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HIGHLIGHTS

The perfect Biochemistry book for Medical PG aspirants:

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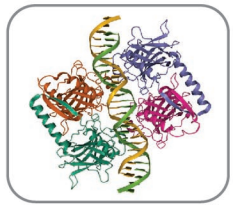

9th Edition

Rebecca James Perumcheril

All Recent Model Questions (2024–2000)
INI-CET (2024–2020), AIIMS (Nov 2019–2000)
AIPGMEE (2012–2000), PGI (Nov 2019–2000)
JIPMER (2019–2000), NEET Pattern (2024)
& Various State and Deemed University Exams

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Contents

Most Important★★★★★ (Learn Completely)
Very Important★★★★ (Learn Completely)
Important★★★ (Selective Reading)
No Star Topics – Selective Reading Based on Check List Given after Every Subchapter

1.1 CHEMISTRY OF AMINO ACIDS

- Structure of Amino Acids
- Beta Alanine
- Classification of Amino Acids.
- Decarboxylation of Amino Acids
- Abbreviations of Amino Acids
- Colour Reactions of Amino Acids
- Derived Amino Acids
- Buffering Action of Amino Acids
- Properties of Amino Acids
- Titration Curve

GENERAL STRUCTURE OF ALPHA AMINO ACID

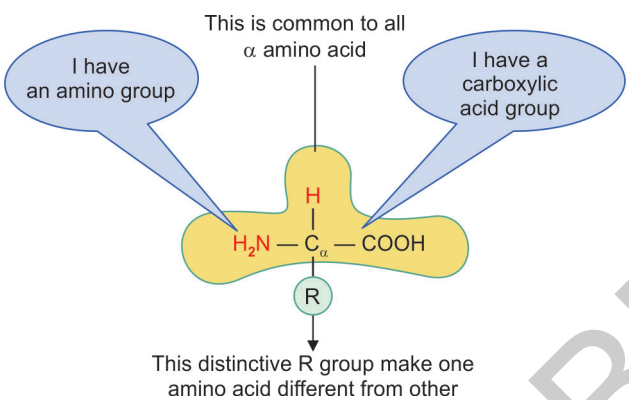


Fig. 1.1.1: Basic structure of amino acid

Alpha Amino Acid

Amino group and carboxyl group attached to the alpha carbon atom.

Most of the amino acids are **alpha amino acid**.

Non-Alpha Amino Acid

Unlike alpha amino acids either carboxyl group or Amino group is not attached to the alpha carbonatom.

Non-alpha amino acids present in tissues in free form are:

- β Alanine
- β Amino Isobutyrate
- γ-Amino Butyrate

Imino Acid—Proline

The α amino nitrogen form a rigid five membered **pyrrolidine ring**. Then this amino group is called a **secondary amino group**. So proline is referred to as an **imino acid.** Still it can form a peptide bond.

- It favors the unique triple helix in collagen.
- But it interrupts the alpha helix found in most globular proteins.

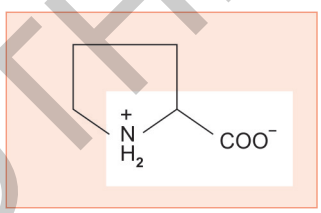
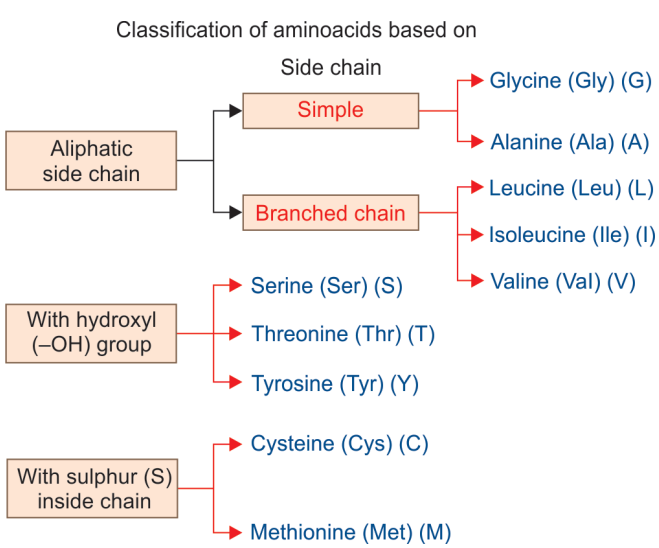


Fig. 1.1.2: Structure of amino acid, proline

CLASSIFICATION OF AMINO ACIDS[Q]

- Based on the variable side chain (R group)
- Based on side chain characteristics (polarity)
- Based on nutritional requirement.
- Based on metabolic fate.

Based on Variable Side Chain[Q]



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- Acidic (–COOH) group in side chain
  - Aspartic acid (Asp) (D)
  - Glutamic acid (Glu) (E)
- Amides ($CO–NH_2$) in the side chain
  - Asparagine (Asn) (N)
  - Glutamine (Glu) (Q)
- Basic ($–NH_2$) group in side chain
  - Histidine (His) (H)
  - Arginine (Arg) (R)
  - Lysine (Lys) (K)
- With aromatic ring
  - Histidine (His) (H)
  - Phenylalanine (Phe) (F)
  - Tyrosine (Tyr) (Y)
  - Tryptophan (Trp) (W)
- Imino acid
  - Proline (Pro) (P)

High Yield Points —Amino acids

- Aromatic amino acid with hydroxyl group is Tyrosine
- Aromatic amino acid with basic properties is Histidine
- Amino acid with secondary amino group is Proline
- Amino acid that form disulphide bond in proteins is Cysteine
- At physiologic pH, negatively charged amino acids are Aspartic acid and Glutamic acid
- At physiologic pH, positively charged amino acids are Arginine, Lysine and Histidine
- Most basic amino acid is Arginine
- Amino acid with maximum number of amino group is Arginine

Based on Side Chain Characteristic (Polarity)Q

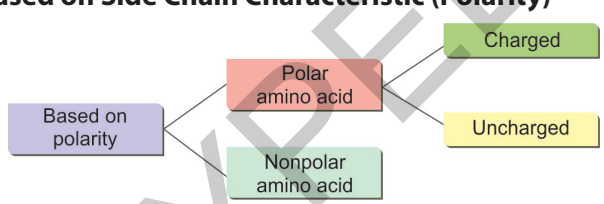


Fig. 1.1.3: Classification of amino acid based on polarity

Flowchart 1.1.1: Classification of amino acid based on side chain characteristics

- Polar (Hydrophilic)
  - Charged
    - I Acidic aa
      1. Aspartic acid
      2. Glutamic acid
    - II Basic aa
      1. Histidine
      2. Arginine
      3. Lysine
  - Uncharged
    - I Amide
      1. Asparagine
      2. Glutamine
    - II Hydroxyl group containing
      1. Serine
      2. Threonine
    - III Simple aa
      1. Glycine only
    - IV Sulphur containing
      1. Cysteine only
- Nonpolar (Hydrophobic)
  - I Branched chain aa
    1. Leucine
    2. Isoleucine
    3. Valine
  - II Aromatic aa
    1. Phehylalanie
    2. Tyrosine
    3. Tryptophan
  - III Simple aa
    1. Alanine only
  - IV Sulphur containing aa
    1. Methionine only

Concept Box

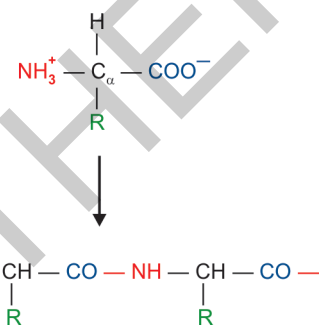
Why amino acids are classified based on its side chain?

