

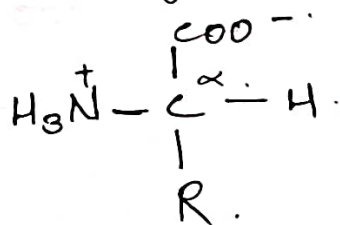
9/9/23

AMINO ACIDS

- * Building blocks of proteins
- * Proteins are polymers of amino acids.
- Proteins are composed of aa linked by peptide bond.
- About 300 aa occur in nature.
- 20 of them are seen in human body.
- Most of the aa. are alpha aa (except proline)

Alpha (α -) amino acids

The amino group is attached to the same carbon atom to which the carboxyl group is attached.



Amino acids: Naming

Biochemical designation: Start from α -carbon and go down the R group.

Classification

- (i) Based on structure
- (ii) " " side chain.
- (iii) " " metabolism.
- (iv) " " nutritional requirement.

(I) Based on structure

- Aliphatic amino acids
- Aromatic amino acids
- Heterocyclic amino acids
- Imino acids
- derived amino acids.

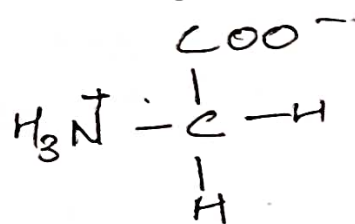
Aliphatic amino acids:

- Mono amino monocarboxylic acid.
- monoamino dicarboxylic acid.
- Dicarboxic monocarboxylic acids.

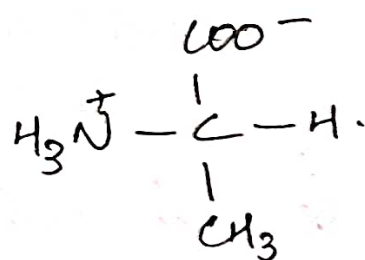
(a) Monoamino monocarboxylic acids

(i) Simple amino acids.
eg: Glycine, Alanine

Glycine (Gly, G).



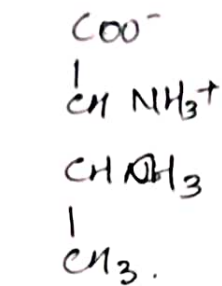
Alanine (Ala, A)



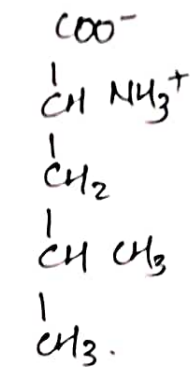
(ii) branched chain amino
eg: Valine, Leucine
Isoleucine.

(1)

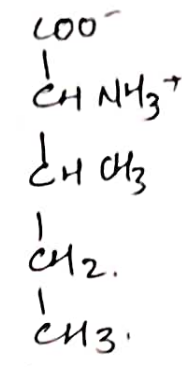
(B)



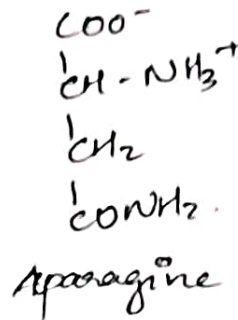
Valine
(Val, V)



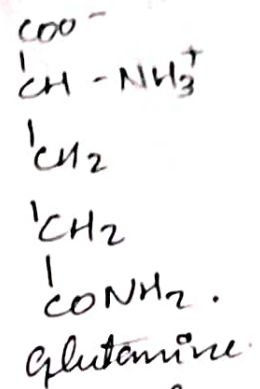
Leucine
(Leu, L)



Isoleucine
(Ile, I)

