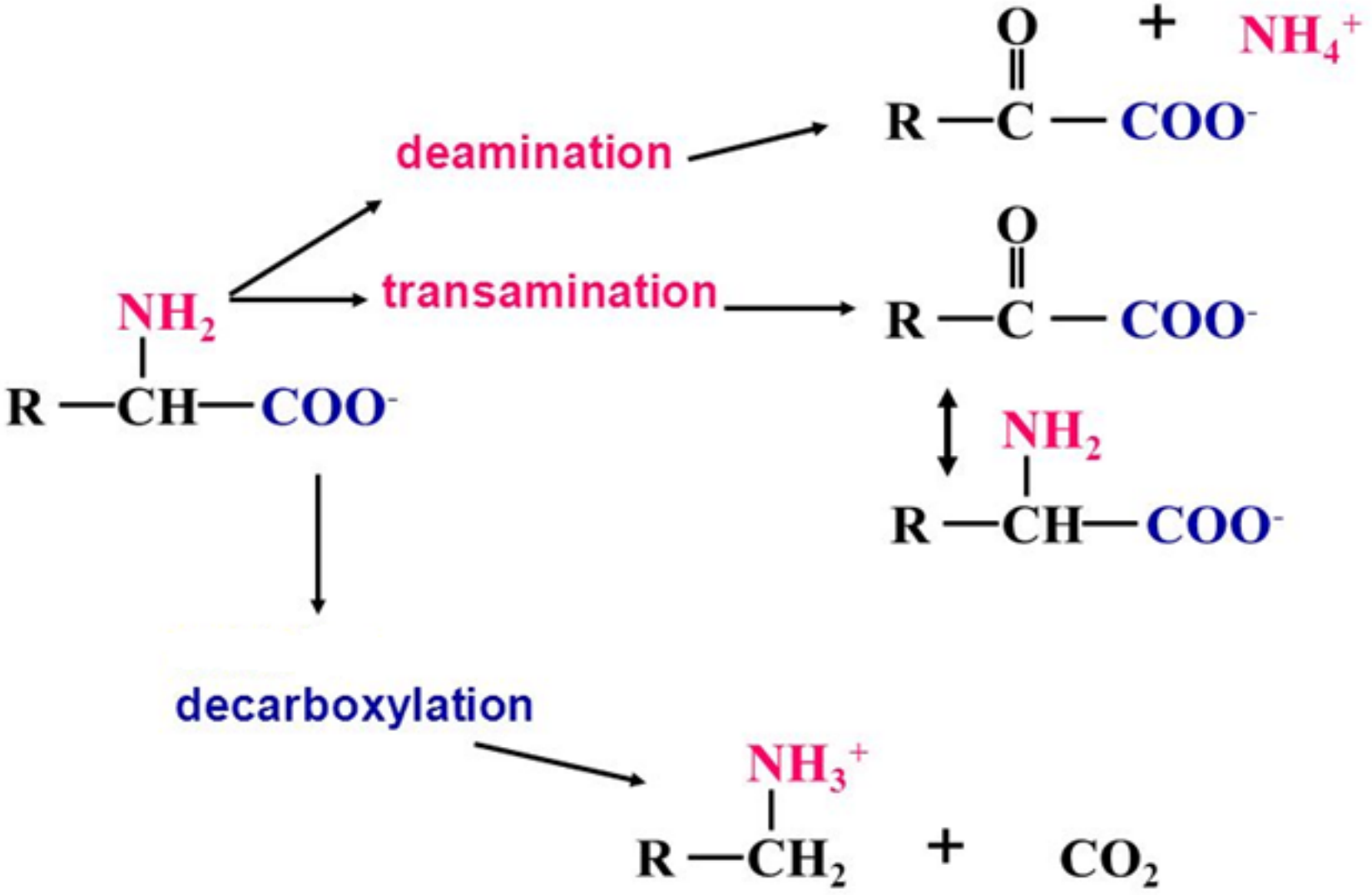
# *METABOLISM OF AMINO ACIDS*

**Lecture II**

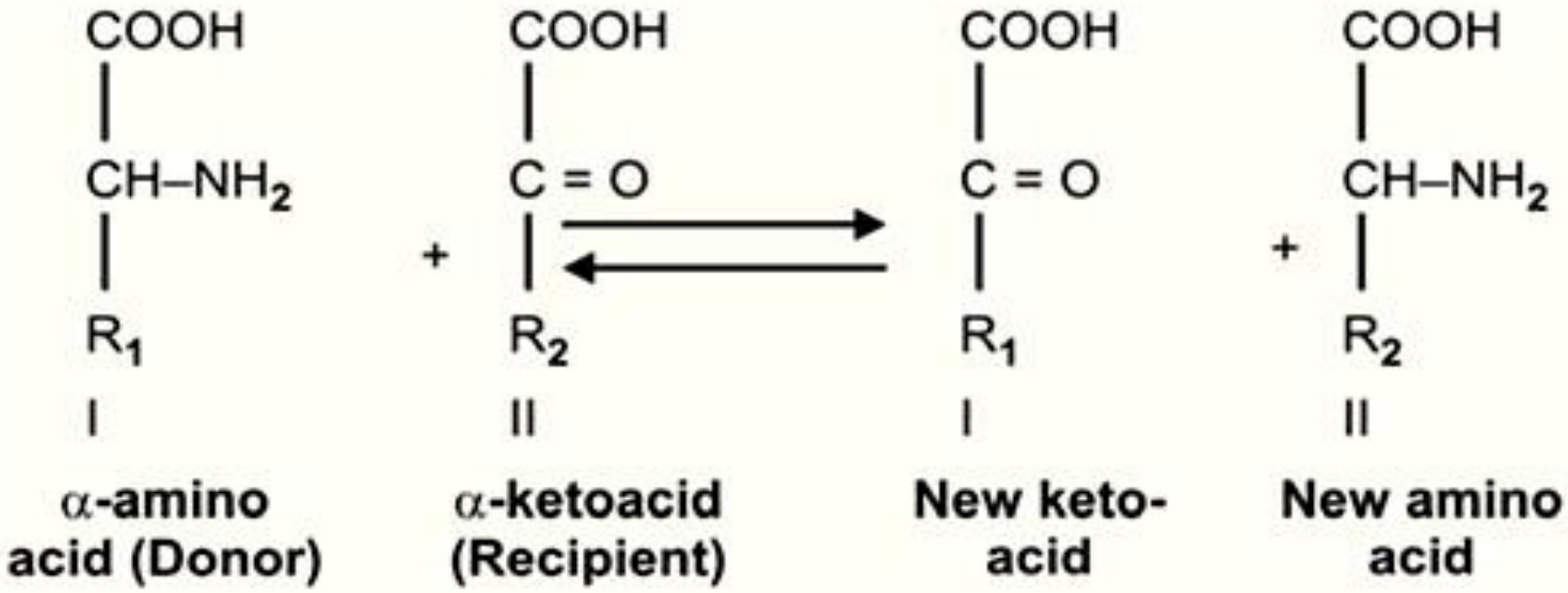
# General reactions of amino acids metabolism



**Transamination**
**typically initiates**
**amino acid catabolism**

# TRANSAMINATION OF AMINO ACIDS

**Transamination is a reversible reaction in which α-amino group of one amino acid is transferred to ketoacid resulting in formation of a new amino acid and a new ketoacid.**




**While most amino acids may act as donor , the recipient ketoacids may be either**

**α-ketoglutarate, oxaloacetate or pyruvate.**

# TRANSAMINATION OF AMINO ACIDS

**The process represents an intermolecular transfer of $NH_2$ group without the splitting out of $NH_3$.**

**(*Ammonia formation does not take place by transamination reaction*)**

**Transamination takes place principally in liver, kidney, heart and brain.**

**But the enzymes are present in almost all mammalian tissues and transamination can be carried out in all tissues to some extent.**

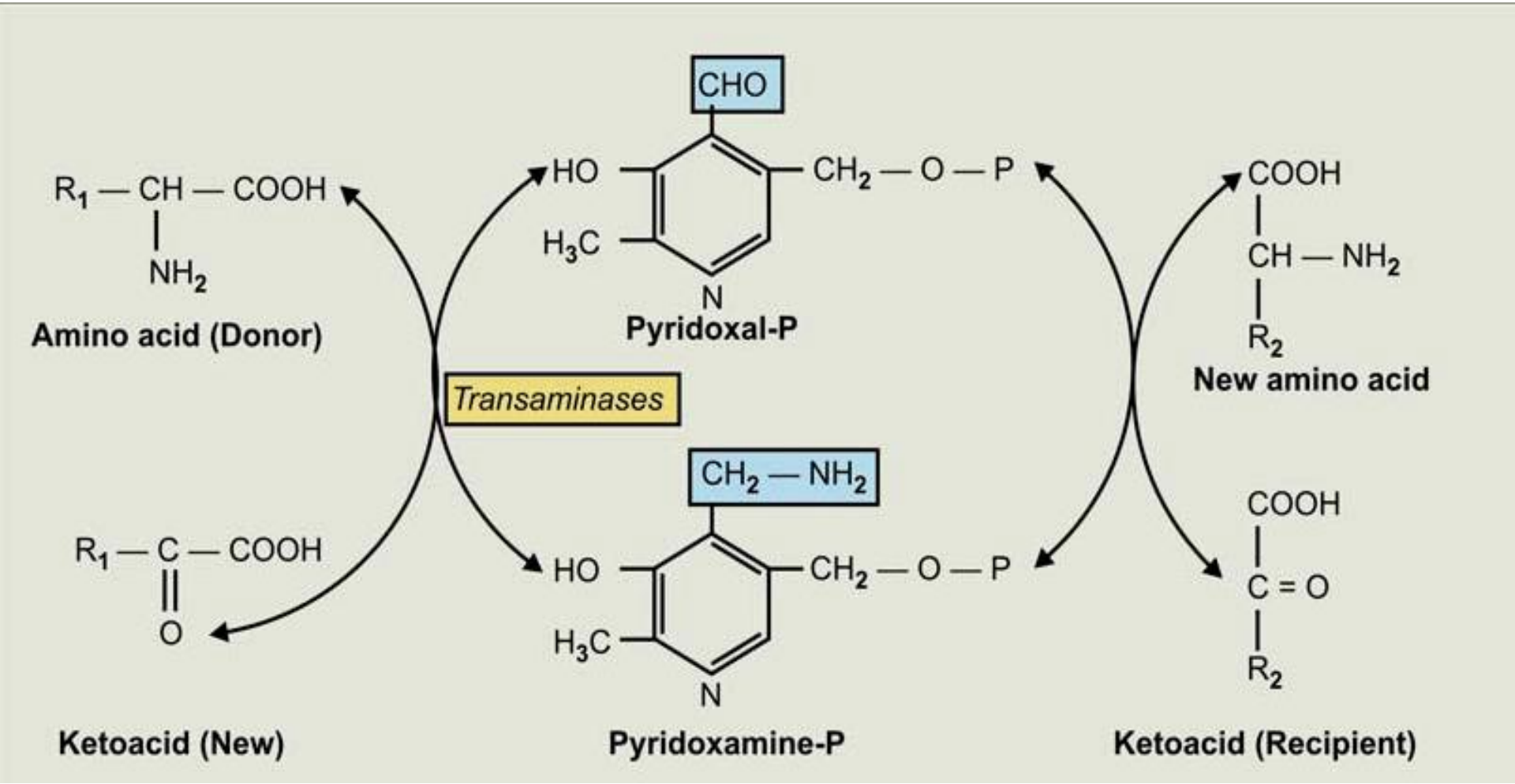
# TRANSAMINATION OF AMINO ACIDS

**The enzymes concerned in transamination are called**

**aminotransferases (or transaminases)**

**The coenzyme required for the reaction is**

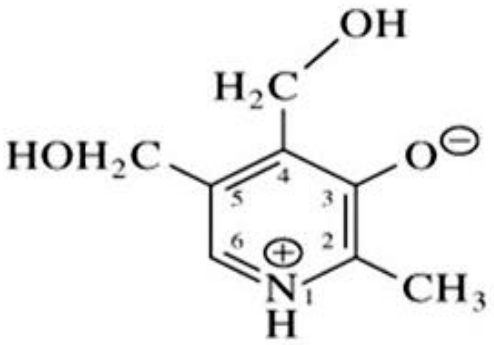
**pyridoxal-phosphate (PLP).**



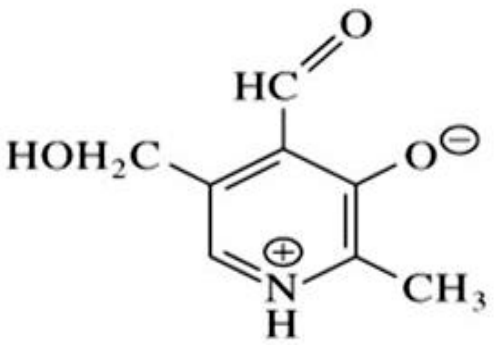
# Pyridoxal-phosphate (PLP)