Alpha amino acids

At physiological pH, alpha carboxyl group is deprotonated and negatively charged COO^- and amino group is protonated and positively charged (NH_3^+) They are reactive group.

Alpha amino acids forming peptide bond

But in proteins the alpha carboxyl group and alpha amino group are combined through peptide bond. So ultimately the side chain R group determines the role of amino acids in proteins. Hence amino acids are classified based on side chain.



Tips to Memorise

Polar and Nonpolar Amino Acid

- *Learn polar and nonpolar amino acid by classifying the amino acid rather than learning name of individual amino acid.*
- *Charged amino acids are Polar. Charged amino acids are Acidic and Basic amino acids.*
- *Mnemonic ABC: Acidic and Basic amino acids are Charged amino acids*
- *All branched chain amino acids are nonpolar.*
- *All aromatic amino acids except Histidine are nonpolar.*

Flowchart 1.1.2: Concept of polar side chain

- Concept of polar side chain
  - Charged
    - At physiological pH its fully ionized
      - Acidic side chain is –vely charged ($– COO^-$)
      - Basic side chain is + vely charged $– NH_3^+$
  - Uncharged
    - At physiological pH they have zero net charge
      - – OH group can form hydrogen bond
      - – SH group can form disulphide bond
      - – OH group are site of attachment of phosphate and other compounds

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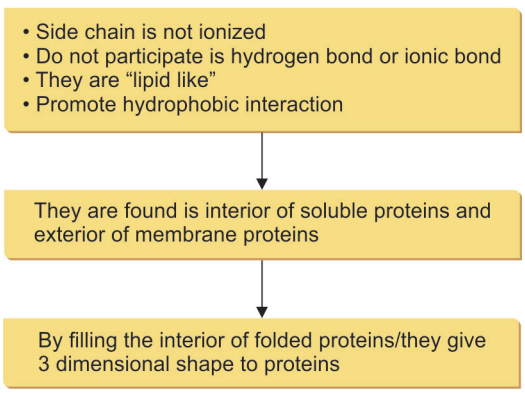
Flowchart 1.1.3: Concept of nonpolar side chain



Practical tips to approach controversial questions.

1. **Glycine polar or nonpolar?**
   Yes, Glycine is polar; but it is least polar among the polar amino acid.
   It exhibits some nonpolar nature also.
2. **Tyrosine polar or nonpolar?**
   Tyrosine is significantly polar amino acid among the nonpolar amino acid.

How to approach such questions?

1. **Which of the following amino acid is polar?**
   a. Glycine
   b. Arginine
   c. Leucine
   d. Isoleucine

Choose arginine as answer NOT Glycine.

2. **Which of the following amino acid is nonpolar?**
   a. Tyrosine
   b. Leucine
   c. Arginine
   d. Lysine

Choose Leucine as the answer

Among the nonpolar amino acids, Tyrosine and Leucine choose leucine as the best answer as Tyrosine has some polar nature due to the hydroxyl group.

Based on Metabolic Fate[Q]

Classified into:

1. **Ketogenic:** Amino acids that are converted to Acetyl CoA and thereby to ketogenic pathway
2. **Glycogenic:** Amino acids that enter into glucogenic pathway
3. **Both glycogenic and ketogenic:** That can enter into both ketogenic and glucogenic pathway.

Classification of Amino	Amino Acid
Purely Ketogenic	Leucine[Q] ***Lysine***
Both Ketogenic and Glycogenic	**P**henylalanine, **I**soleucine, **T**yrosine **T**ryptophan
Glycogenic	Any amino acid that do not belong to the above groups

Tips to Memorise

Classification Based on Metabolic Fate

First learn the amino acids which are Ketogenic, and then learn amino acids which are both Glucogenic and Ketogenic.

Mnemonic to learn both Ketogenic and Glycogenic—PITT (Lysine, Phenylalanine, Isoleucine, Tyrosine, Tryptophan).

All the rest amino acids are purely glycogenic

Practical tips to approach controversial questions

Example: 1 (multiple response PGI type)

1. **Which of the following amino acids are ketogenic?**
   a. Lysine
   b. Leucine
   c. Alanine
   d. Tyrosine
   e. Isoleucine

Answers are a, b, d, e, i.e. Lysine, Leucine, Tyrosine, Isoleucine. Here you have to consider all ketogenic amino acids. Among these options, exclude only Alanine as it is purely glucogenic.

Based on Nutritional Requirement[Q]

- **Essential:** Those amino acids which cannot be synthesized in the body[Q]. Hence these amino acids are to be supplied in the diet.
- **Semiessential:** Growing children require them in the food, but not essential in adults.
- **Nonessential:** Amino acids which can be synthesized in the body[Q], hence not required in the diet.

Nutritionally Essential	Nutritionally Nonessential
Methionine	All the other amino acids
Threonine	
Tryptophan	
Valine	
Isoleucine	
Leucine	
Phenylalanine	
Lysine	
Histidine	
Arginine***	

***Arginine is nutritionally semiessential. Because it is inadequately synthesized in growing children.

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Tips to Memorise

Essential Amino Acids

Mnemonic to learn essential amino acids—MeTT VIL PHLY (read as Met will fly).

Methionine, Threonine, Tryptophan, Valine, Isoleucine, Leucine, Phenylalanine, Lysine.

Practical tips to approach controversial questions

Is histidine essential or semiessential?

Although histidine is considered essential, unlike the other essential it does not fulfill the criteria of inducing negative nitrogen balance promptly upon removal from the diet.

How to approach such question?

Example 1:

- **Which of the following amino acid is semiessential?**

  a. Lysine b. Tyrosine

  c. Arginine d. Histidine

  For single response type of question choose Arginine as the answer NOT Histidine.

Example 2:

- **Which of the following amino acid is semiessential?**

  a. Histidine b. Glycine

  c. Tyrosine d. Glutamate

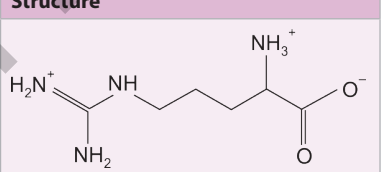
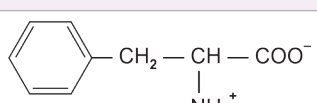
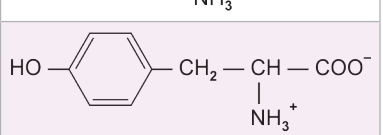
  From these options, Histidine is the single best answer.

Concept Box

What makes certain amino acids nutritionally essential?

The lengthy pathway to synthesize certain amino acids make certain amino acids essential. All nonessential amino acids need 1 or 2 enzymes for its synthesis. But essential amino acids need more than 5 enzymes.

