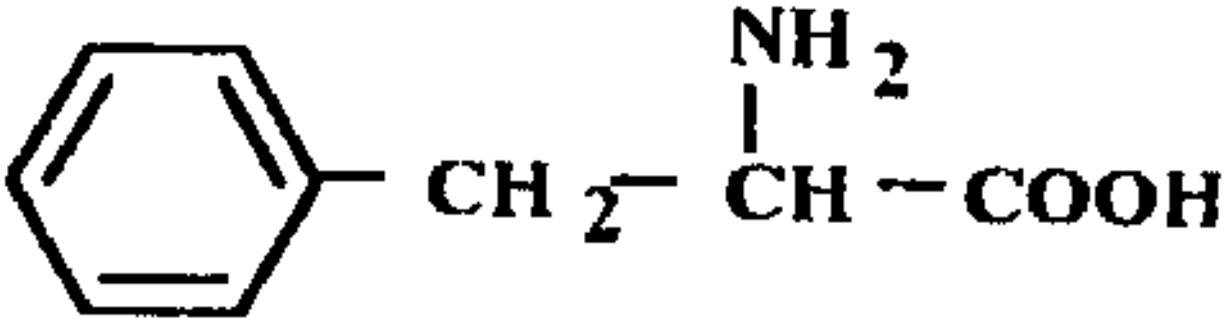
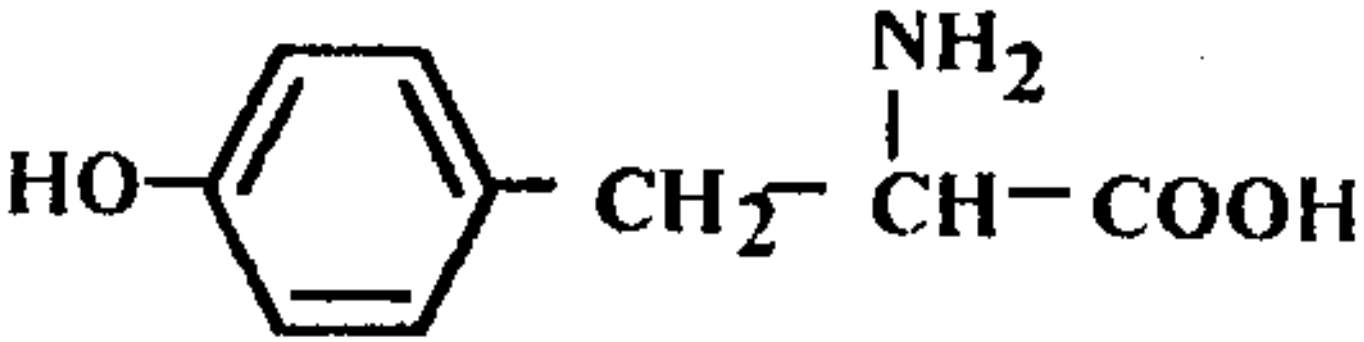
Phenylalanine and Tyrosine

