BP205T · B.PHARM THEORY

BP205T Pharmacognosy and Phytochemistry

Unit I — Metabolic Pathways & Biogenetic Studies

Pills & Python Notes

From-zero teaching standard: every technical term is defined before use.

Syllabus coverage: Unit I (10 hours).

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Chapter 1: Metabolites — What Plants Make and Why

Learning objectives

After studying this chapter you will be able to:

1. Define metabolite, metabolism, primary metabolite and secondary metabolite.
2. Distinguish primary and secondary metabolites with examples.
3. Explain why plants produce secondary metabolites.
4. List the main groups of secondary metabolites and the pathways that make them.

Definitions (from absolute zero)

- **Metabolism:** All the chemical reactions happening inside a living cell. Think of it as the "kitchen work" of the cell — chopping, cooking and packing chemicals.
- **Metabolite:** Any chemical substance made or used during metabolism. A "metabolite" is simply a product of the cell's kitchen.
- **Primary metabolite:** A chemical that every living cell needs for basic life — growth, energy, reproduction. Examples: sugars (glucose), amino acids, proteins, fats, DNA building blocks. Without them the cell dies.
- **Secondary metabolite:** A chemical that is NOT needed for basic survival, but helps the plant survive in the real world — fighting insects, attracting pollinators, healing wounds. Examples: morphine, caffeine, menthol, the colour of flowers.
- **Biosynthesis:** The building-up of a chemical by a living organism, step by step, using enzymes. "Bio" = life, "synthesis" = making.
- **Phytoconstituent:** A chemical constituent found in a plant ("phyto" = plant).
- **Crude drug:** A plant, animal or mineral material used as medicine in its natural, unprocessed form (dried leaves, bark, gum, oil). We study crude drugs in pharmacognosy.

Simple explanation

Every plant cell runs two kinds of business. The **primary business** keeps the cell alive: it burns sugar for energy, builds proteins, copies DNA. The chemicals used here are primary metabolites, and they are almost the same in all living things — your body and a mango tree both use glucose and amino acids.

The **secondary business** is the plant's defence and marketing department. Plants cannot run away from insects or animals, so they make bitter, poisonous or smelly chemicals (secondary metabolites) to protect themselves. They also make sweet smells and bright colours to attract bees and birds. Humans discovered that many of these defence chemicals act as medicines — that is why most plant drugs are secondary metabolites.

Example

- Primary metabolite: **glucose** — fuel for every cell, made by photosynthesis.
- Secondary metabolite: **quinine** (from cinchona bark) — bitter chemical the tree makes to poison insects; humans use it against malaria.

Analogy

> Think of a house. The **primary metabolites** are the bricks, cement, water and electricity — the house cannot exist without them. The **secondary metabolites** are the lock on the door, the fence, the paint and the flower pots — not needed for the house to stand, but they protect it and make it attractive.

Comparison table: primary vs secondary metabolites

Feature	Primary metabolites	Secondary metabolites
Needed for basic life?	Yes, essential	No, not essential for survival
Found in	All living cells (plants, animals, humans)	Mainly plants (and some microbes)
Examples	Glucose, starch, amino acids, proteins, fats, nucleic acids	Alkaloids, glycosides, tannins, volatile oils, flavonoids, resins
Function	Growth, energy, reproduction	Defence, attraction, protection from stress
Amount in plant	Usually large quantities	Usually small quantities
Medicinal use	Mostly as food/nutrition/excipients	Mostly as active drugs

Main groups of secondary metabolites and their origin pathways

Secondary metabolite group	Built mainly from	Made by pathway
Alkaloids (e.g., morphine, quinine)	Amino acids	Amino acid pathway
Phenylpropanoids, flavonoids, tannins	Shikimic acid products	Shikimic acid pathway
Fatty-acid-like compounds, some pigments	Acetyl-CoA units	Acetate (polyketide) pathway
Terpenoids, steroids, volatile oils	Isoprene units	Mevalonate / MEP pathway (basic idea only)

Pharmacy relevance

Almost every plant drug you will study in Units II and III is either a primary metabolite (acacia gum, gelatin, castor oil) or a secondary metabolite (alkaloids in Unit III). Understanding which pathway makes which drug helps you remember drugs in families instead of as isolated facts.

India context

India's traditional systems (Ayurveda, Siddha, Unani) have used secondary-metabolite-rich plants for thousands of years — neem (bitter defence chemicals), turmeric (curcumin, a defence pigment), opium poppy (alkaloids). Modern phytochemistry simply explains *why* these plants work.

Common confusions

- **Confusion:** "Secondary means less important." **Truth:** Secondary only means "not needed for basic cell life." For medicine, secondary metabolites are the MOST important — they are the active drugs.
- **Confusion:** "Primary metabolites have no medicinal use." **Truth:** They do — as bulk drugs and excipients: acacia as emulsifier, gelatin for capsules, castor oil as purgative (Unit II is full of them).

