Taxonomy of the medicinal plants& importance

Dr. Thukaa Z. Abdul-Jalil

Lec 2

Taxonomy is the science of systematically naming and organizing organisms in to similar groups.

Or taxonomy : is the scientific system of classification divided all living things (plants, animals, and microorganisms) into groups called taxa or taxon (kingdom , phylum, order…etc.).

Plant taxonomy has (2) aims :

1- To identify all kinds of plants. This aim requires us to make a complete inventory of all the plants on the face of the earth.

2- To arrange the kinds of plants into a scheme of classification that will show their true relation.

This aim of the taxonomist is to seek out the evidence that will enable to understand the relationships among groups of plants (starting from the lower plants and lesser groups or taxa such as the species).

Common taxonomic of the medicinal plants:

All plants are placed in the kingdom of plantae (planate).

Kingdom: plantae.

The plant kingdom is divided into two taxa called division.

Division1: lower plants.

Division2: higher plants.

Lower plants (nonvascular plants) ex: fungi
Higher plants (vascular plants: plants with vascular system of xylem)
Division 2 i.e. higher or vascular plants are divided into two subgroups called subdivisions:
Subdivision 1: seedless ex: orchid plant.
Subdivision 2: seeds (seed plants).

Subdivision 2 i.e. seed plants are divided into two taxa called phylum.

Phylum 1: angiosperma (مغطاة البذور)

Phylum 2: gymnosperma (معراة البذور)

Angiosperma (produce seeds through flowering)

Gymnosperma (do not produce flower)

In angiosperma: plants are divided into two taxa called order.

Order 1: monocotyledoneae ذوات الفلقة الواحدة

Order 2: dicotyledoneae ذوات الفلقتين

In gymnosperma also the plants are divided into two taxa called order:

Order 1: conifers مخروطيات

Order 2: Gnetales

In all these orders, the plants are divided into many families, then the family is divided into many genus, then the genus is divided into many species, then the species is divided into many variety

Example of Angiosperma

- Kimgdom: Plantae (planate).
- Division: Higher plants.
- Subdivision: Seed plants.
- Phylum: Angiosperma.
- Order: Monocotyledoneae.
- Family: Liliaceae.
- Genus: Aloe
- Species: vera.
- *Aloe vera*

- Kimgdom: Plantae (planate).
- Division: Higher plants
- Subdivision: Seed plants.
- Phylum: Angiosperma.
- Order: Dicotyledoneae.
- Family: Scrophulariaceae.
- Genus: Digitalis.
- Species: lanata or purpurea.
- *Digitatis purpurea*
- *Digitalis lanata*

Example of Gymnosperma

- Kimgdom: Plantae (planate).
- Division: Higher plants.
- Subdivision: Seed plants.
- Phylum: Gymnosperma.
- Order: Conifers.
- Family: Pinaceae.
- Genus: Pinus.
- Species: pinaster.
- *Pinus pinaster*

- Kimgdom: Plantae (planate).
- Division: Higher plants.
- Subdivision: Seed plants.
- Phylum: Gymnosperma.
- Order: Gnetales.
- Family: Ephederaceae.
- Genus: Ephedra.
- Species: sinica.
- *Ephedra sinica.*

The importance or value of natural drug product

The natural drugs and their active constituents play many significant roles in modern medicine and the following points explain this value:

1-Some medicinal plants and their active constituents have a **high healing efficiency** for some diseases especially the heart and cancer disease, until now these drugs are used in many medicinal establishments to treatment these diseases.

Ex: (A) Digitalis plants and their active constituents (digoxin and digitoxin) that used for treatment some heart diseases.

(B) Vinca rosa plant and its active constituents (vincristine and vinblastine) that used for treatment some cancer diseases.

2- Some natural substances are **provide a number of useful drugs** (active constituents) that **are difficult if not possible** to produce them commercially by synthetic (chemical) or microbiological methods. Therefore, the only way to produce these drugs is the plants .

Ex: active constituents of digitalis and Vinca rosa plants (digoxin, digitoxin , vincristine, and vinblastine).

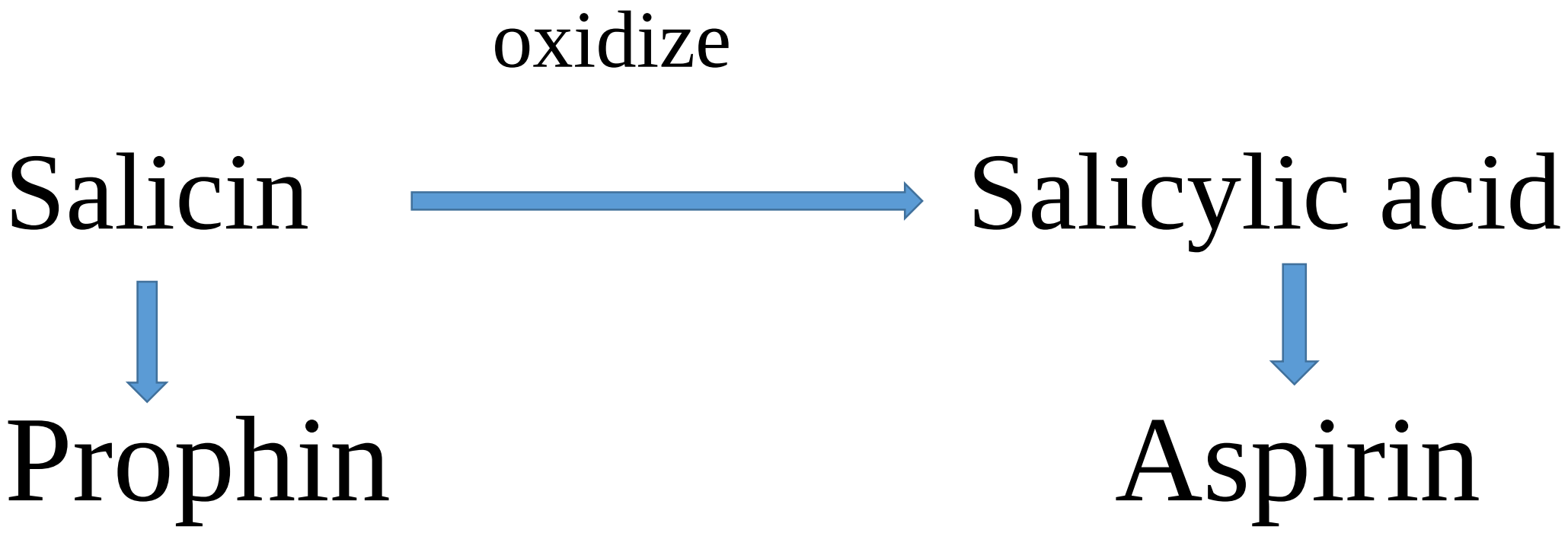
3- Some natural sources **supply basic compounds** that may be **modified** their chemical structures to render them **more effective but less adverse effects**.

Ex: morphine compound from the plant opium poppy (Papaver somniferum). خشخاش

This compound is used as a strong narcotic and lead to habit forming (addiction) but by making changes in its molecular structure it can found other compound named **codeine** which used as narcotic but less habit.

4-Some natural compounds can be used **as a model or prototype** for synthesis some drugs having **pharmacological activity** similar to original compound.

Ex: Salicin compound (alcohol glycoside) obtained from the bark of Salix plant. Salicin drug is used for treatment headache, antimalarial, diaphoretic معرق, in human body salicin compound oxidized to salicylic acid and appear these actions.



5-Some natural sources contain compounds that **demonstrate little or no activity** themselves, but it be **modified their structures** by chemical or microbiological methods to produce potent drugs not easily obtained by other methods.

Ex: Digitonine compound (Saponin glycoside) in the seeds of digitalis plant.

*This compound **has no medicinal activity** and it's poisonous, therefore, it's used for fishing but we can use the **molecular structure** of this compound as precursor to form very important useful drugs. Like: cortisone, sex hormones (testosterone and progesterone) and vit.D.

The sources of these drugs are expensive and limited especially the cortisone like:

**Bile acids of the cattle الاغنام. **Adrenal cortex of whaleحوت.

But the cheap source in the plant by modified the chemical structure of their active constituents.

Commerce and production

Dr . Thukaa Z. Abdul – Jalil

Lec 3

Geographical Distribution of the medicinal Plants:

The plant density varies in quality and quantity according to the environmental conditions of different regions on earth.

The main factors affecting on the plant density:

1-Temperature

2-Moisture

3-Soil (land).

First: The temperature factor:

The main medicinal plants of **hot region**: cacao, kola (cola**), coffee bean**, black pepper, olive, **Citrus spp**. and cinchona.

The main medicinal plants in **cold region**: balsams, pinus, **Digitalis and Crocus**

Second: The moisture factor:

Xerophytes plants (dry region plants): plants can maintain inner water and work to resist dry weather and water shortage: Aretemesia, **Aloe,Henna**

Hydrophytes plants (wet region plants):like *Nerium oleander* and **Salix**

Mesophytes plants (middle region plants): This environment has the most important medicinal plants like: ***Atropa belladonna*** **and Digitalis spp.**

Third: The land (Soil) factor:

Medicinal plants which grow in **acid soils**. Ex: **Digitalis and gardenia**

Medicinal plants which grow in **alkaline soils**. Ex: ***Atropa belladonna*** and cinchona

Production of crude drugs

The process of drug production include three steps which are: collection , drying, and storage.

First: collection (harvesting):

Collection is the most important step which comes after the cultivation. Drugs may be collected from **wild plants** or **cultivated plants**, collection of drugs from **cultivated plants** always ensure a **true natural source** and a **reliable product**. This may or may not be the case when drugs are collected from wild plants. Generally, these drugs are collected by different means. The **mode of collection** varies with each **drug** produced and with the **pharmaceutical requirement**. Some drugs may be collected by **hands workers** (labor) either by **skilled workers** as in case **: Digitalis, belladonna and cinchona** plant, while other plants are collected by **unskilled workers** as in case **Black pepper**, or some drugs are collector by **mechanical** means like fruits of **olive** and **jojoba** plants.

Quantity and quality of active constituents in the drugs (plant materials) are affected by some factors. Therefore, when collected these drugs we must attend to these factors:

1-Collection time: EX. The **leaf** of **peppermint and spearmint** plant collected in spring season because in this season the leaf contain high concentration of **volatile oils.**

2-Plant age :EX. **trees of plant cinchona** have the maximum amount of **alkaloid cinchonine** in their barks when they within 6-9 years old.

3-The growth stage of the plant part :EX. The **leaves** of the following plants: tobacco, senna, and **digitalis**, are collected in the full maturity stage.

Second: Drying:

This process is essential removal of moisture from the plant material to:

1-Ensure keeping qualities
2-Prevent molding and bacterial
3-Prevent the action of enzyme and chemical or other possible change
4-Converts the drug into a more convenient for commercial handling.

The drying process depends **on plant type**, **plant part** and **plant constituents**, if the **enzymatic activity** wanted to **continue**, **slow drying and at moderate temperature used**. Such as in **vanilla pods** which give vanillin (active compound) used as flavoring agent, we should use slow drying at moderate temperature to convert **glucovanilla (inactive compound) into vanillin**.

But in most cases, the enzymatic activity is unwanted and the plant is dried completely to avoid the enzymatic activity which may lead to convert the active constituent into inactive substances which are medicinally unwanted.

****Drying** is very important in case of some plants **contain volatile oil or aromatic substances**. These plants should be **dry as soon as possible or distilled** to get aromatic and volatile material because during **bad drying these materials are lost.**

Drying process occur either by:

1-Open-air drying: in which the drying depending on type of plant that contain high or low moisture, this type is done either by sun for the crude drugs are not affected by light and high temperature. Ex: fruits of black pepper
Or under shade (not apply to sun) for crude drugs are affected by light and high temperature. Ex: fruits of opium poppy.
This type of drying (open-air drying) last from few hours to many weeks depending on type of plant materials.

2-Artificial drying: this type can be done by using oven heat to plant materials in certain conditions which not affect plant constituents. Ex: seeds of coffee bean.

Third: Packaging and Storage:

Packaging is the process by which a newly produced drug is protected by a packet or some kind of bottle or into a container.

The **long storage** although is not recommended but cannot be avoided**. Except** in certain cases such as in **cascara bark** (لحاء نبات الكسكارة) that need long storage in order to get the required active constituents, this process of storage called **curing or sweating** which need one or two years.

*Other drugs such as **Digitalis** should be stored carefully to avoid the absorption of water or moisture which help in mold and bacterial growth and prevent the deterioration of these drugs.

*The **volatile oil, fixed oils** and **other moist sensitive drugs** should be stored in **cool,** fully **closed, dark** and **fully filled container** in order to avoid oxidation or deterioration of these drugs by the **action of light, oxygen** or by other factors **which leads to destruction of active constituents.**

The stored drugs should be checked from time to time to remove any spoil, deteriorated drugs that result from the action of rats and insects.