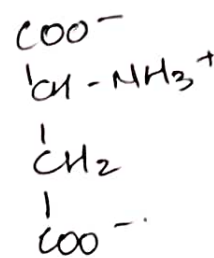


Asparagine

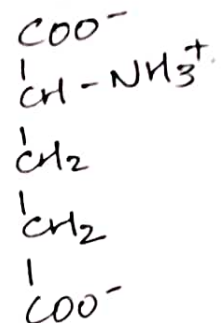


Glutamine

(b) Monoamino dicarboxylic acids

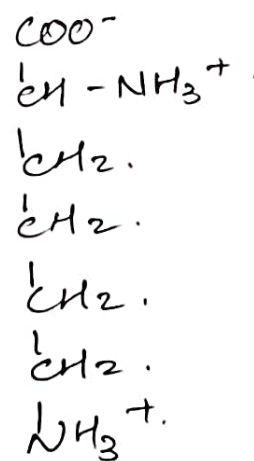


Aspartic Acid
(Asp, D)

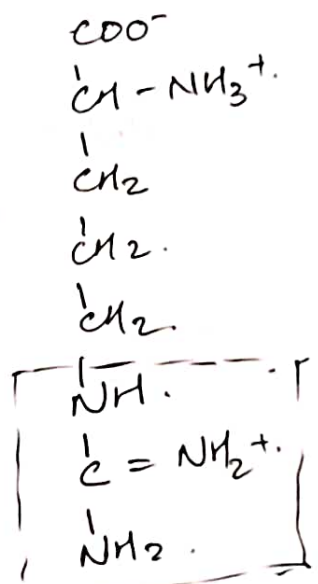


Glutamic acid
(Glu, E)

(c) Dibasic mono carboxylic acids

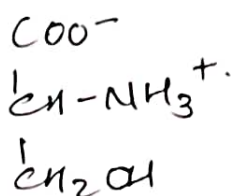


Lysine
(Lys, K)

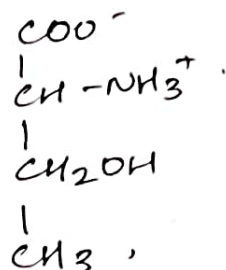


Arginine
(Arg, R)

(ii) Hydroxy amino acids.
Serine, Threonine

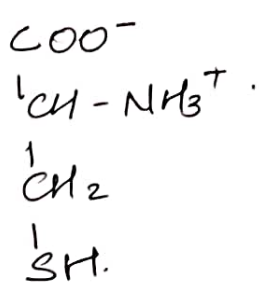


Serine
(Ser, S)

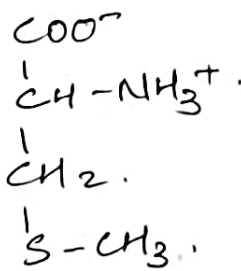


Threonine
(Thr, T)

(iii) Sulphur containing amino acids.



Cysteine
(Cys, C)

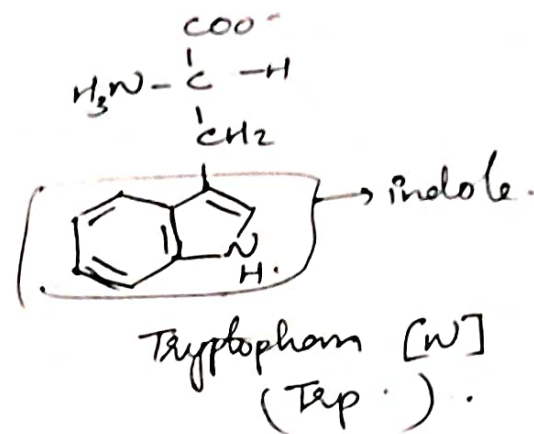
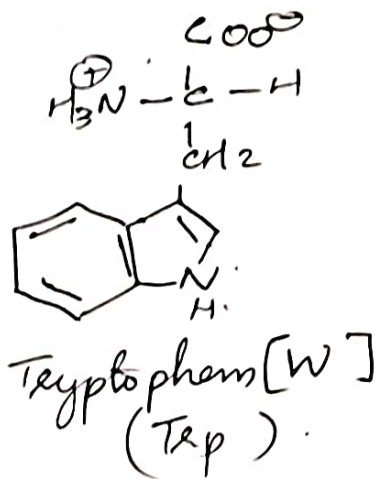
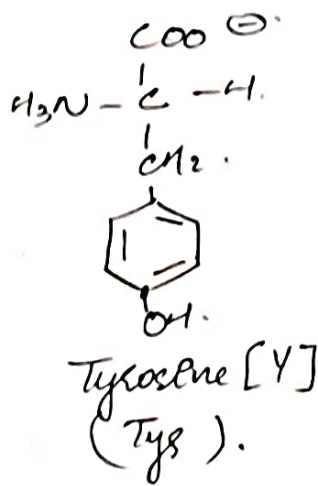
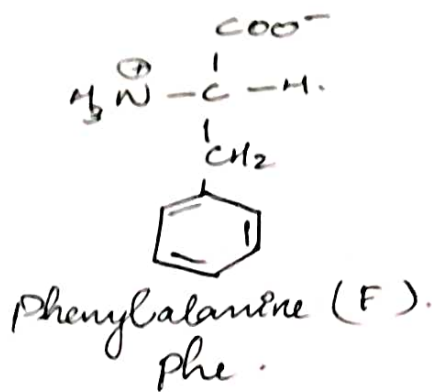