- **Is derived from $B_6$ family of vitamins**
- **Is a coenzyme for enzymes catalyzing reactions of amino acid metabolism (transamination, decarboxilation, isomerisation)**

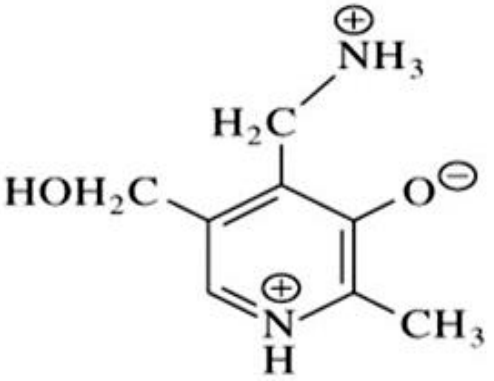
(a)



Pyridoxine

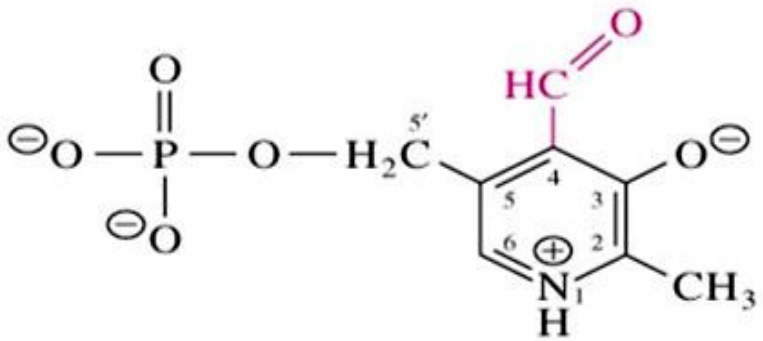


Pyridoxal



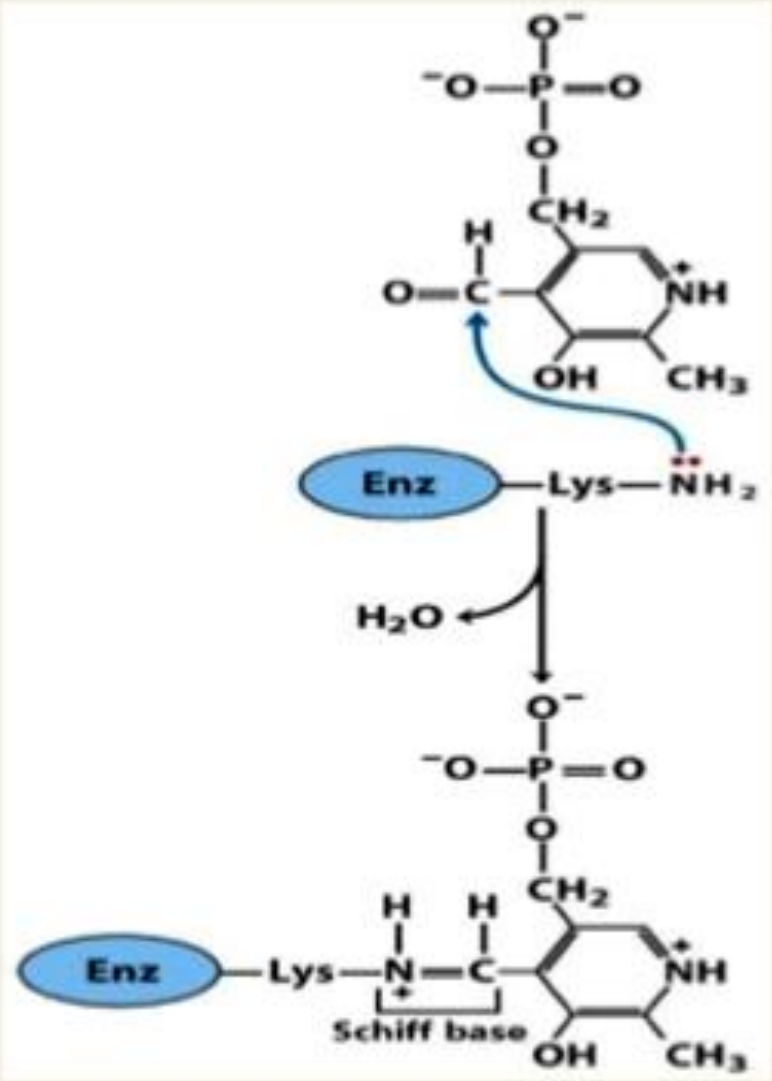
Pyridoxamine

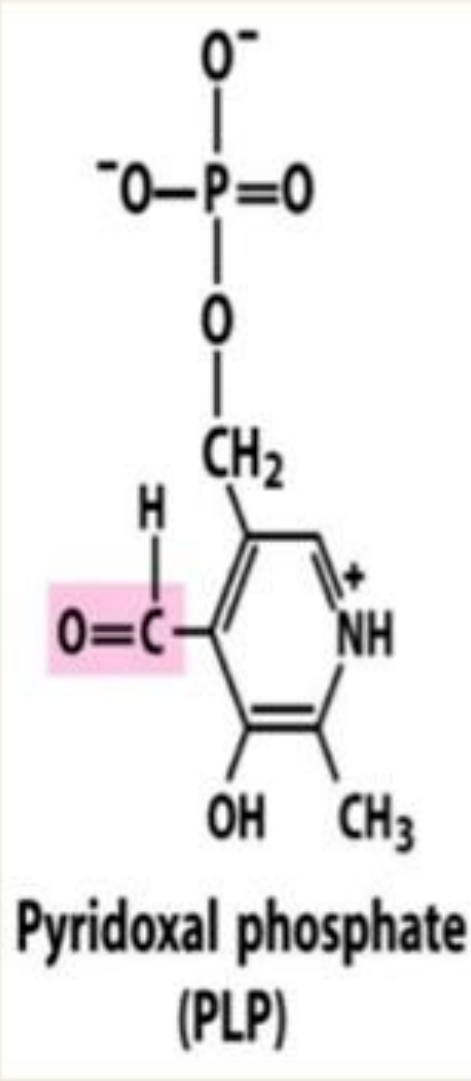
(b)

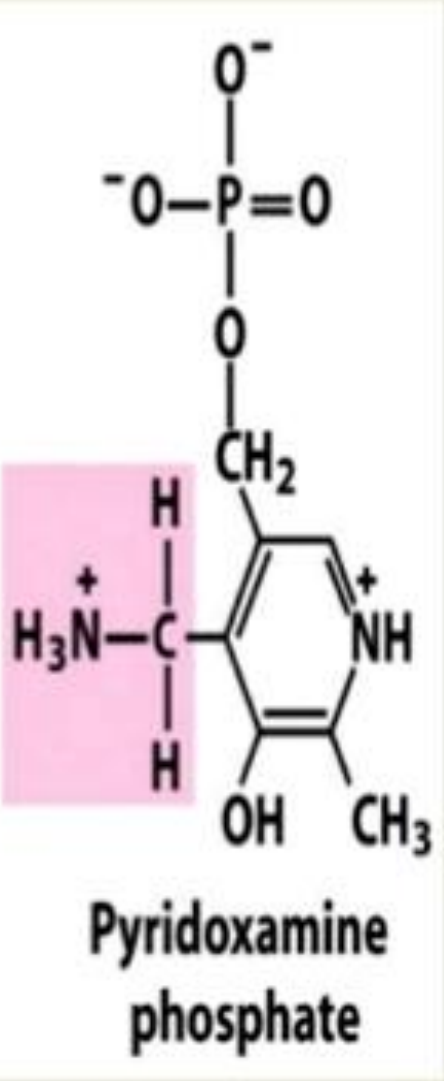


Pyridoxal 5′-phosphate (PLP)

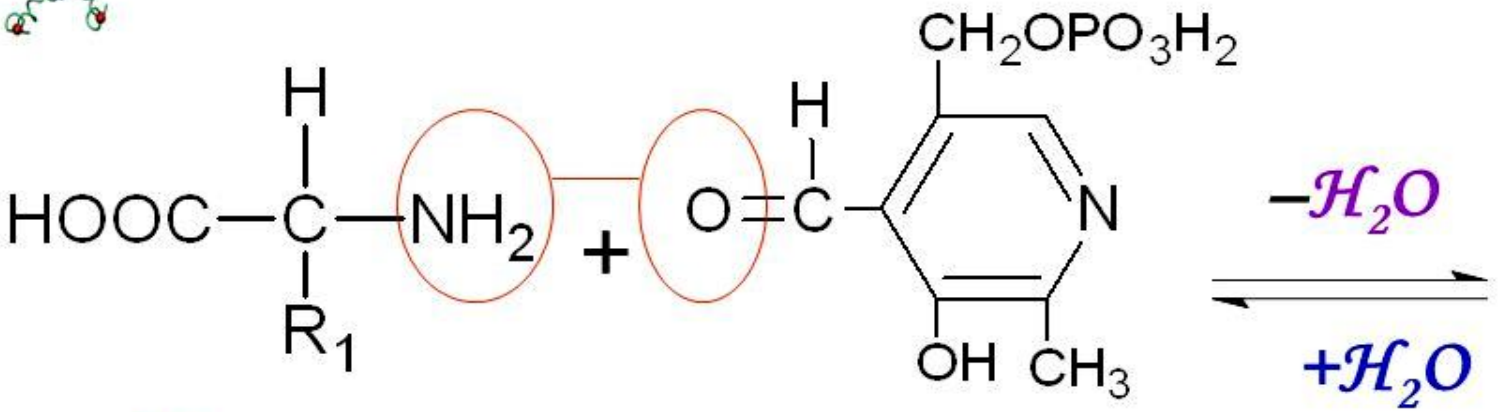
# Role of Pyridoxal-phosphate in transamination