Methods of using plants

Plants may be used as :

1. **Isolated parts** ex: dried leaves of plant **as Digitalis** which contain glycosides as digoxin which is used for the treatment **of heart diseases**

2. **Whole plants** ex**: Vinca rosa** (***Catharanthus roseus***) and its active constituents vincristine and vinblastine which are used as **anticancer**

3. **Extracts of active constituents** ex: extract of unripe fruits of plant as ***Papaver somniferum*** which contain morphine which is used as **narcotic.**

Adulteration and evaluation

Dr. Thukaa Z. Abdul-Jalil

Lec 4

Adulteration of crude drugs:

*__Adulterant:__ herb (drug) which does not confirm to official standards. Usually practiced when the herb (drug) is expensive.

Types or methods of adulteration:

1-Inferiority: this type of adulteration results **naturally** or **by ignorance** or **carelessness of workers** leading to destruction **quality** of herbs then produced substandard herbs.

Ex: Fruits of opium poppy (Papaver somniferum), when the fruits containing less than 10% of anhydrous morphine , in this case this drug is consider inferior drug.

2-Spoilage:

In this type of adulteration normally results from **incorrect storage** (effects of water and temperature). Where, this type of storage will lead to impaired or **destroyed the medicinal value** of herbs by the action of bacterial, fungal, insects, and rodents.

3-Admixture:

In this type of adulteration, the drugs (herb) contain **another species of herbs** or **another plant parts** which are not medicinally valuable or **contain foreign materials** (stones and dirt). This type of adulteration may be results of collection due to unskilled workers.

4-Sophistication:

In this type of adulteration, required drug can **be instead or substituted** by using different **materials** that haven't any medicinal activities.

Example: **Ginger drug** has yellow color, pungent or potency taste and thick form. By this type of adulteration, this drug can be substituted by using the following materials: **curcuma**, **chilies**, and **powdered flour.**

Curcuma: to give this mixture, the yellow color, Chilies: to give this mixture potency taste, Powdered flour: to give this mixture thick form.

5-Deterioration:
In this type, the **crude drugs** exposed to some methods like **extraction** and **distillation.**

6-Substitution:
In this type of adulteration, the **original drug** is **substituted** using **inferior drug** that may be similar in morphological characters, active constituents, or therapeutic activity.
Ex: ***Digitalis thaspi*** substitute for ***Digitalis purpura***, with note: ***Digitalis purpura*** is better than ***Digitalis thaspi*** for treatment some heart diseases

Evaluation of drugs:

Evaluation of a drug **ensures the identity of a drug** and **purity of drugs**.

The **main reasons** behind the need for evaluation of crude drugs are **biochemical variation in the drug**, **adulteration** and **substitutions**, **stability of active compounds**, and **product purity**. All of these gains have resulted in tremendous improvements in the quality of herbal-preparations.

Methods of evaluation:

1. **Organoleptic evaluation:** this method is simple and means the study of drugs using **organs of senses**. It refers to the methods of analysis like: color, odor, taste, size, shape, touch, texture…etc.).
2. **Microscopic evaluation:** in this method, using many **microsocial techniques** in the **identification of plant**, herbs as well as **identifying small fragments of crude or powdered herb** and in **detection of adulterants** by studying:

A. Characteristic of tissue structures (xylem, phloem, fibers, trichomes)

B. Cell wall

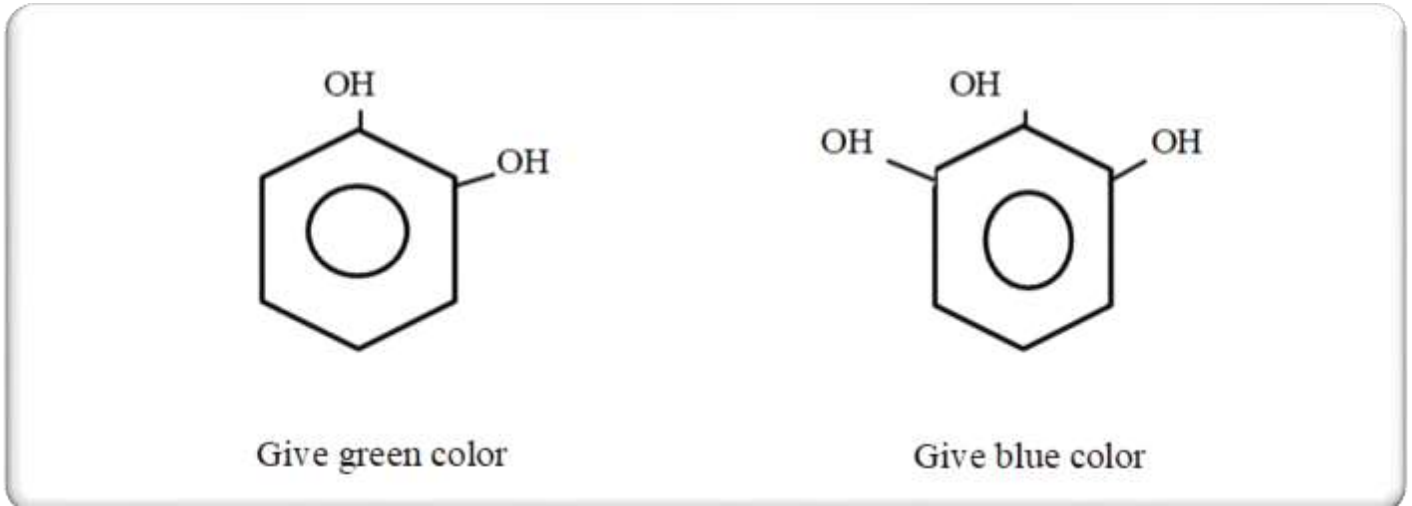
C. Cell content (starch grains, stomata, calcium oxalate crystals, oil crystals, oil drops…etc.).

3-Chemical evaluation: the chemical evaluation includes **qualitative chemical tests**, **quantitative chemical tests(chemical assays** and **instrumental evaluation)**.

- **Qualitative chemical tests:**

Include identification tests (using chemical treatments) for various phytoconstituents like: alkaloids, glycosides, tannins…etc. Examples:

1. Alkaloids with Dragendroff reagent give orange color.
2. Alkaloids with Mayer reagent give white color.
3. Tannins with FeCl3 give either green or blue color depending on the positions and presence of OH group in the aromatic ring.



- **Quantitative chemical tests (Chemical assays):**

Includes assays for alkaloids, glycosides, volatile oils, vitamins or other constituents.

Ex: the assay of total alkaloids in belladonna herb, strychnine alkaloid in Nux vomica. The **results** obtained refers are these **drugs inferior** or **not**.

Instrumental analysis are used to analyze the chemical groups of phytoconstituents using **chromatographic** and **spectroscopic** methods.

A. Chromatographic methods include:

Thin layer chromatography, Paper chromatography, High performance liquid chromatography

B. Spectroscopic methods include:

ultraviolet and visible spectroscopy, infrared spectroscopy, and mass spectroscopy.

4-Physical evaluation:

In crude drug evaluation physical methods are often used to determine the **solubility, melting point**, water content, degree of fiber, **specific gravity**, **optical rotation**, **viscosity**, **refractive index**, and other physical characteristics of the herb material.

5-Biological evaluation:

The plant or extract can then be evaluated by various **biological methods** to **determine pharmacological activity**, **potency**, and **toxicity**. These methods are considered to be **less precise**, **more time consuming** and **more expensive**.

Ex: Mydriatic effects of certain drugs are tested in **rat's eye.**

As for **microbiological assays** are carried out to determine the effects of drug In various methods and this is employed in the **identification on antimicrobial drugs**. The methods used in this type of assays are **agar well diffusion method** and **disk diffusion method**.

Chemistry of Natural Drugs

Dr. Thukaa Z. Abdul-Jalil

Lec 5

On the earth, the green plants are the main source for natural drugs, where many plants accumulate many organic substances have **economically** as **chemical feed stocks** or **raw materials** for various scientific and commercial applications.

These organic substances are synthesis **(Anabolism)** and degradation **(catabolism)**to form another organic substances by series of chemical reactions, these chemical reactions on the whole are named **Metabolism** , therefore these organic substances are classified **as primary** and **secondary** metabolites.

Primary Metabolites Properties:

1-These substances are formed by photosynthesis process (anabolism).

2- They have a high molecular weight.

3- They are found in high concentration in the cells of plant.

4-They are source for energy.

5-They have structural and functional roles in the plant.

Ex: Different sugars (glucose, sucrose…etc.), amino acids, fatty acids, nucleic acids (DNA, RNA), and their derivatives proteins .

Secondary Metabolites Properties:

1-These substances biosynthetically derived from primary metabolites by two main pathways:

A. Shikimic acid pathway.

B. Acetate mevalonate pathway.

2- They have a small molecular weight.

3-They are found in a small concentration in the cells of plant.

4- They are not a source for energy.

5- They have no apparent clear function in a plant, but often they have an ecological role.

Ex: For human, these secondary substances are economically useful, because they are used as drugs like digoxin.

Photosynthesis Process:

In one of the most important biological process occurred on the earth **because it is only source for oxygen**, by this process the green plants take the **photon** and convert it to **chemical energy** and then the plants **use this energy to form different organic compounds**, this process consist of 2 classes of reactions:

1-Light reactions: the main function of these reactions is production **2 types** of **chemical energy** and they **are NADPH, ATP** addition to **give O_2.**

$$2NADP + 3ADP + 3H_3PO_4 + 2H_2O \xrightarrow[\text{Chlorophyll}]{\text{Light}} 2NADPH + 3ATP + O_2 + 2H^+ + 3H_2O$$

2-Dark reactions: They are **enzymatic reactions** that utilize the **energy** from the **light reactions** to fix **carbon dioxide into sugar**, where in these **reactions carbon dioxide** reacts with the compound **RUDP (Ribulose 1,5-phosphate**) to give **2 molecules** of **PGA (3-phosphoglyceric acid).**

$$CO_2 + RUDP \xrightarrow{**} 2PGA\ *$$

**** The enzyme: Ribulose diphosphate carboxylase.**
***PGA: This compound is the first organic compound produced from photosynthesis.**

Then occurred a series of reactions named **(Calvin cycle or Calvin –Benson cycle).**By this cycle ,the plant formed the **first bond sugar** (**Fructose-6-phosphate**), then this sugar converted to **sucrose**, the sucrose is the **first sugar** formed in photosynthesis and it is the **main transport material** in plant and is the **usual precursor for oligo- and polysaccharide synthesis** and a number of reactions occurred on it . **OR hydrolysis** by **invertase enzyme** to formed **monosaccharide (glucose & fructose)** which play very important roles in the synthesis of secondary metabolites.

