



# Pharmacognosy II



## General Biosynthesis Pathways Of Secondary Metabolites

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Lecture 1

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# Lecture content

- Pharmacognosy and drug
- Photosynthesis
- Primary and secondary metabolites
- Building blocks
- Biosynthesis pathways
- Classification of the secondary metabolites

# Pharmacognosy and drug

- Around **25%** of all prescription medicines are from natural sources, this include anticancer medication in which nearly **60%** are from natural sources

## **Botanical drugs are obtained from either:**

1. A plant that converted into a drug by drying certain part of it or all of it
2. A plant, but no longer retains the structure of the plant or its organs and contains a complex mixture of biogenic compounds (e.g., fatty and essential oils, gums, resins, balms)

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## Plant organs (parts) are:

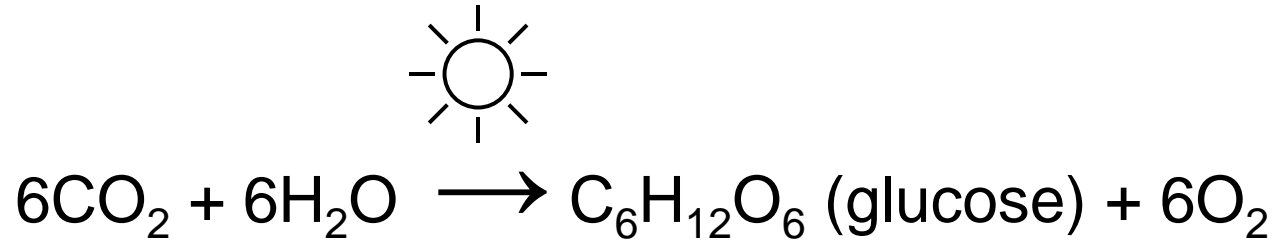
1. Aerial parts ( leaf, flower, fruit, stem)
2. Leaf
3. Flower
4. Fruit
5. Root
6. Bark
7. Rhizome
8. Bulb

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**The nature and quantity of active constituents in plants are affected by:**

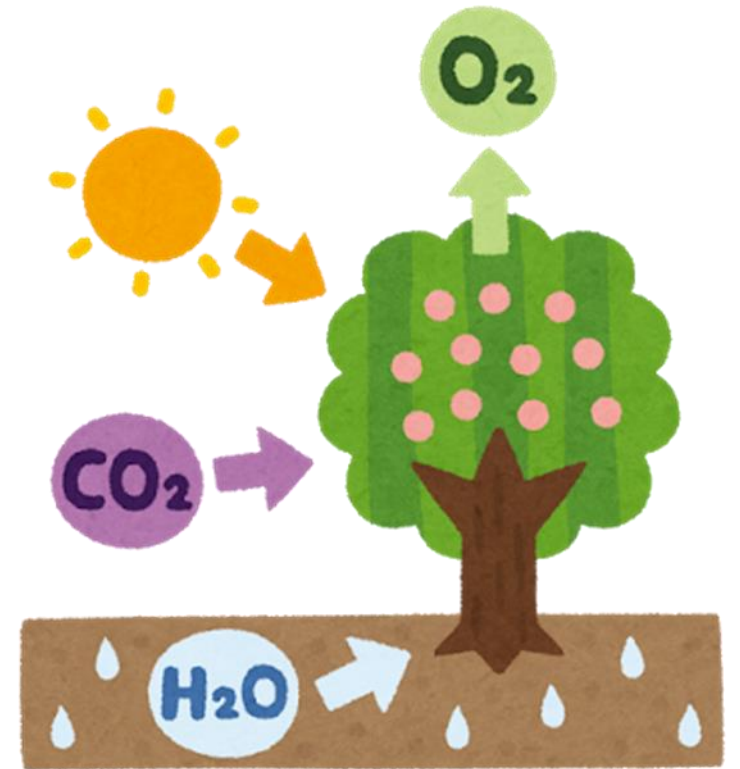
1. Age (developmental stage)
2. Climate
3. Soil
4. Hereditary (genetic differences)

# Photosynthesis



Chlorophyll pigment or any pigment that absorb light

- Photosynthesis can happen in any green part of the plant (not only leaf) if there is chlorophyll.
- It can also occur in certain algae and bacteria too



cont.