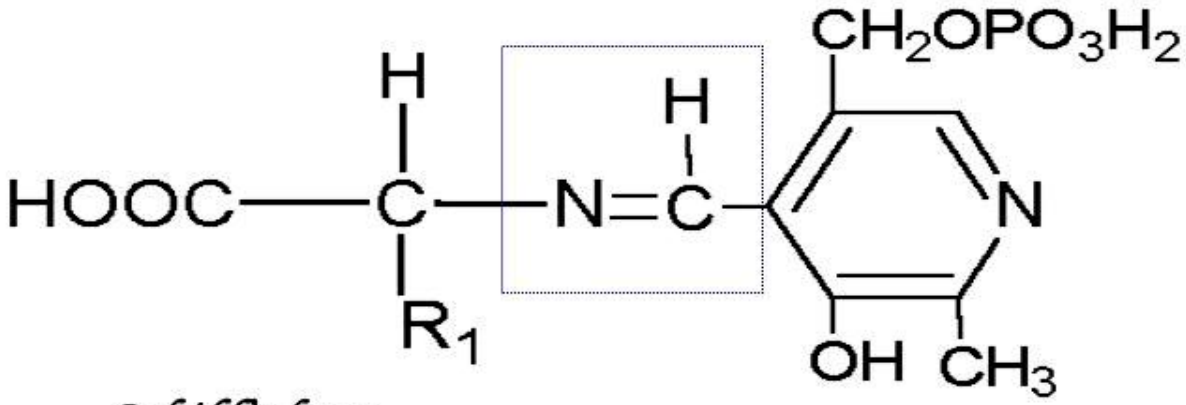



# The mechanism of transamination




AA

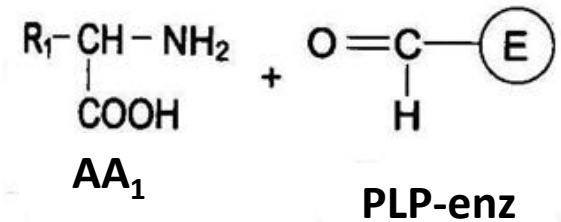
PLP



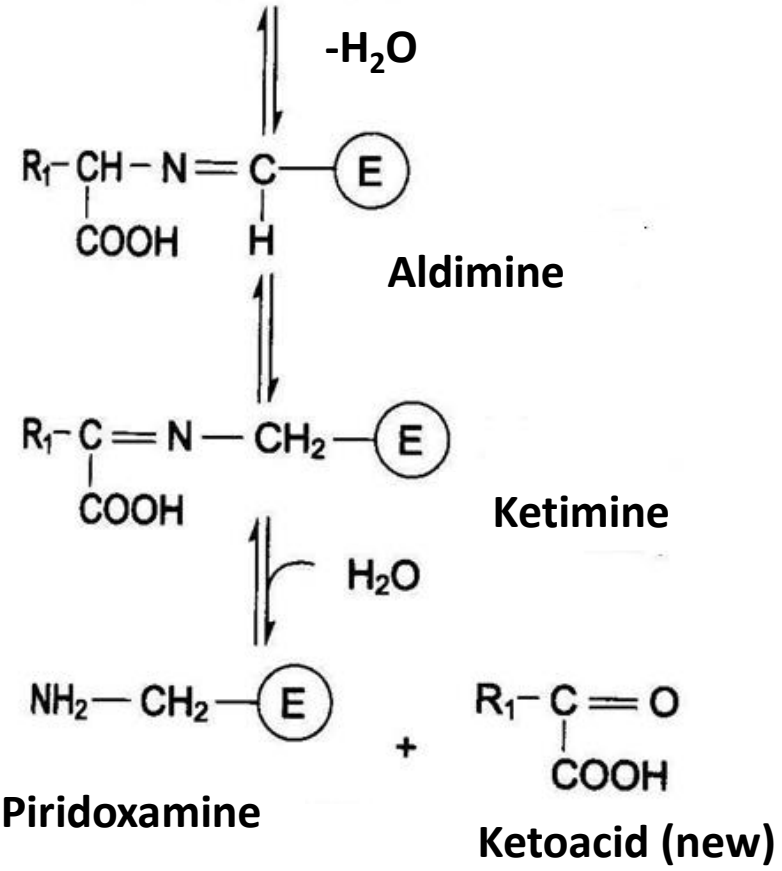

Schiff's base

# Mechanism of transamination

**1st phase**

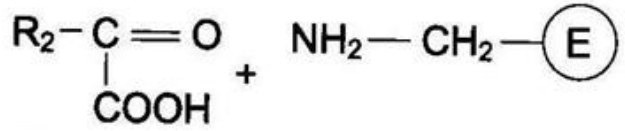



$AA_1$ PLP-enz

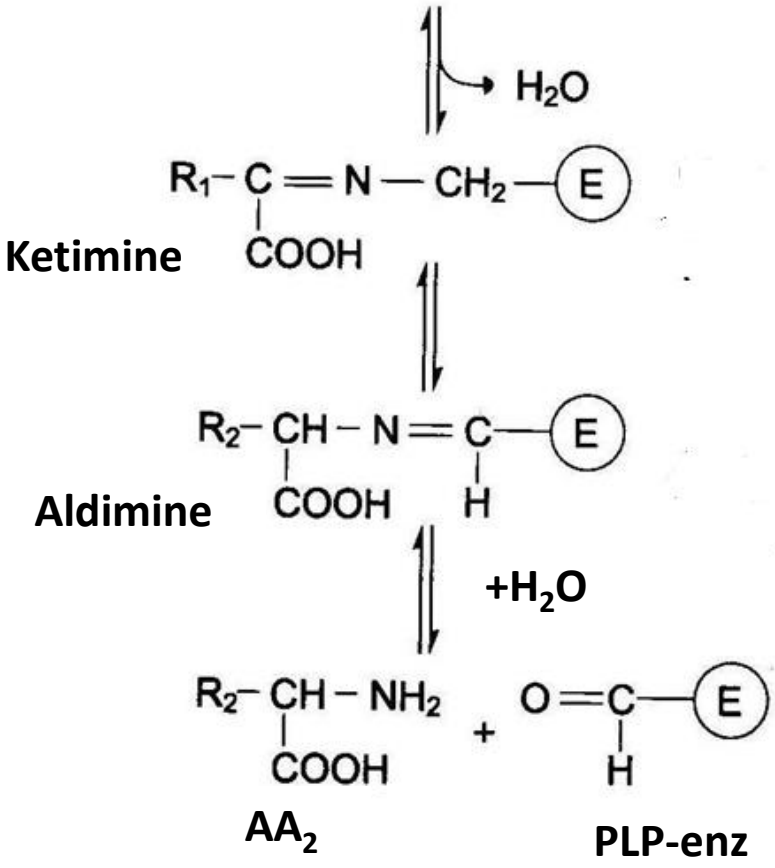



Piridoxamine Ketoacid (new)

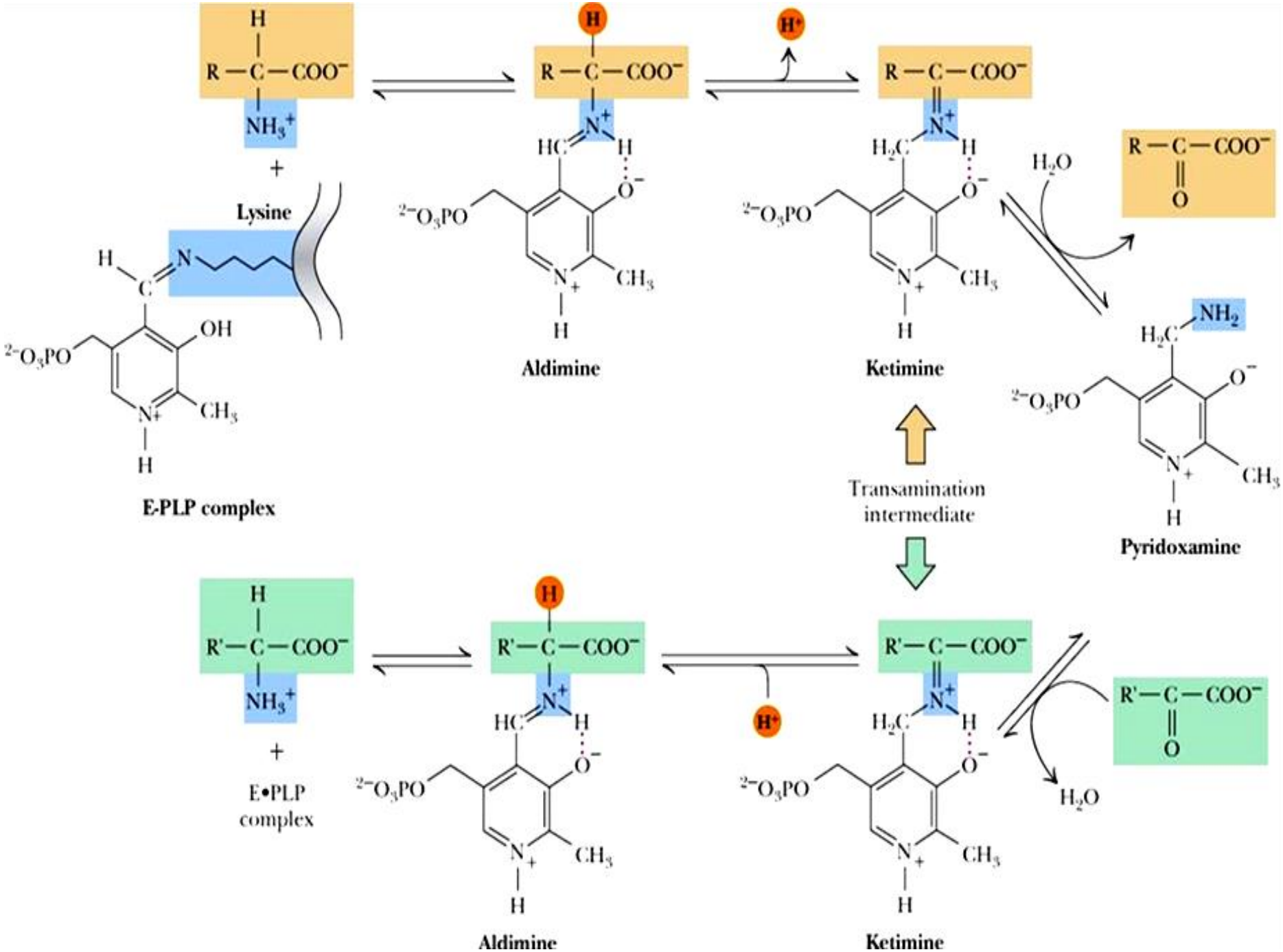
**2nd phase**




Ketoacid Piridoxamine




$AA_2$ PLP-enz


Lysine
E-PLP complex
Aldimine
Ketimine
Transamination intermediate
Pyridoxamine
E•PLP complex
Aldimine
Ketimine

# Biological Significance of Transamination

- Transamination is used both for the catabolic as well as anabolic processes.
- The resultant α-Keto acid can be completely oxidized to provide energy, glucose, fats or ketone bodies depending upon the cellular requirement.
- Since it is a reversible process, it is also used for the synthesis of non essential amino acids.
- In addition to equilibrating amino groups among available α-keto acids, the process of transamination **funnels amino groups** from excess dietary amino acids to those amino acids (e.g., glutamate) that can be **deaminated**.

**The activity of transaminases is high in tissues, and is low in the blood serum. In cell destruction or increased cell membrane permeability, transaminases are released from the tissue into the blood plasma. Clinical determinationof AlAT and AsAT activity in the blood serum is used for diagnostics of certain diseases.**

# Two transaminases are of clinical importance

**Aspartate amino transferase AsAT (SGOT, GOT – serum glutamate oxaloacetate transaminase)**

**Activity of the enzyme is very high in myocardium and also in liver cells.** The enzyme is also distributed in other tissues (muscles, pancreas, kidney, etc. )

**Normal serum activity**

**is 0.1-0.45 mmol/l/h.**

It is increased

in **myocardial infarction**.