Carbohydrate and related compounds

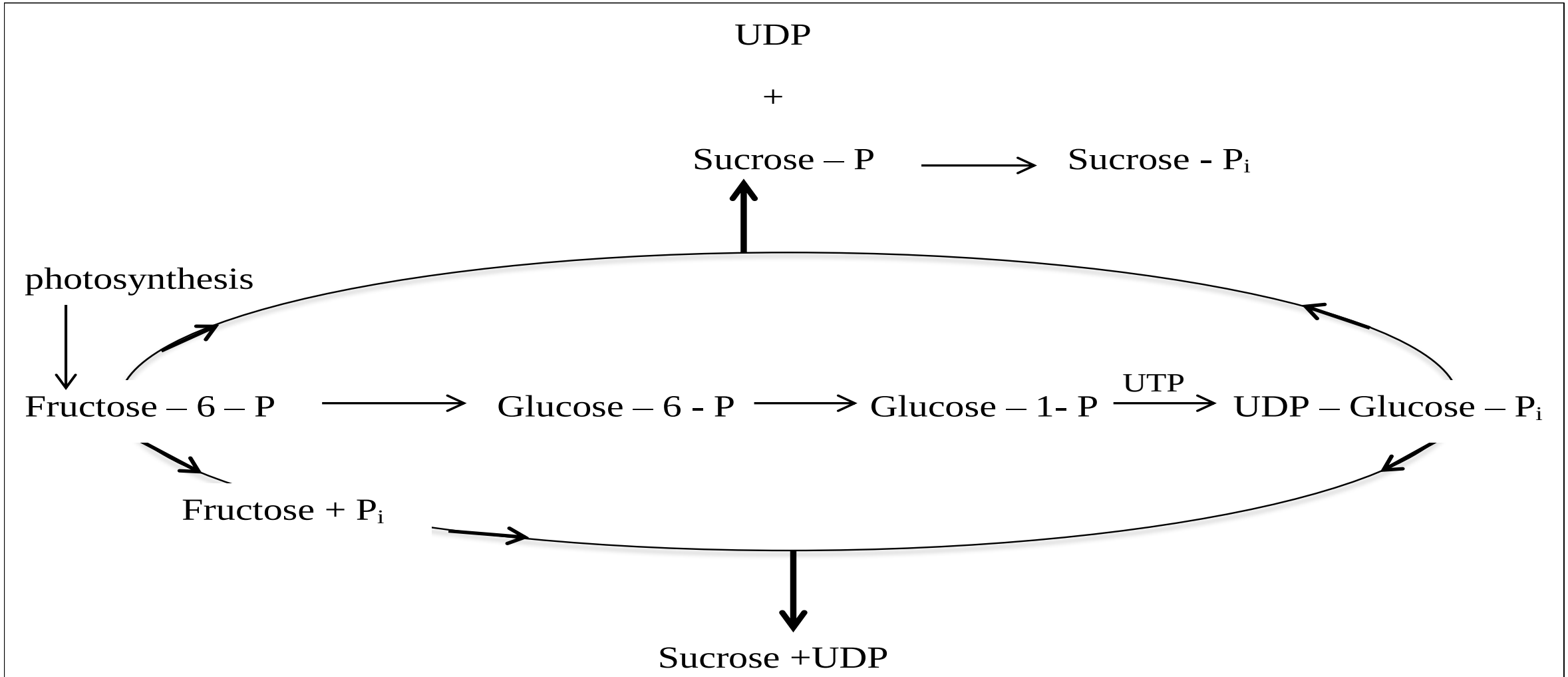
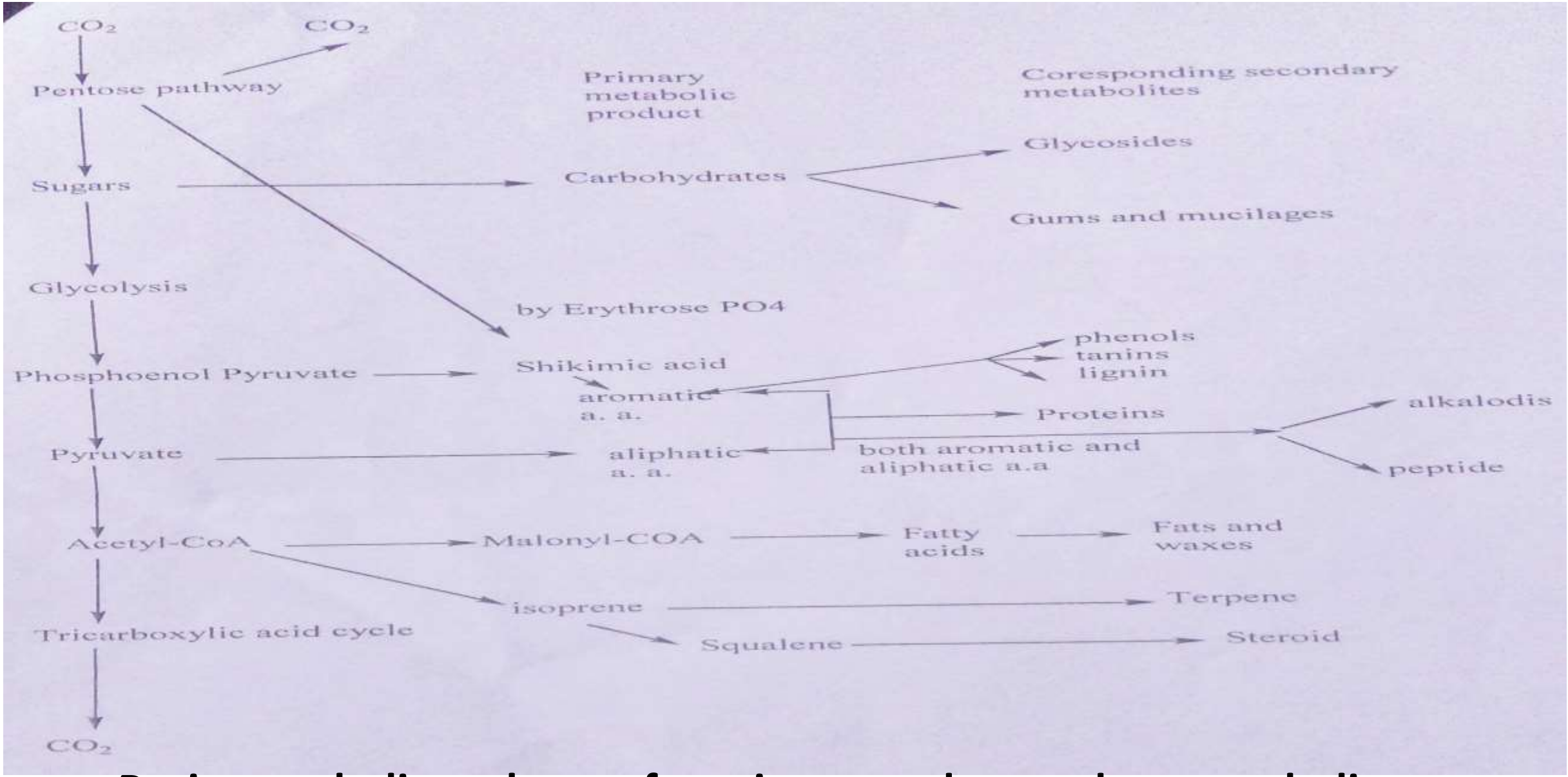


Fig 1: pathways of sucrose biosynthesis



Basic metabolic pathways for primary and secondary metabolites

Classification of Natural Drugs

Dr. Thukaa Z. Abdul-Jalil

Lec 6

In pharmacopeia and Pharmacognosy books, the natural drugs are classified under the following titles:

1-Alphabetical classification:

In this system, the natural drugs are classified into groups according to **alphabetical order** by using **Latin or English** title. European pharmacopeia use Latin title, British pharmacopeia use English title. This classification is complex but is quick reference.

2-Morphological classification:

To identify the specific drug a morphological classification is applicable. In this system the drug are grouped according to the **collection part of plant** or animal ,such as :

Organized drugs (roots ,leaves ,fruits ,seeds ,barks ,flowers)

Unorganized drugs (dried lattices, dried juice, gum, wax, oils)

In commercial market, the drug may by available not in intact form ,in that case the morphological classification is not so suitable and not acceptable.

3- Taxonomic classification

Here drugs are arranged according to the **plant which they are obtained** in **classes ,order ,family ,genus and species**.

So this type of arrangement is sometime called **the botanical arrangement** of plant ,a large number of plant families have certain distinguishing characteristics that permit drugs from these families to be studied at one time.

4-Chemical classification:

In this system, the medicinal plants are classified into groups according to their **active constituent structures** and as follow:

A.Glycosides: Ex: Digitalis

B.Alkaloids: Ex: papaver,

C.Volatile oils:. Ex: peppermint.

D.Fixed oils: Ex: sesame.

E.Resins: Ex: Salix

F.Tannins: Ex: pomegranate

5- Therapeutic classification:

In this system, the medicinal plants are classified into groups according to their **therapeutic uses** and as follow:

A. **Cardiac plants.** Ex: Digitalis plants.
B. **Laxative plants** .Ex: Senna.
C. **Cathartic plants**. Ex: Olive oil.
D. **Narcotic plants** .Ex: papaver.
E. **CNS stimulant plants** .Ex: coffee bean, tea.
F. **Carminative plants** .Ex: peppermint.
G. **Anti-rheumatism plants** .Ex: black and white mustard الخردل الاسود والابيض.
H. **Anticancer: ?**
I. **Hypolipidimic: ?**

Commercial classification:

In this system, the medicinal plants are classified into groups according to their uses in the commercial markets and as follow:

A. Medicinal plants: These plants are selling in the markets for **treatments the disease**.

B. Condiment plants. Ex: black and white mustard.

spices plants.Ex: black pepper.الفلفل الحار

flavoring agents. Ex: cardamom الهيل

coloring matters. Ex: Crocus sativus الزعفران

C. Aromatic plants: these medicinal plants are used for preparing **perfumes** and **cosmetics** like: sweet almond and wild cherry الكرز البري

D. Insecticide plants: these plants are used for **killing the insects** like (**pyrethrum**) or for **killing the rodents** like (**red squil bulb)**, or **for killing the fungi** like **(henna).**

E. Beverages: some medicinal plants can be used as **beverages** like: cola, coffee bean, cacao, and tea.

Separation & isolation of the constituents

Dr:Thukaa Z. Abdul-jalil

Lec 7

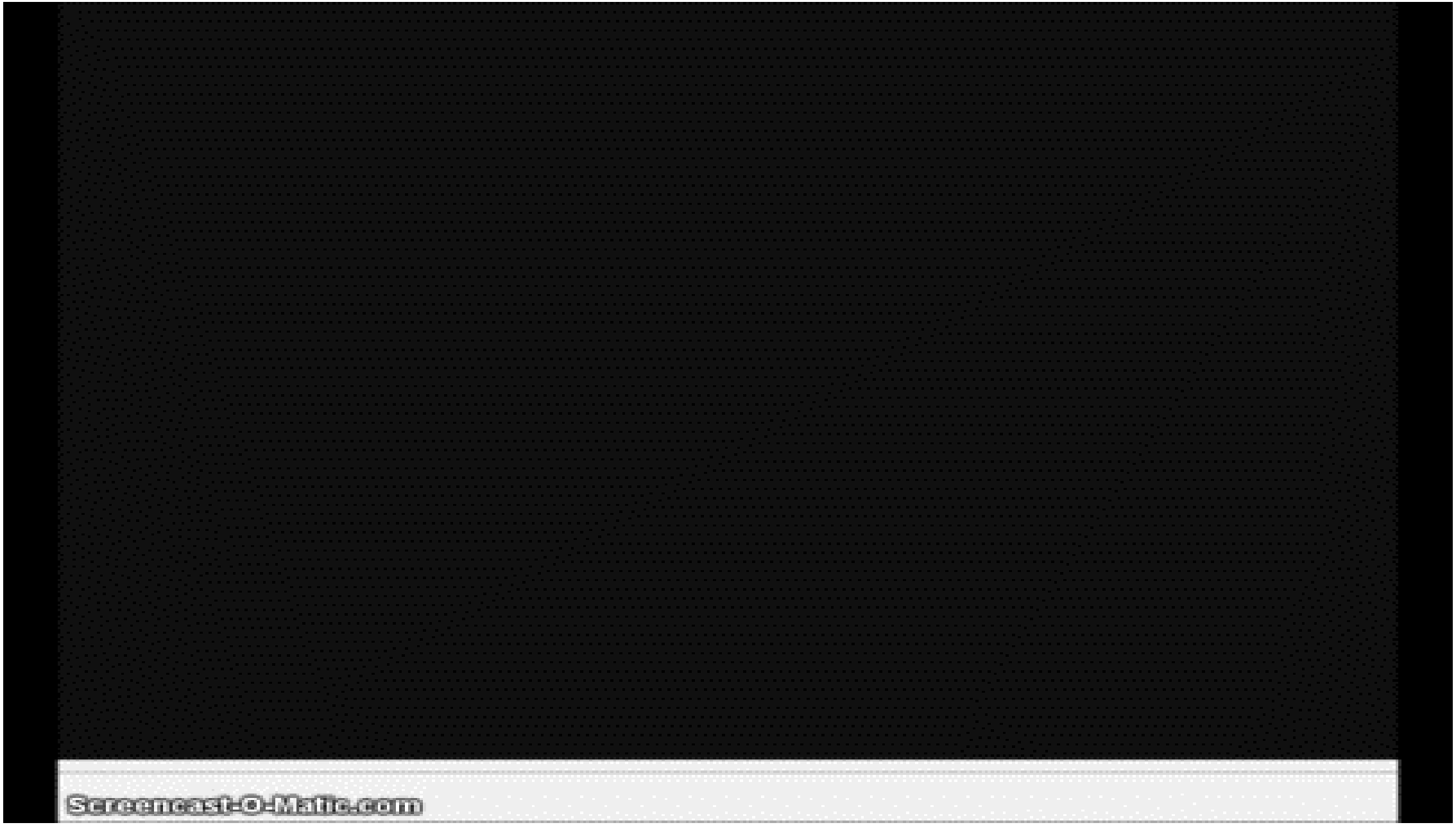
Different methods may be used in this matter ex:

1.Sublimation : which is sometimes used on the whole drug , as in the isolation of caffeine from tea , or for the purification of materials present in a crude extract.

2.Distillation : fractional distillation has been traditionally used for the separation of the components of volatile mixtures , mainly components of volatile oils.

3.Fractional liberation : some groups of compounds may be separated by fractional liberation from a mixture ex: when a mixture of alkaloid bases is shaken with NaOH solution the phenolic alkaloids will be separated as salts.