Methionine
(Met, M)

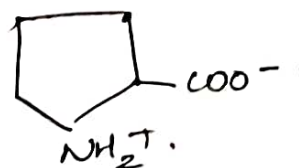
(iv) Amino acids with amide group.

eg: Asparagine (Asn, N)
Glutamine (Gln, Q)

(B) Aromatic amino acids.



(D) Imino acid
proline (Pro, P).



(E) Derived amino acids.

- Found in proteins
- Not seen in proteins
- Non-alpha amino acids.

(i) Derived aa. found in proteins:
Some aa get modified after protein synthesis.

eg: Hydroxyproline, hydroxylysine (components of collagen)

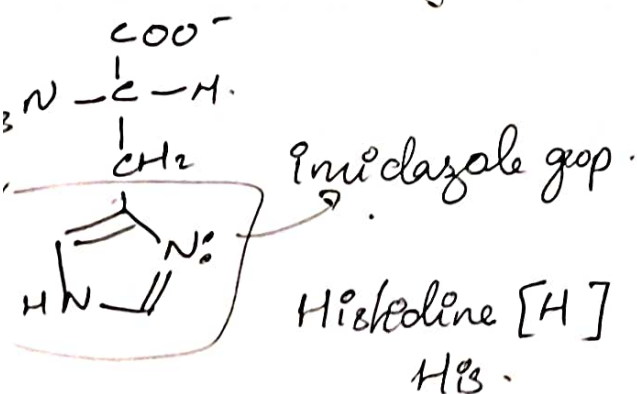
Gamma carboxylation of glutamic acid residues (for clotting).

(ii) Non-alpha amino acids.
Amino group NOT in α position

- Gamma amino butyric acid (GABA) derived from glutamic acid.

(3)

(C) Heterocyclic amino acids
Histidine, tryptophan.



- Beta-alanine
(constituent of Pantothenic acid (vitamin) and coenzyme A)

(iii) Not found in protein
eg: citrulline, ornithine
(compounds of urea cycle)

II Based on Side chain
(a) ^{non charged non polar side chains}
• Hydrophobic (water-repellant)
and lipophilic

Includes

Ala, Val, Leu, Ile (isoleucine)

Met, Pro, Phe, Trp (tryptophan)

(B) Amino acids with uncharged
or non-ionic polar side
chain

→ Hydrophilic in nature

Includes

Gly, Ser, Thr, Asn

Gln, Tyr, Cys

(c) Amino acid with charged
or ionic polar side chain

Hydrophilic

(1) Acidic amino acids

Negative charge on
R group

eg: Asp, Glu

(Tyr is mildly acidic)