- The glucose molecule produced from photosynthesis is involved in the biosynthesis of protein, lipids, nucleic acids and other cell constituents
- This process also help in the production of adenosine triphosphate (ATP) and nicotine adenine dinucleotide phosphate (NADPH)
- Cellular Respiration converts  $O_2$  and glucose into  $H_2O$  and  $CO_2$  in the mitochondria

# Primary and secondary metabolites

- **Primary Metabolites** are compounds, mainly found in all living organism, essential for basic cellular processes and includes **carbohydrates, amino acids, nucleic acids, and lipids** which are vital for energy production, cell structure, and overall metabolism.
- primary metabolites play an essential role in plant growth, development, reproduction, and signal transduction



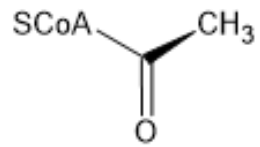
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- **Secondary Metabolites** are, found in only specific organism or group of organism, compounds that does not directly involved in basic cellular functions.
- They often serve specialized roles, such as defense against predators, attraction of pollinators, allelopathy (inhibition of competing organisms)
- Secondary metabolism provides most of the **pharmacologically active natural products.**

# Building blocks

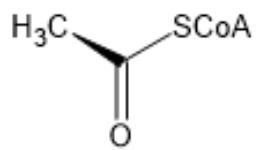
- Most secondary metabolites are derived from just a few building blocks.
- **These building blocks are:**
  1.  $C_1$  : The methylenedioxy group ( $OCH_2O$ )
  2.  $C_2$  : Acetyl-CoA
  3.  $C_5$  : isoprene unite
  4.  $C_6C_3$ ,  $C_6C_2$ ,  $C_6C_1$  : The phenylalanine/ L-tyrosine unite
  5.  $C_4N$ ,  $C_5N$ ,  $C_6C_2N$  : amino acid unites

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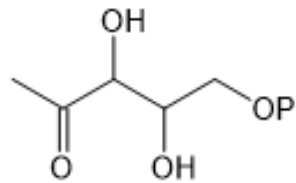


Acetyl-CoA

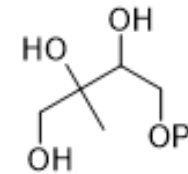
C<sub>2</sub>



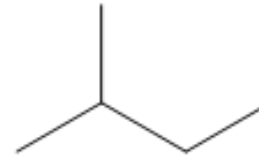
Mevalonic acid



deoxyxylulose phosphate



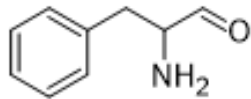
Methylerythritol phosphate



isoprene unite

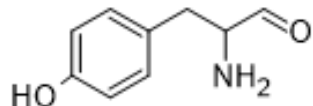
C<sub>5</sub>

L-Phe



C<sub>6</sub>C<sub>1</sub>

L-Tyr



C<sub>6</sub>C<sub>3</sub>

C<sub>6</sub>C<sub>2</sub>

cont.