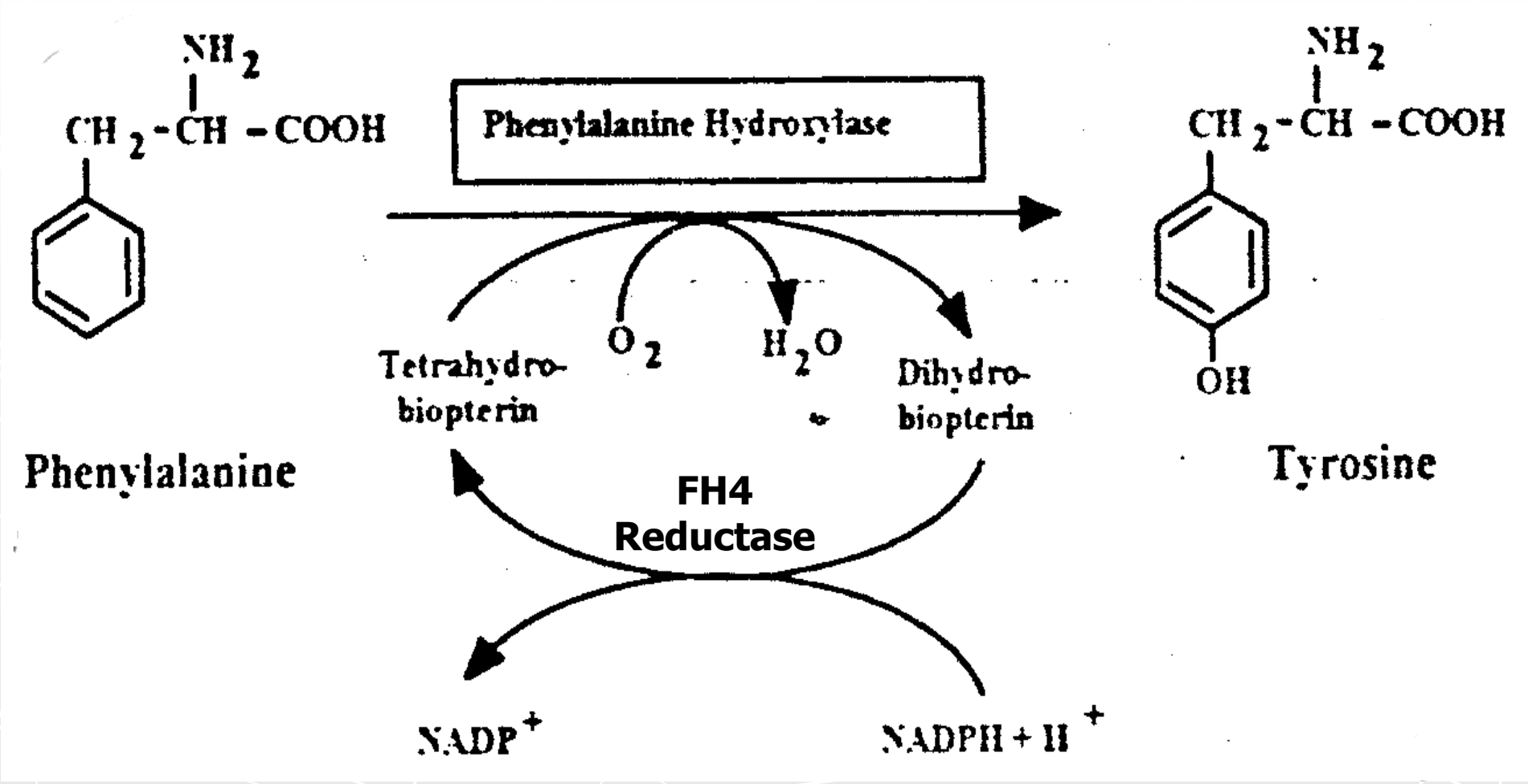

NH 2
CH 2 CH COOH


NH2
HO
CH2 CH COOH

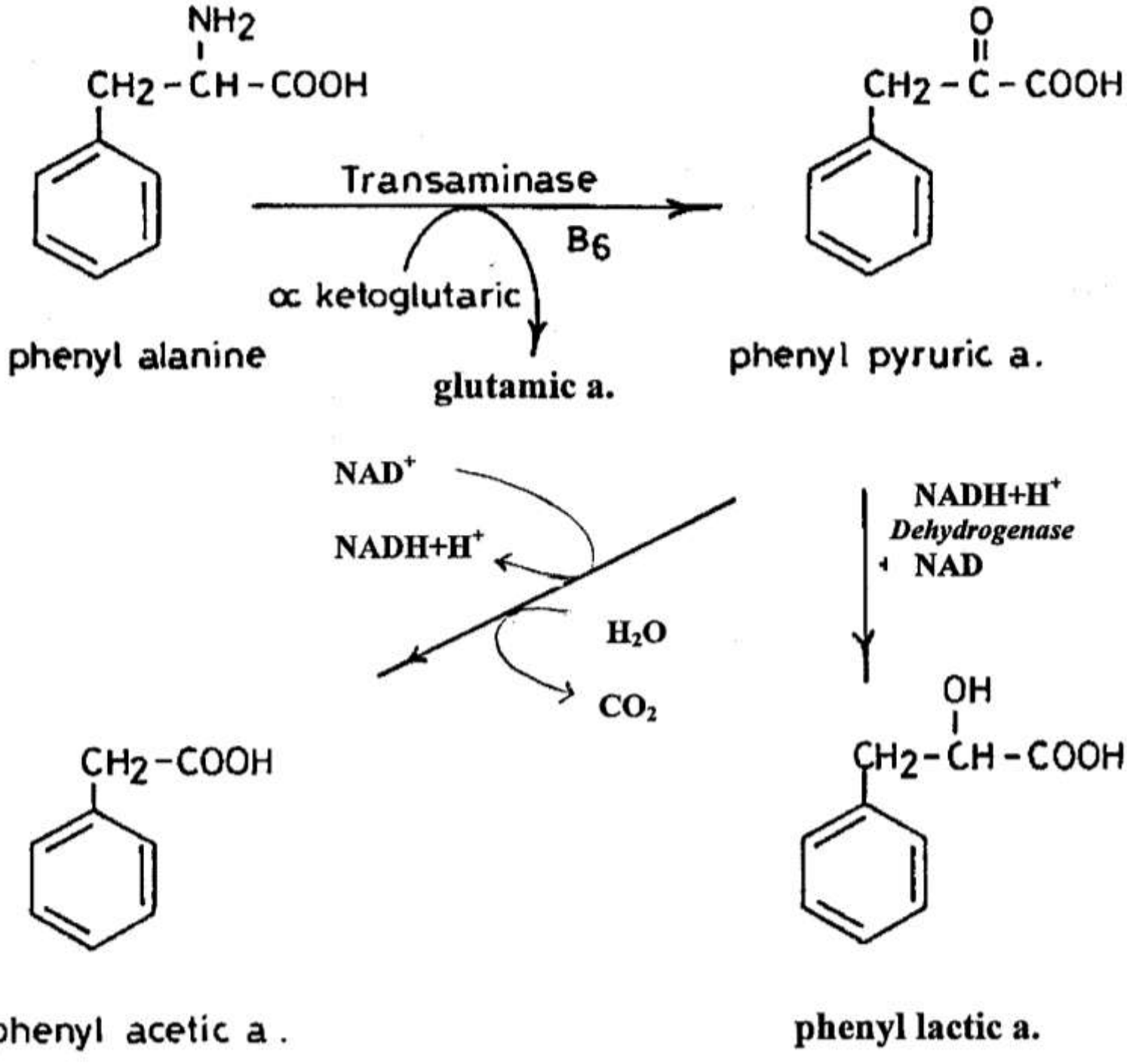
Metabolic pathways of phenylalanine

1. Protein biosynthesis.
2. Tyrosine formation.

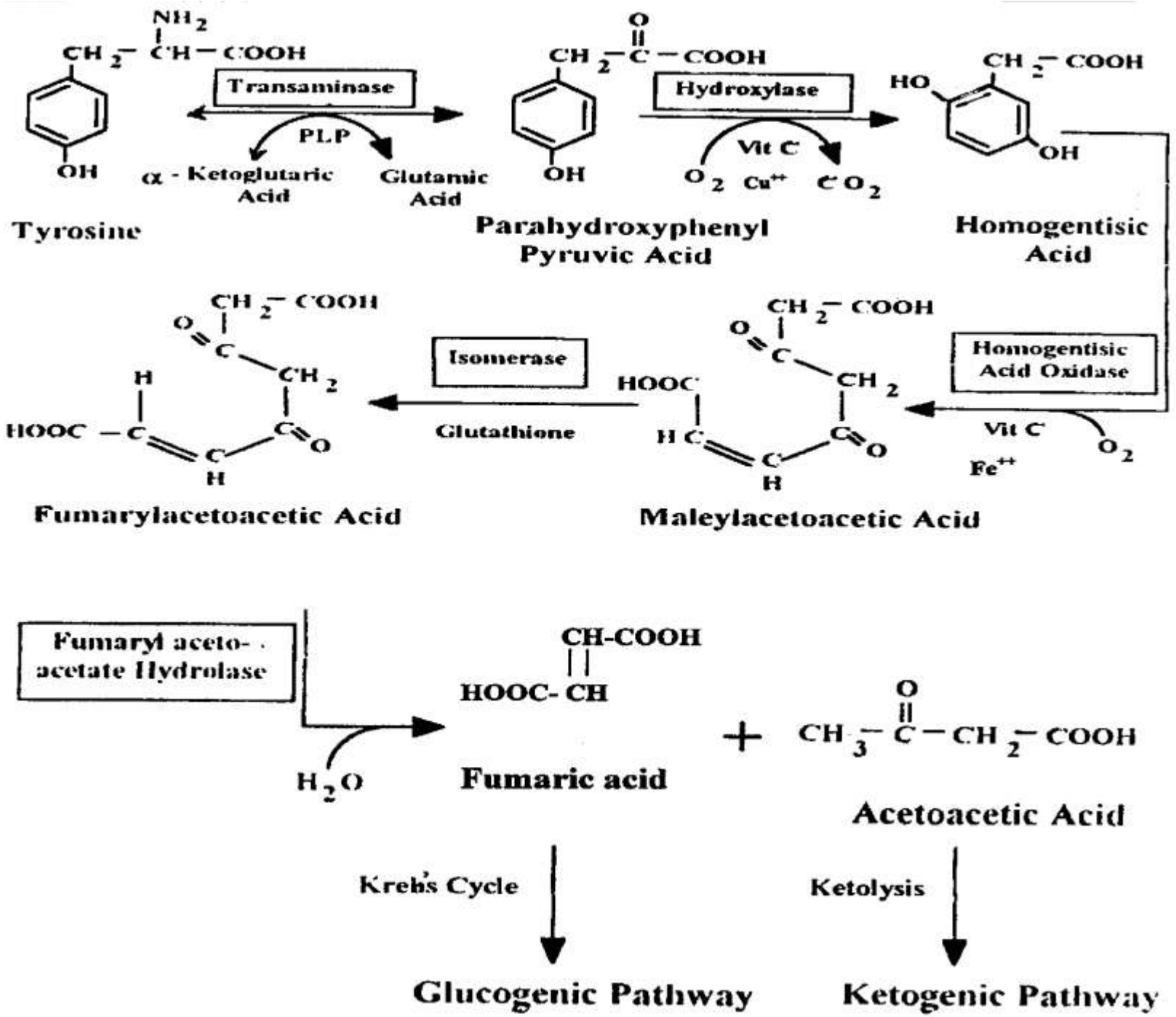
Biosynthesis of Tyrosine



- **Catabolic pathways of phenylalanine:**
- There are 2 pathways for catabolism of phenylalanine:
  - **1) Direct pathway (minor pathway):** where phenylalanine by transamination reaction or oxidative deamination forms phenyl-purvic acid which is secreted in urine via its metabolites, and Phenyl-acetic may react with glutamine to yield phenyl-acetyl-glutamine.


NH2
CH2 - CH - COOH
Transaminase
B6
∝ ketoglutaric
glutamic a.
phenyl alanine
O
CH2 - C - COOH
phenyl pyruric a.
NAD+
NADH+H+
H2O
CO2
NADH+H+
Dehydrogenase
NAD
CH2 - COOH
phenyl acetic a .
OH
CH2 - CH - COOH
phenyl lactic a.

- **2) Phenylalanine is transformed to tyrosine (major pathway):** in the liver then tyrosine is catabolized to fumaric acid and acetoacetic acid.