(b) Basic amino acid
Positive charge on R group
eg: Lys, Arg, His

III Based on Metabolism

A. Purely ketogenic

→ AA that can be
converted to ketone bodies

Eg: Leucine is purely
ketogenic

B. Ketogenic and Glucogenic

During metabolism, part
of these amino acids
will enter ketogenic
pathway and the other
part to glucogenic pathway

eg: lysine, Isoleucine,
phenylalanine, tyrosine,
tryptophan

C. Purely ~~Ketogenic~~ Glucogenic

→ Can enter only into
glucogenic pathway

Remaining amino acids
are purely glucogenic

eg: Alanine, glycine,
Valine, arginine, cysteine,
methionine

IV Based on Nutritional Req. (4 max)

a. Essential / Indispensable aa

b. Partially essential / semi essential

c. Non essential or dispensable

(4)

(d) Conditionally essential.

(a) Essential / Indispensable

Amino acids that cannot be synthesised in the body and have to be supplied through diet.

Lysine, leucine, Isoleucine, methionine, phenylalanine, threonine, valine, tryptophan.

(c) Partially essential or semi essential

Histidine, arginine.

Growing children require these in food. Not essential for adults.

(e) Non-essential or dispensable

→ Remaining 20 aa are non essential

eg. tyrosine, cysteine, aspartic acid, glutamic acid.

→ Their carbon skeleton can be synthesised by the body and need not to be taken only through food.

(d) Limiting amino acids.

→ one or more essential amino acids deficient in certain proteins are called limiting amino acids.

→ Results in improper growth of individual.

→ This problem can be overcome by taking a mixture of proteins in diet (mutual supplementation)

Mutual supplementation

A mixture of proteins are taken in diet to overcome the deficiency of limiting amino acids.

eg: Pulses are deficient in Met. Cereals are deficient in Lys.

So, a combination both of these will cancel each other's deficiency.

Special (functional) groups in amino acids.

- Arginine → Guanidinium.
- Phenylalanine → Benzene ring.
- Tyrosine → Phenol group.
- Tryptophan → Indole group.
- Histidine → Imidazole.
- Proline → pyrrolidine.

Properties of amino acids

Taste Amino acids

Sweet

Gly, Ala, Val, Ser, Trp, His and Ile.

Bitter.

Ile, Arg.

Tartarous

Leu

Flavouring agent

Sodium glutamate

Aspartame, an artificial sweetener contains aspartic acid and phenyl alanine. 1 mark

- All aa have high melting points (more than 300°C)
- Soluble in water and alcohol (polar solvents).
- Insoluble in non polar solvents (benzene).

Optical activity

- exhibit optical activity if asymmetric carbon atom is present.
- Asymmetry arises when FOUR different groups are attached to the same carbon.
- Glycine - simplest aa.

↓
no asymmetric carbon atom

↓
no optical activity

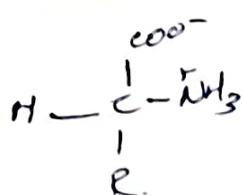
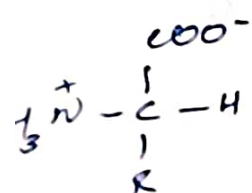
All others are optically active.

D and L Isomers

Mirror image forms produced with reference to α C atom

L Isomer

D Isomer



L-amino acids are in nature and are called natural aa.

→ D-amino acids are seen in small amounts in micro organisms and as constituents of certain antibiotics such as Gramicidin-S, Actinomycin D etc.

* Isoleucine and Threonine have 2 optically active centres and each has 4 diastereoisomers.

Isoelectric Point (pI)

→ Amino acids can exist as ampholytes or zwitter ions (dipolar ions) in solution, depending on the pH of the medium:

Amino group = $-\text{NH}_3^+$

Carboxyl group = $-\text{COO}^-$

The pH at which the molecules carry no net charge is known as isoelectric point or isoelectric pH (pI)

→ At isoelectric point the no. of anions = no. of cations and the net charge is 0.
∴ there is no mobility in an electric field.

