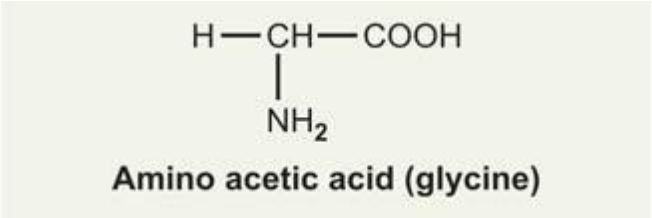
Metabolism of other amino acids

GLYCINE

Glycine is the simplest amino acid. Chemically it is "**amino acetic acid** ".



Amino acetic acid (glycine)

It is non-essential amino acid and can be synthesized in animal tissues. Though it is non- essential but it is an important amino acid as it forms many biologically important compounds in the body.

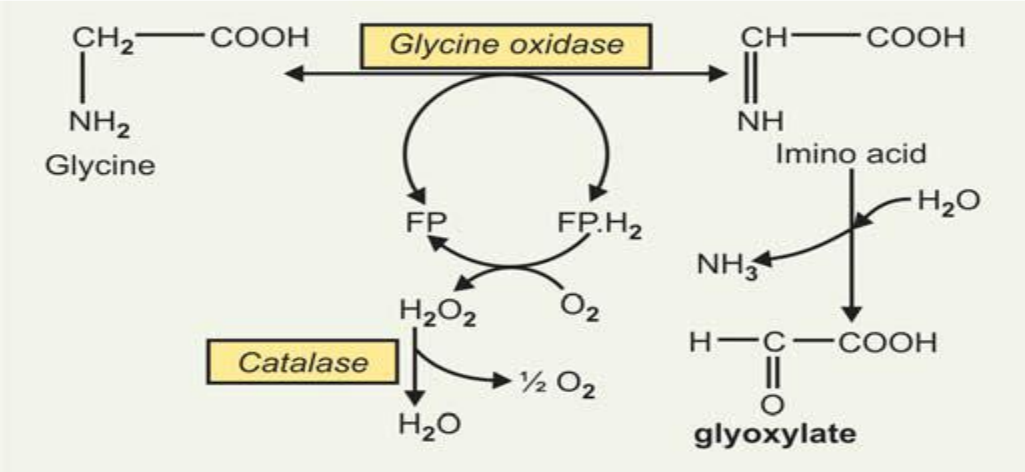
A- Metabolic fate:

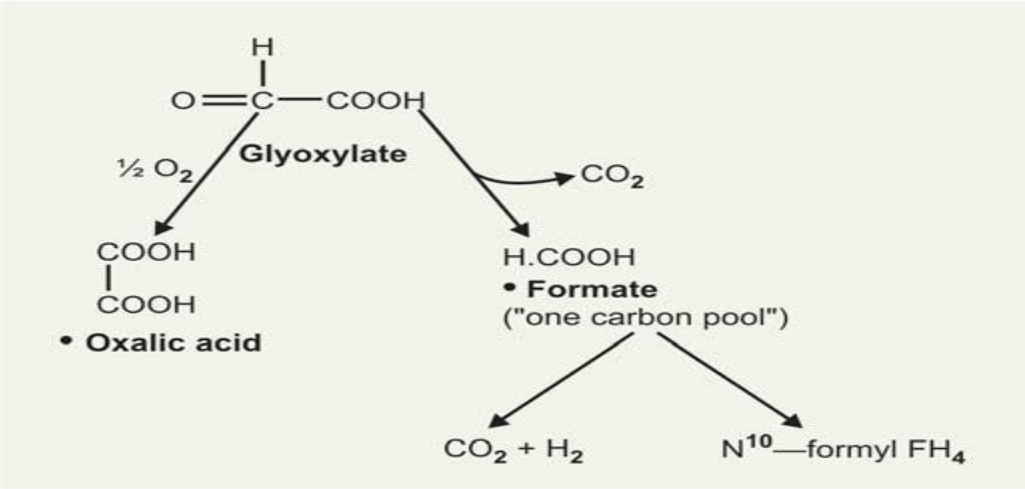
1- Deamination by a specific enzyme ***glycine oxidase*** present in Liver and kidney to produce glyoxylic acid (glyoxylate), which convert to oxalic acid or formic acid and thus enters" one-carbon pool".