4.Fractional crystallization : the method exploits the differences in solubility of the components of a mixture in a particular solvent .


Screencast-O-Matic.com

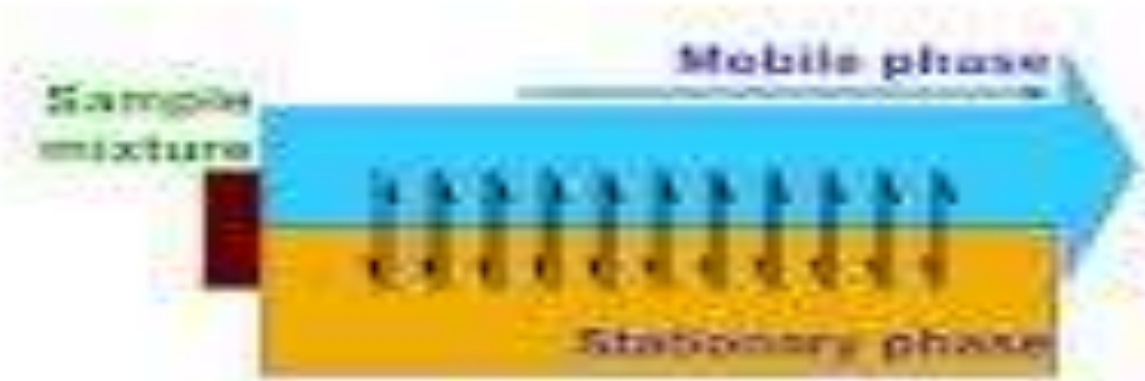
5.Chromatography: This process means a variety of separation technique .The common feature of these technique is that the components of the **sample** mixture are distributed between two phases one of which remains **stationary** while the other phase percolates through or over the surface of the fixed phase. The movement of the **mobile** phase results in a differential migration of the sample components.

- Or chromatography involves the distribution of a **compound** between two phases , a moving (**mobile**) phase that is passed over an immobile (**stationary**) phase . Separation is based on the characteristic way in which compounds distribute themselves between these two phases.

- **What is chromatography?**

Chromatography is a technique for separating mixtures into their components in order **to analyze**, **purify , and /or quantify the mixture or components**. Or separation of a mixture by distribution of its components between a mobile and stationary phase over time.

Chromatographic principle



Equilibrium establishes at each point (ideally)

The molecules of the mixture interact with the molecules of the Mobile and Stationary Phase → Retardation of rate of movement of molecules

Each molecule interacts differently with MP and SP → Different distribution coefficients and different net rates of migration

Chromatography terms:

- **Analyte:** is the substances to be separated during chromatography. Called **solute ,sample**
- **Stationary phase:** is the phase which tries to fix the analyte in it's place during the chromatography procedure .Retarded the movement of sample to be separated .Called **column ,adsorbent ,bed, opposing force, retardation force.**
- **Mobile phase:** is the phase which moves in a definite direction **or** is the solvent that will carry the analyte. Called **developing solvent , eluent**.
- **Developing:** How the mobile phase can cause separation? **Or** the direction of separation. **example ascending ,descending, horizontal**

- **Chromatographic system :** the whole conditions of chromatography **example** temperature, stationary phase, mobile phase, methods of detection, mechanism of separation…….etc.

Methods of detection

1.Physical detection
2.Chemical detection
3.Biological detection
4.Radioactive detection

mechanism of separation: the ways in which analytes distribute themselves between two phases.[stationary phase, mobile phase]

- **Chromatogram:** is the visual output of the Chromatograph **or** the results of the separation procedure.

The **first** detailed description of **chromatography** is credited by Michael Tswett a Russian biochemist who separated chlorophyll from a mixture of plant pigments in 1906.

The **stationary phase** can be either **solid or liquid** & the **mobile phase** can be either **a liquid or gas** thus several combinations are possible. The two combinations which are **not possible** are the **gas-gas** & the **solid-solid.**

Types of chromatography

Mobile phase	Stationary phase	Abbreviation
Liquid	Solid	LSC
Gas	Solid	GSC
Liquid	Liquid	LLC
Gas	Liquid	GLC

LSC & GSC are usually **adsorption chromatography** while in **LLC & GLC** are **partition chromatography.**

There are several ways to carry out a chromatographic process depending on how the sample is introduced & moved through the stationary phase.

Gas – liquid chromatography (GLC)

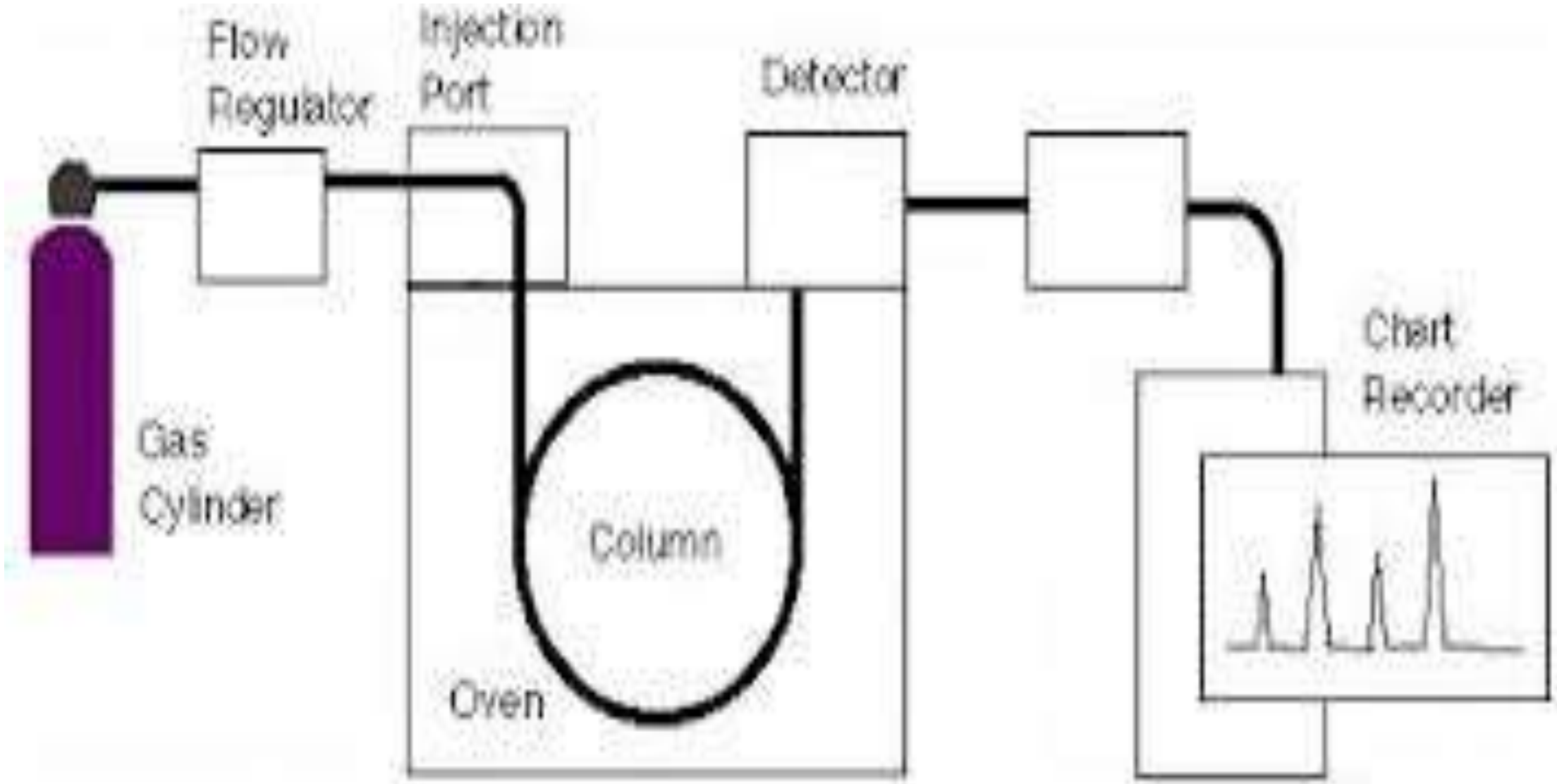
Dr. Thukaa Z. Abdul-Jalil

Lec 9

- **Gas-liquid chromatography** is a **partition type** of chromatography where by the **solute is partitioned between two phases a liquid stationary phase & a gas mobile phase .** The inert carrier gas passes through a pressure regulator into a sample injector & mixing chamber . From here the carrier gas (mobile phase) carries the sample into the column .

- **The column** may be packed with **a porous solid coated with a thin film of a non-volatile liquid (stationary phase) ,** or it may be a long capillary tube with a thin coating of liquid on its wall . The sample components are separated as they pass through the column & one after the other pass through a detector which sends a signal to a recorder .

- Finally , the gas passes through a flow meter & is exhausted to the atmosphere **. A thermo stated oven is provided for the column , injector , & detector , although the last two may be heated separately** .


Flow
Regulator
Injection
Port
Detector
Chart
Recorder
Gas
Cylinder
Column
Oven

- The **sample injection point** in the column is important part & usually **there is a rubber stopper at the top of the column** through which the **syringe needle** containing the sample passes to introduce the sample at **the top of the column** .

- **The whole of the injection point** unit should be at a **higher degree** than the rest of the column & it is usually **kept 10 C** above the **temperature needed for the rest of the column ,** this is important to ensure **the immediate evaporation of the liquid sample once it enters the column** . The column oven may be set at any temperature required **between 0-400 C** . The injection unit has a separated heating control than the rest of the column .

- **The instrument of GLC is composed of the following parts :**
- **Carrier gas supply** :

  In GLC the **carrier gas** (which is supplied by a cylinder) provides transportation for the sample components through the apparatus **. It must be chemically inert & available in pure form & reasonable cost** .The most commonly used gases are **helium , nitrogen, argon, hydrogen & carbon dioxide .**

- **A high density is preferred for best efficiency** & a **low density for maximum speed** . The flow control is obtained from a standard reducing valve & a soap film flow-meter is used almost exclusively to measure the flow rate .

- **Columns** :

  There are **two distinct types** of columns in common use i.e**. packed & open tubular** (capillary) . They are **either stainless steal or glass column** . The column is packed with the **inert support which has been already coated with the liquid phase** . One end of the column is connected to the sample injector that means the place through which the sample or solute is introduced , the other end of the column is connected to the detector which will analyze the signal received.

- **Solid support** :

The ideal solid support should have a **high specific surface (1m^2/gm)** , & the surface must be **chemically inert** also wet able by the liquid phase so that it will spread in a thin layer of **uniform thickness** . In addition it must **have thermal stability** , **mechanical strength** & available in a **uniform size**, nearly **spherical shaped** particles

- **Detectors :**

Detectors detects the emerging sample in the gas form usually the solute or sample emerge from the column in the form of a gas or steam.

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY

Dr. Thukaa Z. Abdul-Jalil

Lec 11

High performance liquid chromatography is now one of the most powerful tools in analytical chemistry. It has the ability to **separate**, **identify, and quantitate** the compounds that are present in any sample that can be dissolved in a liquid. Today, compounds in trace concentrations as low as parts per trillion (ppt) may easily be identified. HPLC can be, and has been, applied to just about any sample, such as **pharmaceuticals, food, nutraceuticals, cosmetics, environmental matrices, forensic samples, and industrial chemicals**.