→ At pH above the isoelectric point (alkaline), protein molecule is negatively charged i.e. behave as anions.

→ At a pH below isoelectric point (acidic), it is positively charged, i.e. behave as cations.

• Solubility and buffering capacity and viscosity are minimum at this pH, hence precipitation is maximum.

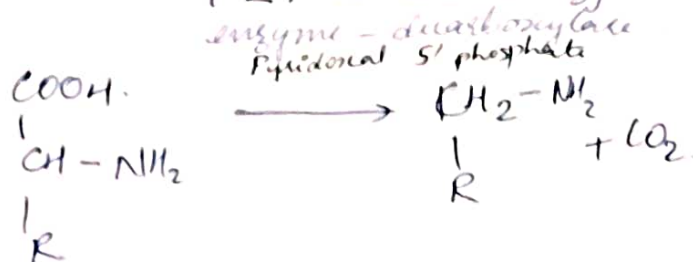
(7) Kaustmethylations

eg: pI of His is 7.6.

General Reactions of Amino acids.

① Decarboxylation Reactions (4 mark)

- Amino acids will undergo alpha decarboxylation to form the corresponding amine. PLP as the coenzyme.



Histidine $\rightarrow$ histamine.

Tyrosine $\rightarrow$ tyramine.

Tryptophan $\rightarrow$ tryptamine.

Lysine $\rightarrow$ cadaverine.

Glutamic acid $\rightarrow$ GABA
gamma amino butyric acid.

5-OH tryptophan $\rightarrow$ Serotonin

DOPA $\rightarrow$ Dopamine.

Amino acid derivatives of Importance:

- GABA (derivative of glutamic acid) and dopamine (derivative of tyrosine) are neurotransmitters.

- Histamine derived from Histidine is the mediator of allergic reactions.

- Thyroxine, from tyrosine is an important thyroid hormone.

- ~~Left~~ Cycloserine, a derivative of serine is an anti tubercular drug.

- Azaserine, acts as an anti cancer drug.

- Ornithine and citrulline are derivatives of arginine and are essential for urea synthesis.

- Beta alanine is a constituent of pantothenic acid coenzyme A.

- Glycine is necessary for heme synthesis.

- Taurine, derived from cysteine is a modulator of calcium fluxes, calcium binding and movement. It is an inhibitory neurotransmitter.

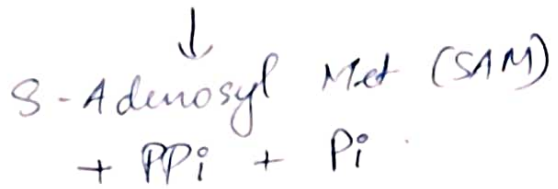
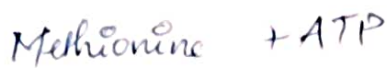
(8 mark)

② Transmethylation reactions (4 mark)

- Methionine plays the key role.
- The transfer of methyl group ($-\text{CH}_3$) from active methionine to another is known as transmethylation.

(7)

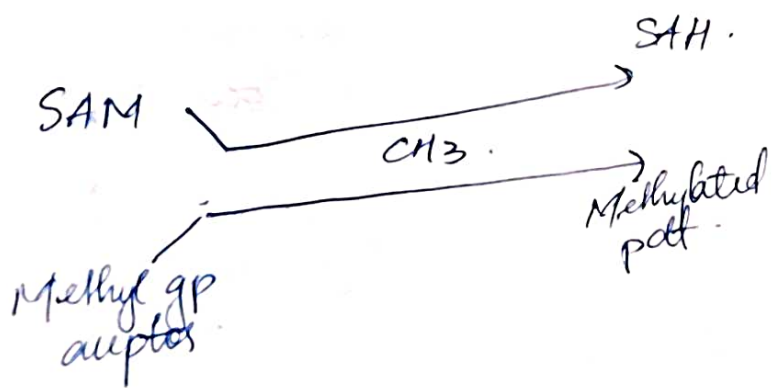
Methionine has to be activated to S-Adenosyl Methionine (SAM) or Active methionine to donate the Methyl group (activated by ATP).