Special Groups Present in Amino Acids

Amino acid	Special group	Structure
Arginine	Guanidinium[Q]	
Phenylalanine	Benzene	
Tyrosine	Phenol	

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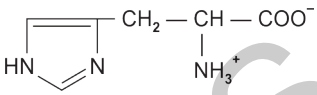
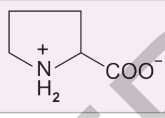
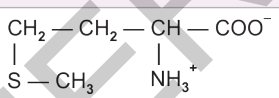
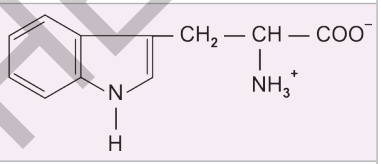
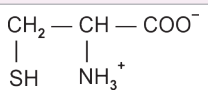
Amino acid	Special group	Structure
Histidine	Imidazole[Q]	
Proline	Pyrrolidine	
Methionine	Thioether Linkage	
Tryptophan	Indole	
Cysteine	Thioalcohol (SH) or Sulfhydryl group or Thiol	

Conservative (Homologous) Substitution

One amino acid replaced by another amino acid of similar characteristics.

Examples of homologous substitution is shown in the diagram given below.

Conservative Mutation

Hydrophilic, Acid	Asp	Glu				
Hydrophilic, Basic	His	Arg	Lys			
Polar, Uncharged	Ser	Thr	Gln	Asn		
Hydrophobic	Ala	Phe	Leu	Ile	Val	Pro

Nonconservative (Nonhomologous) Substitution

One amino acid replaced by another amino acid of different characteristics.

21st and 22nd Amino Acids[Q]

Selenocysteine

- 21st protein forming Amino Acid[Q]
- Precursor amino acid for selenocysteine is Serine[Q]
- **Serine** is modified to cysteine. Selenium replaces sulphur of cysteine cotranslationally
- In humans approximately 2 dozen selenoproteins are there, that includes Peroxidase[Q] and Reductases[Q].

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Seen in the active site of following enzymes and proteins:[Q]

- Thioredoxin reductase
- Glutathione peroxidase
- Iodothyronine deiodinase
- Selenoprotein P

Recoding

- Selenocysteine is coded by a stop codon, UGA
- This process of converting stop codon to a coding codon is called Recoding
- SECIS element in the mRNA help in this process

Pyrrolysine

- 22nd protein forming Amino Acid
- By recoding **UAG** stop codon, helped by PYLIS element in the mRNA.

DERIVED AMINO ACIDS

Classified into:

- Derived amino acids seen in proteins
- Derived amino acids not seen in proteins

Derived Amino Acid seen in Protein[Q]

4-Hydroxy Proline	• Found in Collagen • Vitamin C is needed for hydroxylation.
5-Hydroxy Lysine	
Methyl lysine	• Found in Myosin
Gamma carboxy glutamate	• Found in clotting factors, like Pro-thrombin that bind Ca^{2+} • Vitamin K is needed for Gamma carboxylation
Cystine	• Found in proteins with disulphide bond.[Q] • Two cysteine molecules join to form cystine • For example, Insulin, Immunoglobulin
Desmosine	• Found in Elastin[Q]

Derived Amino Acid not Seen in Protein[Q]

Ornithine	Intermediates of Urea Cycle
Arginosuccinate	
Citrulline	
Homocysteine	Derived from Methionine[Q]
Homoserine	Product of Cysteine biosynthesis
Glutamate-γ Semialdehyde	Serine catabolite

PROPERTIES OF AMINO ACID

More than 300 naturally occurring amino acids exist in nature out of which 20 amino acids constitute monomer units of proteins.

Derived amino acids do not have a genetic code.[Q]
Amino acids coded by stop codon are: Selenocysteine, Pyrrolysine

I. Amino Acids Exist in Different Charged State

Depends on the two factors:

- Isoelectric pH of the amino acid.
- pH of the surrounding medium.

Isoelectric pH of Amino Acids

1. At pH = Isoelectric pH(pI)

- The amino acid carry equal number of positive and negative charge, i.e. **NO NETCHARGE.**
- Amino acid exists as **ZWITTER ION (AMPHOLYTE)**

Zwitter Ions or Ampholytes

Molecules which carry equal number of ionizable groups of opposite charge and therefore bear no net charge are called **Zwitter ions or ampholytes**[Q]**.** Zwitter is agerman word which means hermaphrodite.

High Yield Points

Properties of Amino acid at Isoelectric pH (pI)

- No mobility in electric field.[Q]
- Minimum solubility.
- Maximum precipitability.[Q]
- Minimum Buffering capacity.

2. At pH less than isoelectric pH (pI)

Amino acid exists as protonated or positively charged.

3. At pH greater than isoelectric pH (pI)

Amino acid exists as deprotonated or negatively charged.

The charge of carboxyl group and amino group at physiological pH (pH = 7.4)

- Carboxyl group is negatively charged
- Amino group is positively charged.

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High Yield Points

How to calculate isoelectric pH of amino acid?

Fact-1

Isoelectric pH (pI) is average of pKa of ionisable groups.

First we calculate the pI of Alanine

pK_1 of αCOO^- group is 2.35

pK_2 of αNH_3^+ is 9.69

$$\text{So pI} = \frac{pK_1 + pK_2}{2}$$

$$\textbf{pI of Alanine} = \frac{9.69 + 2.35}{2} = \textbf{6.02}$$

Fact-2

If the amino acid has ionisable group other than alpha carboxylic and alpha amino group, then isoelectric pH is the average of pKa of isoionic group.

Calculate pI of Aspartic acid

Aspartic acid has an extracarboxylic group.

pKa of αCOO^- group = 2.09

pKa of αNH_3^+ group is = 9.9

pKa of COO^- group in the side chain (R) = 3.96

pI = average pKa of isoionic species, which means we have to find the average of pKa of two COO^- group

$$\text{pI} = \frac{2.09 + 3.96}{2}$$

So pI of Aspartic acid is 3.02

II. Amino Acids Exhibit Isomerism

Amino acids have asymmetric (chiral) alpha carbonatom. The mirror images produced with reference to alphacarbon atom, are called D and L forms or enantiomers.

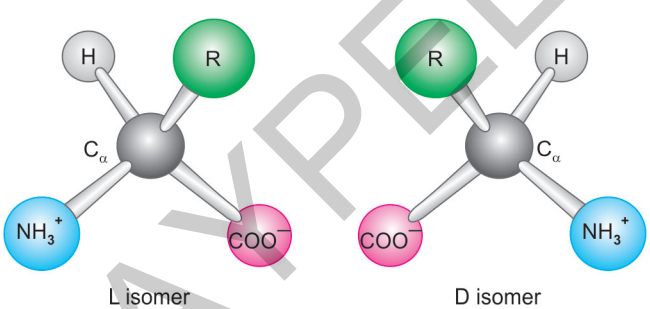

Fig. 1.1.4: L and D amino acid

- Almost all naturally occurring amino acids are **L-Isomers**
- Some naturally occurring amino acids are D **Amino acids**.

Naturally Occurring D Amino Acid

- Free D Aspartate and Free D Serine in brain tissue
- D-Alanine and D Glutamate in cell walls of gram positive bacteria
- *Bacillus subtilis* excretes D-methionine, D-tyrosine, D-leucine, and D-tryptophan to trigger biofilm disassembly
- *Vibrio cholerae* incorporates D-leucine and D-methionine into the peptide component of their peptidoglycan layer.

High Yield Points

- *Amino Acid with No Chiral/No Asymmetric/No Optically Active Carbon* ***Glycine***[Q]
- Source of D-Amino acids in humans is exogenous[Q].
- The enzyme that interconvert D and L isomers is Racemase.