Common mistakes

- Writing that alkaloids come from the acetate pathway. Alkaloids come mainly from **amino acids**.
- Mixing up "metabolite" and "metabolism": metabolism is the *process*, metabolite is the *chemical*.

Mnemonic

"Primary Keeps Alive, Secondary Survives" — primary metabolites keep the cell alive; secondary metabolites help the plant survive attacks.

One-minute revision

Metabolism = all cell chemistry. Primary metabolites (sugars, amino acids, fats) = essential for life, same in all organisms. Secondary metabolites (alkaloids, flavonoids, tannins, volatile oils) = plant defence/attraction chemicals, the source of most plant drugs. Three big building pathways: shikimic acid, acetate, amino acid pathways.

Key takeaway

Plants make two chemical families: primary metabolites for living, secondary metabolites for defending. Pharmacy cares deeply about both.

Practice questions

MCQs

1. Which of the following is a primary metabolite?

a) Morphine b) Glucose c) Quinine d) Caffeine

1. Secondary metabolites are mainly useful to the plant for:

a) Energy production b) DNA copying c) Defence against pests d) Cell division

Short answers

1. Define primary and secondary metabolites with one example each.
2. Why do plants produce bitter or poisonous chemicals?

Long answer

1. Compare primary and secondary metabolites under: necessity for life, distribution, examples and pharmaceutical importance.

Application-based

1. A tribe uses a bitter leaf paste on wounds and the wounds heal faster without infection. Is the active chemical likely a primary or secondary metabolite? Give reasons.

Viva

1. What is biosynthesis? Name the three pathways of secondary metabolite biosynthesis in the syllabus.

Answers: 1-b, 2-c.

Chapter 2: Basic Metabolic Pathways — The Factory Behind the Drugs

Learning objectives

1. Describe in simple words how plants make their basic building blocks.
2. Explain the roles of photosynthesis, glycolysis and the citric acid cycle.
3. Identify the starting materials (precursors) that feed the three secondary pathways.

Definitions

- **Precursor:** A starting chemical from which another chemical is built. Flour is the precursor of bread.
- **Photosynthesis:** The process by which green plants use sunlight to make glucose from carbon dioxide and water.
- **Glycolysis:** The breakdown of glucose into smaller pieces (mainly pyruvate) to release energy. Happens in all cells.
- **Citric acid (TCA) cycle:** A wheel of reactions that burns the small pieces further and releases energy plus useful building blocks.
- **Enzyme:** A protein that speeds up one specific chemical reaction, like a specialised worker on a factory line.
- **Acetyl-CoA:** A small, energy-rich molecule made from glucose breakdown; the starting material of the acetate pathway and of fatty acids.

Simple explanation

Before a plant can make fancy defence chemicals, it must first make simple building blocks. This happens in three connected stages:

1. **Photosynthesis (the farm):** Leaves capture sunlight and make glucose. Glucose is the master raw material.
2. **Glycolysis + TCA cycle (the cutting room):** Glucose is chopped into small standard pieces — pyruvate, acetyl-CoA, and small acids. These pieces release energy AND serve as Lego bricks.
3. **Secondary pathways (the special workshops):** The Lego bricks are sent to three workshops — shikimic acid, acetate and amino acid pathways — where they are rebuilt into defence chemicals (alkaloids, flavonoids, etc.).

Flowchart: from sunlight to medicine

1. **Sunlight + CO_2 + water**
   photosynthesis in leaves

2. **GLUCOSE (master raw material)**
   glycolysis — chopping

3. **PYRUVATE → ACETYL-CoA**
   TCA cycle → small acids (oxaloacetate, α-ketoglutarate…) supply secondary metabolism

1. **SHIKIMIC ACID PATHWAY**
   aromatic rings: flavonoids, tannins...
2. **ACETATE PATHWAY**
   chains built from acetyl-CoA units: fatty acids, pigments
3. **AMINO ACID PATHWAYS**
   alkaloids from amino acids

Key building blocks and where they come from

Building block	Comes from	Feeds which pathway
Phosphoenolpyruvate (PEP) + erythrose-4-phosphate	Glucose breakdown	Shikimic acid pathway
Acetyl-CoA	Pyruvate (from glycolysis)	Acetate pathway
Amino acids (ornithine, lysine, tyrosine, tryptophan)	TCA-cycle acids + nitrogen	Amino acid pathways

Example

The painkiller **morphine** starts as the amino acid tyrosine (made using TCA-cycle materials), then follows the amino acid pathway. The yellow colour **curcumin** in turmeric starts from shikimic-acid-pathway materials. The purgative oil in **castor seeds** is built from acetyl-CoA units.

Analogy

> A car factory first makes standard steel sheets, bolts and wires (primary metabolism). Then three specialist workshops turn those standard parts into (1) painted body panels, (2) long exhaust pipes, and (3) electronic alarms (the three secondary pathways). Same raw steel, three different finished products.