→ The synthesis of SAM occurs by the transfer of an adenosyl group from ATP to S atom of Methionine.

→ The enzyme involved in the transfer of methyl group collectively are called as methyl transferases.

→ SAM transfers the methyl group to an acceptor and gets itself converted to S-Adenosyl Homocysteine (SAH)



Methyl gp
acceptor

methylated ppt.

Guano de albatros → creatinine
 → epinephrine

Nor-epinephrine → epinephrine
 metanephrine

Epinephrine → Metanephrine
 → choline

Epinephrine
Ethanolamine $\rightarrow$ choline

Serine $\rightarrow$ choline

Serine $\rightarrow$ choline
Histidine $\rightarrow$ methyl histidine
 $\rightarrow$ methyl histidine + P.N.

Hisidine $\rightarrow$ Methylated tRNA
tRNA $\rightarrow$ Methylated tRNA

(3) Amide bond formation

3) Amide bond formation
The rest of dicarboxylic amino acids (other than alpha carbonyl) can combine with ammonia to form the corresponding amide.

- Aspartic acid + $\text{NH}_3 \rightarrow$ Asparagine
- Glutamic acid + $\text{NH}_3 \rightarrow$ Glutamine

(4) Peptide Bond formation

Peptide bonds link amino acids in Proteins.

- Peptide bond - linkage b/w amino acids is a secondary amide bond.
- Formed by condensation of the α carbonyl of one amino acid with the α -amino of another amino acid (loss of H_2O molecule)
- 2 amino acids combine to form a dipeptide.

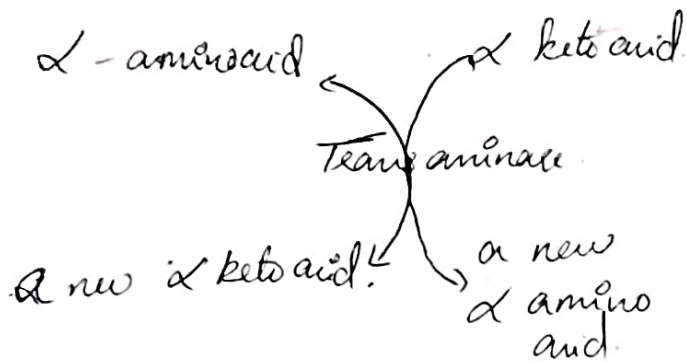
- Dipeptide $\rightarrow$ 1 peptide bond
- Tripeptide $\rightarrow$ 2 peptide bond
- Tetrapeptide $\rightarrow$ 3 peptide bond

• Few amino acids - oligopeptide
10-50 aa - polypeptide

• Big polypeptide chains containing more than 50 aa are called proteins.

5. Transamination ~~5%~~ (Small)

- Transamination means transfer of amino group from α amino acid to α -keto acid with formation of a new α -amino acid and a new α -keto acid.



The liver is the main site for transamination.
All amino acids can be transaminated except lysine, threonine, proline and hydroxy proline.

$\rightarrow$ All transamination reactions are reversible
If catalysed by amino

transferases (transaminases)
It needs pyridoxal phosphate as a coenzyme.

$\rightarrow$ Transamination provides a route for redistribution of amino acid nitrogen.

Two important enzymes in clinical diagnosis

- SGOT: Serum glutamate oxaloacetate transaminase
Aspartate + Glutamate

$\downarrow$
Aspartate + α Ketoglutarate

- SGPT: Serum glutamate pyruvate transaminase
ALT $\rightarrow$ Alanine transaminase
Glutamate + Pyruvate

$\downarrow$
 α -Ketoglutarate + Alanine

Biological Significance of Transamination

- $\rightarrow$ First step of catabolism
- $\rightarrow$ Synthesis of Non-Essential amino acids.
- $\rightarrow$ Interconversion of amino acids.