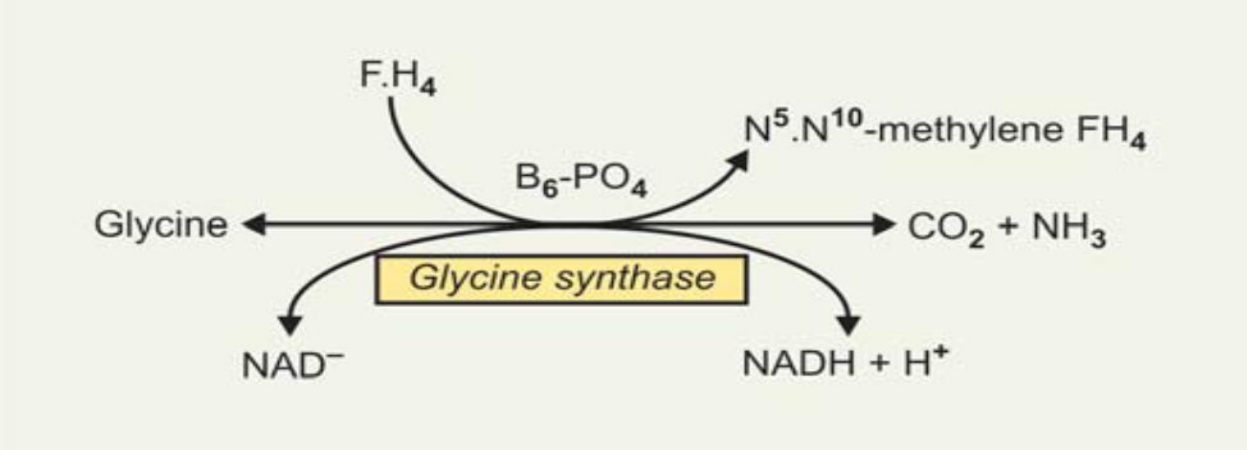
2- Glycine Cleavage to CO2, NH^{+}_{4}, and N^{5}, N^{10}- methylene-FH4 catalyzed by the enzyme ***Glycine Synthase complex*.**

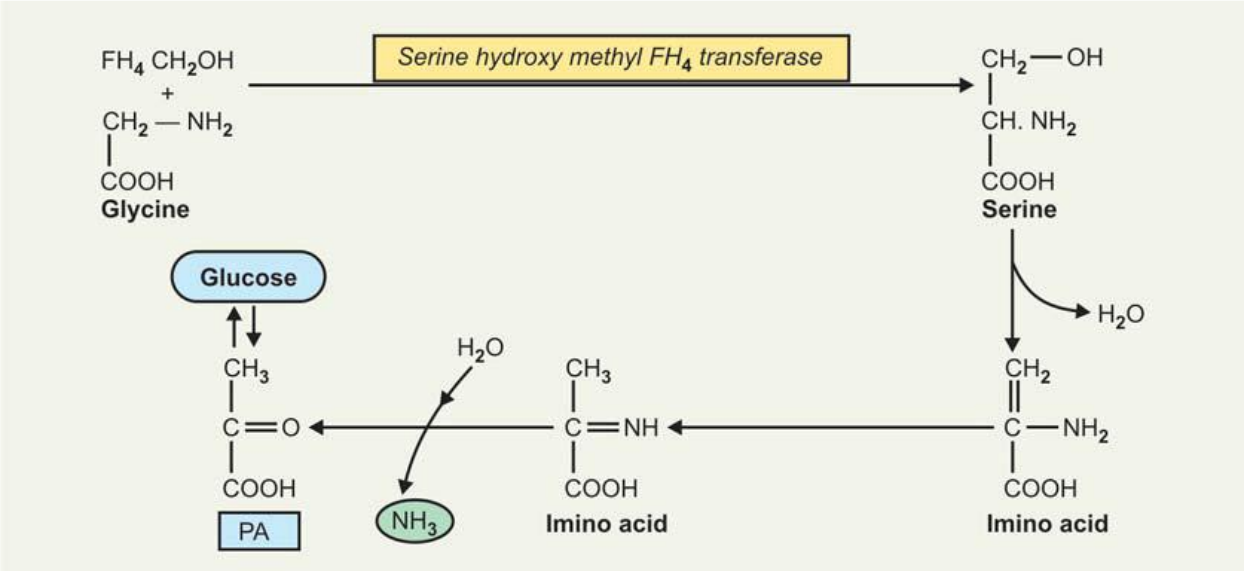
3- Glycine can be converted to serine which by non-oxidative deamination can form pyruvic acid, thus glycine may be ***glucogenic***