Pharmacy relevance

If you know which workshop made a drug, you can predict its chemistry: shikimate products usually have aromatic rings; acetate products are often long chains; alkaloids always contain nitrogen (from amino acids).

Common confusions

- **Confusion:** "Photosynthesis makes alkaloids directly." **Truth:** Photosynthesis makes glucose; glucose is chopped up; the pieces are rebuilt into alkaloids through several pathways.
- **Confusion:** Acetyl-CoA is only for energy. **Truth:** It is also the brick for fatty acids and the acetate pathway.

Common mistakes

- Drawing the pathways as separate and disconnected. They are connected — all start from glucose pieces.

Mnemonic

"Sun → Sugar → Small pieces → Special drugs" — the four S's of plant chemistry.

One-minute revision

Photosynthesis makes glucose → glycolysis/TCA chop it into PEP, acetyl-CoA, small acids → three workshops (shikimic acid, acetate, amino acid pathways) build secondary metabolites → these become plant drugs.

Key takeaway

All plant drugs trace back to glucose; the three secondary pathways are just three different ways of rebuilding glucose pieces.

Practice questions

MCQs

1. Acetyl-CoA is mainly formed from:

a) Sunlight b) Pyruvate from glycolysis c) DNA d) Chlorophyll

1. The shikimic acid pathway starts from:

a) Acetyl-CoA b) Amino acids c) PEP + erythrose-4-phosphate d) Fatty acids

Short answers

1. What is a precursor? Give one example.
2. Draw a simple flowchart from glucose to secondary metabolites.

Long answer

1. Explain how primary metabolism supplies building blocks to secondary metabolism, with a labelled flowchart.

Viva

1. Name two products of the TCA cycle that are useful as biosynthetic building blocks.

Answers: 1-b, 2-c.

Chapter 3: The Shikimic Acid Pathway

Learning objectives

1. State the starting materials and key intermediate of the shikimic acid pathway.
2. Draw the pathway flowchart up to the aromatic amino acids.
3. List the secondary metabolite groups arising from this pathway with examples.

Definitions

- **Shikimic acid:** A ring-shaped molecule that is the central intermediate of this pathway; named after the Japanese *shikimi* plant where it was found.
- **Aromatic compound:** A chemical containing a benzene-like ring (a stable ring of carbon atoms). Many smell nicely — "aromatic".
- **Phenylpropanoid:** A molecule built from a 6-carbon ring plus a 3-carbon side chain (C6–C3 unit), e.g., cinnamic acid.
- **Chorismic acid:** The branch-point molecule after shikimic acid; from here the road splits toward different amino acids.

Simple explanation

The shikimic acid pathway is the plant's **aromatic-ring factory**. It takes two small glucose pieces — PEP (3 carbons) and erythrose-4-phosphate (4 carbons) — and joins them step by step into a ring: shikimic acid. From shikimic acid the path continues to chorismic acid, and then splits into three **aromatic amino acids**: phenylalanine, tyrosine and tryptophan. These amino acids are then converted into a huge family of ring-containing defence chemicals: flavonoids (flower colours), tannins, lignans, coumarins and many alkaloids.

Important: animals and humans do NOT have this pathway — we must get these aromatic amino acids from food. That is why weed-killers blocking this pathway kill plants but are less toxic to humans (basic idea; details beyond syllabus).

Flowchart

1. **PEP (3C, from glycolysis) + Erythrose-4-phosphate (4C, from glucose route)**
   joining steps
2. **SHIKIMIC ACID**
   the pathway’s namesake
3. **CHORISMIC ACID**
   branch point
4. **Phenylalanine**
   Cinnamic acid → phenylpropanoids → flavonoids, tannins, coumarins, lignans
5. **Tyrosine**
   Many alkaloids (e.g., morphine)

1 **Tryptophan**
Indole alkaloids (e.g., vinca alkaloids, rauwolfia)

Products table

Product group	Example drugs/chemicals	Use / note
Phenylpropanoids	Cinnamic acid, eugenol (clove)	Flavour, antiseptic
Flavonoids	Quercetin, rutin	Antioxidant, vein drugs
Tannins (hydrolysable)	Gallic acid derivatives	Astringent
Coumarins	—	Fragrance, some anticoagulant-like
Lignans	—	Plant defence chemicals
Aromatic amino acids	Phenylalanine, tyrosine, tryptophan	Also feed amino-acid pathway alkaloids

Example

The astringent taste of tea and myrobalans (Unit III) comes from tannins built through the shikimate route. The yellow flavonoid colours in flowers are shikimate products that attract bees.

Analogy

> The shikimate pathway is like a **ring-making machine** in a jewellery factory: flat metal strips (straight carbon chains) go in, rings come out, and the rings are then set with different stones to make different jewellery (flavonoids, tannins, alkaloids).