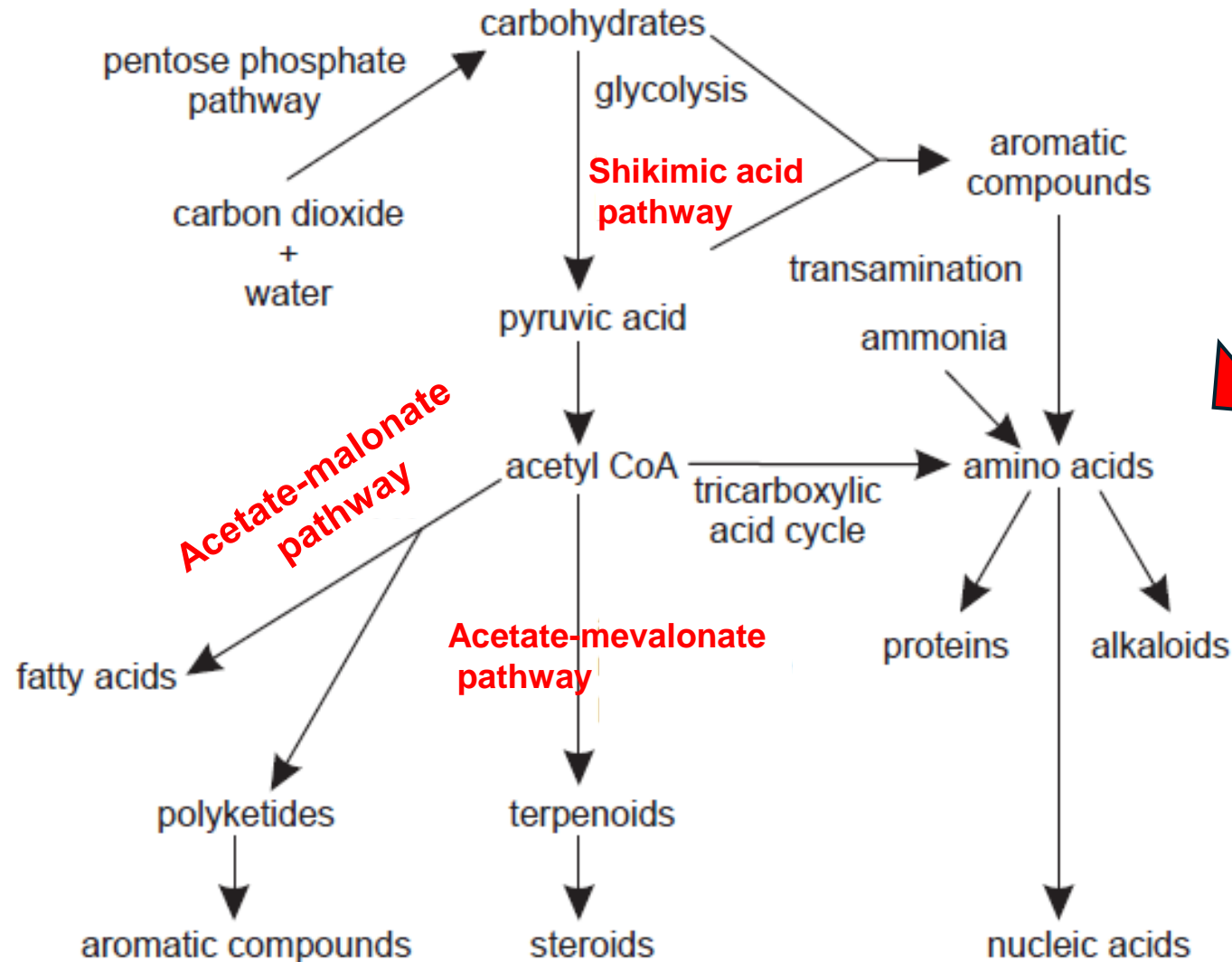
## Functions of Secondary Metabolites In Plants are various:

1. Defense against herbivores and pathogens
2. Protection against UV radiation
3. Attracting pollinators and seed dispersers
4. Allelopathy (inhibit the growth and germination of other plant)
5. Stress responses
6. Wound Healing and Tissue Repair
7. Pharmaceutical and medicinal uses
8. Agricultural and economic value

# Biosynthesis pathways

- Excluding the primary processes of sugar (pentose phosphate pathway) and protein (tricarboxylic acid cycle) biosynthesis, there are **three main routes** to the wealth of chemical compounds found in plants:
  1. Shikimic acid pathway (only in plant, fungi, and bacteria)
  2. Acetate-malonate pathway
  3. Acetate-mevalonate pathway

cont.



Animal can not Produce aromatic Amino acid. Therefore, it is Essential in the diet

Obtained from Textbook of Pharmacognosy And Phytochemistry by Shah and Seth

cont.

- Shikimic acid pathway for phenols, tannins, aromatic alkaloids;
- Acetate malonate pathway for fat, waxes, polyketides, anthraquinones;
- Mevalonic acid pathway for terpenes and steroids.