# Alanine amino transferase AlAT (SGPT, GPT – serum glutamate pyruvate transaminase)

**The enzyme is found mainly in liver.**

**Normal enzyme activity is 0.1-0.68 mmol/L/h.**

**It is increased in hepatitis**

# AST/ALT ratio

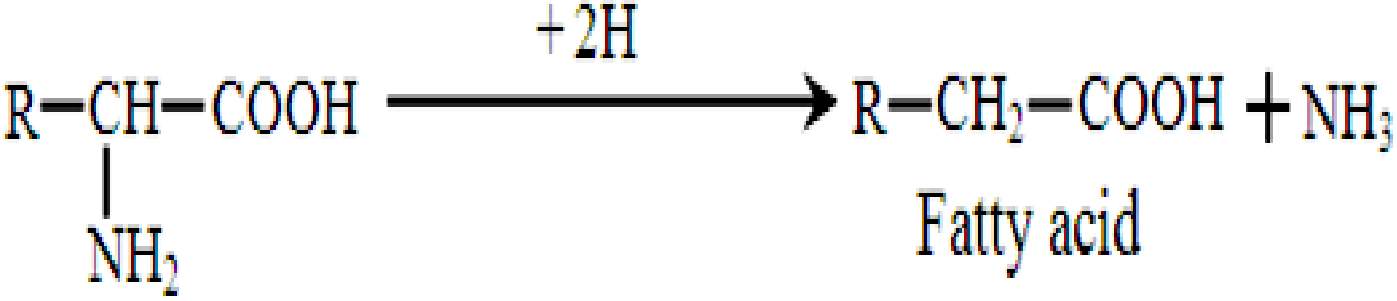
**The AST/ALT ratio is the ratio between activities of the enzymes in the blood. It is useful in medical diagnosis to differentiate between causes of liver damage, or hepatotoxicity.**

# DEAMINATION of AMINO ACIDS

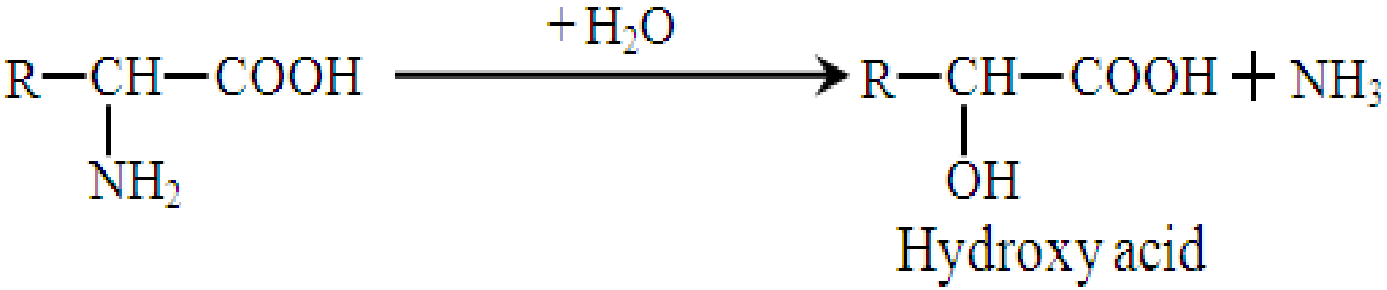
**Deamination is the process by which the amino group from an amino acid is removed as $NH_3$.**

**It can be of 4 types:**

**1. Reductive deamination**

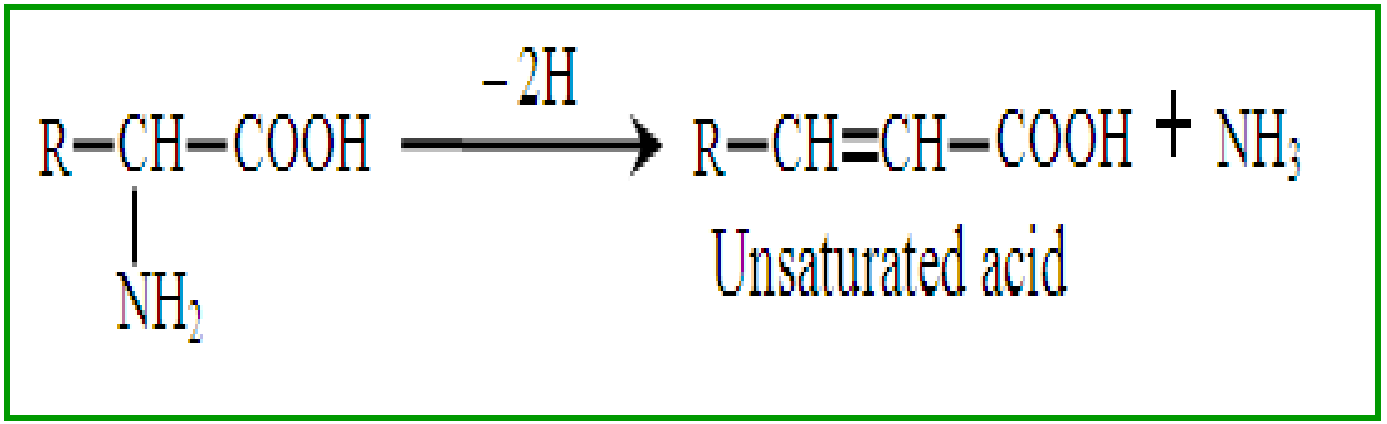



**2. Hydrolytic deamination**

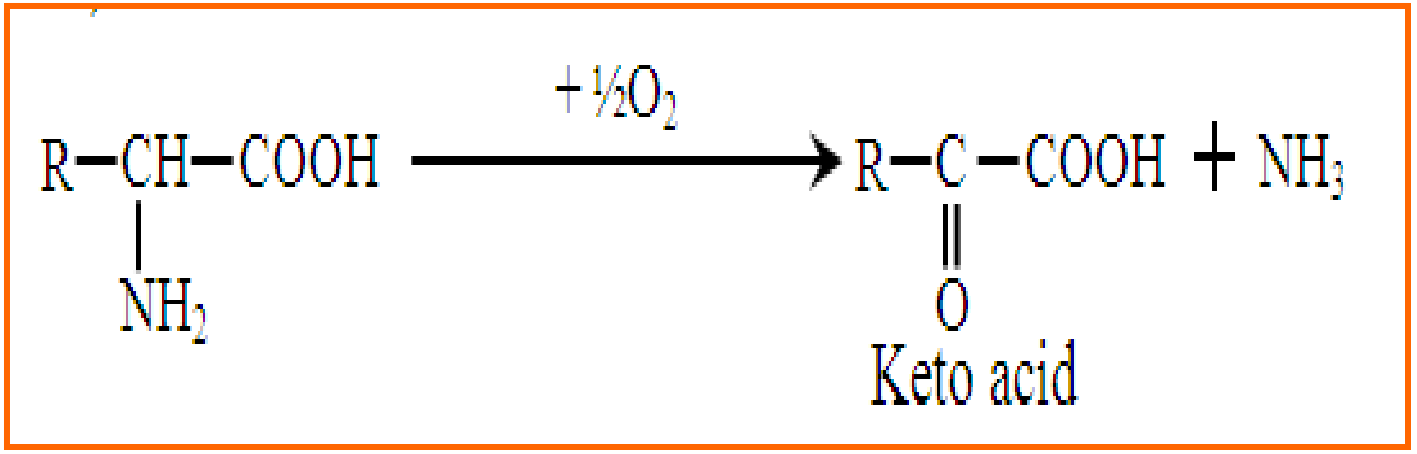


# DEAMINATION of AMINO ACIDS

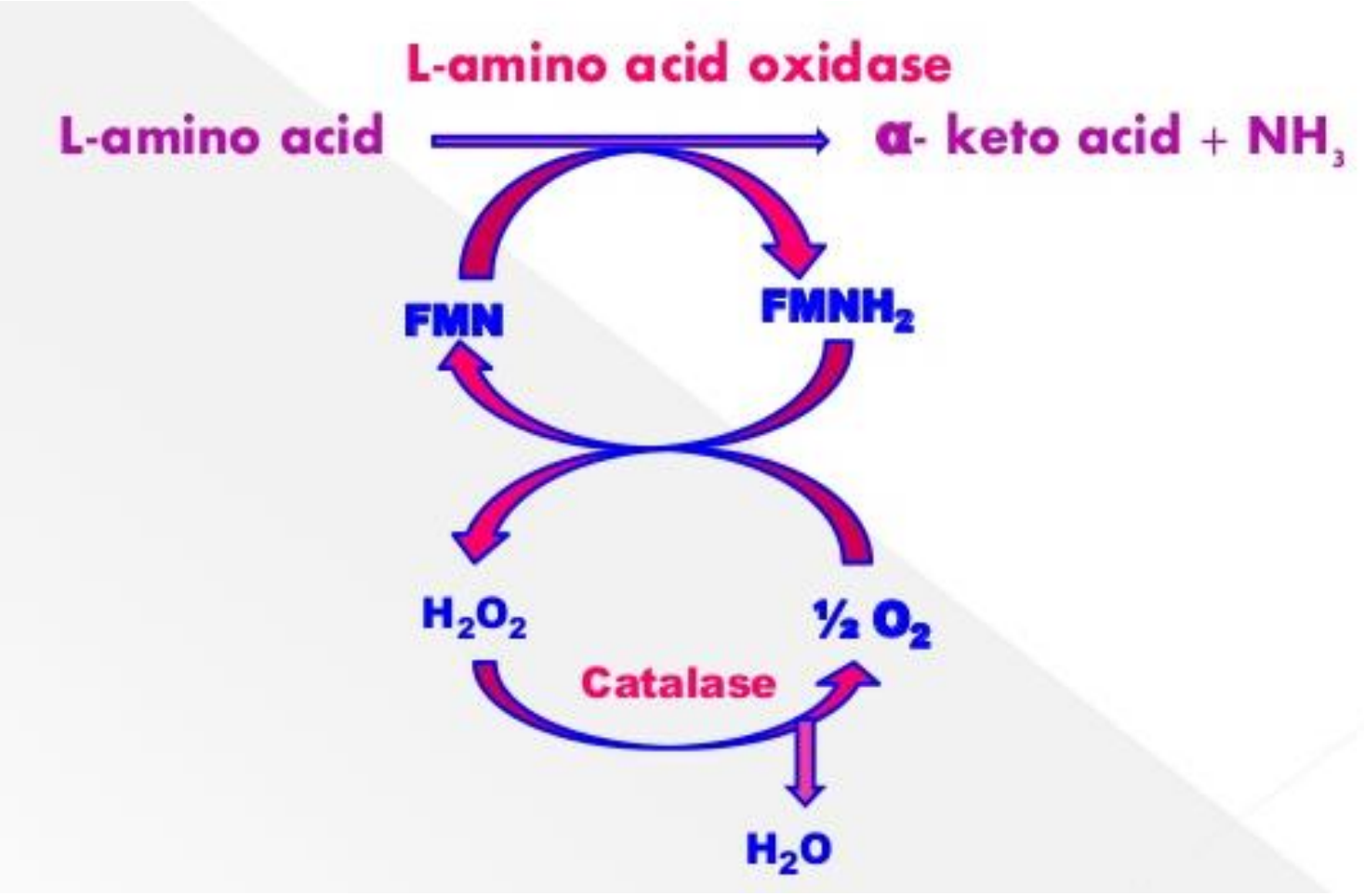
## 3. Intramolecular deamination




## 4. Oxidative deamination



# In humans, the major type is oxidative deamination



# Oxidative deamination

This takes place in **two steps:**

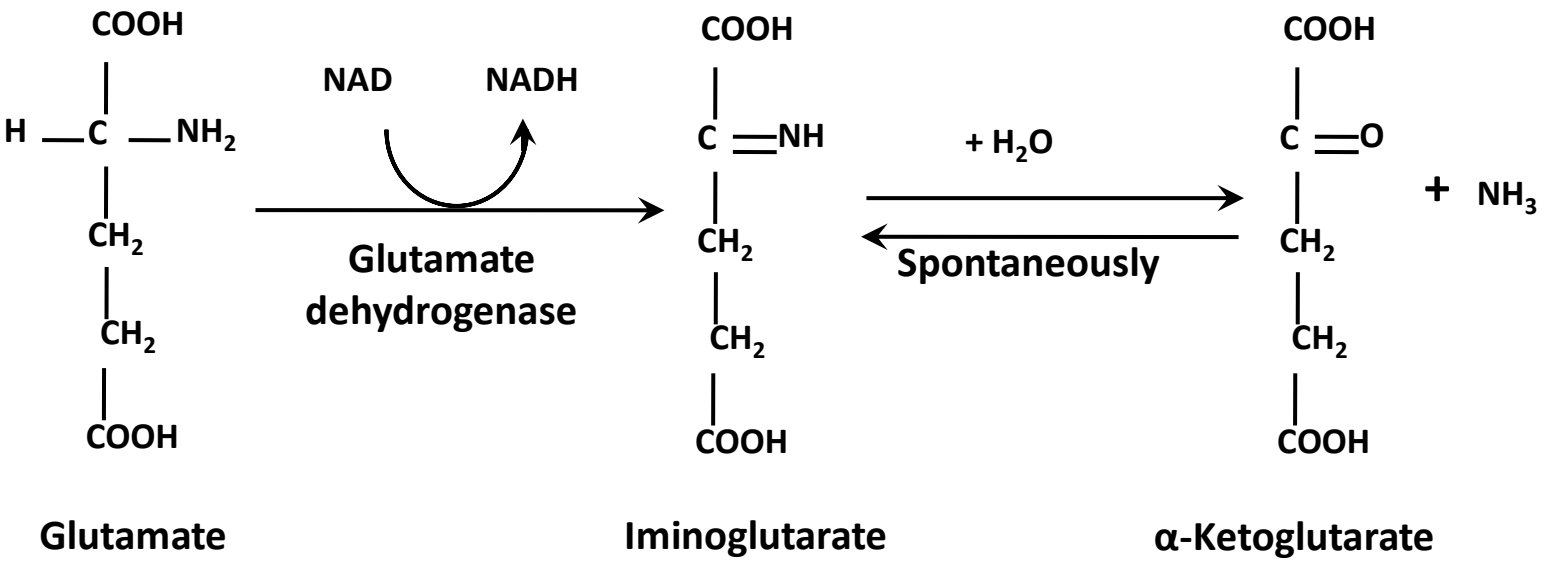
the amino acid is first dehydrogenated by the flavoprotein of the enzyme, ***L-amino acid oxidase,*** forming an **imino acid.**

In the next step, water is added spontaneously, and decomposes to the corresponding ketoacid, with loss of the iminonitrogen as $NH_3$.