Pharmacy relevance

Many Unit III drugs (tannin drugs, flavonoid drugs like ginkgo and green tea) are shikimate children. If an examiner asks "which pathway gives flavonoids?" — answer: shikimic acid pathway.

India context

Shikimic acid itself became famous as the starting material for the antiviral drug oseltamivir (Tamiflu), originally isolated from star anise — showing how a pathway intermediate can become industrially precious. (General knowledge; not a pharmacopoeial claim.)

Common confusions

- **Confusion:** Shikimic acid pathway makes all alkaloids. **Truth:** It makes the *aromatic amino acids* that *some* alkaloids come from; but the actual alkaloid-building steps belong to the amino acid pathways (Chapter 5). Many textbooks group them together — keep the distinction clear for exams.
- **Confusion:** "Shikimic" is spelled/pronounced "shikimik". Note the spelling: s-h-i-k-i-m-i-c.

Common mistakes

- Forgetting the two starting materials (PEP + erythrose-4-phosphate). Examiners love asking this.
- Saying humans have the shikimate pathway. We do not.

Mnemonic

"PEP plus E4P makes Shikimate" — the two starters. Then **"Phe, Tyr, Try"** — the three aromatic amino acids (phenylalanine, tyrosine, tryptophan).

One-minute revision

PEP + erythrose-4-phosphate → shikimic acid → chorismic acid → phenylalanine, tyrosine, tryptophan → phenylpropanoids, flavonoids, tannins, coumarins, lignans, some alkaloids. Absent in humans. The aromatic-ring factory.

Key takeaway

Shikimate pathway = rings from sugar pieces; products = flavonoids, tannins, phenylpropanoids and aromatic amino acids.

Practice questions

MCQs

1. The shikimic acid pathway is absent in:

a) Plants b) Bacteria c) Humans and animals d) Fungi

1. Chorismic acid is the precursor of:

a) Fatty acids b) Aromatic amino acids c) Sugars d) Waxes

Short answers

1. Name the two starting materials of the shikimic acid pathway.
2. List four product groups of the shikimic acid pathway with one example each.

Long answer

1. Draw and explain the shikimic acid pathway up to the formation of secondary metabolites.

Application-based

1. A new herbicide blocks the enzyme that converts shikimic acid to chorismic acid. Predict which plant products will decrease, and explain why the herbicide is relatively safer for humans.

Viva

1. Why is the shikimic acid pathway considered a bridge between primary and secondary metabolism?

Answers: 1-c, 2-b.

Chapter 4: The Acetate Pathway (Polyketide Pathway)

Learning objectives

1. State the building block and key intermediate of the acetate pathway.
2. Explain how fatty acids and polyketides are built.
3. List product groups with examples.

Definitions

- **Acetate pathway:** The route that builds long carbon chains by joining 2-carbon acetate (acetyl-CoA) units head-to-tail. Also called the **polyketide pathway** ("poly" = many, "ketide" = keto-containing units).
- **Malonyl-CoA:** The activated 2-carbon donor unit actually used for chain building (made from acetyl-CoA).
- **Polyketide:** A long chain built from repeated keto units; can fold into rings to make pigments and antibiotics.
- **Fatty acid:** A long chain with a carboxylic acid end — the building block of fats and oils.

Simple explanation

The acetate pathway is the plant's **chain-making factory**. It takes 2-carbon units (as malonyl-CoA) and joins them one after another like train coaches: 2 + 2 + 2 + 2... After joining, each unit can be processed in different ways — fully reduced to make **fatty acids** (smooth chains), or left with keto groups to make **polyketides** (reactive chains that fold into rings, giving coloured pigments and some antibiotics).

So the same Lego-adding process gives two families: fats/oils (Unit II lipids!) and aromatic polyketides like anthraquinone pigments.

Flowchart

1. **ACETYL-CoA (2C)**
   carboxylation
2. **MALONYL-CoA**
   the active 2C donor; repeated joining, 2C at a time
3. **FULLY REDUCED**
   FATTY ACIDS (palmitic, stearic, oleic acids...) → FATS, FIXED OILS, WAXES (Unit II!)
4. **KEPT AS KETO UNITS**
   POLYKETIDE CHAIN → folds into rings → AROMATIC POLYKETIDES (e.g., anthraquinone pigments like emodin; some antibiotics)

Products table

Product group	Examples	Note
Fatty acids	Palmitic, stearic, oleic, ricinoleic acids	Build fats and oils
Fixed oils and fats	Castor oil, olive oil, cocoa butter	Unit II drugs — acetate pathway products!
Waxes	Beeswax components	Long-chain esters
Anthraquinone pigments	Emodin-type compounds	Laxative pigments (senna-type, Unit III glycosides link)
Some antibiotics	(microbial polyketides)	Basic idea only

Example

Castor oil (Unit II) is mostly ricinoleic acid — a fatty acid built by joining 2-carbon units through the acetate pathway. The orange-red pigment in some laxative barks is an anthraquinone — also acetate-built, but folded into rings instead of staying a straight chain.