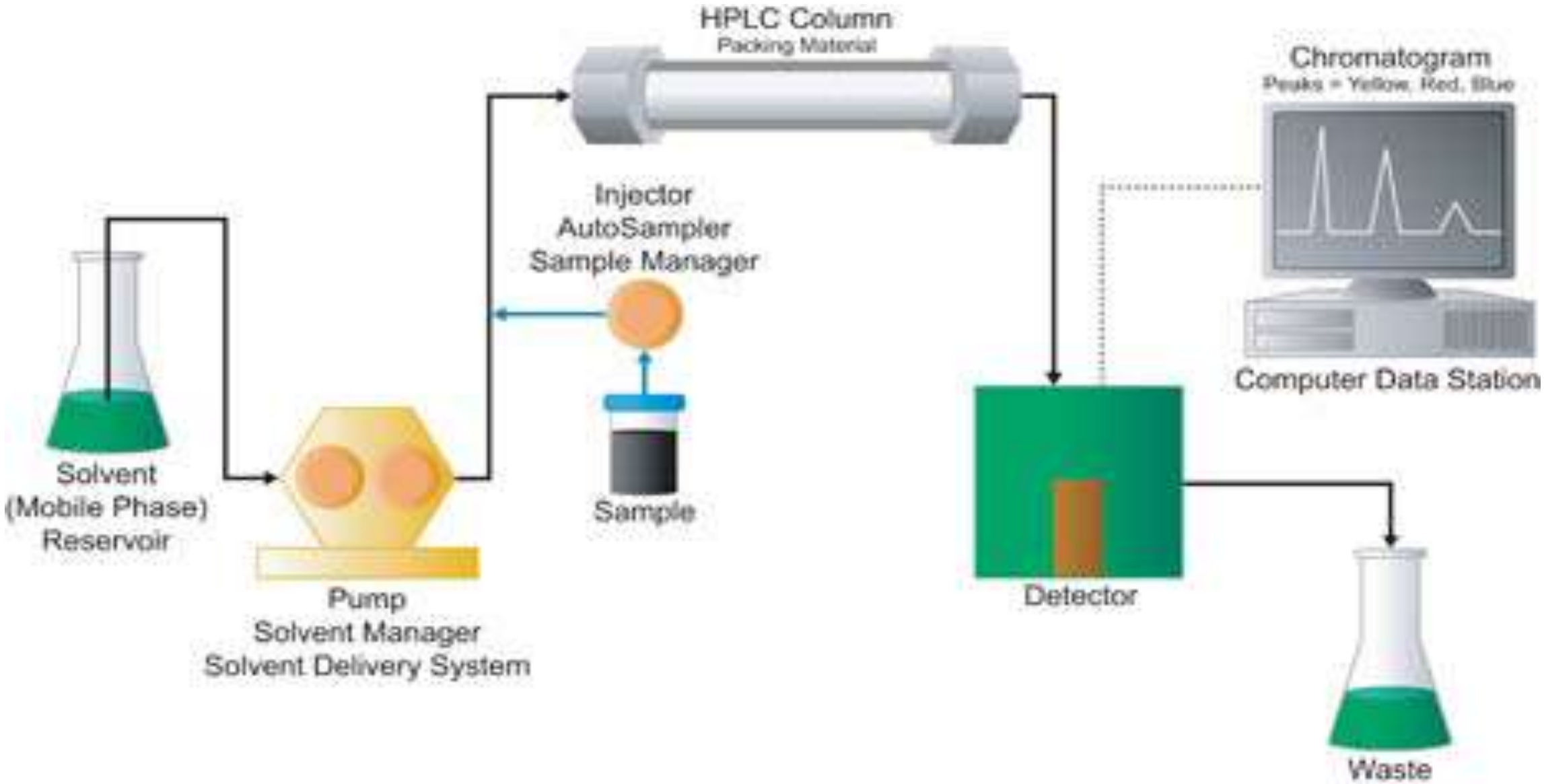
The instrument of HPLC is composed of the following parts :

A reservoir (Solvent Delivery):

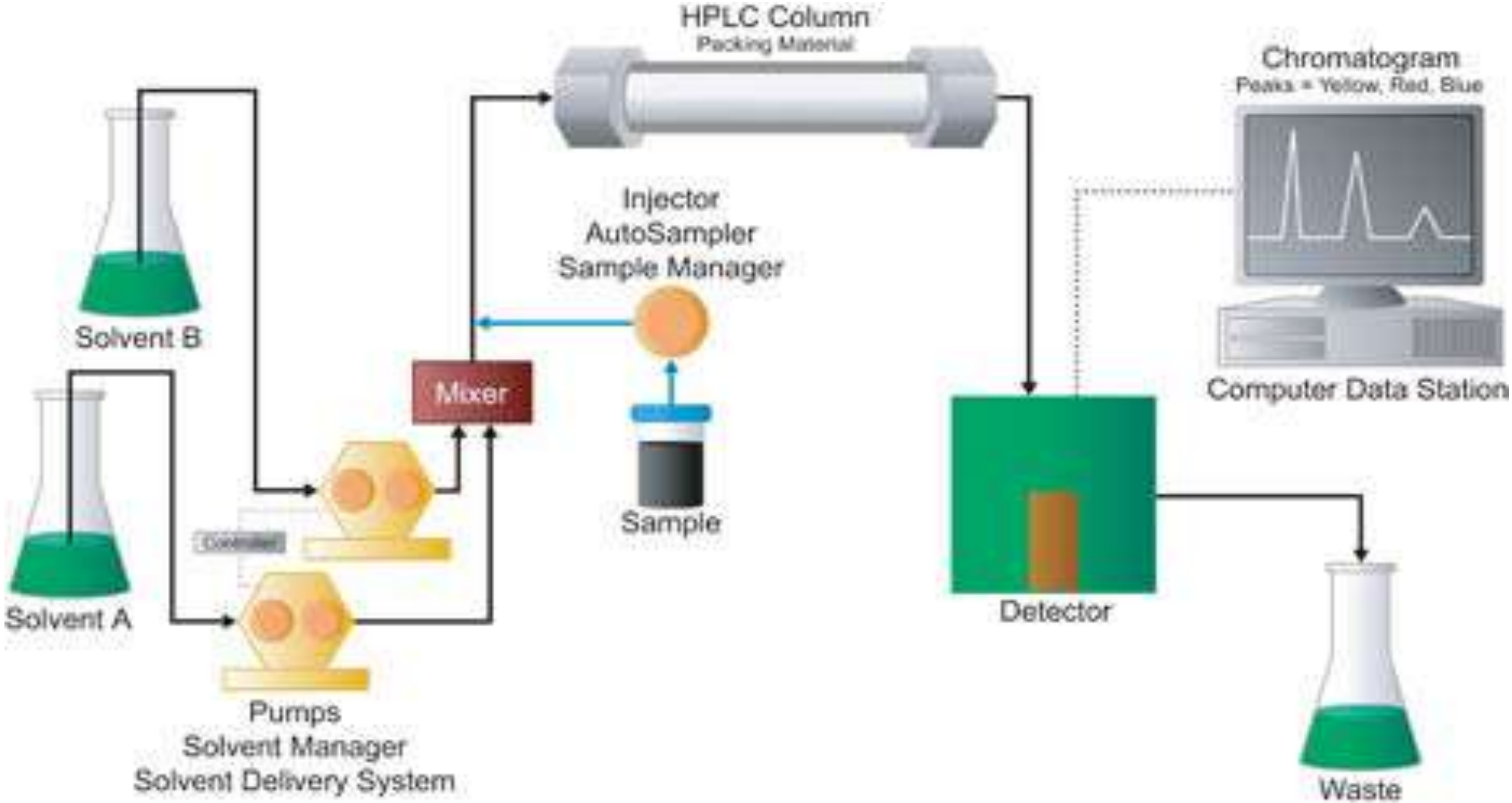
A reservoir (Solvent Delivery) holds the solvent (called the mobile phase, because it moves).

Two basic elution modes are used in HPLC.

The first is **called isocratic elution**. In this mode, the mobile phase, either a pure solvent or a mixture, **remains the same throughout the run.** A typical system is outlined in Figure bellow


HPLC Column
Packing Material
Chromatogram
Peaks = Yellow, Red, Blue
Injector
AutoSampler
Sample Manager
Computer Data Station
Solvent
(Mobile Phase)
Reservoir
Sample
Pump
Solvent Manager
Solvent Delivery System
Detector
Waste

The second type is called **gradient elution**, wherein, as its name implies, **the mobile phase composition changes during the separation.** This mode is useful for samples that contain compounds that span **a wide range of chromatographic polarity**. As the separation proceeds, the elution strength of the mobile phase is increased to elute the more strongly retained sample components


HPLC Column
Packing Material
Chromatogram
Peaks = Yellow, Red, Blue
Injector
AutoSampler
Sample Manager
Solvent B
Mixer
Sample
Computer Data Station
Solvent A
Detector
Pumps
Solvent Manager
Solvent Delivery System
Waste

HPLC PUMPS

A high-pressure pump solvent manager is used to generate and meter a specified **flow rate of mobile phase**, typically **milliliters per minute**. For **analytical purposes**, HPLC pumps should have flow rates that range from **0 to 10 ml/min.**, but for **preparative HPLC**, flow rates in excess of **100 ml/min** may be required.

HPLC SAMPLE VALVES

Since sample valves come between the pump and the column it follows that HPLC **sample valves must also tolerate pressures up to 10,000 psi**. For **analytical HPLC**, the sample volume should be selectable from **sub micro liter to a few micro liters**, whereas in **preparative HPLC** the sample volume may be **even greater than 10 ml.**

HPLC COLUMNS

The column contains the **chromatographic packing material needed to effect the separation**. This packing material is called the stationary phase because it is held in place by the column hardware. . The apparatus is suitable for **all types of column chromatography (adsorption, partition, gel filtration, ion exchange, etc.)**

In most **modern HPLC separations** are carried out by using either a **silica microporous particle column for non polar compounds** or a **reverse – phase C18 bonded phase column for polar compounds.**

HPLC DETECTORS

UV/Vis spectrophotometers, including diode array detectors, are the most commonly employed detectors. **Fluorescence spectrophotometers**, differential refractometers, electrochemical detectors, **mass spectrometers**, **light scattering detectors**, **radioactivity detectors** or other special detectors may also be used.

The mobile phase exits the detector and can be sent to waste, or collected, as desired. When the mobile phase contains a separated compound band, **HPLC** provides the **ability to collect this fraction of the eluate** containing that purified compound for further study. This is called **preparative chromatography**.

HPLC is analogous to GLC in its **sensitivity** and **ability to provide both quantitative and qualitative data** in the single operation. It differs in that the **stationary phase** bonded to a porous polymer is held in a narrow stainless steel column and the liquid **mobile phase** is forced through under considerable pressure. The apparatus for **HPLC is more expensive** than GLC, mainly **because** a suitable pumping system is required and all connections have to be screw-jointed to withstand the pressure involved.

The mobile phase is a miscible solvent mixture, which either remains constant (isocratic separation) or may be changed continuously in its proportions, by including a mixing chamber (gradient elution).The **major differences between HPLC and GLC** is that the separation in HPLC normally operates **at ambient temperature,** so that the **HPLC** is mainly used for those classes of compounds which **are non-volatile**, e.g. higher **terpenoinds, phenolics** of all types, **alkaloids, lipids** and **sugars**. It works best for compounds which can be detected in the ultra- violet or visible regions of the spectrum.

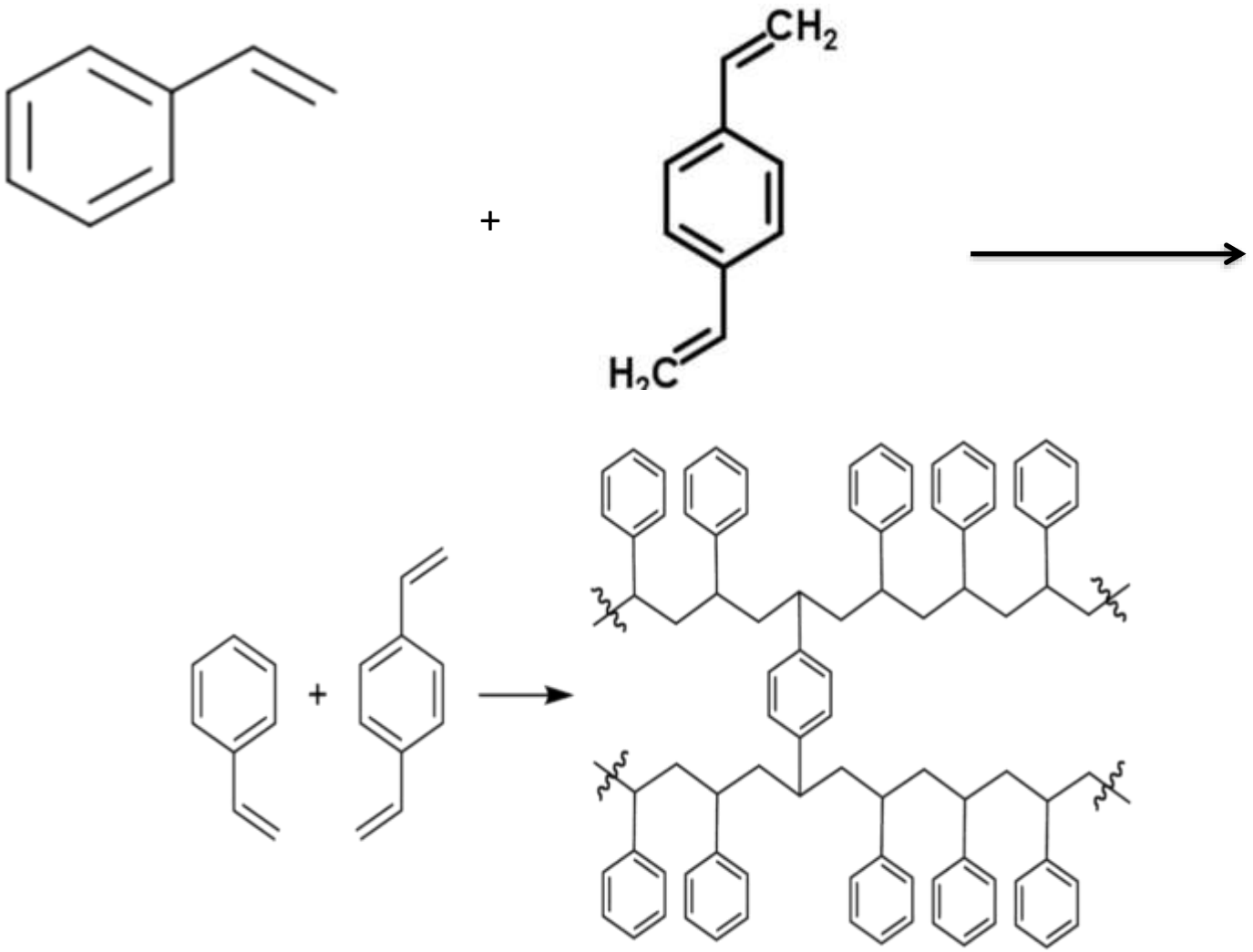
Ion exchange methods

Dr. Thukaa Z. Abdul-Jalil

Lec 12

- An ion exchanger is a material which consists of **resin or matrix carrying certain ion** , this material is **packed in a column** & is used for the same purpose as the column chromatography but here the separation will take place by exchange of the ions between the resin material & the solute . Thus , there is an **insoluble phase with fixed ionic sites of one charge , while the oppositely charged species are free to move about & be replaced by other ions of like charge .**