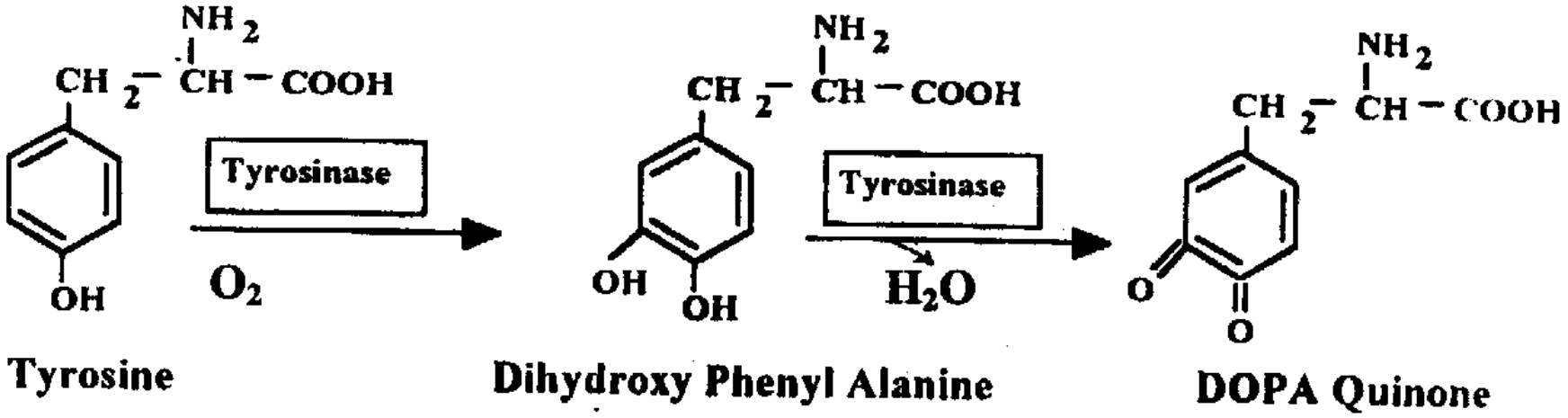

Transaminase
PLP
α - Ketoglutaric Acid
Glutamic Acid
Tyrosine
Hydroxylase
Vit C
Parahydroxyphenyl Pyruvic Acid
Homogentisic Acid
Homogentisic Acid Oxidase
Vit C
Fe++
Isomerase
Glutathione
Maleylacetoacetic Acid
Fumarylacetoacetic Acid
Fumaryl aceto- acetate Hydrolase
Fumaric acid
Acetoacetic Acid
Krebs Cycle
Ketolysis
Glucogenic Pathway
Ketogenic Pathway

Metabolic pathways of Tyrosine

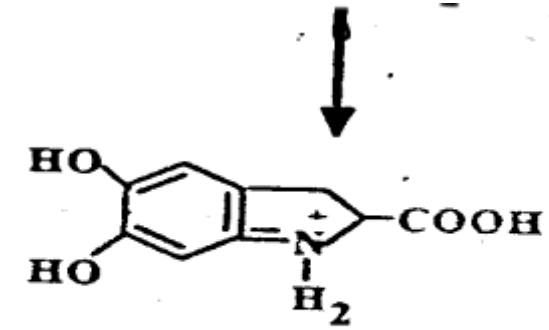
1. Formation of melanin pigment of skin
2. Formation of phenol
3. Biosynthesis of epinephrine and nor epinephrine
4. Biosynthesis of thyroid hormone.

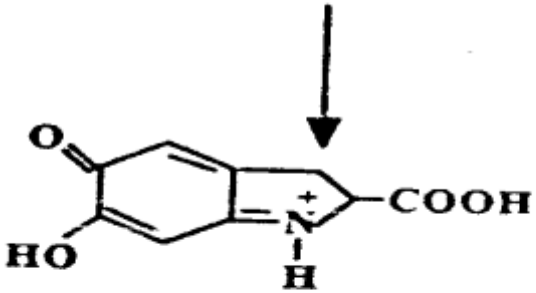
Formation of Melanin of skin:

- This reaction takes place in the melanocytes (pigment cells).
- When there is defect in melanin synthesis in the skin, hair and eye, this leads to albinism.



Dopaquinone is a very reactive molecule that cyclizes and condenses to form melanin polymers containing <u>eumelanin</u> and <u>pheomelanin</u> in varying proportions.



