WELCOME

TO

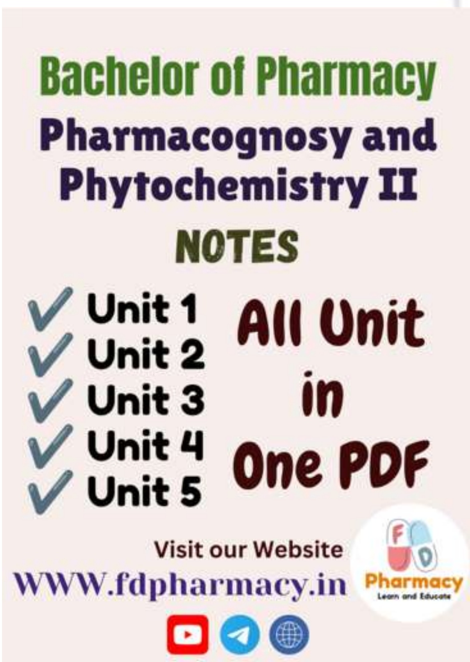
Pharmacy
Learn and Educate

Pharmacy
Learn and Educate


Bachelor of Pharmacy
Pharmaceutical Jurisprudence
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Industrial Pharmacy I
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Medicinal Chemistry II
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Pharmacognosy and Phytochemistry II
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Bachelor of Pharmacy
Pharmacology II
NOTES
Unit 1
Unit 2
Unit 3
Unit 4
Unit 5
All Unit in One PDF
Visit our Website
WWW.fdpharmacy.in
Pharmacy
Learn and Educate


Pharmacy
Learn and Educate
FDPharmacy
Diploma in Pharmacy
Download
Bachelor of Pharmacy
Download
D.Pharma
B.Pharma
PDF Notes
Practical Manual
Important Questions
Assignment etc
Download Now
ANDROID APP ON
Google play
www.fdpharmacy.in

PHARMACOGNOSY AND PHYTOCHEMISTRY - II

UNIT 1

TOPIC :

- **Metabolic pathways in higher plants and their determination**
  a) Brief study of basic metabolic pathways and formation of different secondary metabolites through these pathways- Shikimic acid pathway, Acetate pathways and Amino acid pathway.
  b) Study of utilization of radioactive isotopes in the investigation of Biogenetic studies.

Pharmacy Learn and Educate

Metabolic Pathways In Higher Plants And Their Determination

Plants synthesize a variety of chemical compounds for growth, defense, and adaptation. These compounds are classified into:

1. **Primary metabolites** – essential for growth (carbohydrates, proteins, lipids).
2. **Secondary metabolites** – non-essential for basic metabolism but important for defense, attraction of pollinators, and medicinal properties (alkaloids, flavonoids, terpenoids, phenolics).

Secondary metabolites are formed via specific metabolic pathways, which are interconnected with primary metabolism.

Shikimic Acid Pathway

- The Shikimic Acid Pathway is a metabolic route in plants, fungi, bacteria, and some protozoa for the biosynthesis of aromatic amino acids and a wide range of secondary metabolites.
- Animals, including humans, do not have this pathway, so aromatic amino acids like phenylalanine, tyrosine, and tryptophan are essential in the diet.
- It is named after Shikimic acid, an important intermediate.

Importance in Pharmaceutical Sciences:

- Precursors for alkaloids, flavonoids, lignins, tannins, and phenolic compounds.
- Target pathway for herbicides and antimicrobial agents.
- Shikimic acid is also a starting material for the synthesis of oseltamivir (Tamiflu).

Key Features

Feature	Description
Location	Cytoplasm of plant, bacterial, and fungal cells
End Products	Aromatic amino acids (Phe, Tyr, Trp), alkaloids, phenolics, flavonoids
Precursor Molecules	Phosphoenolpyruvate (PEP) and Erythrose-4-phosphate (E4P)
Number of Steps	7 enzymatic steps from PEP & E4P to chorismate
Enzymes	DAHP synthase, Shikimate dehydrogenase, Shikimate kinase, EPSP synthase, Chorismate synthase, etc.