III. Amino Acids Absorb UV Light

Amino acids which absorb **250–290 nm** (Maximum at **280 nm**) UV light are **tryptophan, phenylalanine, tyrosine.** Maximum absorption of UV light by **tryptophan.**[Q]

High Yield Points

- Aromatic amino acids absorb UV light.
- Amino acids are color less because they do not absorb visible light.

Image-Based Information

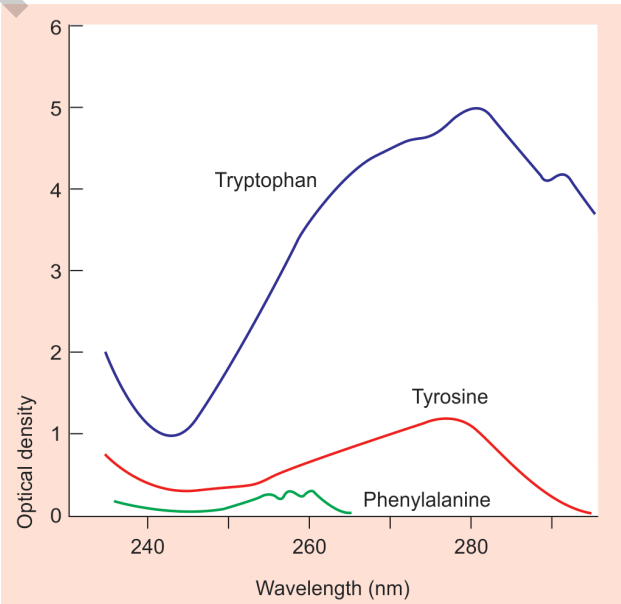

Fig. 1.1.5: Ultraviolet absorption spectra of aromatic amino acids

BETA-ALANINE

Formed from **Cytosine and Uracil.**[Q]

Other sources of Beta Alanine is hydrolysis of Beta alanyl dipeptides.

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Beta Alanine is seen in[Q]
- Pantothenic Acid
- Coenzyme A
- Acyl Carrier Protein
- Beta Alanyl Dipeptides.

Beta Alanyl Dipeptides are
- Carnosine [Histidine + Beta alanine]
- Anserine [N methyl Carnosine]
  Both present in **Skeletal muscle**

Uses of Carnosine
- Activate Myosin ATPase.
- Chelate Copper
- Enhance Copper uptake
- Buffers the pH of anaerobically contracting muscle.

High Yield Points
- Homocarnosine is GABA + Histidine
- There is no beta alanine in homocarnosine

DECARBOXYLATION OF AMINO ACID

- The amino acid undergo alpha decarboxylation to form corresponding Amines
- **PLP**[Q] **is the coenzyme for this reaction.**

Examples of Amino Acid Decarboxylation

Amino acid	Biologic Amines
Histidine	Histamine
Tyrosine	Tyramine
Tryptophan	Tryptamine
Lysine	Cadaverine
Glutamic acid[Q]	Gamma Amino Butyric Acid (GABA)
Serine	Ethanolamine
Cysteine	Betamercapto Ethanolamine

High Yield Points
- Amino acids undergo decarboxylation to form corresponding amines.
- **PLP** is the coenzyme for Amino Acid Decarboxylation
- Amino acids undergo deamination to form corresponding Ketoacids.
- Most common amino acid that undergo Oxidative deamination is **Glutamic Acid (Glutamate)**
- Glutamic acid undergo decarboxylation to form **GABA**
- Glutamic Acid undergo deamination to form **Alpha Keto Glutarate**

COLOUR REACTIONS OF AMINO ACIDS

Biuret Test

- General test for Proteins
- Cupric ions in alkaline medium forms violet colour with peptide bond nitrogen.

Remember

Dipeptides and individual amino acid do not answer biuret test because this test needs a minimum of two peptide bonds.

Ninhydrin Test

General test for all alpha Amino Acid + 2 mols of Ninhydrin ⟶ Aldehyde with 1 carbon atom less + CO_2 + Purple Complex (Ruhemann's Purple).

Remember

- Amino acid which do not give purple colour are:
  - Proline and Hydroxy proline (Yellow colour)
  - Glutamine and Asparagine (Brown colour)

Colour Reactions	Test answered by
Xanthoproteic Test **(Conc HNO_3 is a reagent**[Q]**)**	Aromatic Amino Acid[Q] *DNB* (Phenylalanine, Tyrosine, Tryptophan)
Millon's test	Tyrosine (Phenol)
Aldehyde test can be done in two methods: • Acree Rosenheim Test (Formaldehyde and Mercuric Sulphate is used) • Hopkin's Cole Test[Q] • (Glyoxylic Acid is used)	Tryptophan (Indole group)
Saka **G**uchi's test	Arginine (**G**uanidinium group) Mnemonic–G is common to all
Sulphur test	Cysteine
Cyanide Nitroprusside Test	Homocysteine
Pauly's Test	Histidine (Imidazole) Tyrosine (Phenol)

Methionine does not answer Sulphur test because sulphur in methionine is in the thioether linkage which is difficult to break.

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BUFFERING ACTION OF AMINO ACIDS

- Buffers are solutions which can resist changes when acid or alkali is added.

Henderson Hasselbalch Equation

pH = pKa + log [Base]/[Acid]

When [Base] = [Acid] pH = pKa

Maximum buffering capacity is at **pH = pKa**. So amino acid which has pKa range near physiologic pH can act as an effective buffer.

pKa of Imidazole group of histidine is 6.5–7.4.

Hence at physiologic pH, **Imidazole** group of Histidine has the maximum buffering capacity.[Q]

TITRATION CURVE

Titration is done to find out the amount of acid in a given solution. To find out that a measured volume of acid is titrated against a strong alkali. The endpoint of titration is the point at which the pH of solution is 7. A plot called titration curve is obtained.

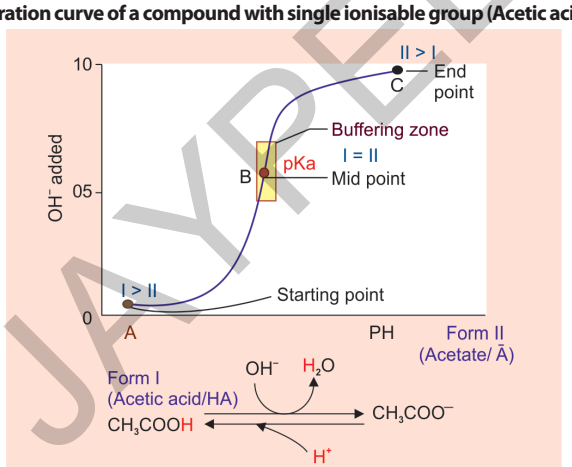
Definition of titration curve

A plot of (OH–) added (represented in equivalents) against pH is called Titrarion curve.

- Let us see the important landmarks in Titration curve of weak acids and certain amino acids in the Image-based Information boxes.

IMAGE-BASED INFORMATION

Titration curve of a compound with single ionisable group (Acetic acid)



At point A-Most of the Acetic acid is **unionized**

At point B-the pH = pKa and Acetic acid is **partially ionized** ($CH_3COOH = CH_3COO^-$).