4- Oxidation to form Aminoacetone, which further be metabolized through *methyl glyoxal* to Lactic acid and Pyruvic acid


CH2—COOH
NH2
Glycine
Glycine oxidase
CH—COOH
NH
Imino acid
H2O
NH3
FP
FP.H2
H2O2
O2
Catalase
½ O2
H2O
H—C—COOH
O
glyoxylate


H
O=C—COOH
Glyoxylate
½ O2
CO2
COOH
COOH
• Oxalic acid
H.COOH
• Formate
("one carbon pool")
CO2 + H2
N10—formyl FH4


F.H4
N5.N10-methylene FH4
B6-PO4
Glycine
CO2 + NH3
Glycine synthase
NAD−
NADH + H+



B- Metabolic Role of Glycine:

1- Synthesis of Heme: glycine is necessary in the first reaction of heme synthesis.

2- Synthesis of Glutathione: glutathione is a tripeptide formed from three amino acids; glutamic acid, cysteine and glycine.

3- Synthesis of Purine Nucleus.

4- Synthesis of Creatine.

5- Conjugation with benzoic acid to form hippuric acid and excreted in urine. In similar way with cholic acid to form glycocholic acid, a bile acid which is excreted in bile as sodium salts.

6- Glycine is Glucogenic.

7- Source of formate (" one carbon pool") and oxalate.