# Classification of the secondary metabolites

## Secondary metabolites

### Terpenoids

- MONOTERPENES
- SESQUITERPENES
- DITERPENES
- SESTERPENES
- TRITERPENES
- TETRATERPENES

### Phenolics

- Flavonoids
- Isoflavonoids
- Tannins
- Lignins
- Coumarin
- Furano-coumarin

### Nitrogen containing compounds

- Alkaloids
- Cyanogenic glucosides
- Non-protein amino acid



# Terpenoids

- Terpenes are the largest class of secondary metabolites in plants include a wide variety of compounds that are **insoluble in water** such as essential oils, carotenoids, and steroids
- The building blocks for it is **isoprene (2 Methyl 1,3 butadiene)**. (**C<sub>5</sub>**) therefore terpenes are referred to as isoprenoids
- Isoprene itself is volatile and contributes to the **distinctive aroma** of some flowers
- has many members that are **chiral** and have extensive functional group chemistry.

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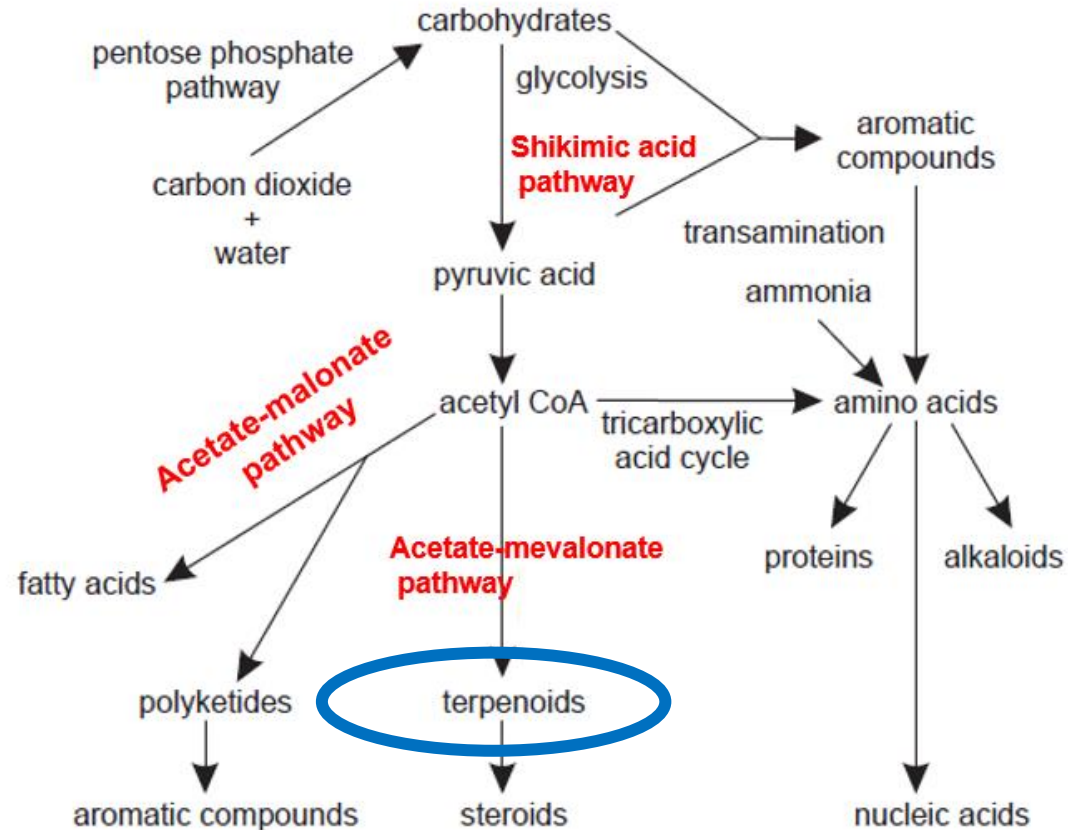
• **Terpenes can be classified based on the number of isoprene units they contain:**

1. **Monoterpenes:** has two isoprene units ( $C_{10}$ ) e.g., limonene
2. **Sesquiterpenes:** has three isoprene units ( $C_{15}$ ) e.g., Artemisinin
3. **Diterpenes:** has four isoprene units ( $C_{20}$ ) e.g., Hardwickiic acid
4. **Sesterterpenes:** has five isoprene units ( $C_{25}$ ) e.g., polygodial
5. **Triterpenes:** has six isoprene units ( $C_{30}$ ) e.g., limonin
6. **Tetraterpenes:** has eight isoprene units ( $C_{40}$ ) e.g., carotenoids