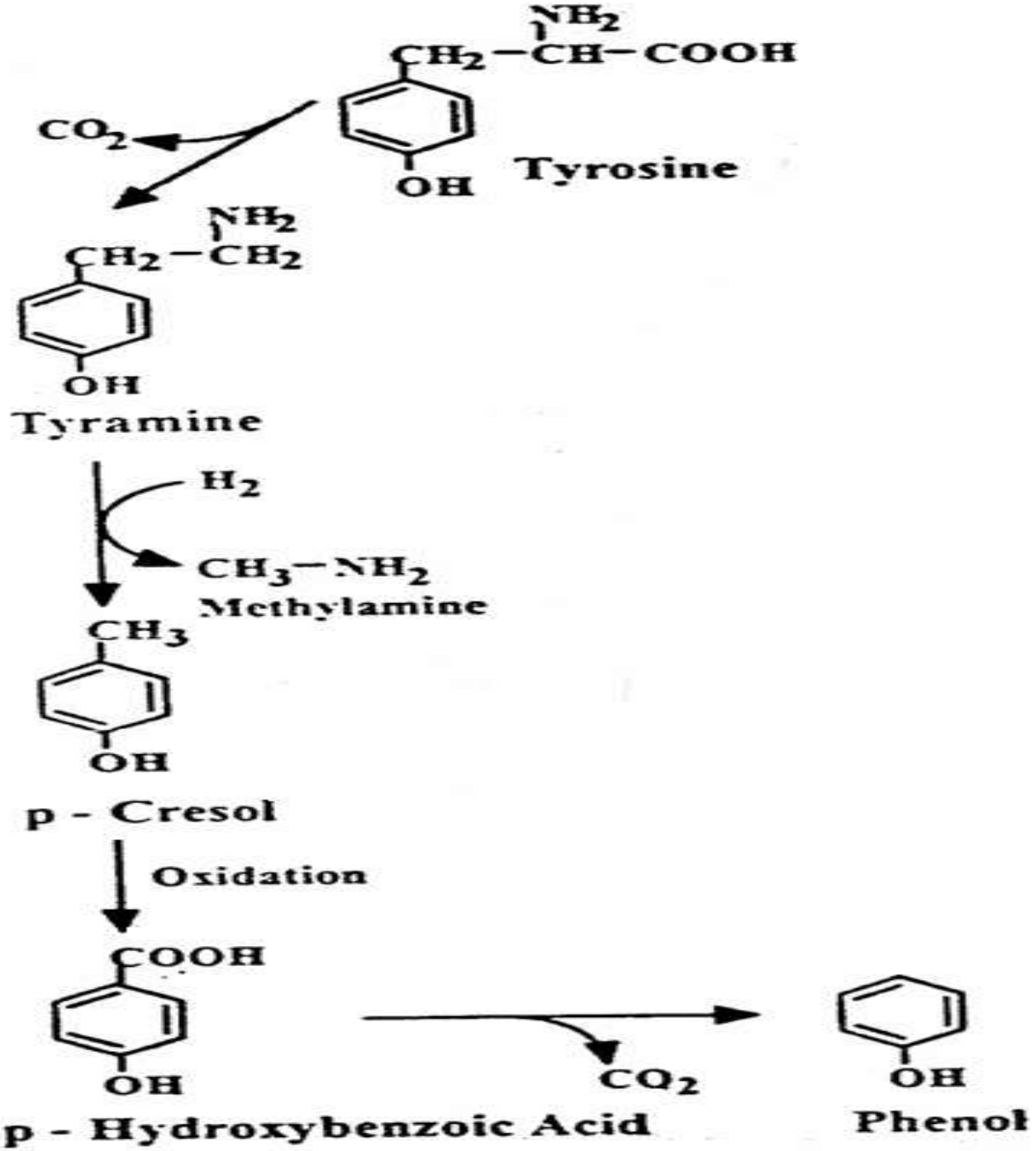


Melanin

2) Formation of Phenol:

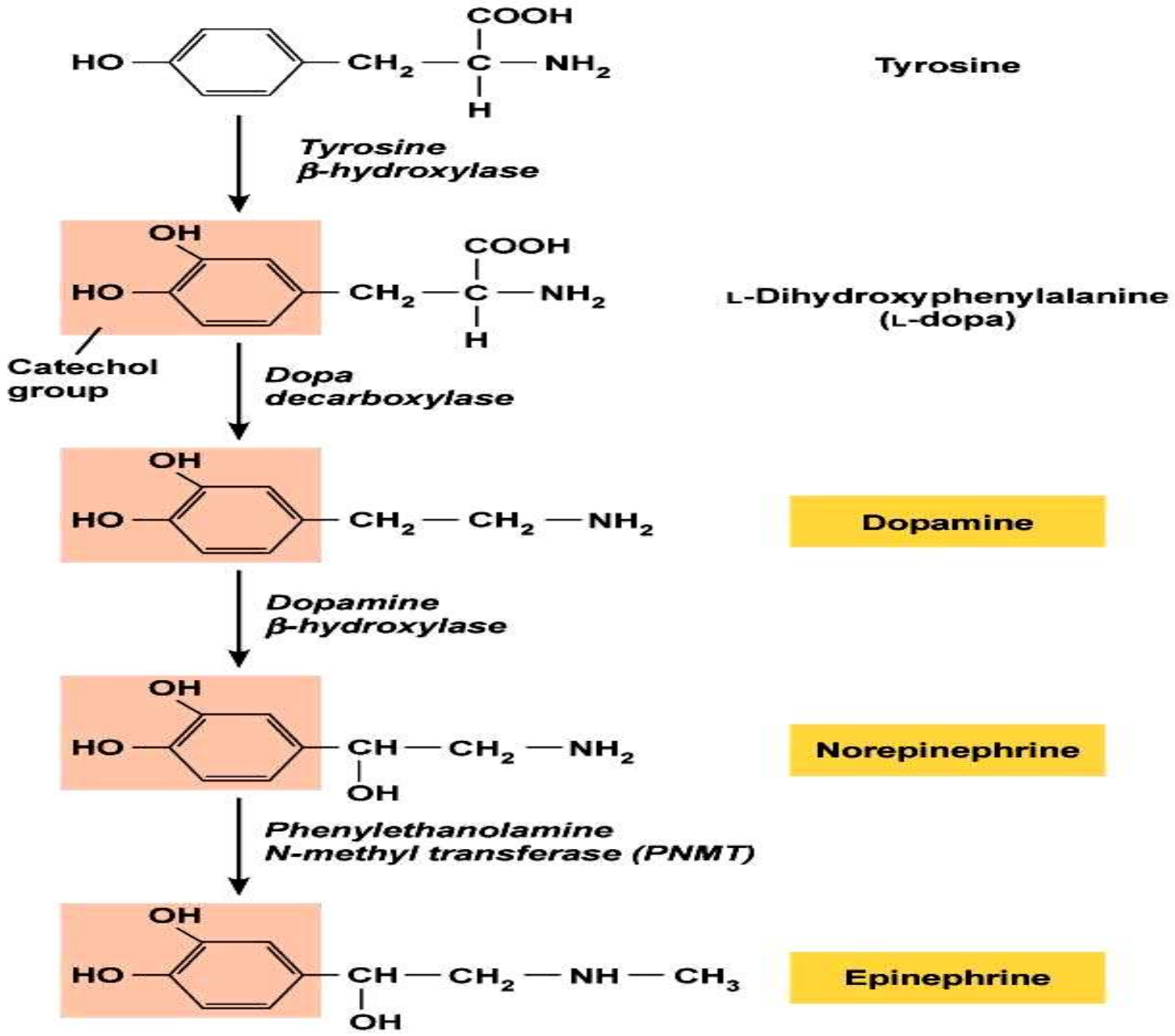
- **Through 4 steps:**

- Decarboxylation – deamination – oxidation - decarboxylation

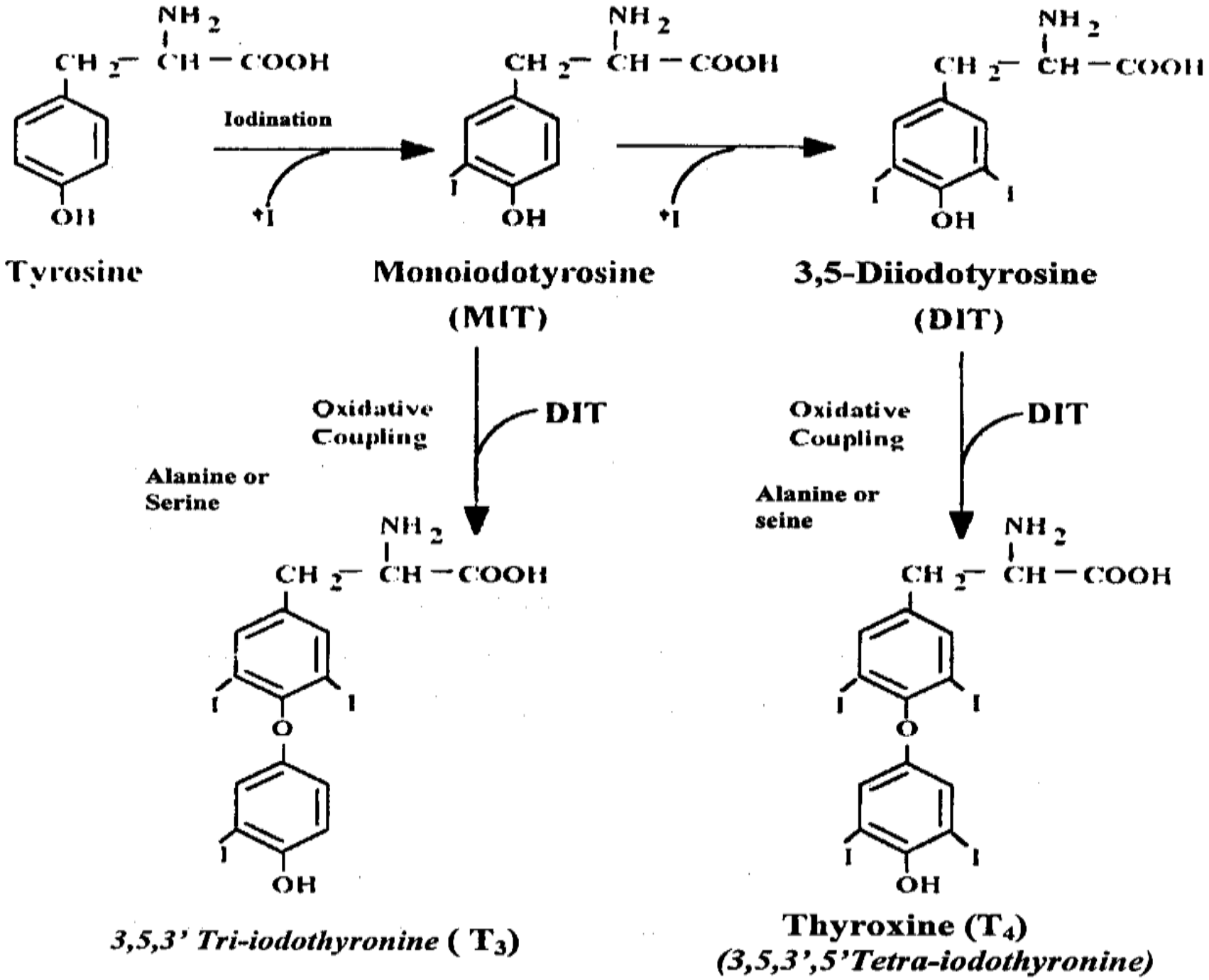

NH2
CH2—CH—COOH
CO2
OH
Tyrosine
NH2
CH2—CH2
OH
Tyramine
H2
CH3—NH2
Methylamine
CH3
OH
p - Cresol
Oxidation
COOH
OH
CO2
OH
p - Hydroxybenzoic Acid
Phenol

3) Biosynthesis of epinephrine and norepinephrine:

- This occurs in cells of neural origins and in adrenal medulla.


Tyrosine
Tyrosine β-hydroxylase
L-Dihydroxyphenylalanine (L-dopa)
Catechol group
Dopa decarboxylase
Dopamine
Dopamine β-hydroxylase
Norepinephrine
Phenylethanolamine N-methyl transferase (PNMT)
Epinephrine

4) Biosynthesis of Thyroid hormones.


Iodination
Tyrosine
Monoiodotyrosine
(MIT)
3,5-Diiodotyrosine
(DIT)
Oxidative
Coupling
DIT
Alanine or
Serine
Oxidative
Coupling
DIT
Alanine or
seine
3,5,3' Tri-iodothyronine (T3)
Thyroxine (T4)
(3,5,3',5'Tetra-iodothyronine)

Metabolic Disorders of Phenylalanine and Tyrosine Catabolism:

1. Phenylketonuria:

- It is inherited metabolic disorder of phenylalanine caused by **defective liver phenylalanine hydroxylase.**
- The disease is characterized by increased phenyl-pyruvic and phenyl-lactic acid in blood and urine and hence, the name of phenylketonuria.

- **The signs and symptoms**

1. Mental retardation
2. Eczema of the skin
3. Mousy odor of urine.

- The disease could be **diagnosed** by increased plasma and urinary levels of phenylalanine and by using ferric chloride test which gives green color.
- **Treatment** is through a diet low in phenylalanine which is terminated at the age of 6 years when high phenylalanine and its derivatives no longer injure the brain. The treatment with low-protein diet continues.