# Oxidative deamination

**Glutamate dehydrogenase is the only enzyme involved in oxidative deamination in the body.**

**The enzyme directly deaminates only glutamate.**



# Biological role of oxidative deamination

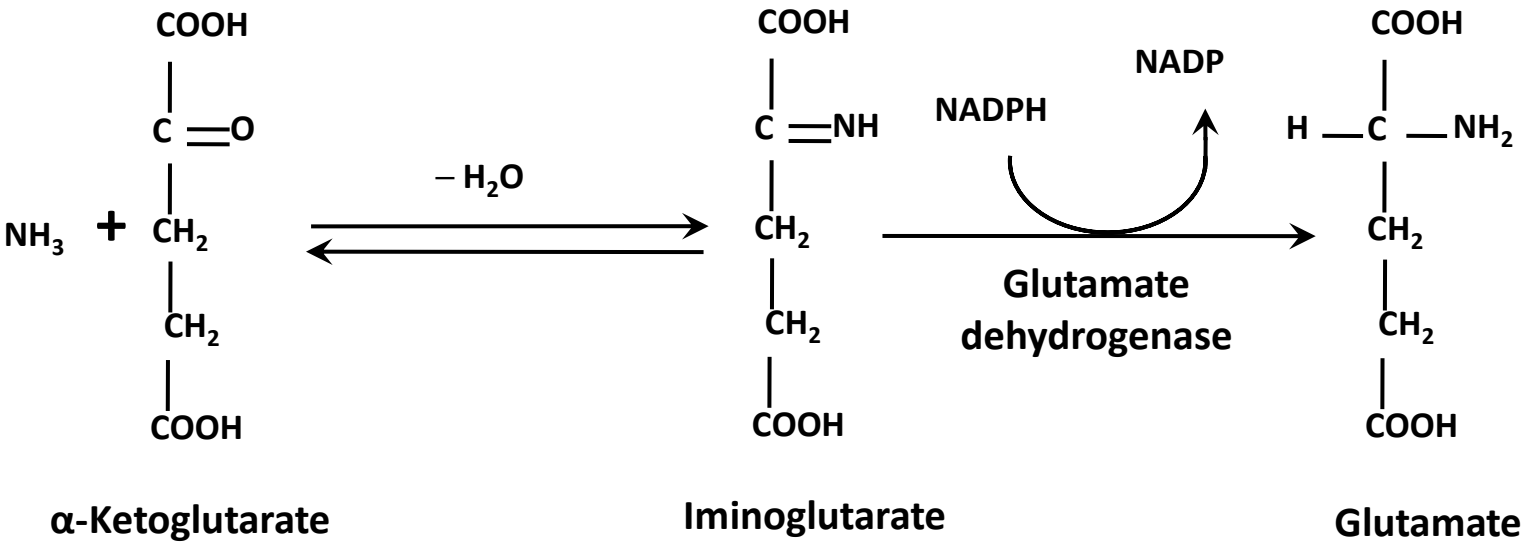
1. **Deamination of excess molecules of glutamate.**

2. **Helps deaminate other amino acids by way of indirect deamination (transdeamination).**

3. **The reaction produces toxic ammonia which has to be detoxified.**

# REDUCTIVE AMINATION

**This is the reverse reaction of oxidative deamination with participation of NADPH as a coenzyme:**




**This is the way for detoxification of $NH_3$.**
**Due to this reaction, synthesis of the new glutamate molecules occurs.**

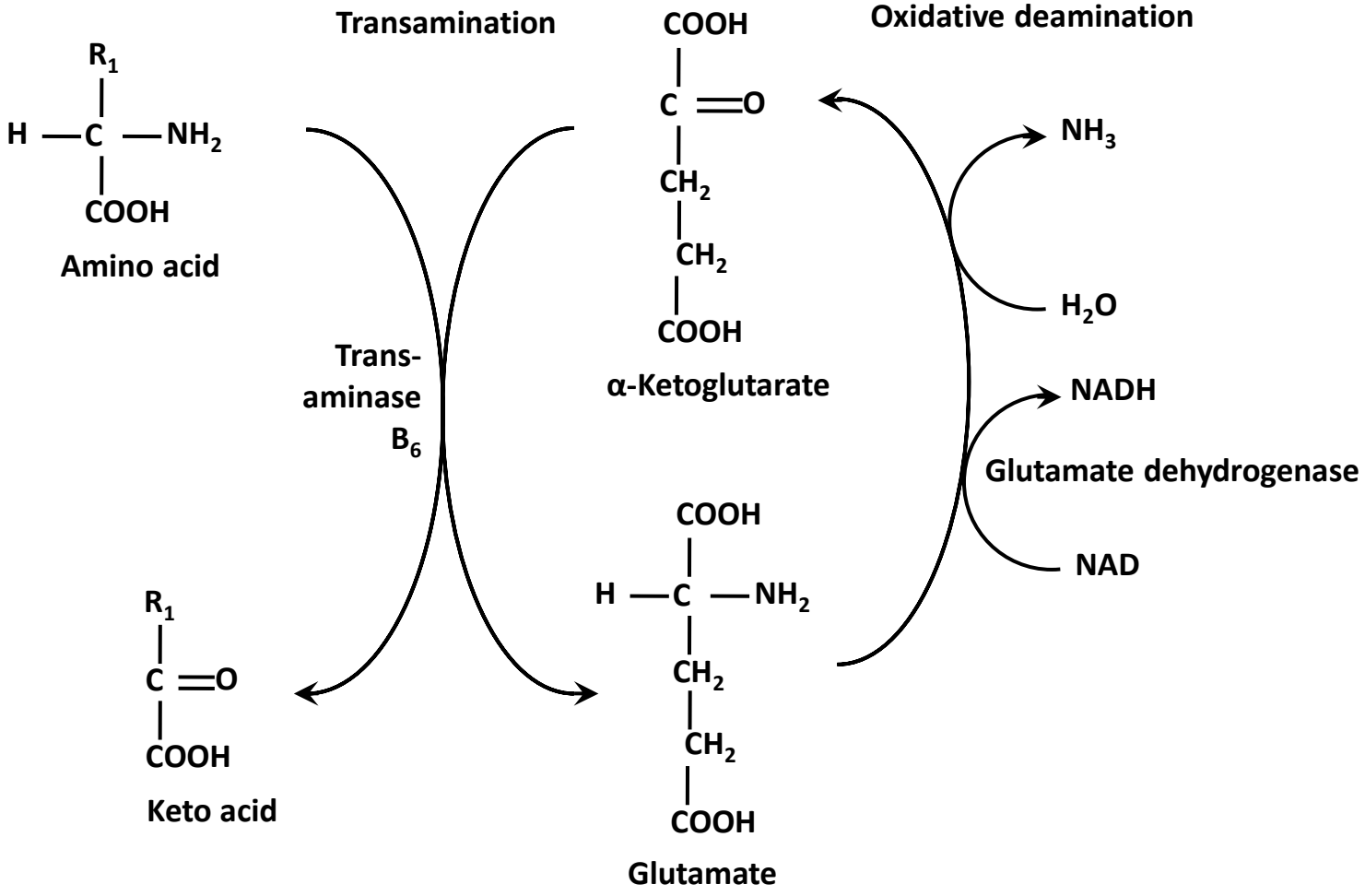
# TRANSDEAMINATION

**Glutamate is the only amino acid which undergoes direct deamination.**

**There are no enzymes for direct deamination of other amino acids.**

**Therefore, other amino acids may be deaminated only indirectly.**

**That is, to be deaminated, all the other amino acids have to undergo initially transamination with α-ketoglutarate to form glutamate. The glutamate undergoes then oxidative deamination with the release of ammonia.**

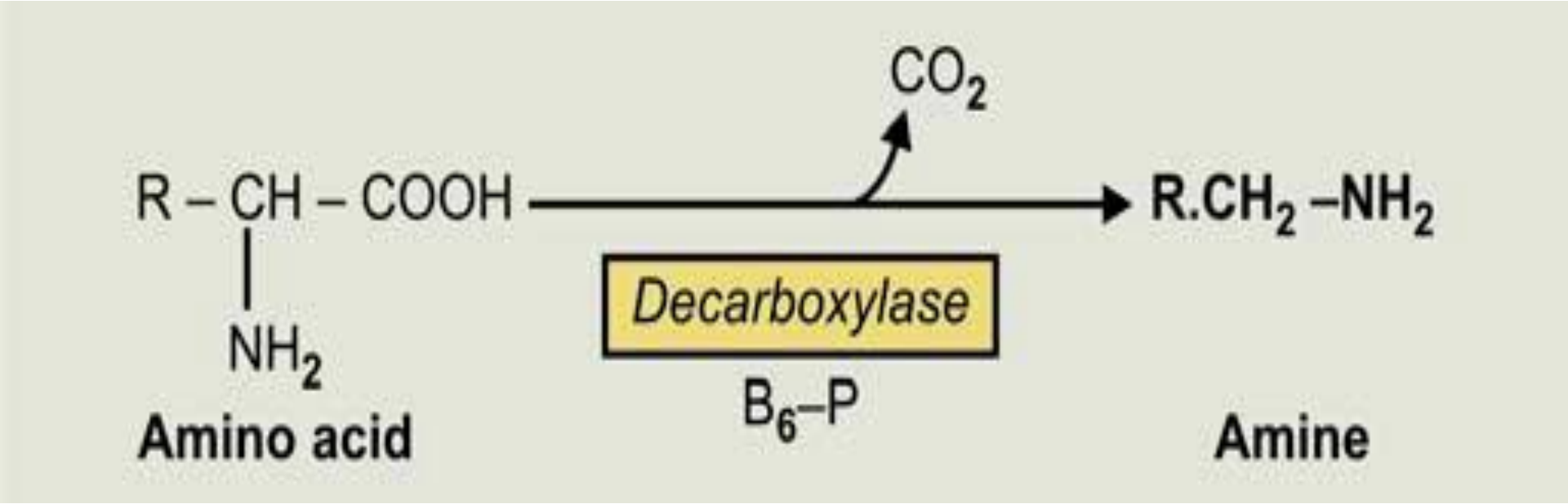



**Thus, transdeamination represents combination of transamination and oxidative deamination**

# DECARBOXYLATION

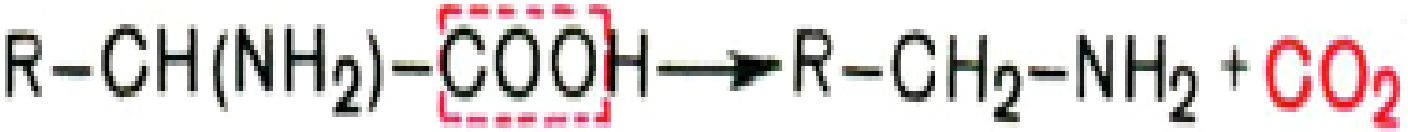
Decarboxylation is the reaction by which $CO_2$ is removed from the -COOH group of an amino acid as a result ***an amine is formed.***

The reaction is catalysed by the enzyme ***decarboxylase,*** which requires pyridoxal phosphate as coenzyme.