Buffering region of Acetic acid is at pH = pKa + / -1

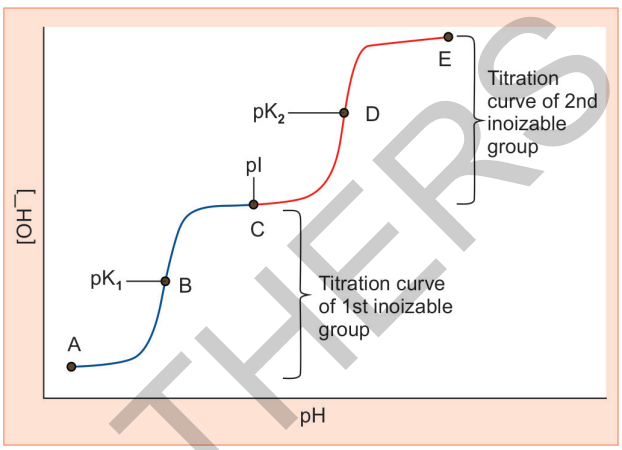
The **horizontal segment of titration curve shown in blue colour is the buffering region.**

At point C-Acetic acid completely ionized (CH_3COO^-)

IMAGE-BASED INFORMATION

Titration Curve of Amino acid, Glycine

Titration curve of a compound with 2 ionizable group



pK_1 = Ionization constant of Ist ionizable group

pK_2 = Ionization constant of IInd ionizable group

$pI = \frac{pK_1 + pK_2}{2}$ = isoelectric pH

Titration curve of compound with two ionizable groups

Ionization constant of each ionisable group is the midpoint of each curves.

Buffering region is at pH ± 1 of pKa of ionisable group.

Buffering region is shown in blue colour.

Point C is the isoelectric pH(pI)

IMAGE-BASED INFORMATION

Titration Curve of Amino acid, Histidine

Titration curve of a compound with three ionisable group

TC-1 Titration Curve of first ionisable group

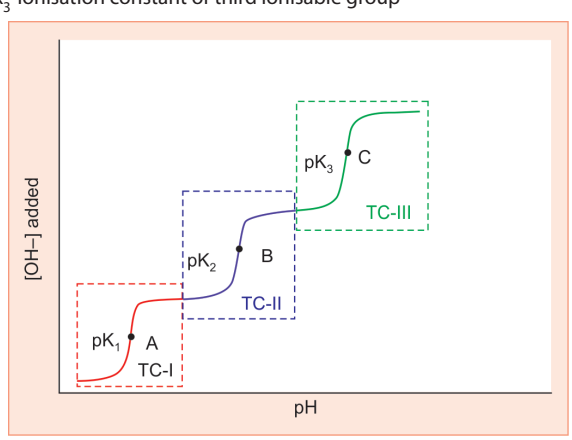
TC-2 Titration curve of second ionisable group

TC-3 Titration curve of third ionisable group

pK_1-Ionisation constant of first ionisable group

pK_2-Ionisation constant of second ionisable group

pK_3-Ionisation constant of third ionisable group



As histidine has three ionisable group three curves TC-I, TC-II and TC-III are present.

TC = Titration curve; pK = ionization constant

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High Yield Points

Amino Acids

- Simplest Amino acid: Glycine
- Most hydrophobic (nonpolar) Amino acid: Isoleucine
- Second most nonpolar amino acid is Valine
- Most polar amino acid is Arginine
- Most abundant amino acid in the proteins present in the body is Alanine.
- Most abundant amino acid in the plasma: Glutamine
- Least polar amino acid is Glycine
- Least nonpolar is Proline

Amino Acids and its derivatives as Neurotransmitters

- Glycine: Major inhibitory neurotransmitter in brain-stem and spinal cord
- Glutamate: Major excitatory neurotransmitter.

Amino Acid derivative as Neurotransmitter

- Dopamine
- Epinephrine
- Norepinephrine
- Serotonin
- Gamma Amino Butyric Acid (GABA).

DIGESTION OF PROTEINS

Native proteins are resistant to digestion because few peptide bonds are accessible to the proteolytic enzymes without prior denaturation of dietary proteins (by heat in cooking and by the action of gastric acid).

Enzymes Catalyze the Digestion of Proteins

There are two main class of proteolytic digestive enzymes (proteases).

I. **Endopeptidases** hydrolyze peptide bonds between specific amino acids throughout the molecule.
   - **Pepsin** in the gastric juice catalyzes hydrolysis of peptide bonds adjacent to amino acids with bulky side-chains (aromatic and branched-chain amino acids and methionine).
   - **Trypsin, chymotrypsin, and elastase** are secreted into the small intestine by the pancreas.
   - Trypsin catalyzes hydrolysis of **lysine and arginine esters**.
   - Chymotrypsin catalyzes hydrolysis esters of **aromatic amino acids**.
   - Elastase catalyzes hydrolysis esters of small **neutral aliphatic amino acids**.

II. ***Exopeptidases catalyze the hydrolysis of peptide bonds, one at a time, from the ends of peptides.***
   - **Carboxypeptidases**, secreted in the pancreatic juice, release amino acids from the free carboxyl terminal.
   - **Aminopeptidases**, secreted by the intestinal mucosal cells, release amino acids from the amino terminal.
   - **Dipeptidases and tripeptidases** in the brush border of intestinal mucosal cells catalyze the hydrolysis of di- and tripeptides, which are not substrates for amino- and **carboxypeptidases**.

The proteases are secreted as inactive **zymogens;** the active site of the enzyme is masked by a small region of the peptide chain that is removed by hydrolysis of a specific peptide bond.

Pepsinogen is activated to pepsin by gastric acid and **by activated pepsin**.

In the small intestine, trypsinogen, the precursor of trypsin, is activated by **enteropeptidase**[Q], which is secreted by the duodenal epithelial cells; trypsin can then activate chymotrypsinogen to chymotrypsin, proelastase to elastase, procarboxypeptidase to carboxypeptidase, and proaminopeptidase to aminopeptidase.

Absorption of Amino Acid

Free amino acids are absorbed across the intestinal mucosa by **sodium-dependent active transport**. There are several different amino acid transporters, with specificity for the nature of the amino acid side-chain.

Transporters of Amino Acids

- For Neutral Amino acids
- For Basic Amino acids and Cysteine.
- For Imino Acids and Glycine
- For Acidic Amino acids
- For Beta Amino Acids (Beta Alanine).

Quick Revision

- Most of the amino acids are alpha amino acids.
- Imino acid—Proline has Pyrrolidine ring
- Two amino acids are that are coded by stop codons are:
  1. Selenocysteine-by UGA
  2. Pyrolysine –by UAG
- Amino acids have maximum buffering capacity at pH = pKa.

Contd...

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Contd...

- Imidazole group of histidine has maximum buffering action at physiological pH.
- Aromatic amino acids (Trp, Phe,Tyr) absorb UV light at 250–290 nm.
- Pantothenic acid contain beta alanine.

This table is a workbook model table for quick review before exams. Two are done for you. Try the rest! Based on the classification of amino acids we have learnt in the chapter.

Amino acid	Based on side chain	Based on side chain characteristic	Nutritional classification	Metabolic fate
Glycine	Simple amino acid	Polar	Nonessential	Glycogenic
Alanine				
Cysteine				
Methionine				
Serine				
Threonine				
Aspartate				
Glutamate				
Asparagine				
Glutamine				
Arginine				
Histidine	Heterocyclic Aromatic, Basic	Polar	Essential (Can be semiessential)	Glycogenic
Lysine				
Phenylalanine				
Tyrosine				
Tryptophan				
Proline				
Leucine				
Isoleucine				
Valine				

Check List for Revision

- This chapter is high yield topic.
- Classification of amino acids,Selenocysteine are the must learn topic
- Isoelectric pH,Derived amino acids,Beta alanine-text with bold letters is most important.
- Titration curve is an IBQ hence learn in that aspect.