Starting Materials / Precursors

1. Phosphoenolpyruvate (PEP) – from glycolysis.
2. Erythrose-4-phosphate (E4P) – from the pentose phosphate pathway.

Major Steps in the Pathway

1. Formation of 3-Deoxy-D-arabino-heptulosonate-7-phosphate (DAHP)
   - Enzyme: DAHP synthase
   - Reaction: PEP + E4P → DAHP
   - Significance: First committed step of the pathway.
2. Conversion to 3-Dehydroquinate (DHQ)
   - Enzyme: DHQ synthase
   - DAHP → 3-Dehydroquinate
   - Ring formation begins.
3. Formation of 3-Dehydroshikimate
   - Enzyme: Dehydroquinate dehydratase
   - DHQ → 3-Dehydroshikimate
4. Formation of Shikimate
   - Enzyme: Shikimate dehydrogenase
   - 3-Dehydroshikimate → Shikimate
5. Phosphorylation of Shikimate
   - Enzyme: Shikimate kinase
   - Shikimate + ATP → Shikimate-3-phosphate
6. Formation of 5-Enolpyruvylshikimate-3-phosphate (EPSP)
   - Enzyme: EPSP synthase
   - Shikimate-3-phosphate + PEP → EPSP
7. Formation of Chorismate
   - Enzyme: Chorismate synthase
   - EPSP → Chorismate
   - Chorismate is the key branch point for aromatic amino acids and secondary metabolites.

Branching from Chorismate

1. Phenylalanine and Tyrosine
   - Chorismate → Prephenate → Phenylalanine / Tyrosine
2. Tryptophan
   - Chorismate → Anthranilate → Tryptophan
3. Other secondary metabolites
   - Isoquinoline, indole alkaloids, flavonoids, tannins, lignins.

Pharmacy Learn and Educate

Significance of the Pathway

- **Pharmaceutical relevance:**
  - Many plant-derived drugs originate from aromatic amino acids.
    - Alkaloids: Morphine, quinine, vincristine
    - Flavonoids: Quercetin, rutin
    - Phenolic acids: Cinnamic acid derivatives
- **Industrial application:** Shikimic acid is used in antiviral drug synthesis (Tamiflu).
- **Agricultural importance:** Herbicides like glyphosate inhibit EPSP synthase.

Utilization of Radioactive Isotopes

- C-14 or H-3 labeled PEP/E4P can trace the biosynthesis of aromatic compounds.
- Helps in studying biogenetic pathways and secondary metabolite formation.

Pharmacy
Learn and Educate

Acetate Pathway (Polyketide Pathway)

- The Acetate Pathway, also called the Polyketide Pathway, is a major biosynthetic route in plants, bacteria, fungi, and some algae for the formation of secondary metabolites.
- It primarily uses acetyl-CoA units to build complex molecules.
- It leads to the formation of fatty acids, polyketides, terpenoids, flavonoids, and certain phenolic compounds.
- This pathway is distinct from the shikimic acid pathway, which uses sugar derivatives as precursors.
- Produces compounds of pharmacological importance, like antibiotics (tetracyclines), anticancer drugs (anthracyclines), and steroids.

Precursors

1. Acetyl-CoA – derived from glycolysis or β-oxidation of fatty acids.
2. Malonyl-CoA – formed by carboxylation of acetyl-CoA.
    - Enzyme: Acetyl-CoA carboxylase
    - Reaction: Acetyl-CoA + CO_2 + ATP → Malonyl-CoA + ADP + Pi

Note: These two-carbon units are the building blocks for polyketides.

General Steps of the Acetate Pathway

1. **Initiation**
    - Acetyl-CoA serves as the starter unit.
    - Malonyl-CoA units are added sequentially.
2. **Chain Elongation**
    - Each malonyl-CoA contributes 2 carbons to the growing chain (with release of CO_2).
    - Enzymes involved: Polyketide synthases (PKS), similar to fatty acid synthase.
3. **Cyclization**
    - Linear chains can undergo cyclization and aromatization.
    - Forms polyketide rings, aromatic compounds, and phenolics.
4. **Modifications**
    - Post-synthesis modifications like methylation, hydroxylation, glycosylation, or oxidation produce a wide range of secondary metabolites.