# There are 4 types of the amino acid decarboxylation

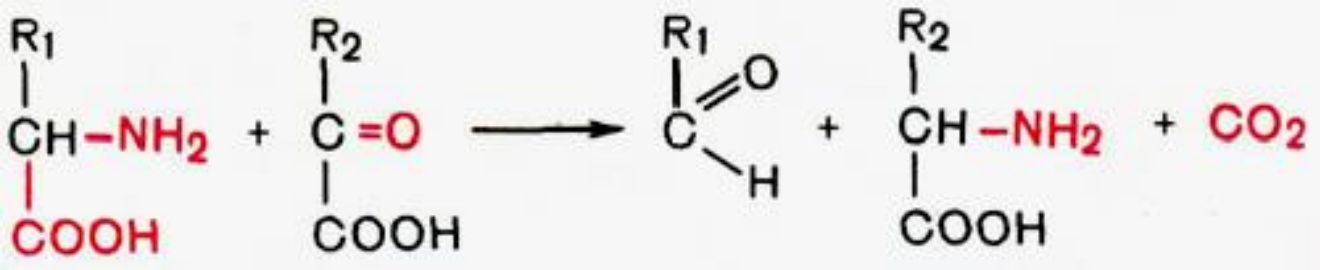
1) α-Decarboxylation (is typical of animal tissues)



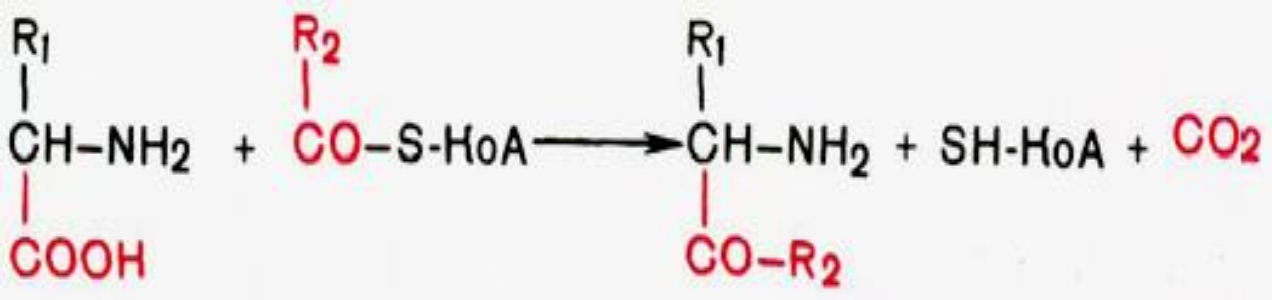
2) ω-Decarboxylation (This type of decarboxylation is typical of microorganism)

# There are 4 types of the amino acid decarboxylation

**3) Decarboxylation involving a transamination reaction.**



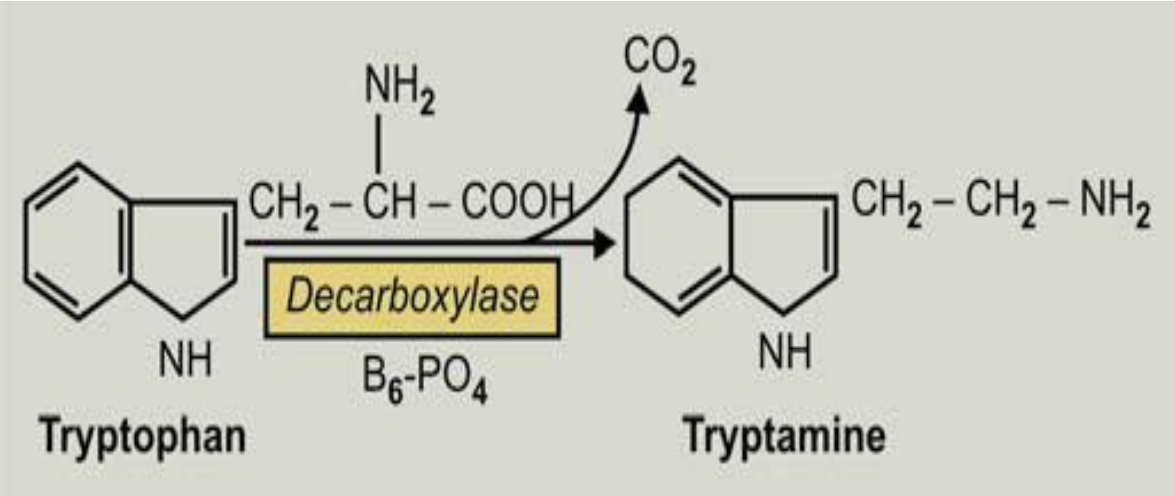

**4)Decarboxylation involving condensation reaction of two molecules.**



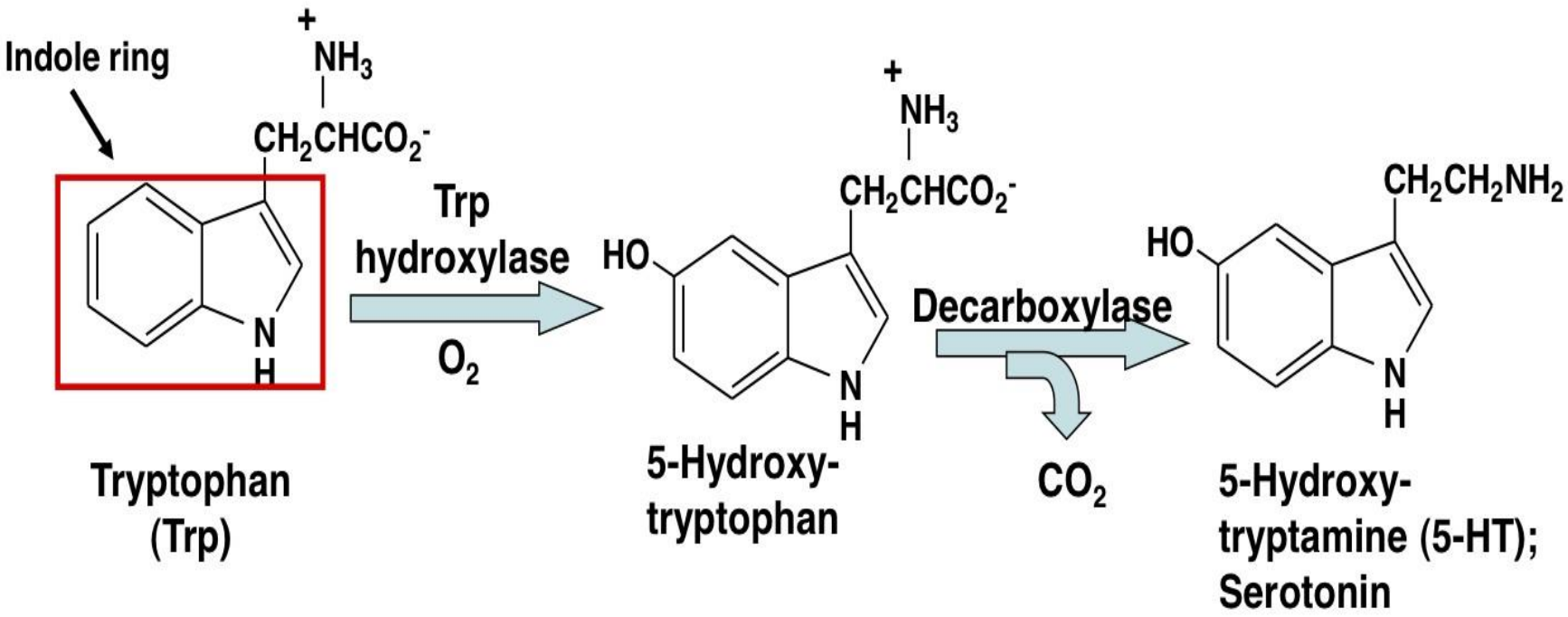
# Tryptamine

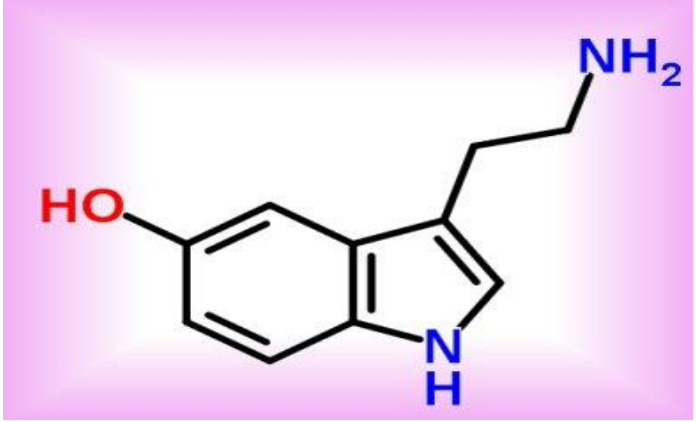
Mammalian kidney, liver and bacteria of gut can decarboxylate the amino acid, tryptophan to form the amine ***tryptamine***.

Tryptamine elevates blood pressure (exhibits **vasoconstrictive** action)



# Serotonin


Indole ring
+
NH3
CH2CHCO2-
N
H
Tryptophan
(Trp)
Trp
hydroxylase
O2
HO
+
NH3
CH2CHCO2-
N
H
5-Hydroxy-
tryptophan
Decarboxylase
CO2
HO
CH2CH2NH2
N
H
5-Hydroxy-
tryptamine (5-HT);
Serotonin




# Serotonin

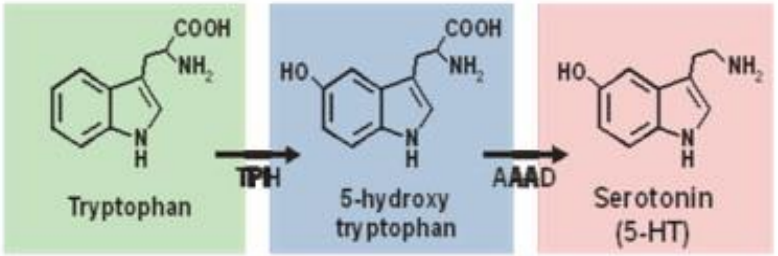
- **Serotonin** is a powerful **vasoconstrictor**, increases **motility of GIT**, takes part in the regulation of **body temperature**, rate of **respiration**, **renal filtration.** Serotonin may induce **sleep**, may participate in the development of **allergy**.
- Serotonin is also central **neurotransmitter**; its excess may cause panic attacks.

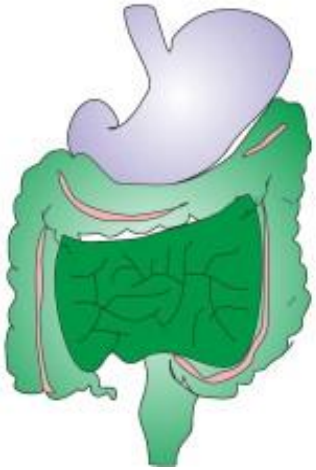
## Behavioural Effects

Visceral pain
Emotion
Stress response
Appetite
Addiction
Sexuality

## CNS Effects

Motor control
Circadian rhythm
Cerebellar regulation
Body temperature
CNS vascular tone



## GI Effects

Gastric secretion
Gastrointestinal motility
Intestinal secretions
Colonic tone
Pancreatic secretion