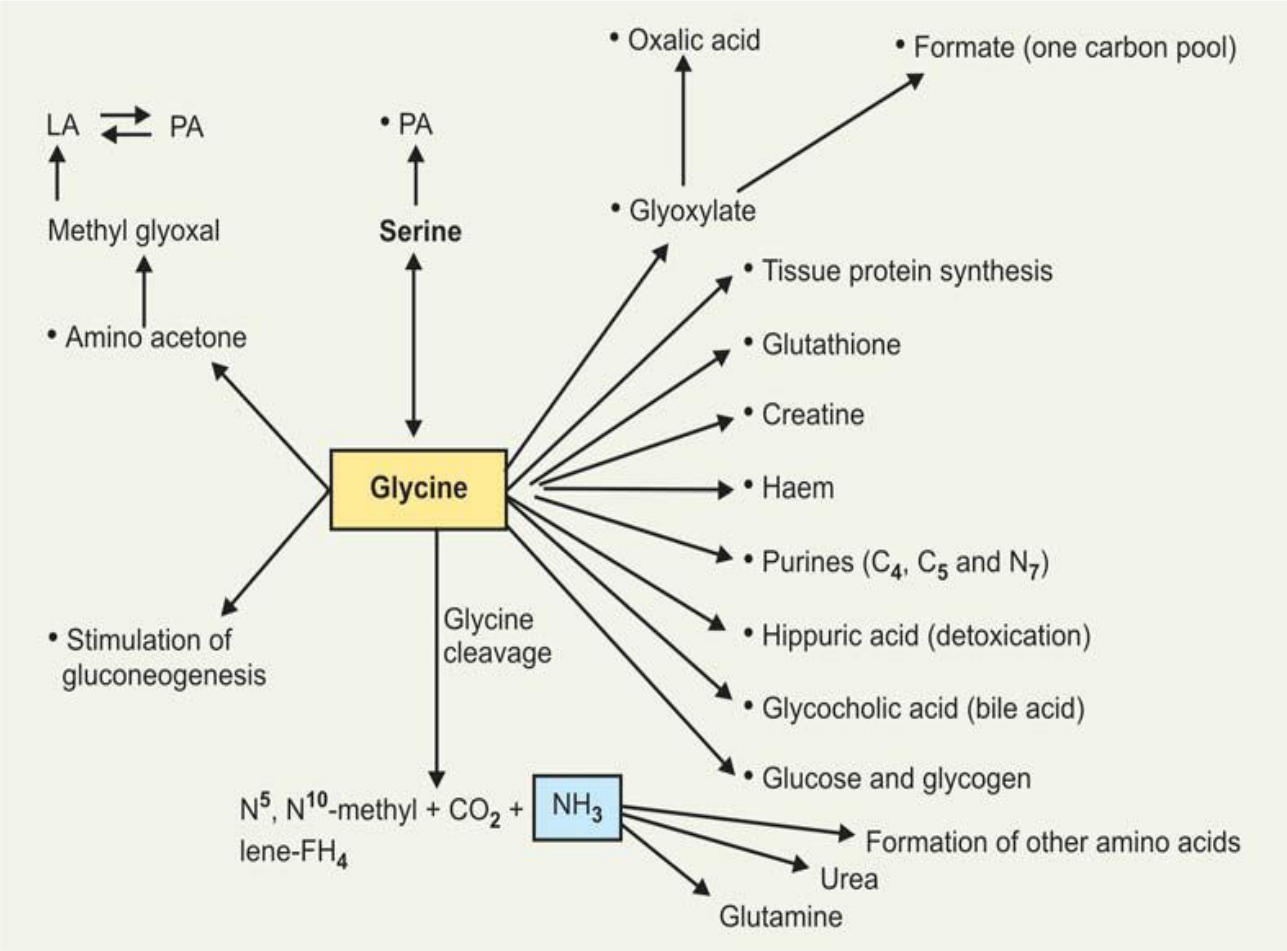


Figure: Glycine, showing metabolic fate and metabolic role

Inherited Disorders of Glycine Metabolism

Two disorders are associated with glycine metabolism:

1. Glycinuria:

The disease is characterized by excess urinary excretion of glycine.

Inheritance: Autosomal dominant may be X-linked trait.

Defect: There is no enzyme deficiency. Defect is attributed to renal tubular reabsorption of glycine.

Clinically: Tendency to formation of oxalate stones in kidney though the amount of oxalate excreted in urine is normal. Plasma level of glycine is normal. Urinary excretion of glycine ranges from 600 to 1000 mg/dl.

2. Primary Hyperoxaluria

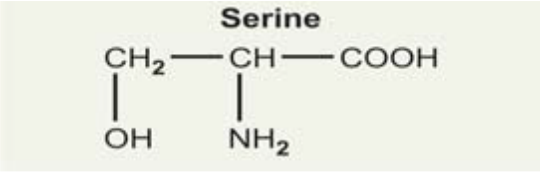
An inherited disorder characterized by continuous high urinary excretion of oxalates. Not related to dietary intake. Excess oxalate arises from glycine.

Defect: Exact biochemical defect is not known. May be **glycine transaminase** deficiency together with some impairment of oxidation of glyoxylate to formate. Glyoxylate formed from glycine by oxidative deamination is channelised to oxalate formation.

Clinical features: Progressive bilateral calcium oxalate urolithiasis, oxalate stone formation in genitourinary tract, also may be nephrocalcinosis, and recurrent infection of the urinary tract.

Prognosis: Death occurs in childhood or early adult life from renal failure or hypertension.