Analogy

> Imagine making two things from the same paper chain: if you press it flat and smooth, you get a ribbon (fatty acid); if you let it curl and glue the loops, you get a rosette badge (aromatic polyketide). Same paper, different finishing.

Pharmacy relevance

Unit II's entire lipid section (castor oil, olive oil, cocoa butter, wool fat, beeswax) is the pharmacy face of the acetate pathway. When you study those drugs, remember: their fatty acids are acetate-pathway children.

Common confusions

- **Confusion:** "Acetate pathway makes alkaloids." **Truth:** No — alkaloids need nitrogen from amino acids. The acetate pathway makes nitrogen-free chains and rings.
- **Confusion:** Polyketide = plastic/polymer. **Truth:** In biochemistry, polyketide means a chain built from keto-acid units — a natural product family.

Common mistakes

- Writing acetyl-CoA as the direct chain donor. The actual donor added each round is **malonyl-CoA** (made from acetyl-CoA). Examiners award marks for this detail.

Mnemonic

"ACetate Adds Chains" — 2 carbons at a time. **"Reduce → fat, Ring → pigment."**

One-minute revision

Acetyl-CoA → malonyl-CoA → repeated 2C joining → fatty acids (reduced) or polyketides (folded into aromatic pigments). Products: fats, fixed oils, waxes, anthraquinones. The chain factory.

Key takeaway

Acetate pathway joins 2-carbon units into chains: smooth chains become fats and oils; folded chains become pigments.

Practice questions

MCQs

1. The active 2-carbon donor in the acetate pathway is:

a) Acetyl-CoA b) Malonyl-CoA c) Pyruvate d) Shikimic acid

1. Anthraquinone pigments are biosynthesised mainly by the:

a) Shikimate pathway b) Acetate (polyketide) pathway c) Amino acid pathway d) TCA cycle

Short answers

1. Distinguish fatty acids from polyketides in terms of biosynthesis.
2. Name two Unit II drugs whose constituents come from the acetate pathway.

Long answer

1. Describe the acetate pathway with a flowchart and list its major product groups with examples.

Viva

1. Why is the acetate pathway also called the polyketide pathway?

Answers: 1-b, 2-b.

Chapter 5: Amino Acid Pathways (Alkaloid Biosynthesis)

Learning objectives

1. Define alkaloids and their key chemical feature.
2. Explain the general steps: amino acid → decarboxylation → alkaloid.
3. Match major amino acids to the alkaloid families they produce, with examples.

Definitions

- **Alkaloid:** A naturally occurring, nitrogen-containing, basic (alkali-like) compound, usually with strong effects on the body. Examples: morphine, quinine, caffeine, nicotine. ("Alkali" + "oid" = alkali-like.)
- **Decarboxylation:** Removal of carbon dioxide (CO_2) from a molecule — a key first step that turns an amino acid into an amine.
- **Amine:** A molecule containing nitrogen derived from ammonia; the stepping stone between amino acids and alkaloids.
- **True alkaloid:** An alkaloid whose nitrogen comes from an amino acid and sits inside a ring (heterocyclic) structure.

Simple explanation

Amino acid pathways are the plant's **nitrogen workshop**. The recipe is simple and repeats for every alkaloid family:

1. Take an amino acid (which already contains nitrogen).
2. **Decarboxylate** it — knock off CO_2 — to get an amine.
3. Build rings around the nitrogen, add decorations → **alkaloid**.

Different amino acids give different alkaloid families, like different doughs give different breads.

General scheme

1. **AMINO ACID (contains N)**
   $-CO_2$ (decarboxylation)
2. **AMINE**
   ring building, oxidations, methylations...
3. **ALKALOID**
   nitrogen in/beside rings, basic, bioactive

Amino acid → alkaloid family table (must memorise)

Amino acid	Alkaloid family	Example drugs
Ornithine	Tropane alkaloids; nicotine	Atropine (belladonna), cocaine, nicotine
Lysine	Quinolizidine alkaloids	Lupin alkaloids (basic idea)
Tyrosine	Isoquinoline alkaloids	Morphine, codeine (opium, Unit III)
Tryptophan	Indole alkaloids	Vincristine/vinblastine (vinca), reserpine (rauwolfia) — Unit III!
Histidine	Imidazole alkaloids	Pilocarpine (basic idea)
Phenylalanine	(via shikimate link) some alkaloids	Ephedrine-type (basic idea)

Example

Morphine (Unit III, opium): tyrosine → decarboxylation → dopamine-like amine → ring building → morphine. **Reserpine** (Unit III, rauwolfia): tryptophan → indole alkaloid. Same workshop logic, different starting amino acid.

Analogy

> Think of a potter's workshop: the amino acid is the lump of clay (already containing the "nitrogen colour"), decarboxylation is wedging the clay (removing air/CO_2), and ring-building is shaping it into different pots — round tropane pots from ornithine clay, tall indole vases from tryptophan clay.