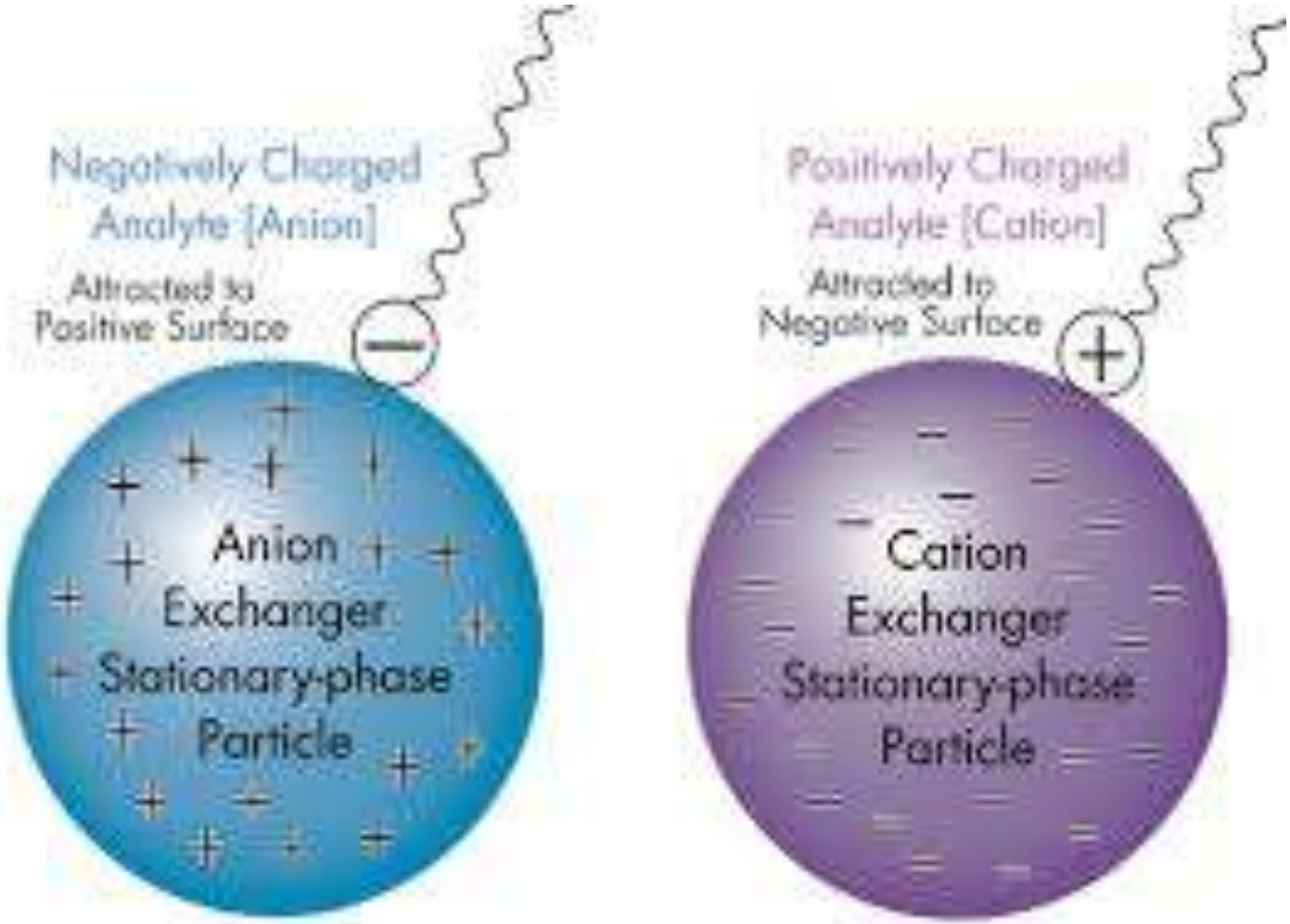
- **Types of resins** : A typical resin is prepared by **polymerization of styrene & divinely benzene** :



Matrix

There are two major types of ion exchangers:

- **Cationic exchanger** : **Acidic functional** groups are easily introduced ex : by **sulfonation** in which a sulfonic acid group is attached to nearly every aromatic nucleus .**Sulfonic acids** are **strong acids** with essentially **completely dissociated protons** , these protons are **not free to leave the resin unless replaced by other positive ions**.


Negatively Charged
Analyte [Anion]
Attracted to
Positive Surface
Anion
Exchanger
Stationary-phase
Particle
Positively Charged
Analyte [Cation]
Attracted to
Negative Surface
Cation
Exchanger
Stationary-phase
Particle

- **Anionic exchanger** : If **basic** functional groups are introduced , then the resin can exchange anions rather than cations . **Strong anion exchangers** are prepared with a **tertiary amine** , yielding a strongly **basic quaternary ammonium group** . **Weaker** anionic exchangers can be prepared **with secondary amines** , yielding a weakly basic **tertiary amine.**

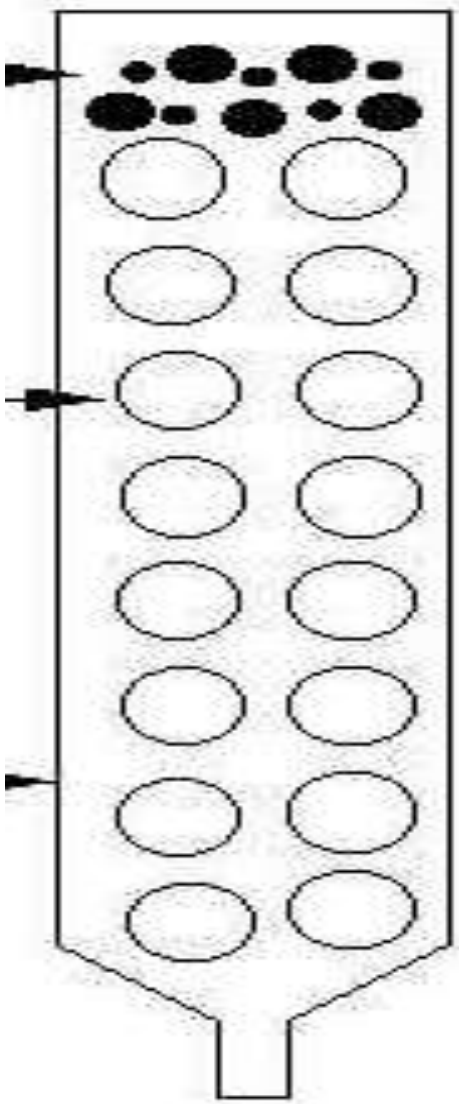
- The **principle of action** is that the **insoluble resin** has a **chemically bound charge** group & there is a **mobile phase** carrying a **solute** which has **a different ion of the same charge** . The different ions may be exchanged with other ions of the same charge without any change in the insoluble resin . The **net result** of an ion exchange reaction can be expressed as a **replacement of equivalent quantities** of like-charged ions :

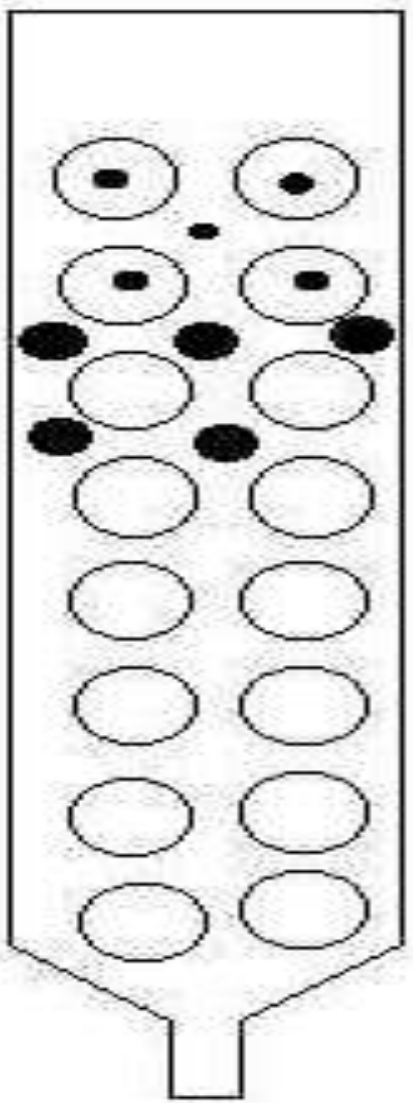
- $HR + Na^{+} = NaR + H^{+}$
- $2HR + Ca^{++} = CaR_2 + 2H^{+}$
- $RCl + OH^{-} = ROH + Cl^{-}$

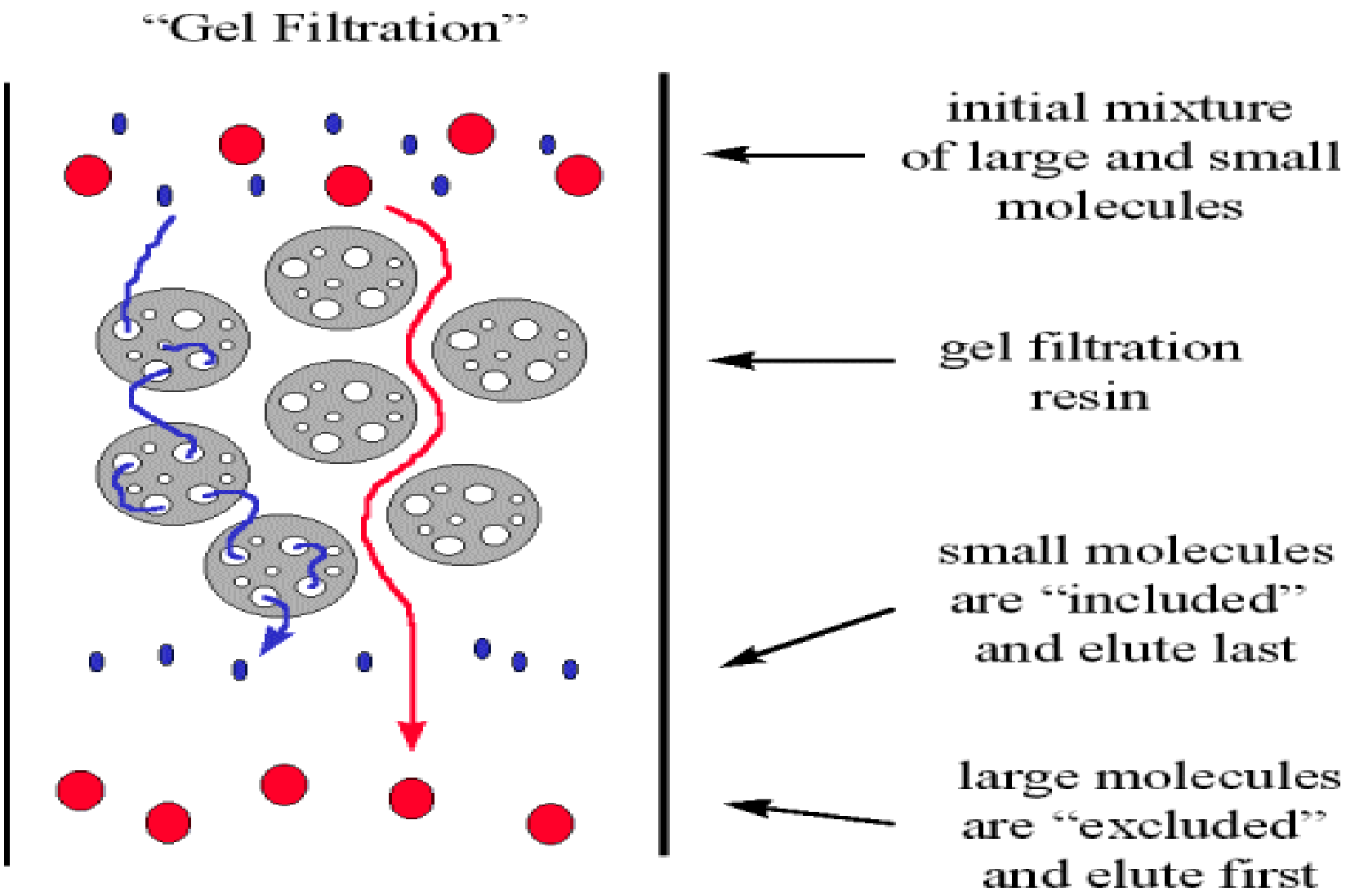
- Where **R** represents the **resin matrix .** This method of ion exchange is used in cases of the **formation of salts** & also for the **quaternary alkaloids** which are separated from plant as **reinekate** salts then they are changed into **another salt** ex: **chlorides** by passing them on a **chloride ions containing resin .**

Gel chromatography(Gel filtration)

- The separation of **very high molecular weight** substances is most readily accomplished by the use of **columns packed with gel** . Several varieties of gel have recently become available , all of which separate molecules primarily on the bases of their sizes by a “ sieving “ or “ filtering “ process . Hence , the names “ **gel filtration** “ used by **biochemists** & “ **gel permeation chromatography** “ used by **polymer chemists** describe the same general technique.