SERINE



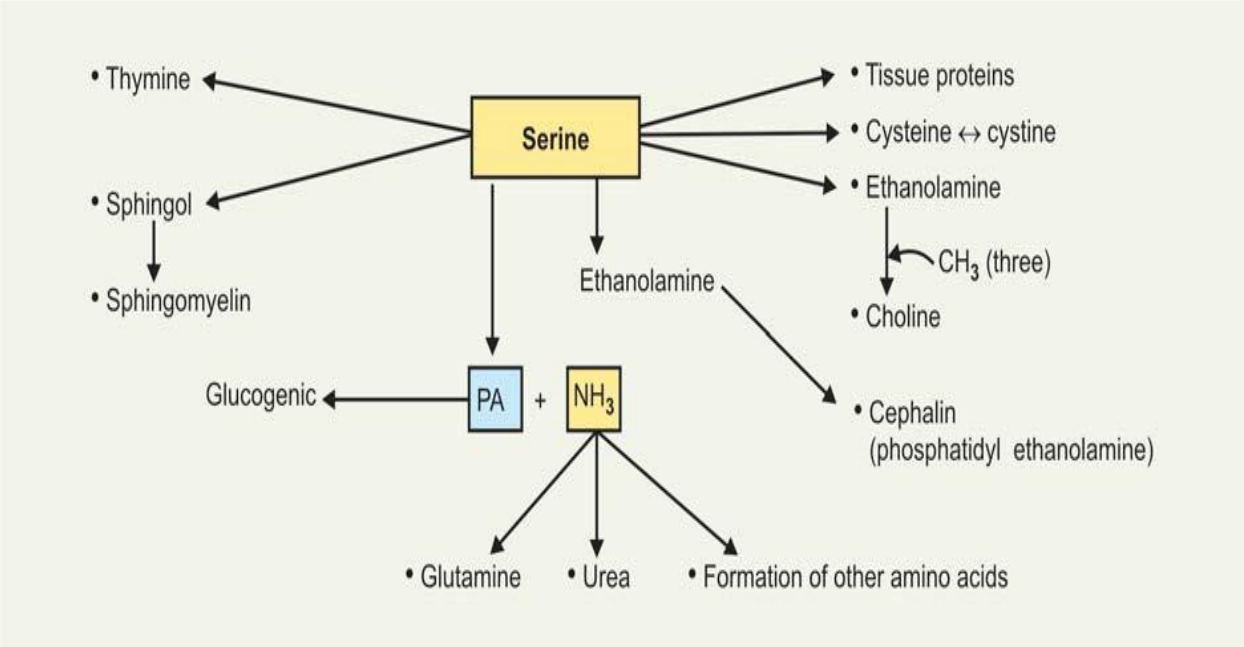
A. Metabolic Fate

It is deaminated by ***L-serine-dehydrase*** in Liver to form **Pyruvic acid** (non-oxidative deamination).

B. Metabolic Role

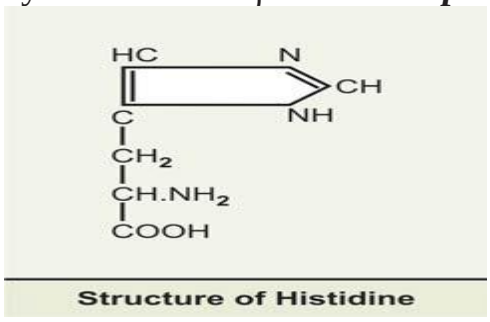
• As serine produces pyruvic acid, it is ***glucogenic.***
• Serine can be utilized, like all amino acids for formation of tissue proteins.
• Serine is a ***"carrier" of PO4 group*** in phosphoproteins.
• ***Serine contributes the carbon-skeleton to form cysteine. Sulphur of cysteine comes from methionine.***
• Serine undergoes decarboxylation to form ***Ethanolamine*** by the enzyme *decarboxylase* in presence of B6-PO4. This is very important reaction as 'ethanolamine' is the precursor for Formation of phosphatidyl ethanolamine (cephalin).
– Formation of 'choline' (a lipotropic factor) by three successive methylations, ~ CH3 group is donated by S-adenosyl methionine ("Active" methionine).
• Serine is used for synthesis of sphingol.
• β-Carbon of serine used for thymine formation.

• Hydroxyl group of serine in an enzyme protein is phosphorylated/ dephosphorylated to form active/inactive forms of the enzyme



HISTIDINE

Nutritionally **semiessential** amino acid. Histidine is required in the diet in growing animals and in pregnancy and lactation. ***Under these conditions, the amino acid becomes essential.*** Chemically it is α-***amino***-β-***imidazole propionic acid***



Structure of Histidine

A. Metabolic Fate

• Histidine on deamination produces urocanic acid, which is converted to 4-imidazolone-5-propionate by the enzyme *urocanase*. This product on addition of water produces ***formiminoglutamic acid (Figlu),*** which is converted to glutamate, the latter is transaminated to α- ketoglurate, which is an intermediate of TCA cycle.

B. Metabolic Role

• It is **glucogenic** through formation of glutamate to α-ketoglutarate.
• **Histamine** formation: Decarboxylation of histidine produces histamine.

• ***Formate*** can serve as one carbon moiety. The 'onecarbon' fragment of histidine is taken up by folic acid and metabolised by transformylation reaction normally.