Pharmacy relevance

Unit III is dominated by alkaloid drugs (vinca, rauwolfia, opium). Knowing "tryptophan → indole → vinca/rauwolfia" and "tyrosine → isoquinoline → morphine" turns three separate drugs into one logical story.

Common confusions

- **Confusion:** "All nitrogen compounds in plants are alkaloids." **Truth:** Proteins and amino acids also contain nitrogen but are primary metabolites, not alkaloids. Alkaloids are secondary, basic, usually ring-structured.
- **Confusion:** Caffeine's origin. Caffeine is a purine alkaloid (from nucleic-acid building blocks, not a standard amino acid) — a special case; don't force it into the table above.

Common mistakes

- Skipping the decarboxylation step when describing alkaloid biosynthesis.
- Assigning morphine to the wrong amino acid — it is **tyrosine** (isoquinoline), not tryptophan.

Mnemonic

"Ornithine Opens Tropanes; Tryptophan Turns Indole; Tyrosine Yields Isoquinoline" — O-T-T-Y. Or shorter: **"OTT-Y"**.

One-minute revision

Amino acid –CO_2 → amine → ring building → alkaloid. Ornithine → tropane (atropine); tyrosine → isoquinoline (morphine); tryptophan → indole (vinca, rauwolfia). Nitrogen comes from the amino acid — that is the signature of alkaloids.

Key takeaway

Alkaloids are amino acids transformed: lose CO_2, build rings around nitrogen. The starting amino acid decides the alkaloid family.

Practice questions

MCQs

1. The first step in alkaloid biosynthesis from an amino acid is:

a) Hydroxylation b) Decarboxylation c) Glycosylation d) Methylation

1. Reserpine (rauwolfia) is derived from:

a) Ornithine b) Lysine c) Tryptophan d) Tyrosine

Short answers

1. Define alkaloid. What is its characteristic chemical feature?
2. Complete: Ornithine → _____ alkaloids; Tyrosine → _____ alkaloids.

Long answer

1. Describe the general scheme of alkaloid biosynthesis from amino acids, giving the amino acid precursors of the tropane, isoquinoline and indole families with one drug example each.

Application-based

1. A newly isolated plant base contains nitrogen in a heterocyclic ring and shows strong physiological activity. Which biosynthetic pathway most likely produced it, and what experiment (using the tracer technique from Chapter 6) could confirm the precursor amino acid?

Viva

1. Why do alkaloids always contain nitrogen?

Answers: 1-b, 2-c.

Chapter 6: Radioactive Isotopes in Biogenetic Studies (Tracer Technique)

Learning objectives

1. Define isotopes, radioactive isotopes and the tracer technique.
2. Explain how labelled precursors reveal biosynthetic pathways.
3. List commonly used isotopes and their applications.
4. State the precautions in handling radioactivity (basic idea).

Definitions

- **Isotope:** Different forms of the same element with the same protons but different neutrons — e.g., carbon-12 (normal) and carbon-14 (heavy, radioactive).
- **Radioactive isotope (radioisotope):** An unstable isotope that gives off radiation as it decays, e.g., ^{14}C, ^{3}H (tritium), ^{32}P, ^{35}S.
- **Labelled compound:** A normal molecule in which one or more atoms are replaced by a radioactive isotope — like tagging a sheep with a coloured collar so you can follow it in a flock.
- **Tracer technique:** Feeding a labelled precursor to a plant and tracking where the label ends up in the final product, to discover the biosynthetic route.
- **Autoradiography:** A technique that makes a photographic image of where radioactivity sits in a plant tissue or chromatogram.
- **Biogenesis:** The origin and formation of a natural product in the living organism (same idea as biosynthesis, emphasising the "life story").

Simple explanation

How do scientists *prove* that morphine comes from tyrosine? They **tag** tyrosine with radioactive carbon (^{14}C), feed it to the poppy plant, wait, then extract morphine and check: is the morphine radioactive? If yes, tyrosine really becomes morphine. They can even find *which carbon* of tyrosine became *which carbon* of morphine by breaking the product apart — like following a marked banknote through the economy.

Steps of a tracer experiment:

1. **Synthesise** the suspected precursor with a radioactive label (e.g., ^{14}C-tyrosine).
2. **Feed** it to the plant (through cut stem, leaf, or hydroponic solution).
3. **Wait** for metabolism (hours to days).
4. **Extract** the suspected product (e.g., morphine).
5. **Detect** radioactivity in the product (scintillation counter, autoradiography).
6. **Degrade** the product stepwise to locate the label — confirming the exact atom mapping.