"Gel Filtration"
initial mixture of large and small molecules
gel filtration resin
small molecules are "included" and elute last
large molecules are "excluded" and elute first

- **The gels** a very open **, three dimensional network** formed by **cross-linking long polymeric chains .** Instead of ion exchange sites , most **of these gels have polar groups** capable of **adsorbing water or other polar solvents** . A few are able to adsorb non-polar solvents . In either case , the adsorption causes **an opening of the structure, or" swelling " leaving interstices within the gel .**

- Depending on the extent of cross-linking , there will be a critical size of a molecule that can just penetrate the interior . **Larger molecules** will pass through **the column with no retardation** because **they cannot enter the gel . Smaller molecules** will **penetrate** the **interior** to a degree determined by their size i.e. these pores are formed from the molecular structure of the gel .

- when the gel is packed in a column & percolated with a solution they will let the large molecules of the solute to pass quickly down the column with the solvent , the large molecules of a solute pass through the inter granular spaces of the gel because these molecules of a solute do not enter the pores of the gel. Smaller molecules of the solute which are able to enter the pores of the gel will remain in the gel .These molecules will pass more slowly down the column .

This method is most **useful to separate** mixtures containing **large molecules of various sizes &** also to the separation of **large molecules from small molecules** . It is mostly used for **fractionation of proteins , amino acids , peptides & poly saccharides** . An **example** of **gel** used is **sephadex** which is **prepared** from **polysaccharide detrains** & is **used** for **proteins** & other **large molecules .**

Gas – liquid chromatography (GLC)
2

Dr. Thukaa Z. Abdul-Jalil

Lec 10

Type of detectors

1- Destructive usually integrated for **quantitative** analysis and include:

- **Mass spectral**
- **Flame ionization**
- **Nitrogen-phosphorus (NPD)**
- **Flame –photometric (FPD)**
- **Electrolytic conductivity**

2- **Non destructive** usually integrated for **qualitative** analysis and include:

- **Thermal conductivity (TCD)**
- **Electron capture (ECD)**
- **Photo ionization (PID)**

Qualitative analysis in GLC:

One of the important parameters used in qualitative analysis in GLC is the **retention time R_t**

The time taken for a particular compound to travel through the column to the detector is known as its **RETENTION TIME.**

This time is measured from the time at which the sample is injected to the point at which the display shows a maximum peak height for that compound.

Different compounds have different retention times.

For a particular compound retention time will vary depending on:

- **Length of the column** ex : when the column is short , then the retention time is reduced because it will take shorter time for solute to emerge from 3ft column than 5ft column .

- **The boiling point of the compound**. A compound which boils at a temperature higher than the column temperature is going to spend nearly all of its time condensed as a liquid at the beginning of the column, so high boiling means a long retention time.

- **The solubility in the liquid phase**. The more soluble a compound is in the liquid phase, the less time it will spend being carried along by the gas. High solubility in the liquid phase means a high retention time.
- **The temperature of the column**. A higher temperature will tend to excite molecules into the gas phase-either because they evaporate more readily, or because they are so energetic that the attractions of the liquid no longer hold them. A high column temperature shortens retention times for everything in the column.
- **The gas flow** has also a big role in controlling the retention time , if the flow of the gas increase the retention time decrease because the gas will flow faster carrying the vaporized solute & so the solute will emerge faster & hence the Rt is decreased.

Quantitative analysis :

- Quantitative estimation in GLC is done by measuring the area under the peak . This area is measured by several techniques :
- Estimate the area by **triangulation** i.e. draw tangents to the points of inflection on the peak sides & compute the area of the triangle formed with the base line.
- Use a **mechanical or electronic** accessory to the recorder which will automatically integrate the area (some devices operate directly from the detector).

- If the peak is too sharp (narrow) then the area can not be measured accurately , in this case we use the peak height as a measure of the amount provided a proper calibration factor is determined .

Advantages of gas chromatography

- **Very good separation**
- **Time (analysis is short)**
- **Small sample is needed-ml**
- **Good detection system**
- **Quantitative analysis**

Disadvantages of gas chromatography or limitations of its use

- **Require specific workers with very high training and experience**

Pharmacognosy & Nomenclature

Lecture 1

Dr. Thukaa Zuhair Abdul-Jalil

Pharmacognosy

- Defined as an applied science that deals with natural drugs and their constituents biological, biochemical and economic features from different originating sources in plant, animal and microorganisms kingdoms. Its an applied science that deals with study of crude drugs and their natural derivatives
- Pharmacognosy is derived from two Greek words:
- Pharma: is derived from the Greek word “pharmacon” means drug.
- cognosy: is derived from the Greek word “gnosis” means knowledge.
- The term “Pharmacognosy” was introduced by C.A.Seydler (medical student) in Germany in 1815.

Plant Nomenclature:
It can be noticed in the pharmacopeia books, in pharmacognosy and other related publications:

1. The medicinal plants have scientific (botanical) names.
This name consist of two names: The first name start with capital letter and represent the name of genus, while the second name start with small letter which represent the species name, with noticed: put line under these names in order to recognize the plant from others.
2. The botanical name of plant is followed by the name of person such as **Linneus** and **Sole**. This name referred to the person who describe the genus, species or variety firstly Ex: Digitalis purpurea Linn

3. In sometimes : the name of plant is derived from morphological characters of plant or property of plant part or the name of person or the names of some countries…etc.).

Example:

Atropa belladonna Linna (السيدة الجميلة)

Atropa: this name is derived from the Latin name Atropa means poisonous.

The species belladonna consist from to Italian words

Bella means beauty

Donna means lady.

Pharmacognosy science concerned with studying the following subjects:

1-Taxonomy of natural drugs (i.e. the natural source of the drugs).

2- Distribution of natural source for the drug in the world.

3-Description of the natural source.

Ex: if the natural source for the drug is the plant; then description this plant as follow: Tree (like Salix) or shrub (like pomegranate) herbal (peppermint), annual حولي (digitalis), biannual(ذات حولين يعيش لمدة سنتين) like caraway , perennial معمر (peppermint).

4- The active constituents of the natural drugs like: glycosides, alkaloids, tannins,…etc.).

5- Biosynthesis and storage places or sites of the active constituents in the natural source.
6- Physical, chemical, and biological properties of the active constituents.
7- The part used from the natural source in the treatment of disease. (Like: roots, seeds, stem…etc.).
8- Collection and storage of the part used.
9- The correct prescription of natural drug in the treatment of the disease.

Some definitions:

1-Drugs: Is a natural or synthetic substance having therapeutic properties.

2-Natural substances: Means, the substances that have not had changes made in their molecular structures as found in nature ,they include :

***Whole plants** (leaf, stem, root, seed, fruit, and flower) and **their parts** (like: only the seeds) and **anatomic parts** there of ex: vegetables saps and mucilage.

***Whole animals and their anatomic parts** like for ex: glands and their secretions.

3- Crude drug: any natural substance that has not been advanced in value or improved in its condition when exposed to some processes like: drying, crushing, extracting, grinding, and distilling.

i.e. crude drugs: Means, natural drugs that have undergone only the processes of collection and drying (no change in their molecular structures).

4- Active constituents: Are those chemical compounds or organic substances or chief principle constituents of natural drugs (natural substance) which give the natural drug its pharmacological activities, these found whether a single substance or mixture of substances and used as therapeutic agents, and when separated these constituents by different methods of extraction in this case these constituents called extractives or derivatives. Like: the active constituents of digitalis plants (digoxin and digitoxin).

5- Phytochemistry: A branch of chemistry that deals with chemical processes associated with plant life and the chemical compounds produced by plants (the chemistry of plants, plant processes and plant product).

6- Medicinal plants: are those plants having pharmacological or therapeutic activities.

7- Indigenous plans: are those plants that grow in their native countries or lands.

8-Exogenous plants: are those plants that grow in other than their native home.

9-Cultivated plants: are those plants that grow under controlled conditions to improve quality and quantity of produce drugs.

10- Pharmacopeia: it's a word book or dictionary that contains the true names of natural drugs and publishing by the authority or a government or medical or pharmaceutical society ex:

British pharmacopeia

European pharmacopeia

United states pharmacopeia.

11- Official drug: is the drug which is found and recognized in pharmacopeia books ex: the leaf of digitalis plant and their active constituents (digoxin and digitoxin).

12- Unofficial drug: is the drug which is found and recognized in pharmacopeia books, but presently not found in current issues .Like: khat plant which is used as narcotic.

13- Nonofficial drugs: these drugs are not appeared in pharmacopeia books.

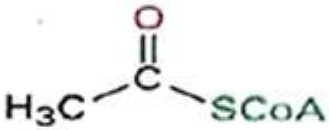
14- Extraction: Methods of obtaining the active principle found in plants. Extraction removes only those substances that can be dissolved in the liquids (single or mixture) which are referred **as solvent or menstrums**. Undissolved portion of the remains after the extraction processes is completed called **marc**. Solvent used after extraction is called **extract** and product of the extraction process is known as **extractive** which is a mixture of substances.

Biosynthesis of aliphatic compounds

Dr. Thukaa Zuhair Abdul-Jalil

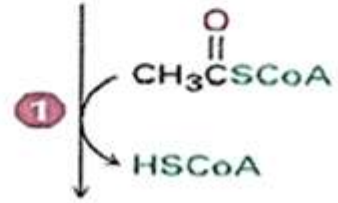
Lec 2

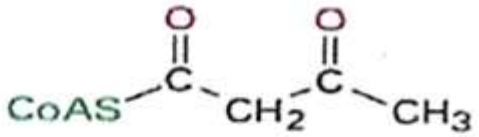
Biosynthesis of isoprenoid compounds(Acetate-Mevalonate pathway)



Acetyl CoA

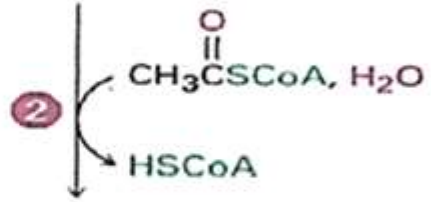
1. Claisen condensation of two molecules of acetyl CoA gives acetoacetyl CoA.

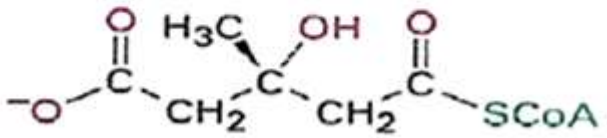




Acetoacetyl CoA

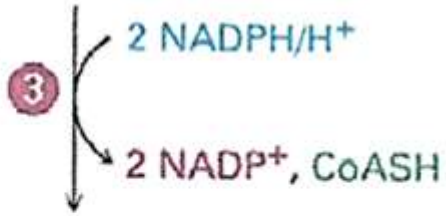
2. Aldol-like condensation of acetoacetyl CoA with a third molecule of acetyl CoA, followed by hydrolysis, gives (3*S*)-3-hydroxy-3-methylglutaryl CoA.