In deficiency of folic acid, the histidine derivative, formiminoglutamic acid, (figlu) accumulates and excreted in urine, used as a test for folic acid deficiency

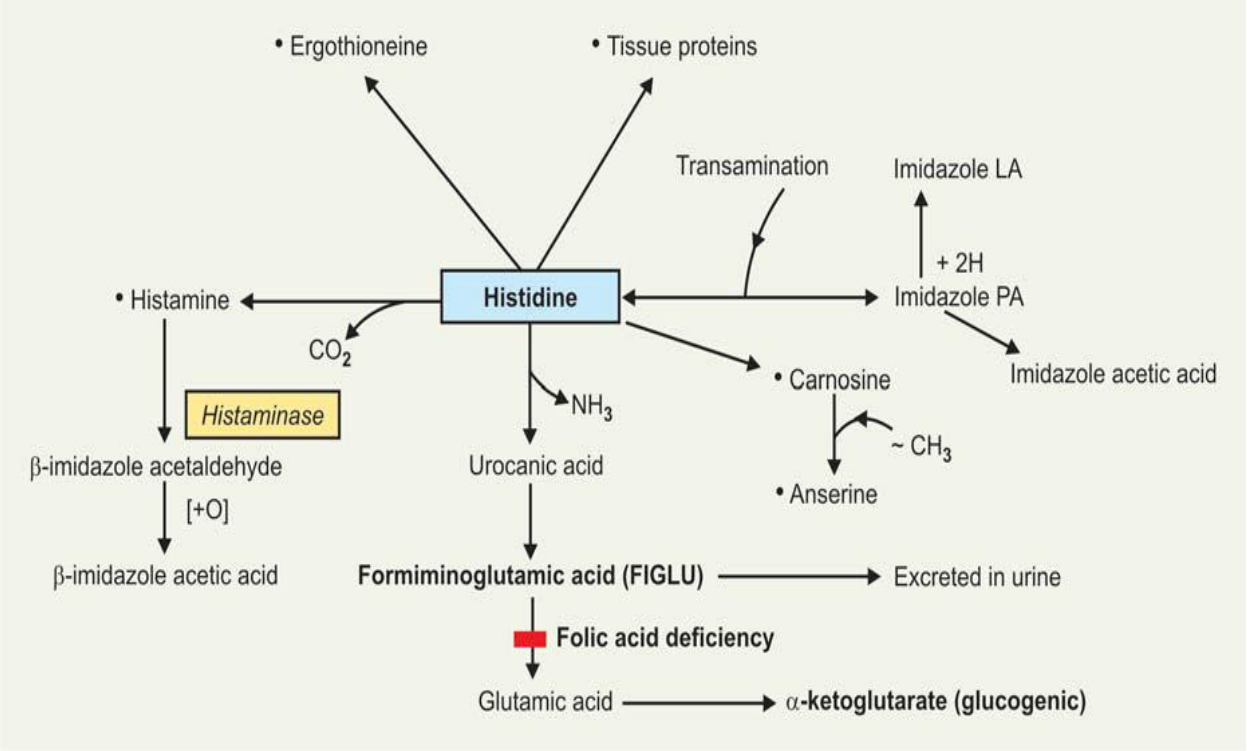
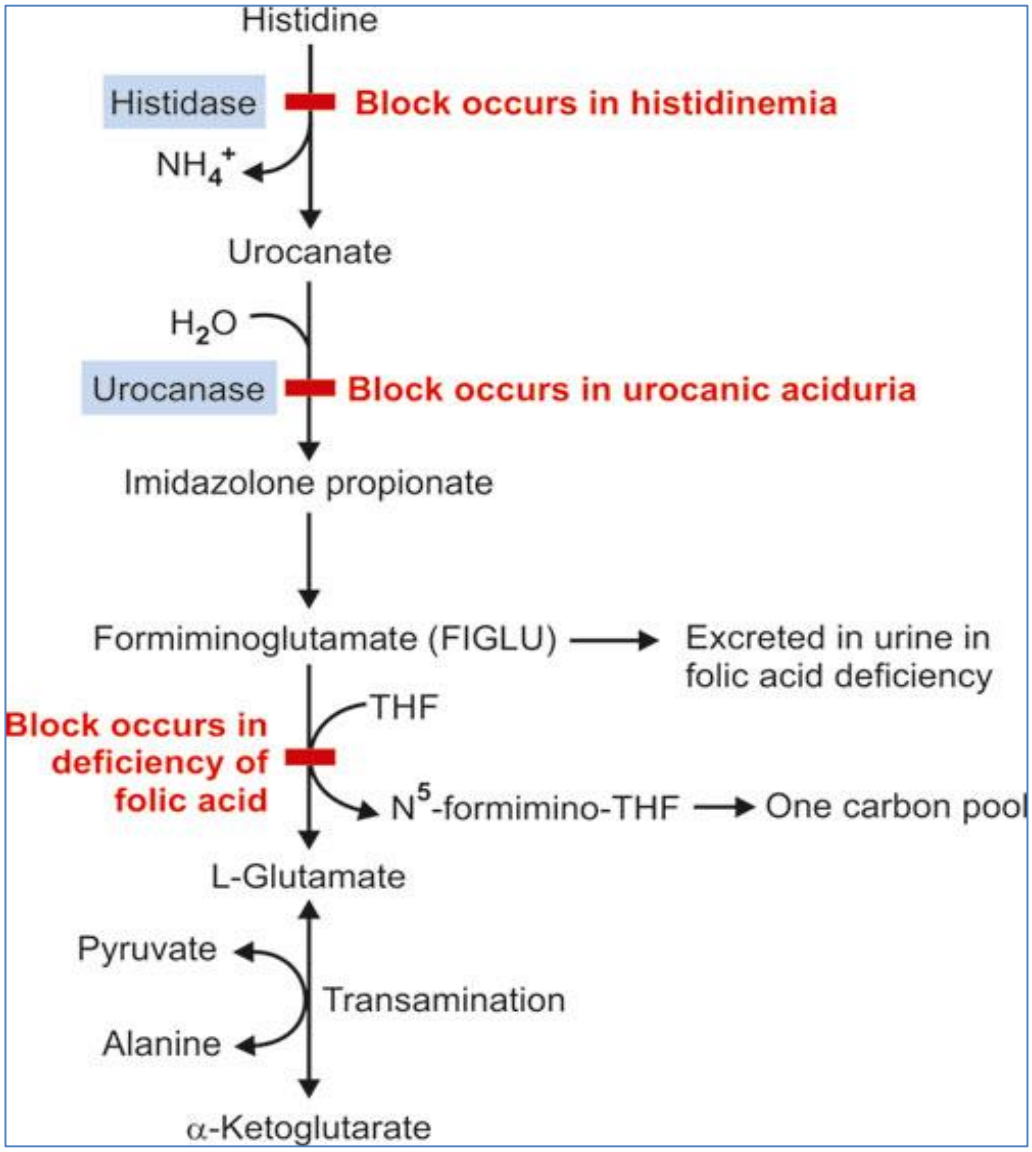