Commonly used isotopes table

Isotope	Symbol	What it labels	Typical use
Carbon-14	^{14}C	Carbon skeleton	Main workhorse — follows carbon atoms through pathways
Tritium	^{3}H	Hydrogen positions	Studies hydrogen transfers, stereochemistry

Isotope	Symbol	What it labels	Typical use
Phosphorus-32	^{32}P	Phosphate groups	Nucleic acids, phosphorylated intermediates
Sulphur-35	^{35}S	Sulphur atoms	Sulphur-containing metabolites

Example

To prove the shikimate pathway: feed ^{14}C-labelled glucose to a plant → isolate shikimic acid → find radioactivity in it → the label pattern shows glucose carbons became shikimate carbons. Classic experiments of this type established every pathway in Chapters 3–5.

Analogy

> It is like the police marking banknotes with invisible ink and releasing them to catch a thief's route: the marked notes (labelled precursor) travel through shops (enzymes) and end up in the thief's wallet (final alkaloid), revealing the whole path.

Pharmacy relevance

Every biosynthetic pathway in your syllabus was mapped using tracers. In industry, tracer studies also check how a medicinal plant makes its active constituent under different growing conditions — helping standardise herbal drugs.

India context

Indian research institutes (such as CSIR laboratories working on medicinal plants) have used tracer and related techniques to study the biosynthesis of important phytoconstituents from Indian medicinal plants.

Safety note (basic idea)

Radioisotopes are handled in licensed laboratories with shielding, distance and time limits, and waste disposal rules. You will not handle them in B.Pharm practicals; this chapter is for understanding the concept.

Common confusions

- **Confusion:** "The tracer changes the chemistry." **Truth:** Isotopes behave chemically almost identically to normal atoms; the label is just a silent tag.
- **Confusion:** Tracer technique vs. "tracing" a criminal. Same word logic — following a marked object — different field.

Common mistakes

- Saying the plant is "made radioactive and dangerous forever." The amounts used are tiny (tracer doses), and short-lived isotopes decay away.
- Confusing ^{14}C (carbon) with ^{32}P (phosphorus) applications.

Mnemonic

"Feed, Wait, Extract, Detect, Degrade" — the five steps of a tracer experiment. Or **"C-14 Carries Carbon Clues."**

One-minute revision

Tag a suspected precursor with a radioisotope (usually ^{14}C) → feed to plant → extract product → detect radioactivity → degrade to map atoms. Proves precursor–product relationships and pathway order.

Key takeaway

The tracer technique uses radioactive labels as silent tags to follow atoms through biosynthesis, proving which precursor becomes which drug.

Practice questions

MCQs

1. The most commonly used isotope in biogenetic tracer studies is:

a) ^{32}P b) ^{14}C c) ^{35}S d) ^{131}I

1. In a tracer experiment, radioactivity found in the isolated product proves:

a) The product is dangerous b) The labelled precursor was converted into the product c) The plant is mutated d) Nothing at all

Short answers

1. Define the tracer technique in two sentences.
2. List the five steps of a tracer experiment.

Long answer

1. Describe how radioactive isotopes are used in biogenetic studies, with a labelled-precursor example.

Application-based

1. You suspect compound X in a leaf is made from phenylalanine. Design a tracer experiment to test this, including controls.

Viva

1. What is autoradiography, and why is it useful in tracer studies?

Answers: 1-b, 2-b.

Chapter 7: Pathway Prediction Tools and Modern Genetic Tools (CRISPR/Cas9)

Learning objectives

1. Explain what pathway prediction tools do, in simple words.
2. Describe CRISPR/Cas9 and its basic components.
3. State applications of these tools in medicinal plant research.

Definitions

- **Pathway prediction tool:** Computer software/databases that predict the biosynthetic route of a natural product from known reactions, enzymes or genes — like a GPS that suggests the road map between a starting material and a product.
- **Genome:** The complete set of DNA (all genes) of an organism — its full instruction book.
- **Gene cluster:** A group of neighbouring genes that work together to make one natural product (common in microbes, also found in plants).
- **CRISPR/Cas9:** A gene-editing tool: a guide RNA leads the Cas9 "molecular scissors" to an exact DNA spot, where Cas9 cuts the DNA so scientists can delete, repair or replace a gene.
- **Knockout:** Deleting or disabling a gene to see what happens without it — proves what the gene does.
- **Metabolic engineering:** Re-designing an organism's chemistry (adding/removing genes) to make more of a useful compound.

Simple explanation — prediction tools

After decades of tracer work, scientists stored thousands of known reactions in databases. A **pathway prediction tool** takes a target molecule (say, a new flavonoid) and searches backwards: "which known reactions could build this?" It proposes likely routes, which scientists then test in the lab. Related tools scan a plant's genome for gene clusters that look like biosynthetic machinery (**genome mining**). In short: the computer suggests the map; the lab verifies the roads.

Simple explanation — CRISPR/Cas9

Bacteria invented CRISPR as an immune system to cut virus DNA. Scientists borrowed it as **programmable scissors**:

1. Design a small **guide RNA** matching the target gene's DNA address.
2. The guide RNA carries the **Cas9 protein** to that exact spot.
3. Cas9 **cuts** the DNA; the cell's repair either disables the gene (knockout) or inserts a new sequence.