Major Products

Class	Examples
Fatty acids	Palmitic acid, stearic acid
Polyketides	Tetracyclines, erythromycin, anthracyclines
Flavonoids and phenolics	Chalcones, flavones, coumarins
Terpenoids (some via acetate-malonate hybrid)	Steroids, saponins

Mechanism Insight

- Chain elongation is repetitive: Acetyl-CoA (starter) + n Malonyl-CoA → Linear polyketide → Cyclization → Aromatic/polycyclic metabolite.

Pharmacological Importance

1. **Antibiotics:**
    - Many antibiotics like tetracyclines, erythromycin are polyketides derived from acetate units.
2. **Anticancer drugs:**
    - Anthracyclines and some cytotoxic flavonoids are acetate pathway products.
3. **Plant secondary metabolites:**
    - Phenolics, flavonoids, and lignans with antioxidant, anti-inflammatory, and antimicrobial activities.
4. **Steroids and terpenoids:**
    - Some steroids in plants and microbes are partly synthesized via acetate units.

Use of Radioactive Isotopes

- C-14 labeled acetate or acetyl-CoA can trace incorporation into polyketides and fatty acids.
- Useful in biogenetic studies and drug precursor identification.

Amino Acid Pathway (Amino Acid Derived Secondary Metabolites)

- The Amino Acid Pathway refers to the biosynthesis of secondary metabolites from amino acids in plants, fungi, and microorganisms.
- It involves aromatic and non-aromatic amino acids as precursors for a wide range of bioactive compounds.
- These secondary metabolites include alkaloids, amines, glucosinolates, cyanogenic glycosides, and phenolics.

Importance in B.Pharm:

- Many pharmacologically active compounds, especially plant alkaloids, are synthesized via this pathway.
- Provides insight into drug precursors and phytochemistry.

Key Precursor Amino Acids

Amino Acid	Major Products / Metabolites
Phenylalanine	Phenylpropanoids, flavonoids, lignans, coumarins
Tyrosine	Alkaloids (e.g., morphine), isoquinoline alkaloids, catecholamines
Tryptophan	Indole alkaloids (e.g., vincristine, serotonin, indole-3-acetic acid)
Ornithine / Arginine	Pyrrolizidine and tropane alkaloids
Lysine	Piperidine and quinolizidine alkaloids
Methionine	Sulfur-containing alkaloids and glucosinolates
Cysteine / Serine	Glucosinolates, thioalkaloids

General Mechanism

1. **Amino Acid Activation**
   - Amino acids are activated by decarboxylation, transamination, or hydroxylation.
2. **Formation of Key Intermediates**
   - Decarboxylated amino acids → Amines
   - Hydroxylated amino acids → Phenols or catechols
3. **Cyclization / Condensation**
   - Linear intermediates undergo cyclization, condensation, or methylation to form complex structures.
4. **Final Modifications**
   - Glycosylation, acetylation, or methylation gives rise to stable bioactive compounds.

Examples of Amino Acid Derived Metabolites

A. Alkaloids

Amino Acid	Alkaloid Example	Pharmacological Use
Phenylalanine	Ephedrine	Stimulant, bronchodilator
Tyrosine	Morphine, Codeine	Analgesic
Tryptophan	Serotonin, Vincristine	Neurotransmitter, anticancer
Ornithine	Hyoscyamine, Atropine	Anticholinergic
Lysine	Sparteine	Antiarrhythmic

B. Phenolic Compounds

- Phenylalanine → Phenylpropanoids → Flavonoids, Coumarins
- Tyrosine → Catechols → L-DOPA, Dopamine

C. Cyanogenic Glycosides

- Amino acids like tyrosine and phenylalanine give rise to cyanogenic glycosides, which release hydrogen cyanide (HCN) as a defense mechanism in plants.

Pharmacy Learn and Educate

Pharmacological Relevance

1. Alkaloids – analgesic, antimalarial, anticancer, antiarrhythmic, anticholinergic activities.
2. Phenolics & Flavonoids – antioxidant, anti-inflammatory, antimicrobial properties.
3. Indole derivatives – neurotransmitters (serotonin, melatonin) and plant growth regulators (IAA).

Use of Radioactive Isotopes

- C-14 or N-15 labeled amino acids can be used to trace the incorporation into secondary metabolites.
- Helps in studying biosynthesis pathways and drug precursor formation.