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- There are **two distinct routes** of terpenes biosynthesis that occur in nature:

## 1. The acetate -mevalonate pathway

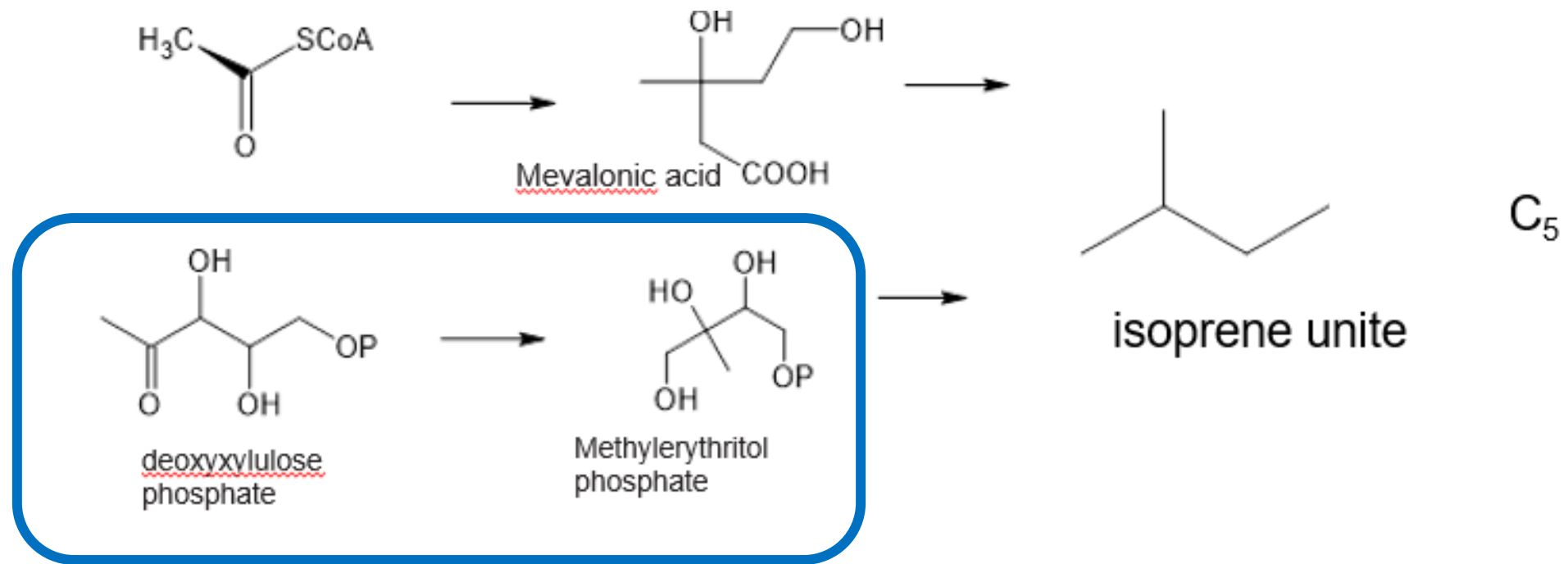


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## 2. Deoxyxylulose phosphate pathway or methylerythritol phosphate pathway (MEP pathway)

- The formation of two main intermediates Isopentenyl pyrophosphate (IPP) and Dimethylallyl pyrophosphate (DMAPP)
- Both units yield geranyl pyrophosphate (C<sub>10</sub> monoterpenes) which further association with IPP to produces farnesyl pyrophosphate (C<sub>15</sub> sesquiterpenes)

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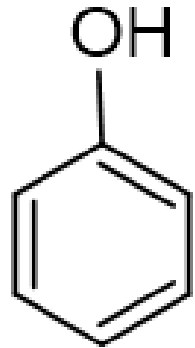


# Phenolics

- Plant phenolics are a chemically heterogeneous group of compounds Some are **soluble only in organic solvents** and others are **water soluble**
- **Phenylalanine** is an intermediate in the biosynthesis of most plant phenolics
- They include compounds like flavonoids, tannins, lignins and other polyphenols
- They have antioxidant properties, contribute to pigmentation, and play roles in defense against pathogens, herbivores, and UV radiation