In medicinal plants, CRISPR lets researchers switch off a competing pathway so more raw material flows into the drug pathway (higher yield), or prove a gene's function by knocking it out and watching the product disappear.

Flowchart: CRISPR editing

1. **Design guide RNA**
2. **Guide RNA + Cas9**
3. **Finds exact DNA address**
4. **Cas9 CUTS DNA**
5. **Cell repairs badly → GENE KNOCKED OUT**
   function proven, pathway blocked
6. **Insert new DNA piece → GENE REPLACED/ADDED**
   new trait introduced, pathway improved

Applications table

Tool	What it does	Use in pharmacognosy
Pathway prediction software/databases	Proposes biosynthetic routes	Faster discovery of how new phytoconstituents are made
Genome mining	Finds biosynthetic gene clusters in DNA	Discovers new natural products without chemistry-first screening
CRISPR/Cas9 knockout	Disables a gene precisely	Proves which gene makes which compound
CRISPR-based activation/engineering	Tunes gene activity	Increases yield of valuable phytoconstituents; removes toxic by-products

Example

Suppose a medicinal plant makes a useful anti-inflammatory flavonoid but also a bitter unwanted compound sharing an early precursor. CRISPR could knock out the gene leading to the bitter branch, channelling more precursor into the useful flavonoid — a cleaner, higher-yielding plant.

Analogy

> Prediction tools are like **route-planning apps** for chemistry; CRISPR is like **precision roadworks** — closing exactly one lane (gene) to redirect traffic (metabolites) where you want it.

Pharmacy relevance

These tools are the future of herbal drug standardisation and production: high-yielding, uniform medicinal plants and plant cell cultures producing consistent phytoconstituents — directly relevant to quality and supply of crude drugs.

Cautious wording (as required)

Exact software names and capabilities change rapidly; examination answers should describe the *principles* (prediction from reaction databases; genome mining; CRISPR cutting via guide RNA) rather than naming specific commercial tools, unless your teacher specifies them.

Common confusions

- **Confusion:** "CRISPR creates new genes from nothing." **Truth:** It edits existing DNA — cutting, disabling or replacing — with precision; it does not invent DNA code from scratch.
- **Confusion:** Prediction tools replace lab work. **Truth:** They propose; experiments confirm.

Common mistakes

- Writing "CRISPER" — the correct spelling is **CRISPR** (Clustered Regularly Interspaced Short Palindromic Repeats).
- Saying Cas9 is the guide. **Cas9 is the scissors; the guide RNA is the address label.**

Mnemonic

"Guide Guides, Cas9 Cuts" — the two jobs. And **"Predict with computer, Prove with CRISPR."**

One-minute revision

Prediction tools = computer maps of possible biosynthetic routes + genome mining. CRISPR/Cas9 = guide RNA delivers Cas9 scissors to an exact gene → cut → knockout or replacement. Uses: prove gene function, boost yield of phytoconstituents, cleaner medicinal plants.

Key takeaway

Computers now predict biosynthetic pathways, and CRISPR/Cas9 lets us edit the genes behind them — the modern toolkit of pharmacognosy.

Practice questions

MCQs

1. In CRISPR/Cas9, the component that finds the target DNA sequence is the:

a) Cas9 protein b) Guide RNA c) Plasmid d) Primer

1. A gene knockout experiment is mainly used to:

a) Increase mutation rate randomly b) Prove the function of a gene c) Sequence DNA d) Extract proteins

Short answers

1. What is a pathway prediction tool?
2. Expand CRISPR and state the role of Cas9.

Long answer

1. Describe the principle of CRISPR/Cas9 gene editing with a flowchart and discuss two applications in medicinal plant research.

Application-based

1. A plant cell culture produces a valuable drug but also a toxic side-product from a branching pathway. How could CRISPR/Cas9 and pathway prediction tools together solve this problem?

Viva

1. What is genome mining, and how does it help discover new natural products?

Answers: 1-b, 2-b.

UNIT I — INFOGRAPHIC CONCEPT

From sunlight to medicine

Sun → Sugar → Small pieces → Special drugs

1. **Sunlight + CO_2 + water** → photosynthesis in leaves → **glucose (master raw material)**.
2. **Glycolysis and the TCA cycle** chop glucose into **PEP, erythrose-4-phosphate, pyruvate, acetyl-CoA and small acids**.
3. **Shikimic acid pathway** → aromatic rings: flavonoids, tannins and phenylpropanoids.
4. **Acetate pathway** → chains built from acetyl-CoA units: fatty acids, fixed oils, waxes and polyketide pigments.
5. **Amino acid pathways** → nitrogen-containing alkaloids.
6. **Tracer technique** follows labelled atoms to prove the route; **pathway prediction tools** propose routes; **CRISPR/Cas9** tests or edits the genes behind them.

UNIT I — COMBINED REFERENCES

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