

- **CHOLENESTERASE**
- PRESENT IN NERVOUS TISSUE AND RBCs. AND IN LIVER
- NORMAL SERUM LEVEL 0.6-2.4 U/L

- **SIGNIFICANT DECREASE**
- ORGANOPHOSPHORUS INSECTISIDE PIOSONING
- LIVER DISEASE

CLINICAL ENZYMOLOGY

AMYLASE

- PRESENT IN SALIVA AND PANCREATIC JUICE. MAY BE EXTRACTED FROM GONADS, SKELETAL MUSCLES AND ADIPOSE TISSUE
- NORMAL SERUM LEVEL 28 –100 U/L

MODERATE INCREASE

- ACTUE CHOLECYSTITIS
- INTESTINAL OBSTRUCTION
- MUMPS
- SALIVARY CALCULI
- ABDOMINAL TRAUMA

SIGNIFICANT INCREASE

- ACUTE PANCREATITIS
- PERFORATED PEPTIC ULCER

CLINICAL ENZYMOLOGY

ACID PHOSPHATASE (ACP)

- PRESENT IN PROSTATE LIVER, R.B.C. PLATELETS
- NORMAL SERUM LEVEL UPTO 4 U/L
- **MODERATE INCREASE**
- AFTER RECTAL EXAMINATION
- AFTER PASSAGE OF CATHETER
- **SIGNIFICANT INCREASE**
- CARCINOMA OF PROSTATE
- BONE DISEASE LIKE PAGET'S DISEASE

CLINICAL ENZYMOLOGY

- **ISOCITRIC DEHYDROGENASE**
- LIVER AND CEREBRAL TUMORS, MENINGITIS
- **LEUCINE AMINOPOLYPEPTIDASE**
- HEPATOBILIARY AND PANCREATIC DISEASE

- **5, NUCLEOTIDASE**
- OBSTRUCTIVE JAUNDICE
- **GLUTATHIONE REDUCTASE**
- HEPATITIS AND MALIGNANCY

- **ALDOLASE**
- PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHIES

CLINICAL APPLICATIONS OF ENZYMES

- PROTEASES, RNASES ARE USED IN DEBRIDEMENT OF WOUNDS
- STREPTOKINASE USED FOR CLEARING BLOOD CLOTS AFTER ACUTE MYOCARDIAL INFARCTION & IN LOWER EXTREMITIES. IT ACTIVATES PLASMINOGEN INTO PLASMIN, A SERINE PROTEASE THAT CLEAVES FIBRIN IN BLOOD CLOTS INTO SEVERAL SMALLER SOLUBLE COMPONENTS.

CLINICAL APPLICATIONS OF ENZYMES

- t-PA(HUMAN TISSUE PLASMINOGEN ACTIVATOR) COMERCIALLY PRODUCED FROM *'E.coli'* IS USED IN DISSOLVING BLOOD CLOTS IN ACUTE MI BY ACTIVATING PLASMINOGEN INTO PLASMIN.