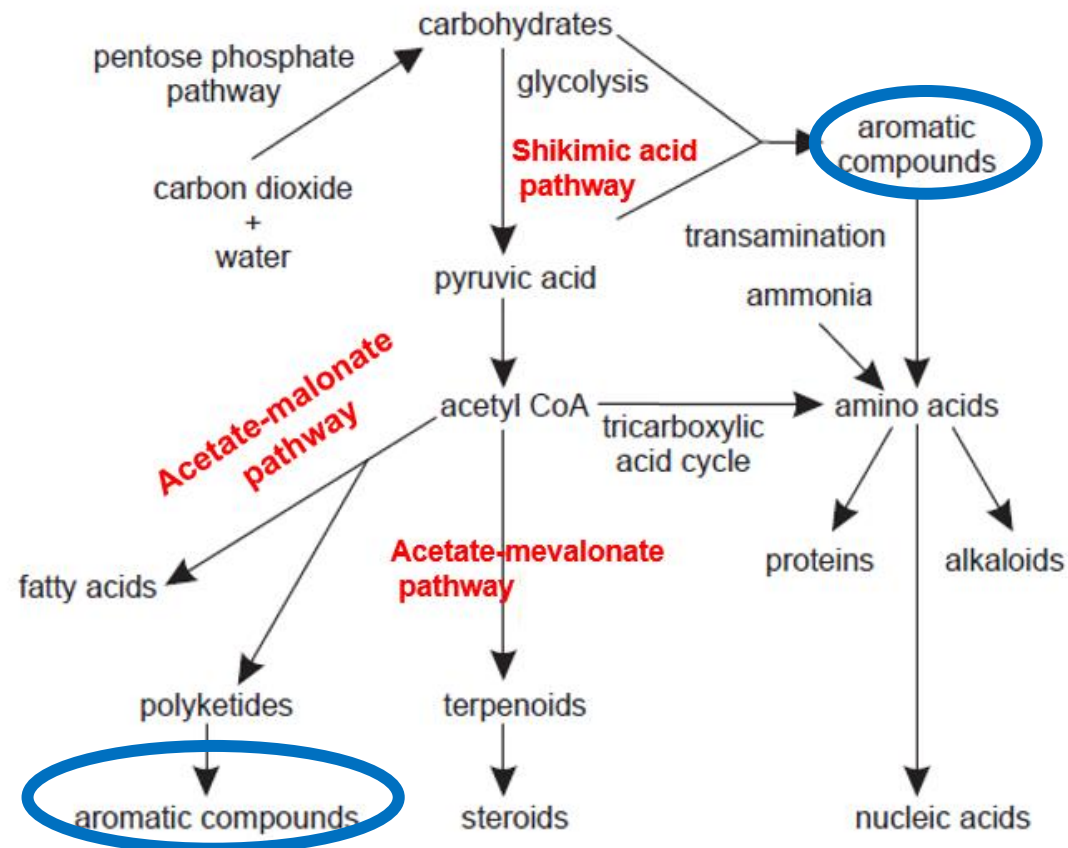
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- Phenolic compounds are characterized by the presence of a phenol ring (a hydroxyl OH) group attached to a carbon atom in a benzene ring)



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- There are two routes for the biosynthesis of phenol:
  1. The shikimic acid pathway
  2. The Acetate-malonate pathway (Malonic acid pathway)