Tryptophan

↓

Serotonin

↓

Melatonin

Sun and vitamin D

Darkness

Tryptophan

Fe, Mg, Ca, Vit B6, Folic acid

5-HTP

Vit C, Vit B6, Zn, Mg

SEROTONIN

Gut and Heart Problems

Fibromyalgia and other pain conditions

Sleep Problems

Cravings for carbohydrates, alcohol, and certain drugs

Melatonin

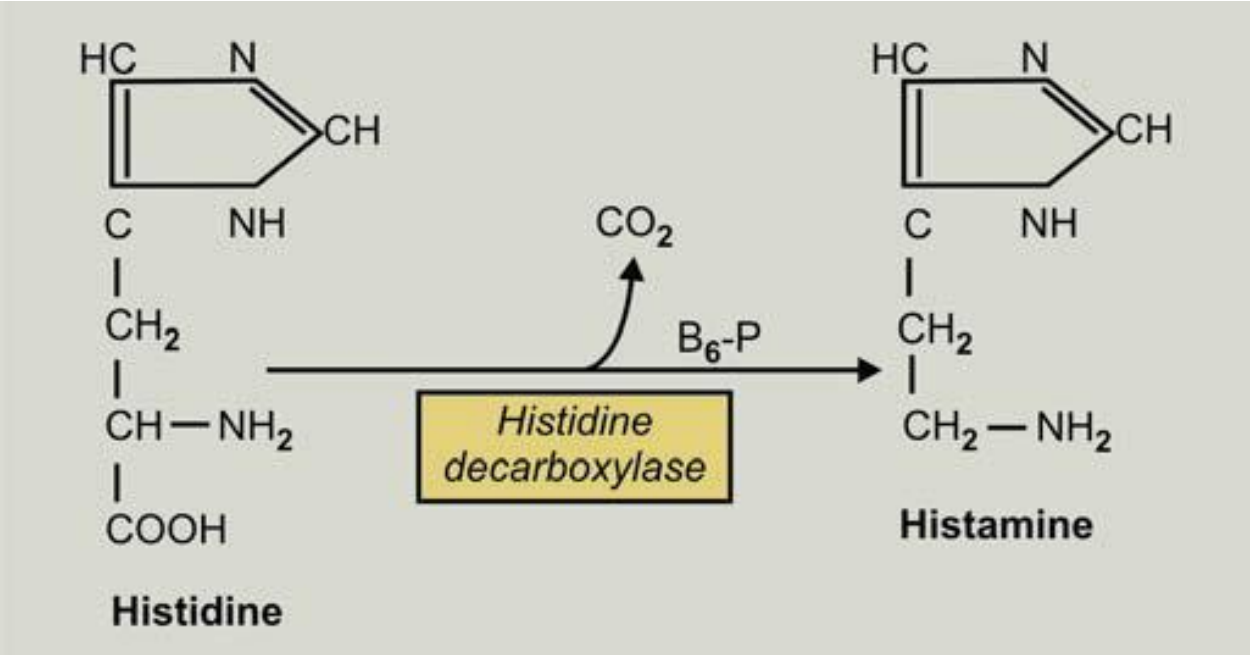
# Serotonin Deficiency

**Serotonin deficiency leads to increases in:**

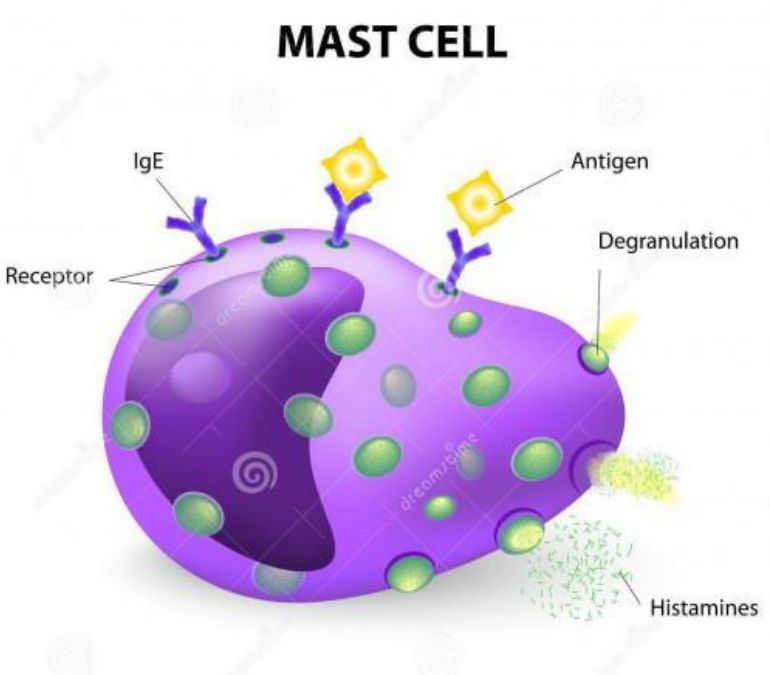
- irritability
- aggression
- pain
- depression
- suicide
- alcohol and drug use
- eating and bingeing
- sexual activity
- obsessive compulsive disorder
- chronic pain
- seizures
- hypoglycemia
- insomnia
- disruption of circadian rhythms

# Histamine

Histamine is formed by decarboxylation of histidine by the enzyme ***histidine decarboxylase***

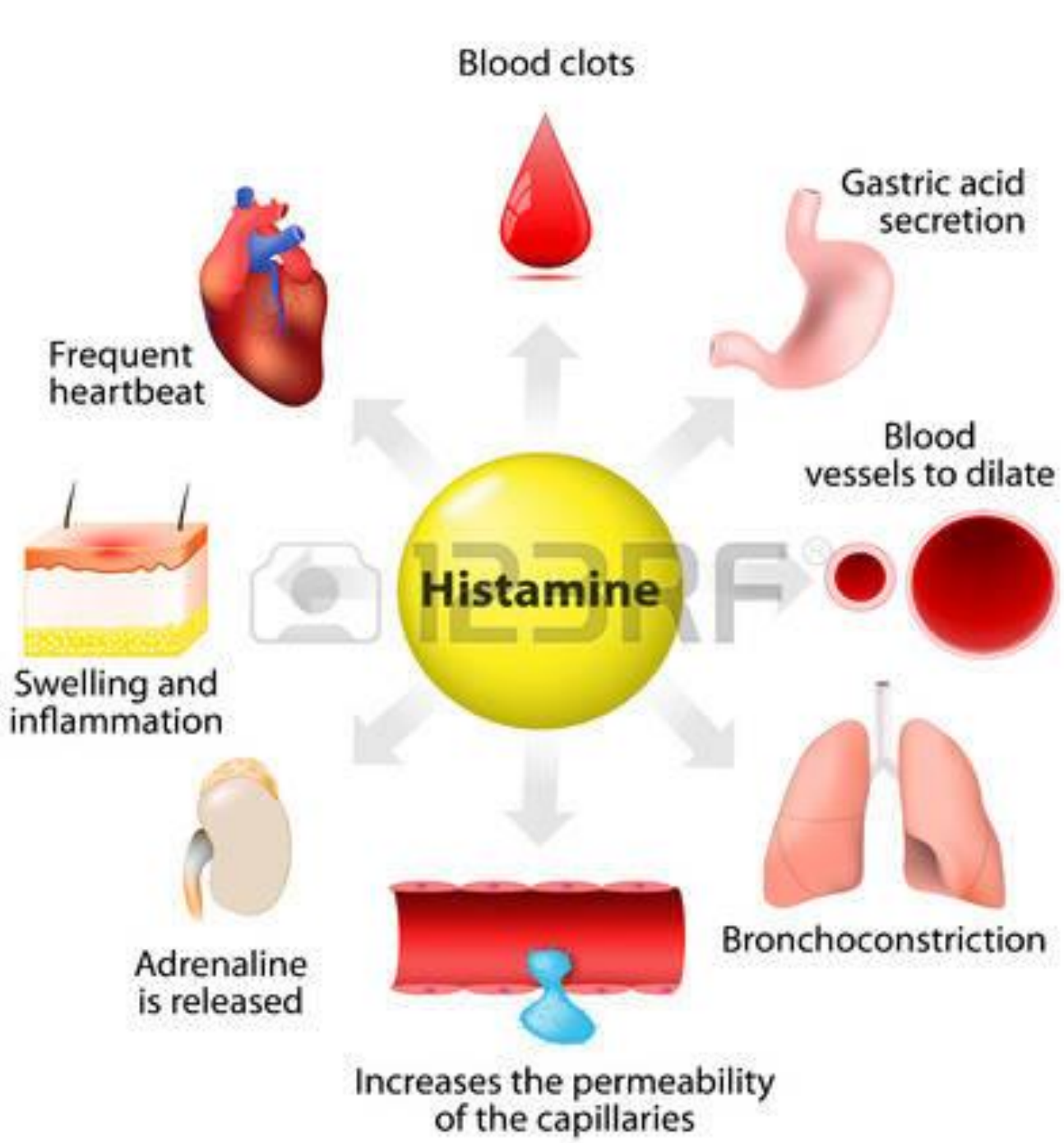


- Mast cells are the chief source of histamine in the tissues. Also produced by gastric mucosa cells and histaminergic neurones of the central nervous system.



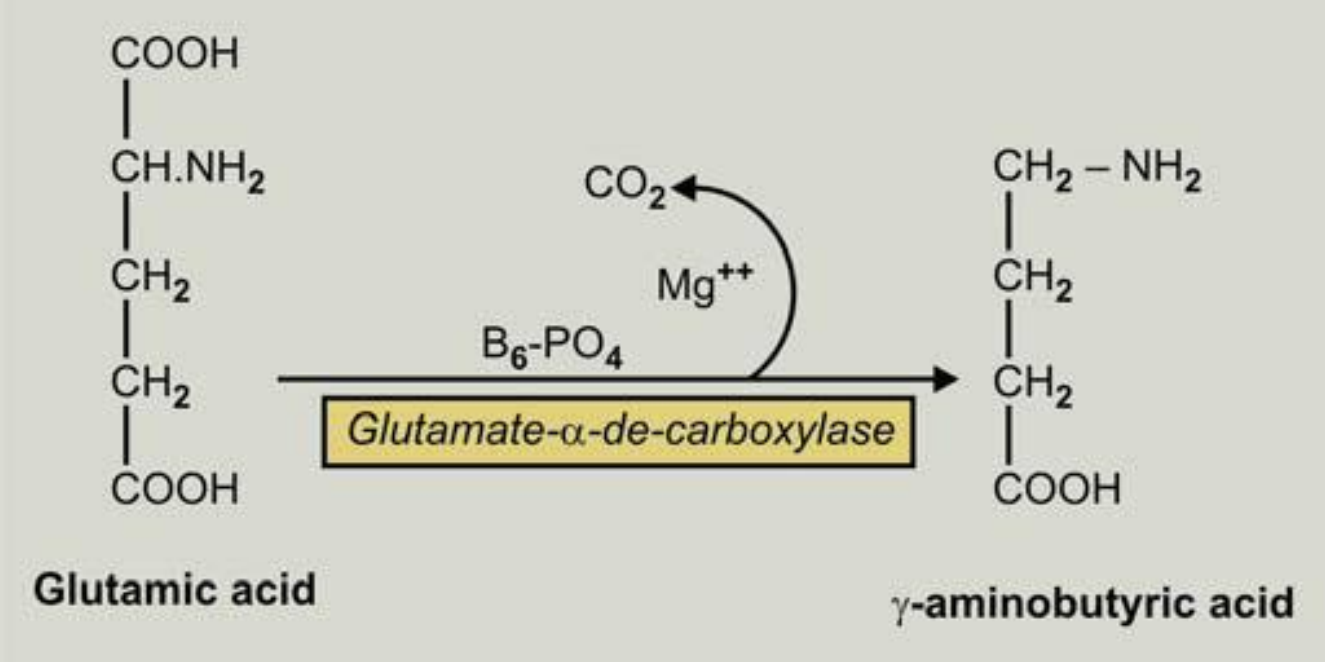

- ***Basophils are the chief source of histamine in the circulating cells.***

- ***Histamine acts as a neurotransmitter, particularly in the hypothalamus.***
- It acts as an anaphylactic and inflammatory agent on being released from mast cells in response to antigens.