Figure: Histidine showing metabolic role



ALANINE

Chemistry and Functions

Little free β-alanine is present in tissues. It is found in combination as:

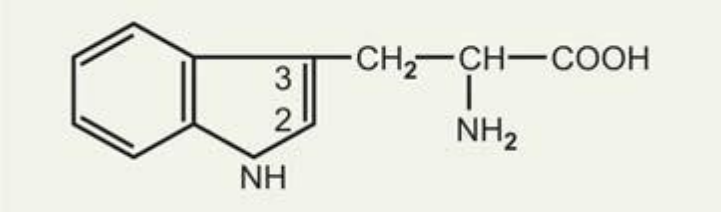
- **β-alanyl dipeptides, e.g. carnosine and anserine;**
- **As a constituent of coenzyme A.**

Source: In mammalian tissues: β-alanine arises principally from catabolism of uracil, carnosine and anserine.

Catabolism: Catabolism of β-alanine in mammals involves transamination to form ***malonate semialdehyde***, which is oxidized to acetate and thence to CO2.

TRYPTOPHAN

• It is an essential amino acid. Omission of tryptophan in diet of man and animals is followed by tissue wasting and negative nitrogen balance.
• It is both glucogenic and ketogenic.
• Tryptophan can synthesize niacin (nicotinic acid), a vitamin of B-complex group.
• It is a heterocyclic amino acid and chemically it is "α-amino--3-indole propionic acid". It is the only amino acid with an indole ring.



A- Metabolic Fate

Tryptophan is finally converted to glutaric acid, which in turn gives two molecules of acetyl-CoA (thus it is ***ketogenic***) from acetoacetyl- CoA. It also produces alanine which on transamination can form ***Pyruvic acid*** (thus it is ***glucogenic***).