Clinical Significance of Transamination

- AST and ALT are induced by glucocorticoids which

favor gluconeogenesis

→ AST and ALT are markers of liver diseases
AST also increased in myocardial infarction

6. Deamination

The removal of ~~amino~~ amino group from the amino acids as NH_3 .

- Oxidative deamination
- Non oxidative deamination.

Oxidative Deamination

An amino acid is converted into the corresponding keto acid by the removal of the amino functional group as ammonia.

AND

the amino functional group is replaced by the ketone group.

the ammonia essentially goes into the urea cycle.

→ Oxidative deamination occurs primarily on glutamic acid because glutamic acid is the end product of many transamination reactions.

→ MAO is the coenzyme.

→ ~~Oxidative~~ Only liver mitochondria contains glutamate dehydrogenase (GDH)

→ All amino acids are first transaminated to glutamate and then deaminated

→ Amino acids are deaminated at the rate of 50-100 g/day.

3 ways pathway of deamination

a) L-amino acid oxidase

(FAD is the coenzyme)

- It acts on all amino acids except hydroxy and dicarboxylic amino acids.

b) D-amino acid oxidase:-

(FAD is the coenzyme)

- It can oxidize glycine and any D-amino acids that form from bacterial metabolism.

(10) • Action of MAO (mono amino oxidase)

Non-Oxidative Deamination

A) Dehydrogenases - acts on hydroxy amino acids.

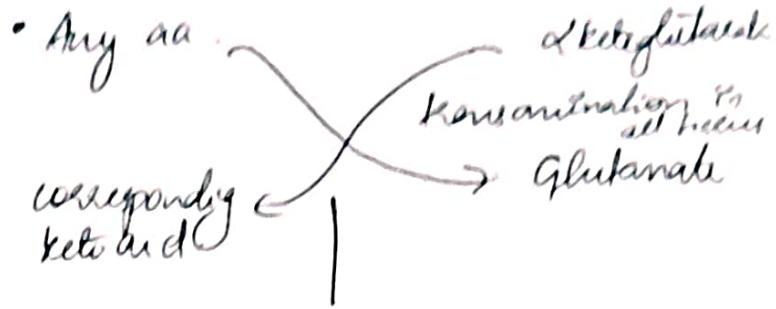
- See forms pyruvate.
- The forms ~~amino~~ keto butyrate.

B) Desulfhydrases - Cysteine undergoes deamination and simultaneous trans-sulphuration to form pyruvate.

- Histidine converted to urocanic acid by histidase.
- Ammonia is formed in GIT by bacterial putrefaction.

Transdeamination

- The amino group of most of the amino acid is released by a coupled reaction.
- Transdeamination - transamination followed by oxidative deamination.
- Transamination takes place in cytoplasm of all cells; ammonia is transported to liver as glutamate.
- Glu is finally oxidatively deaminated in liver mitochondria.



2. Transport of ammonia

- Glutamine is the transport form of ammonia from brain and intestines to liver.
- Alanine is the transport form of ammonia from muscles to liver.

Specialised products formed by amino acid

- | Amino acid | product |
|------------|--|
| Glycine | Creatine, glutathione, Heme, purines, conjugated bile acid |
| Tyrosine | Thyroxine, epinephrine, norepinephrine, dopamine, melanin |
| Methionine | Active methionine, creatine, epinephrine, polyamines |

Tryptophan - NAD⁺, NADP⁺
(coenzymes of Niacin),
Serotonin, Melatonin.

Cysteine - Glutathione, Taurine,
coenzyme A

Histidine - Histamine.

Glutamate → GABA, glutathione.

Arginine - Creatinine

Glutamine - Purines, pyrimidines,
~~amino~~ amino sugars.

Lyxine - Carnitine.

Aspartate - Purines, pyrimidines.

Serine - Phosphatidyl
serine, sphingomyelin,
choline.

Beta alanine - Coenzyme A.