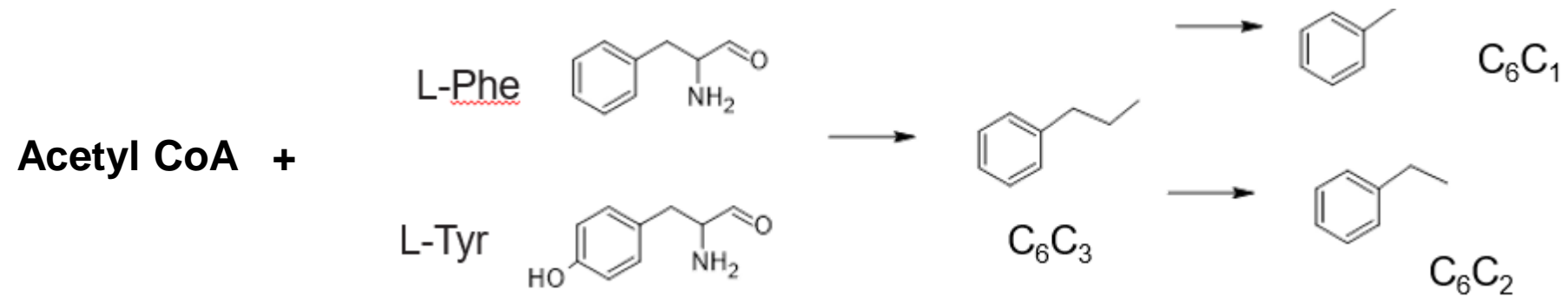


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- In the Shikimic acid pathway, simple carbohydrate precursors derived from glycolysis and the pentosphosphate pathway are converted into the three aromatic amino acids (**phenylalanine, tyrosine, and tryptophan**)
- The elimination of an ammonia molecule from phenylalanine is catalyzed by phenylalanine ammonia lyase (PAL) to form cinnamic acid
- The activity of PAL is increased by environmental factors such as low nutrient levels, light (through its effect on phytochromes and fungal infection)

cont.

- In malonic acid pathway

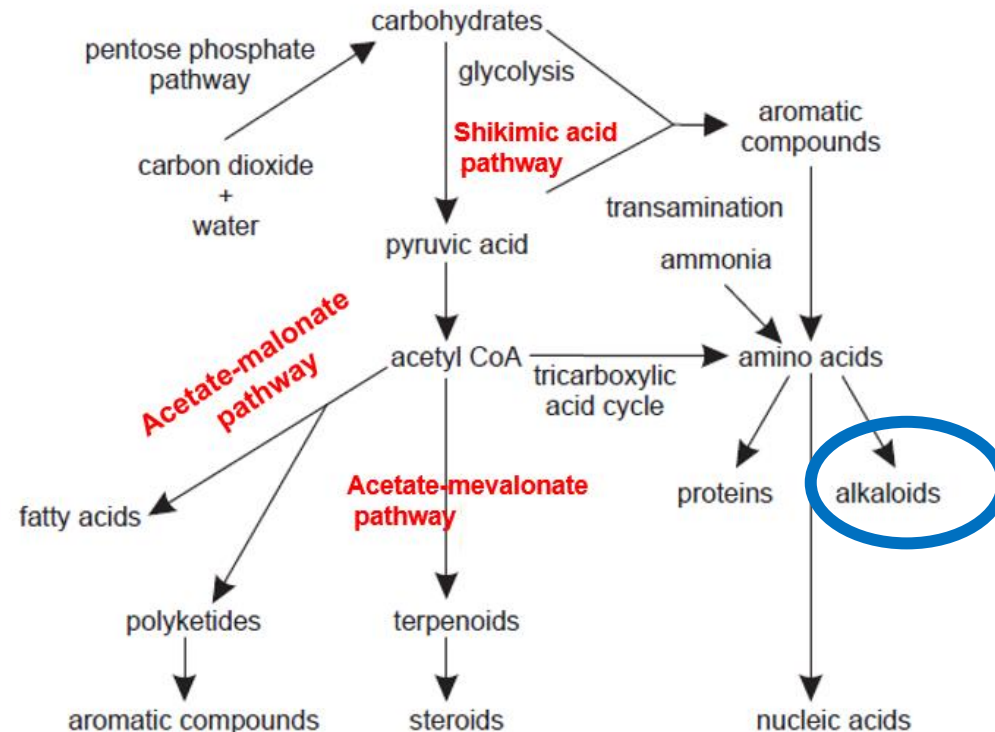


# Nitrogen containing Compounds

- Alkaloids are a large family of nitrogen containing secondary metabolites, including **caffeine**, **nicotine**, **morphine**, and **quinine**
- Alkaloids have diverse pharmacological activities and considered as a **target of abuse**.
- Alkaloids also serve as a protective agent against herbivores and pathogens for the plants
- The nitrogen atom is protonated hence alkaloids are positively charged and are generally **water soluble**

cont.

- Alkaloids are usually synthesized from one of a few common amino acids in particular, lysine, tyrosine, or tryptophan. However, the carbon skeleton of some alkaloids contains a component derived from the terpene pathway.



**Thank you for listening**