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MCQ
Review Questions

Amino Acid Classification

1. **Replacing alanine by which amino acid, will increase UV absorbance of protein at 280 nm wavelength?** *(NEET Pattern 2020)*
   a. Tryptophan b. Arginine
   c. Alanine d. Glycine

2. **Consider the following enzymes:**
   1. Glutathione peroxidase
   2. Glutathione synthetase
   3. Deiodinase
   4. Thioredoxin reductase *(INI-CET November 2022)*
   Which of the following enzymes use Selenocysteine?
   a. 1, 2, 3 b. 2, 3, 4
   c. 1, 3, 4 d. 1, 2, 4

3. **Amino acids with hydroxyl group:** *(PGI Nov 2016)*
   a. Threonine b. Tyrosine
   c. Serine d. Tryptophan
   e. Valine

4. **Fibropeptidase A & B are highly negative due to presence of which amino acids?** *(Recent Question Nov 2017)*
   a. Glutamate and Aspartate b. Serine and Threonine
   c. Lysine and Arginine d. Valine and Lysine

5. **Which of the following special amino acid is not formed by post-translational modification?** *(AIIMS Nov 2017)*
   a. Triodothyronine b. Hydroxyproline
   c. Hydroxylysine d. Selenocysteine

6. **Which of the following have a positive charge in physiological pH?** *(AIIMS Nov 2016)*
   a. Arginine b. Aspartic acid
   c. Isoleucine d. Valine

7. **What is the pH of the solution if the Hydrogen ion concentration is 5 millimoles/L?** *(AIIMS Nov 2016)*
   a. 2.3 b. 3.7
   c. 6.6 d. 3.5

8. **Selenocysteine is coded by:** *(AIIMS Nov 2015)*
   a. UAG b. UGA
   c. UAA d. GUA

9. **All of the following are essential amino acids *except*:** *(AIIMS May 2006)*
   a. Methionine b. Lysine
   c. Alanine d. Leucine

10. **Polar amino acids is/are:** *(PGI May 2012)*
    a. Serine b. Tryptophan
    c. Tyrosine d. Valine
    e. Lysine

11. **Nonpolar amino acid are:** *(PGI Nov 2010)*
    a. Alanine b. Tryptophan
    c. Isoleucine d. Lysine
    e. Tyrosine

12. **Hydrophobic amino acids are:** *(PGI May 2010)*
    a. Methionine b. Isoleucine
    c. Tyrosine d. Alanine
    e. Asparagine

13. **Basic amino acids is/are:** *(PGI Dec 2013)*
    a. Leucine b. Arginine
    c. Lysine d. Histidine

14. **Guanidinium group is associated with:** *(PGI June 2009)*
    a. Tyrosine b. Arginine
    c. Histidine d. Lysine
    e. Tryptophan

15. **Sulphur containing amino acid is:**
    a. Cysteine b. Leucine
    c. Arginine d. Threonine

16. **Which of the following is a non-aromatic amino acid with a hydroxyl R-group?**
    a. Phenylalanine b. Lysine
    c. Threonine d. Methionine

17. **Which is not an essential amino acid?**
    a. Tryptophan b. Threonine
    c. Histidine d. Cysteine

18. **Which of the following is not an aromatic amino acid?**
    a. Phenylalanine b. Tyrosine
    c. Tryptophan d. Valine

19. **Which of the following group contains only non-essential amino acid?** *(Recent Question 2012)*
    a. Acidic amino acid
    b. Basic amino acid
    c. Aromatic amino acid
    d. Branched chain amino acid

20. **Amide group containing amino acid is:** *(Recent Question)*
    a. Glutamate b. Glutamic acid
    c. Glutamine d. Aspartate

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21. Which of the following is semiessential amino acid? *(Recent Question)*

a. Arginine
b. Histidine
c. Glycine
d. Phenylalanine

22. Aminoacyl t-RNA is required for all except: *(AI 2000)*

a. Hydroxyproline
b. Methionine
c. Cysteine
d. Lysine

Properties of Amino Acids

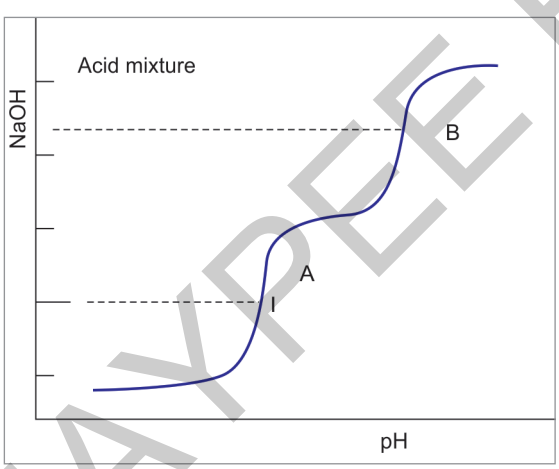
23. pKA = pH when: *(Recent Question Nov 2017)*

a. Solute is completely ionised
b. When the concentration of ionised and unionized form is same
c. Solute is completely unionized
d. All of the above

24. HCO_3^-/H_2CO_3 is considered most effective buffer at physiological pH because: *(AIIMS Nov 2016)*

a. It has pKa close to physiological pH
b. It is formed from a weak acid and base
c. Its components can be increased or decreased by the body
d. It can donate and accept H+

25. The graph shown below is the titration curve of a biochemical compound. Which of the following statement is true? *(AIIMS May 2016)*



a. The maximum buffering capacity of the compound is represented by points A and B
b. The points A and B represent the range of maximum ionisation of the amine and carboxyl group
c. The compound has three ionisable side chains
d. The compound has one ionisable group

26. Which of the following amino acid is responsible for the absorption of UV light in proteins?

a. Leucine
b. Proline
c. Arginine
d. Tryptophan

27. Which of the following proteins cannot be phosphorylated using protein kinase in prokaryotic organisms? *(AI 2012)*

a. Leucine
b. Proline
c. Arginine
d. Asparagine

28. Carboxylation of clotting factors by vitamin K is required to be biologically active. Which of the following amino acid is carboxylated? *(AIIMS Nov 2008)*

a. Histidine
b. Histamine
c. Glutamate
d. Aspartate

29. Which of the following is/are not optically inactive amino acids? *(PGI May 2014)*

a. Threonine
b. Tyrosine
c. Valine
d. Glycine
e. Serine

30. The property of proteins to absorb ultraviolet rays of light is due to: *(AIIMS June99)*

a. Unsaturated amino acid
b. Aromatic amino acid
c. Monocarboxylic acid
d. Dicarboxylic acid

31. All biologically active amino acids are: *(AIIMS Nov 93)*

a. L-forms
b. D-forms
c. Mostly D-forms
d. D and L-forms

32. Replacing alanine by which amino acid will increase UV absorbance of protein at 280 nm wavelength?

a. Unsaturated amino acid *(AIIMS Nov 2008)*
b. Aromatic amino acid
c. Monocarboxylic acid
d. Dicarboxylic acid