Pharmacy Learn and Educate

Utilization Of Radioactive Isotopes in Biogenetic Studies

- Biogenetic studies involve tracing metabolic pathways and understanding biosynthesis of biomolecules.
- Radioactive isotopes (radioisotopes) are atoms that emit radiation (α, β, γ rays) and can act as tracers in biological systems.
- They allow scientists to track the fate of molecules in cells, tissues, or whole organisms without altering their chemical properties.

Principle

- Incorporate a radioactive isotope into a precursor molecule.
- The biological system metabolizes the labeled compound as it would normally.
- The radioactivity is detected in products using instruments like:
  - Geiger–Müller counter
  - Scintillation counter
  - Autoradiography
  - Liquid scintillation spectrometry
- The pattern of radioactivity indicates the biosynthetic pathway of the molecule.

Commonly used radioisotopes

Radioisotope	Type of Radiation	Typical Use in Biogenetic Studies
^{14}C (Carbon-14)	β^-	Tracing carbon atoms in carbohydrates, amino acids, lipids
^{3}H (Tritium)	β^-	Labeling small molecules, fatty acids, nucleotides
^{15}N (Nitrogen-15)	Stable isotope	Protein and amino acid metabolism (non-radioactive)
^{32}P (Phosphorus-32)	β^-	Nucleic acids and phosphate group metabolism
^{51}Cr, ^{57}Co, ^{99}mTc	γ	Tracing metals and cofactors in enzymes

Applications in biogenetic studies

A. Study of Carbohydrate Metabolism

- Example: ^{14}C-glucose used to study glycolysis, pentose phosphate pathway, and starch/sugar biosynthesis in plants.

B. Study of Amino Acid and Protein Biosynthesis

- Example: ^{14}C-phenylalanine or ^{3}H-leucine used to follow incorporation into proteins or secondary metabolites like alkaloids.

C. Study of Lipid Biosynthesis

- Example: ^{14}C-acetate incorporated into fatty acids, sterols, and terpenoids.

D. Study of Nucleic Acid Biosynthesis

- Example: ^{32}P-orthophosphate used to trace DNA/RNA synthesis in cells.

E. Study of Secondary Metabolites

- Alkaloids, flavonoids, lignans: Labeled precursors (^{14}C- or ^{3}H-labeled amino acids) are fed to plants → incorporation traced in secondary metabolites.

F. Enzyme Pathway Elucidation

- Determine which intermediates are converted into which products.
- Example: Use of ^{14}C-shikimic acid to trace phenylpropanoid and flavonoid biosynthesis.

Methods of detection

1. Autoradiography: Visualizes distribution of radioactive molecules in tissues or gels.
2. Liquid scintillation counting: Quantifies β-emitting isotopes.
3. Gamma counters: Detect γ-emitting isotopes.
4. Chromatography coupled with radio-detection: Tracks labeled molecules in mixtures.

Advantages of radioisotopes

- High sensitivity: Detect minute amounts of compounds.
- Can trace dynamic metabolic changes in real time.
- Non-destructive to biological systems when used at appropriate doses.
- Useful for mapping metabolic pathways and identifying precursors and intermediates.

Limitations

- Requires special safety measures due to radiation hazards.
- Expensive instrumentation for detection and measurement.
- Radioactive decay limits half-life of tracers; not all isotopes suitable for long-term studies.
- Ethical concerns in human studies; mostly used in plant and animal models.

Examples of biogenetic studies using radioisotopes

Study	Radioisotope Used	Outcome
Alkaloid biosynthesis (e.g., morphine, quinine)	^{14}C-tyrosine, ^{14}C-tryptophan	Identified precursor amino acids and biosynthetic intermediates
Flavonoid biosynthesis	^{14}C-phenylalanine	Traced carbon flow from Phe → cinnamic acid → flavonoids
Steroid biosynthesis	^{14}C-acetate	Traced acetyl units incorporation into cholesterol and steroid hormones
DNA replication study	^{32}P-orthophosphate	Determined rate and site of DNA synthesis

Safety and handling

- Use shielding and personal protective equipment (PPE).
- Proper waste disposal according to radiation safety guidelines.
- Monitor radiation exposure for laboratory personnel.