Blood clots
Gastric acid secretion
Frequent heartbeat
Blood vessels to dilate
Histamine
Swelling and inflammation
Adrenaline is released
Bronchoconstriction
Increases the permeability of the capillaries

# γ-aminobutyric acid (GABA)

## Decarboxylation of glutamic acid produces γ-aminobutyric acid (GABA)



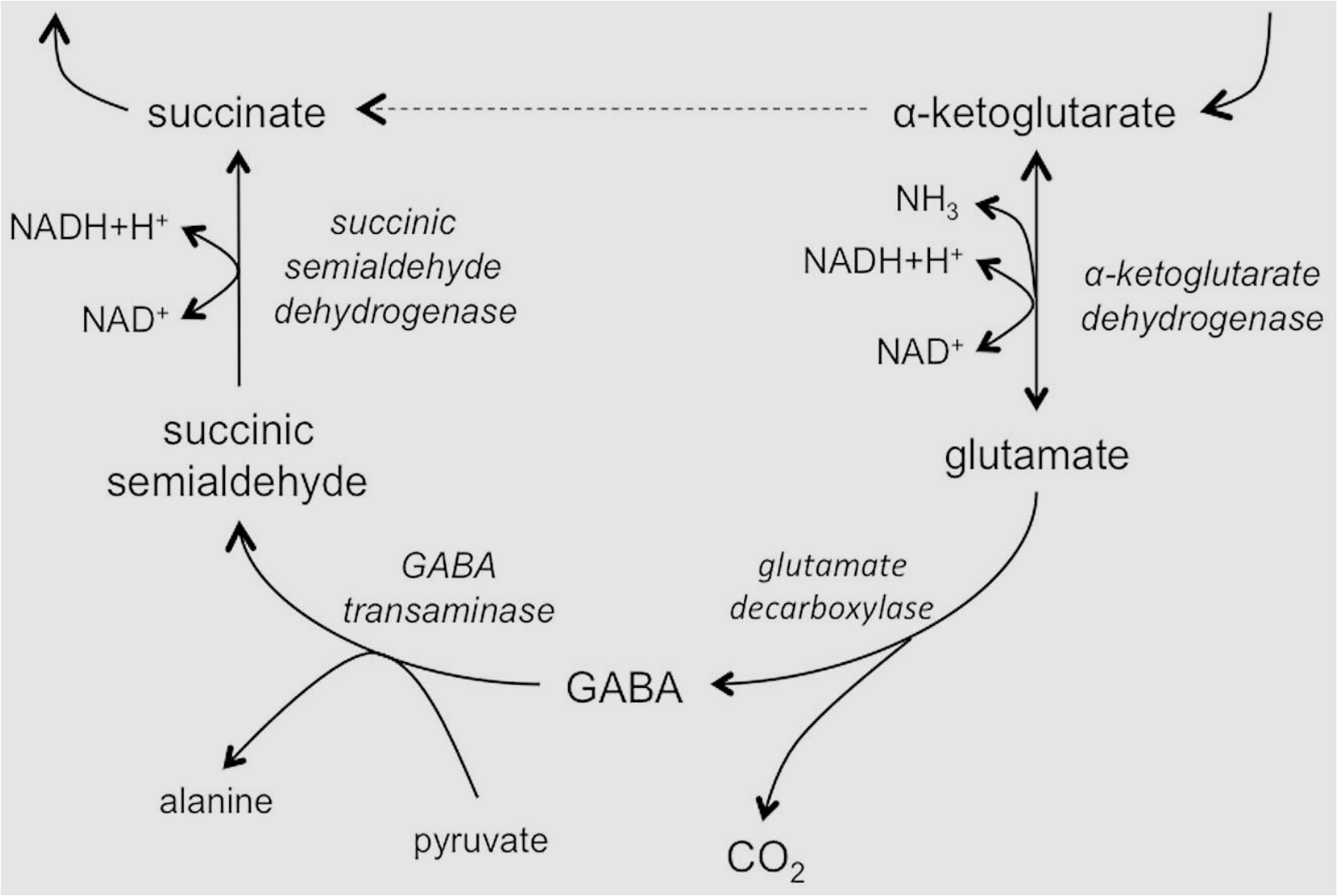
- ***Formed in CN system in the gray matter.***

GABA is known to serve as a normal regulator of neuronal activity being active as an inhibitor **(pre-synaptic inhibition).**

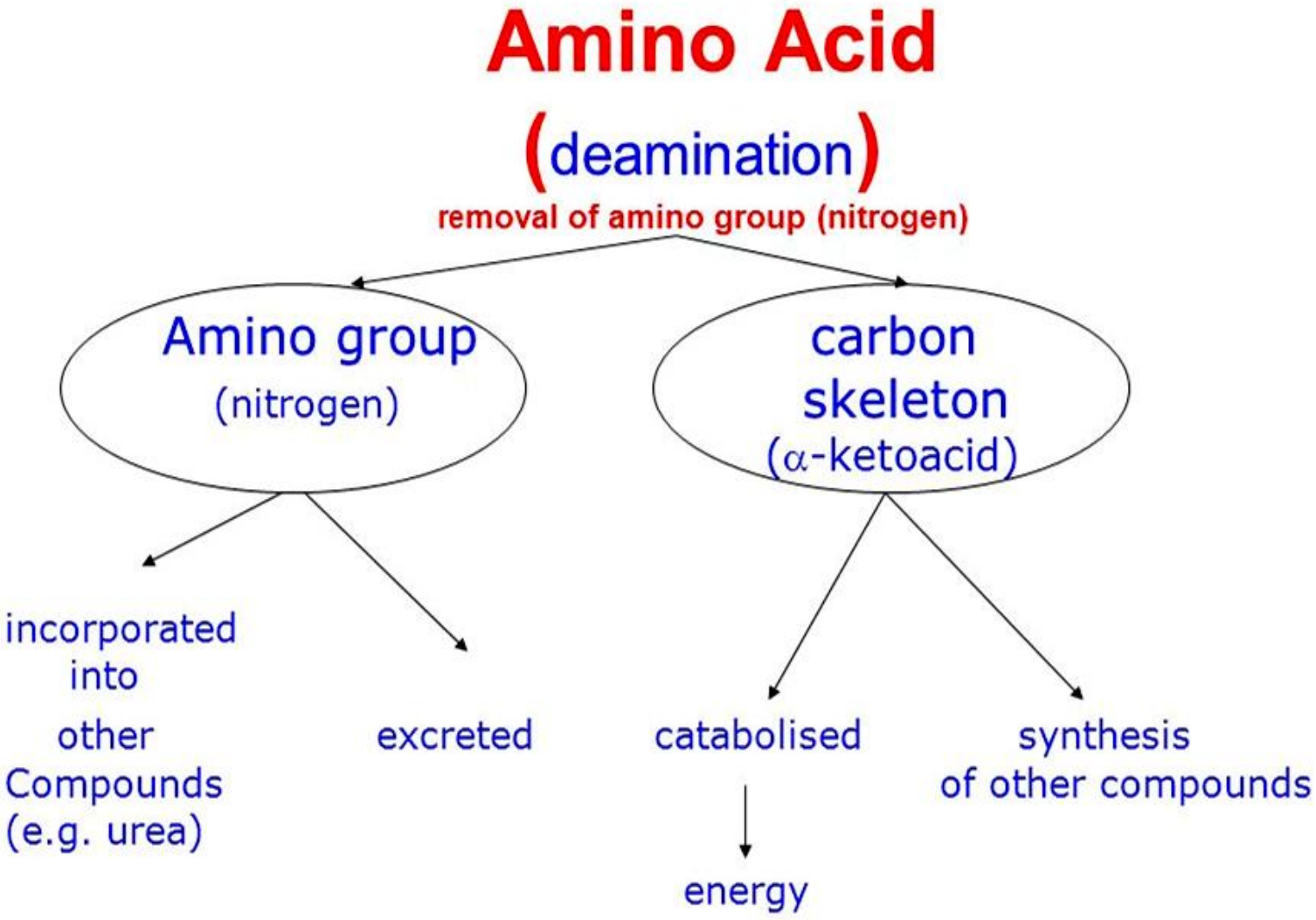
GABA is metabolised by deamination to form succinic semialdehyde.

GABA by its conversion to succinic acid **can form a "bypass" in TCA cycle** and this is called as GABA-shunt.

# GABA-shunt


succinate
α-ketoglutarate
NADH+H⁺
NAD⁺
succinic semialdehyde dehydrogenase
NH₃
NADH+H⁺
NAD⁺
α-ketoglutarate dehydrogenase
succinic semialdehyde
glutamate
GABA transaminase
glutamate decarboxylase
GABA
alanine
pyruvate
CO₂

# CATABOLISM OF CARBON SKELETONS OF AMINO ACIDS



# GLUCOGENIC OR KETOGENIC AMINO ACIDS

- A **glucogenic amino acid** is an amino acid that can be converted into **glucose** through gluconeogenesis

- A **ketogenic** amino acid is an amino acid that can be degraded directly into **acetyl-CoA**, which is the precursor of ketone bodies, or into acetoacetyl CoA

| Glucogenic amino acids | Glucogenic and ketogenic | Ketogenic amino acids |
|---|---|---|
| Alanine, Arginine, Asparagine, Aspartate Asparagine, Cysteine, Methionine Glutamate, Glutamine, Glycine, Histidine Proline, Serine, Threonine,Valine | Tyrosine Isoleucine Phenylalanine Tryptophan | Leucine Lysine |

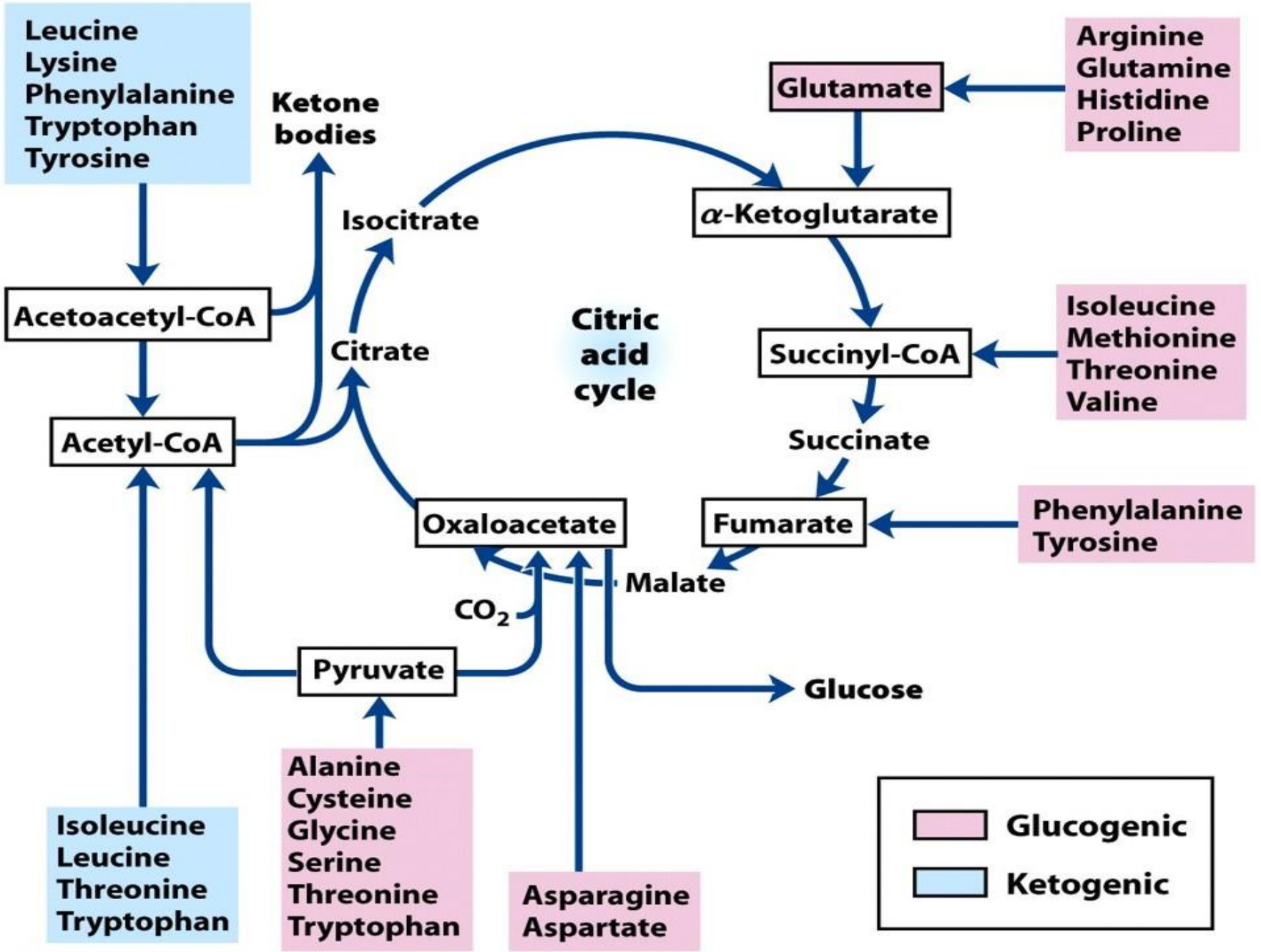



**Figure 18-15**
*Lehninger Principles of Biochemistry, Fifth Edition*