33. Flexibility of protein depends on: *(AI 1994)*

a. Glycine
b. Tryptophan
c. Phenylalanine
d. Histidine

34. Which amino acid can protonate and deprotonate at neutral pH? *(AIIMS May 95)*

a. Histidine
b. Leucine
c. Glycine
d. Arginine

35. Phosphorylation of amino acid by: *(PGI June 98)*

a. Serine
b. Tyrosine
c. Leucine
d. Tryptophan

36. Which of the following amino acid is purely Glucogenic? *(Recent Question)*

a. Valine
b. Lysine
c. Alanine
d. Glycine

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Recent Questions

NEET PG AUG 2024

1. **A patient diagnosed with rare homozygous recessive condition presented with ectopia lentis. In peripheral smear, there was no megaloblastic anemia. Later, was found to have methionine deficiency. Which of the following supplementation will help the patient?**
   a. Thiamine
   b. Biotin
   c. Riboflavin
   d. Pyridoxine

2. **A young female comes to the emergency department after ingesting 10 tablets of Phenobarbital. Which of the electron transport chain is prevented by this drug?**
   a. Succinate - Fe
   b. Cytochrome III
   c. Complex 1 to Q
   d. Complex IV

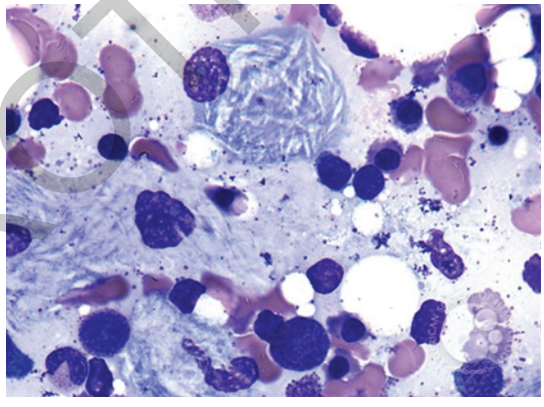
3. **A 3-year-old child is brought to the OPD with complaints persistent delayed developmental milestones, macular lesions on the body, hyperpigmented which are more pronounced on exposure to sunlight. What is the error in DNA multiplication?**
   a. Base excision repair
   b. Nucleotide excision repair
   c. DNA mismatch repair
   d. Homologous recombination

4. **Which food item among this the primary source of thiamine in Indians?**

   a. Chapati and rice
   b. Cucumbers and onions
   c. Curd
   d. Vegetable curry

5. **A neonate was brought with features of lethargy, poor oral intake. On examination, cataract was seen. Urine Benedict's test was positive, but negative for Glucose. What is the enzyme deficient in this condition?**
   a. Hexokinase
   b. Galactosyl-1 phosphate uridyl transferase
   c. Galactokinase
   d. Phosphofructokinase

6. **A child presents to you with bone pain, hepatosplenomegaly and pancytopenia. A trephine biopsy aspirate shows the following finding. Which of the following is the most likely enzyme deficient in this patient?**



   a. Glucocerebosidase
   b. Galactocerebosidase
   c. Sphingomyelinase
   d. Alpha glucosidase

7. **A 10-year-old child from a southern Indian state, hailing from a poor family presents with symptoms of rough and scaly skin. The child's diet hardly has any vegetables, fruits. After treatment with linseed oil, Vitamin A and B, the symptoms subside. What is the most likely diagnosis?**
   a. Phrynoderma
   b. Lichen planus
   c. Erythroderma
   d. Keratosis pilaris

8. **After the age of 12, the boy had intellectual disability. On examination, finger nail abrasions, excessive bitting of lips and increased levels of serum uric acid. What is the diagnosis?**
   a. Lesch Nyhan syndrome
   b. Hurler syndrome
   c. Hunter syndrome
   d. Von Gierke syndrome

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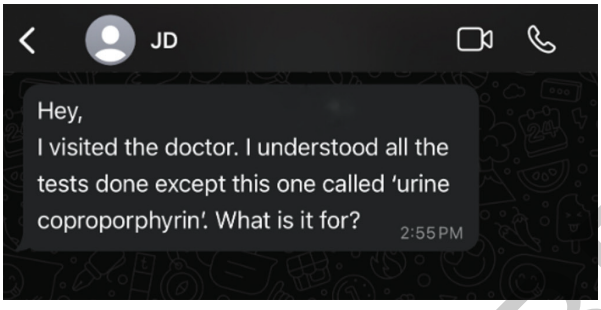
9. **Pain abdomen, vomiting, loss of appetite with serum triglyceride levels >2000 mg/dL. This is due to deficiency of?**
   a. Apolipoprotein C II
   b. Apolipoprotein b48
   c. Apolipoprotein b100
   d. Apolipoprotein A I

10. **Family history of CAD and tendon xanthomas. Cholesterol levels are elevated. Triglyceride levels 398 mg/dL and LDL levels were 280:**
   a. LDL metabolism
   b. VLDL metabolism
   c. LDL receptor defect
   d. Lipoprotein lipase deficiency

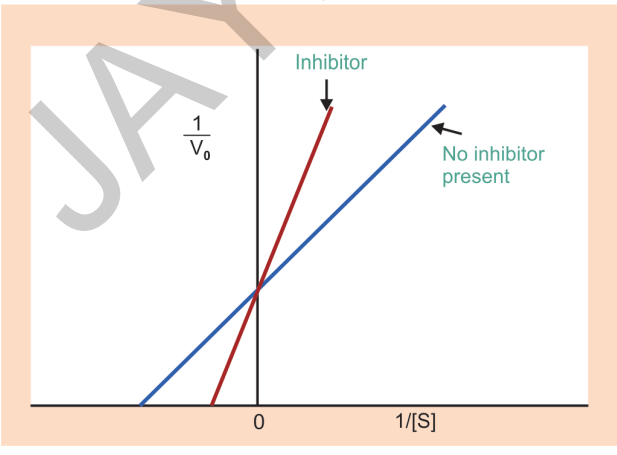
11. **You receive a text message from your friend JOHN DOE about occupational exposure after he visited his doctor, What is the test use to diagnose?**



Whats app message box with urine corporphyrin
   a. Lead poisoning
   b. Anthracosis
   c. Silicosis
   d. Asbestosis

12. **A patient underwent gastrectomy for gastric adeno ca, which of the following vitamin needs to be supplemented in this patient?**
   a. Vitamin A
   b. Vitamin B12
   c. Vitamin B1
   d. Vitamin D

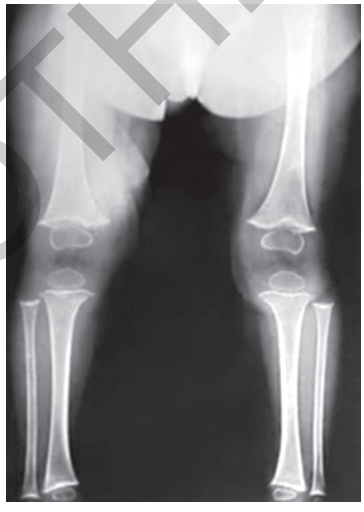
13. **In the given Lineweaver-Burk plot, the blue shows normal enzyme action and red shows the action of the same enzyme with an inhibitor. What is the type of inhibition seen here?**



   a. Allosteric inhibition
   b. Competitive inhibition
   c. Uncompetitive inhibition
   d. Noncompetitive inhibition

14. **A child presented with recurrent abdominal pain, vomiting and diarrhea following ingestion of a milk based product. Which enzyme is likely to be deficient?**
   a. Lactase
   b. Maltase
   c. Lipase
   d. Amylase