B- Metabolic Role

1- Tryptophan is both glucogenic and ketogenic.
2- Nicotinic acid formation
3- Formation of Tryptamine
4- Transamination
5- Formation of xanthurenic acid: xanthurenic acid excretion in urine is an index for B_6- deficiency.
6- ***Formation of serotonin: Another major pathway. Synonyms:*** other names of serotonin are "enteramine" or "thrombocytin

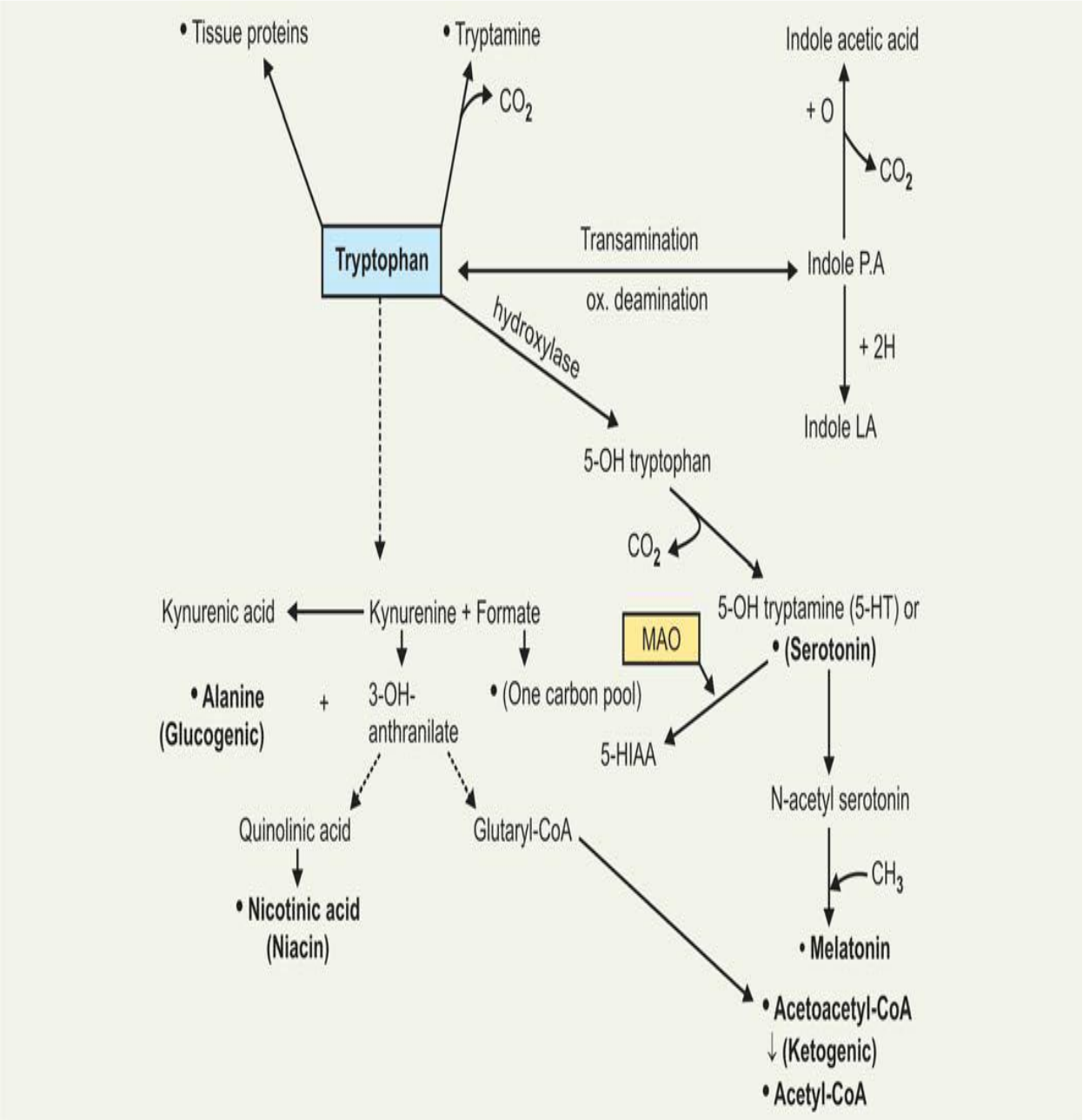


Figure: Tryptophan—showing metabolic role