15. **Which micronutrient is most likely deficient in a patient with the radiographic findings given below along with anaemia, neutropenia, depigmented hair and skin?**



   a. Iron
   b. Copper
   c. Zinc
   d. Fluoride

16. **A child was suffering from phenylketonuria. Necessary dietary control was done the but neurological symptoms persisted. Serum shows normal levels of phenylalanine. Which of the following enzymes is likely to be deficient in this condition?**
   a. DOPA decarboxylase
   b. Tyrosine hydroxylase
   c. Tetrahydrobiopterine synthase
   d. Phenylalanine hydroxylase

17. **A mother came back home to see her child suffering from difficulty breathing. The child had contact with rotenone while trying to bathe their pet. She was taken to the emergency department and later passed away. Inhibition of which of the following enzymes was the likely cause of her death?**
   a. Cytochrome c reductase
   b. Succinate dehydrogenase
   c. NADH ubiquinone reductase
   d. Cytochrome oxidase

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18. Child presented with fatigue and muscle weakness on exercising. Laboratory investigations found that LCFA oxidation was affected. Muscle biopsy revealed the presence of fat vacuoles. What is the probable diagnosis?

a. Carnitine deficiency
b. FA synthase deficiency
c. LPL defect
d. LDL defect

19. A patient presented with multiple yellowish raised spots on eyelids, xanthomas on Achilles tendon. What is the likely cause for the patient's presentation?

a. Tangiers disease
b. Familial hypercholesteremia
c. Fabrys disease
d. Xanthamatosis

20. A 3-month-old child presented with hypotonia, floppiness, difficulty feeding and failure to thrive, macroglossia. O/E cardiomegaly was seen. Weight : 2.8 kg, length : 48 cm What's the diagnosis?

a. Ebstein's anomaly
b. Transposition of great arteries
c. Von Gierke disease
d. Pompe's disease

21. A 32-year-old middle lady comes with the complaints of erythematous scaly rash, loose stools and cognitive dysfunction. The rash involved her forearm, neck and face. She seems to have difficulty in remembering things from the recent past. Her electrolytes are within normal range. She admits to having shifted to a corn based diet due to economical reasons. Which of the following would improve her symptoms?

a. Oral nicotinamide supplementation
b. High dose of IV thiamine
c. High dose Vitamin C
d. Stop corn diet

22. A patient of hypertriglyceridemia was started on medication. He then developed flushing, hyperglycemia and elevated liver enzymes. Identify the drug?

a. Rosuvastatin
b. Ezetemibe
c. Nicotinamide
d. Fenofibrate

ANSWERS WITH EXPLANATION

1. d. Pyridoxine

As there is methionine deficiency this is a metabolic disorder that is associated with methionine metabolism. In Methionine metabolism, homocysteine has two fates either combine with serine to form cysteine and homoserine or remethylate with the help of N5 methyl THFA and Methyl B12 to form methionine. In this case, there is hypomethioninemia so the remethylation fate is affected. So this is a case of nonclassic homocystinuria. Nonclassic homocystinuria with no megaloblastic anemia is Methylene Tetrahydro folate reductase defect which affect N5 methyl THFA formation defect. In nonclassic homocystinuria the treatment is a combination of folic acid, B12 and B6. From the given option B6 is the answer. Moreover in the presence of B6 accumulated homocysteine is converted to cysteine and homoserine as the enzyme cystathionine beta synthase which catalyse this reaction require B6.

2. c. Complex I to Q

Phenobarbital is an inhibitor of Complex I which transfer electrons to CoQ.

Inhibitors of Complex I are:

1. Barbiturates
2. Rotenone
3. Piercidin A

3. b. Nucleotide excision repair

This given question is scenario of Xeroderma pigmentosa. Its due to defect in nucleotide excision repair .

Disorders associated with Nucleotide excision repair are:

1. Xeroderma pigmentosa
2. Trichothiodystrophy
3. Cockayne syndrome

4. a. Chapati and rice

In Indian diet richest source of thiamine is whole grain (aleurone layer of grains is rich in thiamine). Other sources are liver, fish, yeast etc.

5. b. Galactose 1 Phosphate uridyl transferase

This is a case of galactosemia. The enzyme defect are Galactose 1 Phosphate uridyl transferase.

6. a. Glucocerebrosidase

This is a case of Gaucher's disease. The enzyme defect is beta glucosidase or beta Glucocerebrosidase. The image shown is crumpled tissue paper appearance in Gaucher cell.

7. a. Phrynoderma

Follicular hyper keratosis or Phrynoderma or Toad skin is a condition caused due to deficiency of Vitamin A, Essential fatty acids and many B complex vitamin deficiency.

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8. a. Lesch Nyhan Syndrome

This is due to deficiency of HGPRtase enzyme in purine nucleotide salvage pathway.

9. a. Apolipoprotein C II

This is a case of Type I Hyperlipoproteinemia. This is caused due to defect in Lipoprotein lipase or apolipoprotein CII which activate Lipoprotein lipase.

10. c. LDL receptor defect

This is a case of Type II Hyperlipoproteinemia where the defect. Here two close answers are there LDL metabolism and LDL receptor defect .But more precise answer is LDL receptor defect.

11. a. Lead poisoning

Lead inhibit enzymes in heme synthesis like ALA Dehydratase and Ferro chelatase. There are few articles concluding that it also inhibit Coproporphyrinogen oxidase. So as Coproporphyrinogen is a porphyrin and lead inhibit heme synthesis pathway the answer here is lead poisoning.

12. b. Vitamin B12

Vitamin B12 absorption require intrinsic factor. It is secreted by gastric parietal cells. So intrinsic factor deficiency can result in

13. b. Competitive inhibition

X intercept moves closer to zero and Y intercept remains the same in competitive inhibition.

14. a. Lactase

A case of hereditary lactose intolerance.

15. c. Copper

Copper deficiency can cause anaemia, neutropenia and depigmentation in skin and hair. Radiological features of copper deficiency are:

- Symmetric metaphyseal irregularity
- Loss of cortical sharpness
- Metaphyseal cupping
- Metaphyseal spurs in medial distal femurs
- Osteopenia
- Increased density in zone of provisional calcification

16. c. Tetrahydrobiopterine synthase

This is a case of nonclassic phenyl ketonuria where even after dietary treatment with normal phenyl alanine level neurological symptoms are persisting. So this is due to any enzyme in the tetrahydrobiopterin biosynthetic pathway like:

- GTP Cyclohydrolase
- Pyruvoyl Tetrahydrobiopterin synthase
- Sepiaterin reductase
  Any enzyme in recycling of Tetrahydrobiopterin
- Dihydrobiopterin synthetase
- Dihydrobiopterin reductase

17. c. NADH ubiquinone reductase

Rotenone is an inhibitor of complex I of ETC

18. a. Carnitine deficiency

Carnitine is transporter of LCFA for oxidation

19. b. Familial hypercholesterolemia (FH)

Clinical Features of FH are:

- Tendon Xanthoma
- Corneal arcus
- Xanthelasma palpebrarum
- High cholesterol level
- High LDL level

20. d. Pompe's disease

Cardiomegaly with hypotonia is a manifestation of lysosomal storage disorder which is muscle glycogen storage disorder. The enzyme defect is Acid maltase

21. a. Oral nicotinamide supplementation

This is a case od niacin deficiency due to excessive corn based diet. In Corn or maize tryptophan level which is source of niacin is deficient.

22. c. Nicotinamide

Niacin toxicity causes cutaneous flushing due to hyper secretion of prostaglandin

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