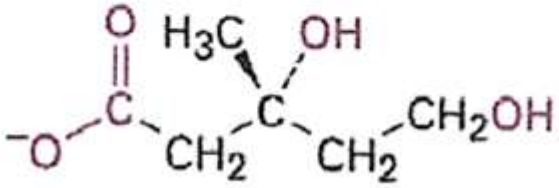


(3*S*)-3-Hydroxy-3-methylglutaryl CoA

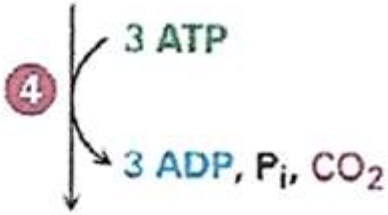
(3*S*)-3-Hydroxy-3-methylglutaryl CoA



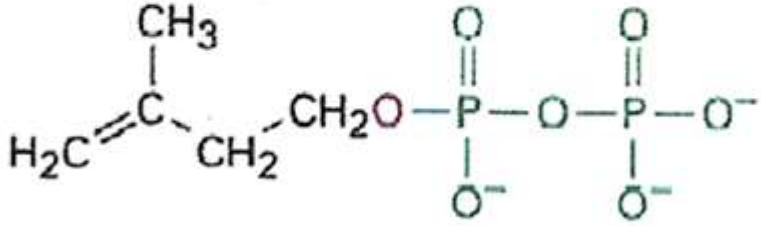
3. Reduction of the thioester group by 2 equivalents of NADPH gives (*R*)-mevalonate, a dihydroxy acid.



(*R*)-Mevalonate



4. Phosphorylation of the tertiary hydroxyl and diphosphorylation of the primary hydroxyl, followed by decarboxylation and simultaneous expulsion of phosphate, gives isopentenyl diphosphate, the precursor of terpenoids.



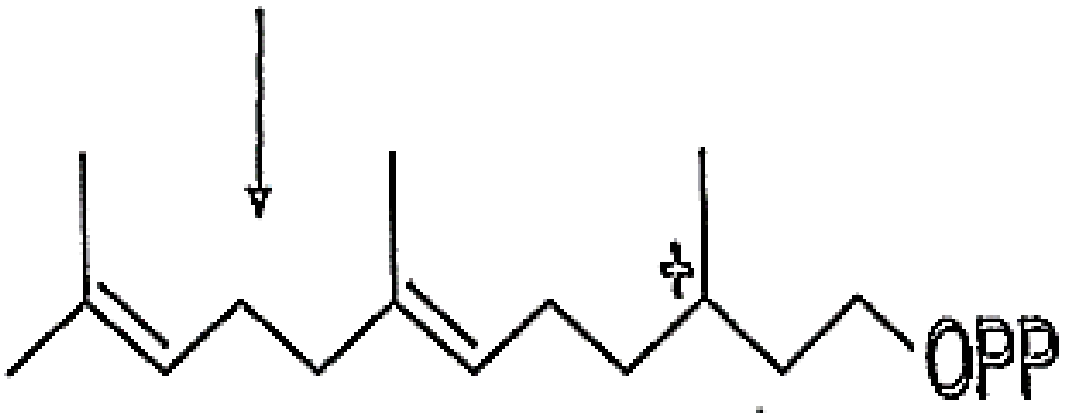
Isopentenyl diphosphate

Isopentenyl pyrophosphate is interconvertible with 2-methylallyl pyrophosphate.

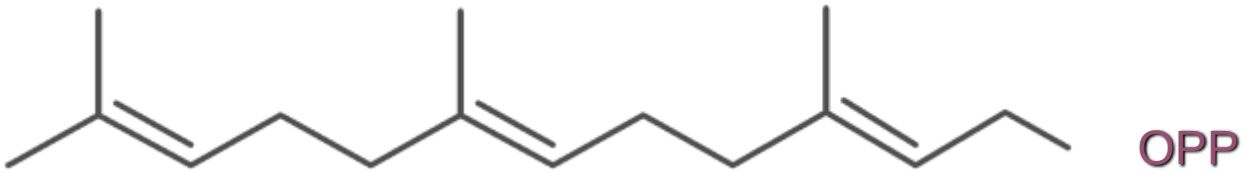
Dimethylallyl pyrophosphate has a leaving group (pyrophosphate) at an allylic carbon; it is reactive toward nucleophilic substitution at this position.

Geranyl pyrophosphate with one molecules of isopentenyl pyrophosphate in the same manner mention previously will give (15 C) atom compound called farnesyl pyrophosphate

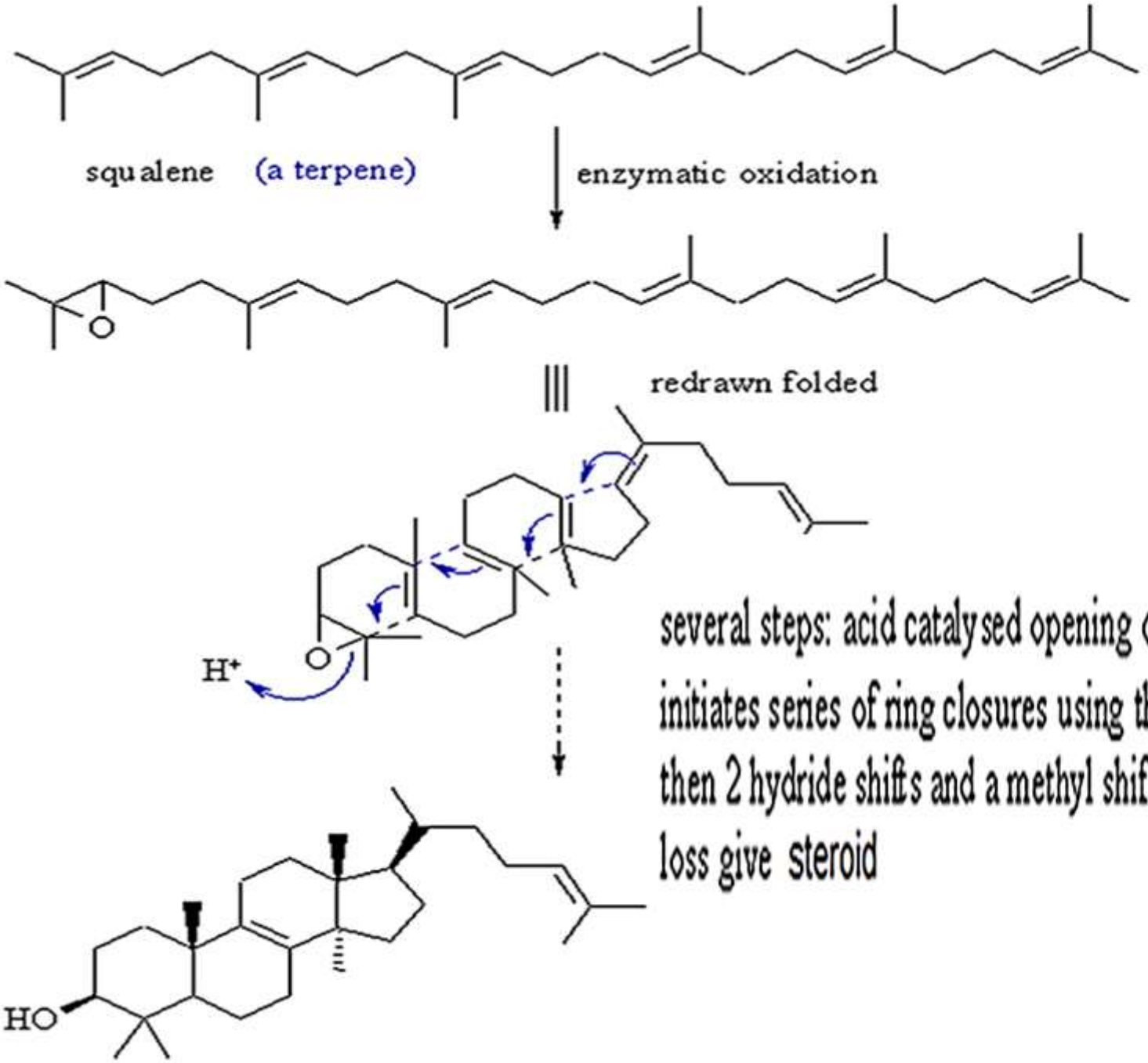
Geranyl pyrophosphate



From 10 Carbons to 15



This compound is called farnesyl pyrophosphate (15C) then when two farnesyl pyrophosphate react together with NADPH will give squalene which is a direct precursor for steroidal nucleus



several steps: acid catalysed opening of the epoxide initiates series of ring closures using the π electrons, then 2 hydride shifts and a methyl shift, and proton loss give steroid

Biosynthetic pathway of natural drugs

Dr. Thukaa Z. Abdul-Jalil

Lec 1

According to the biosynthetic pathways, the natural compounds are classified into:

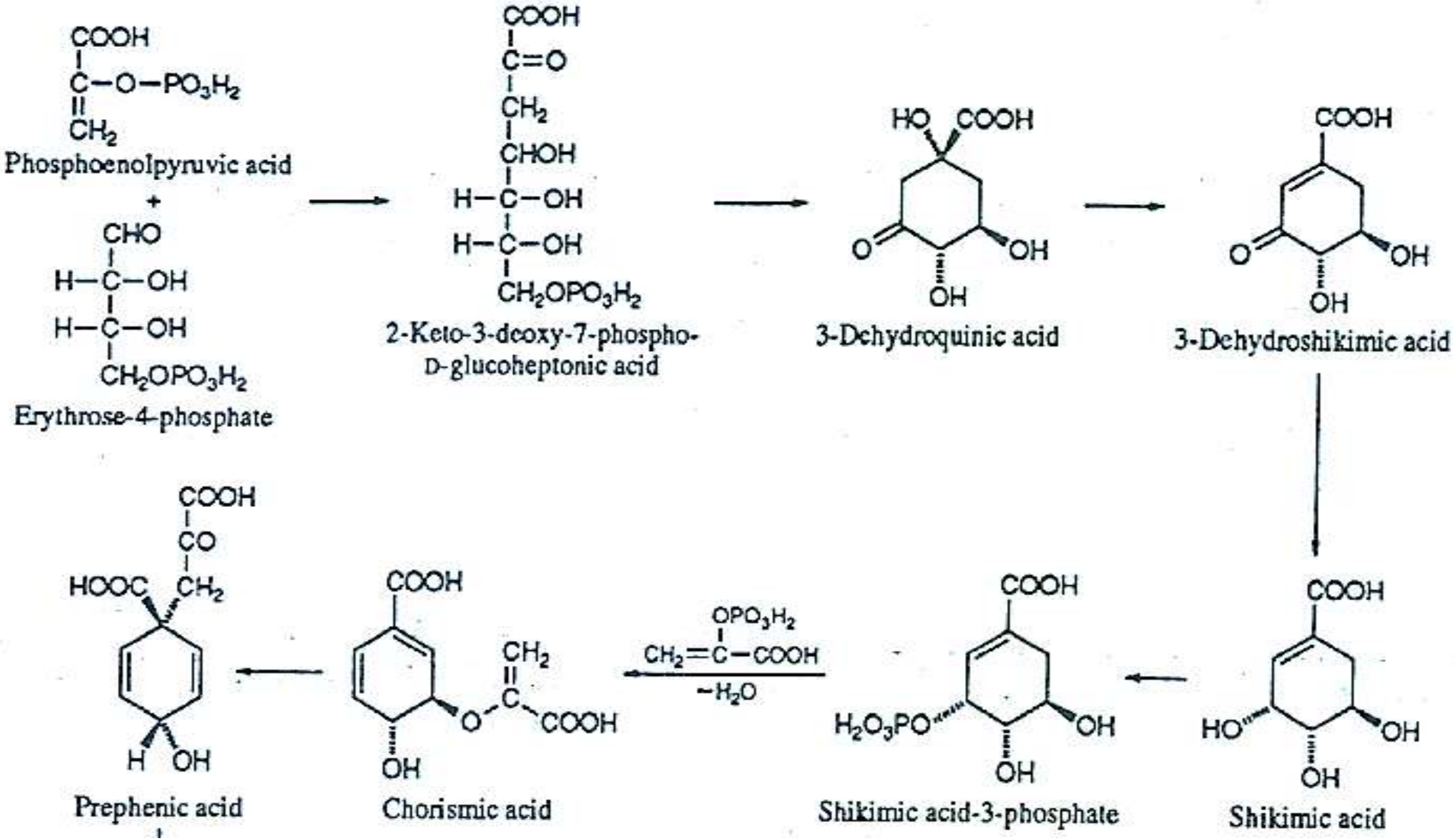
1- Active compounds derived from shikimic acid pathway (Aromatic compounds)

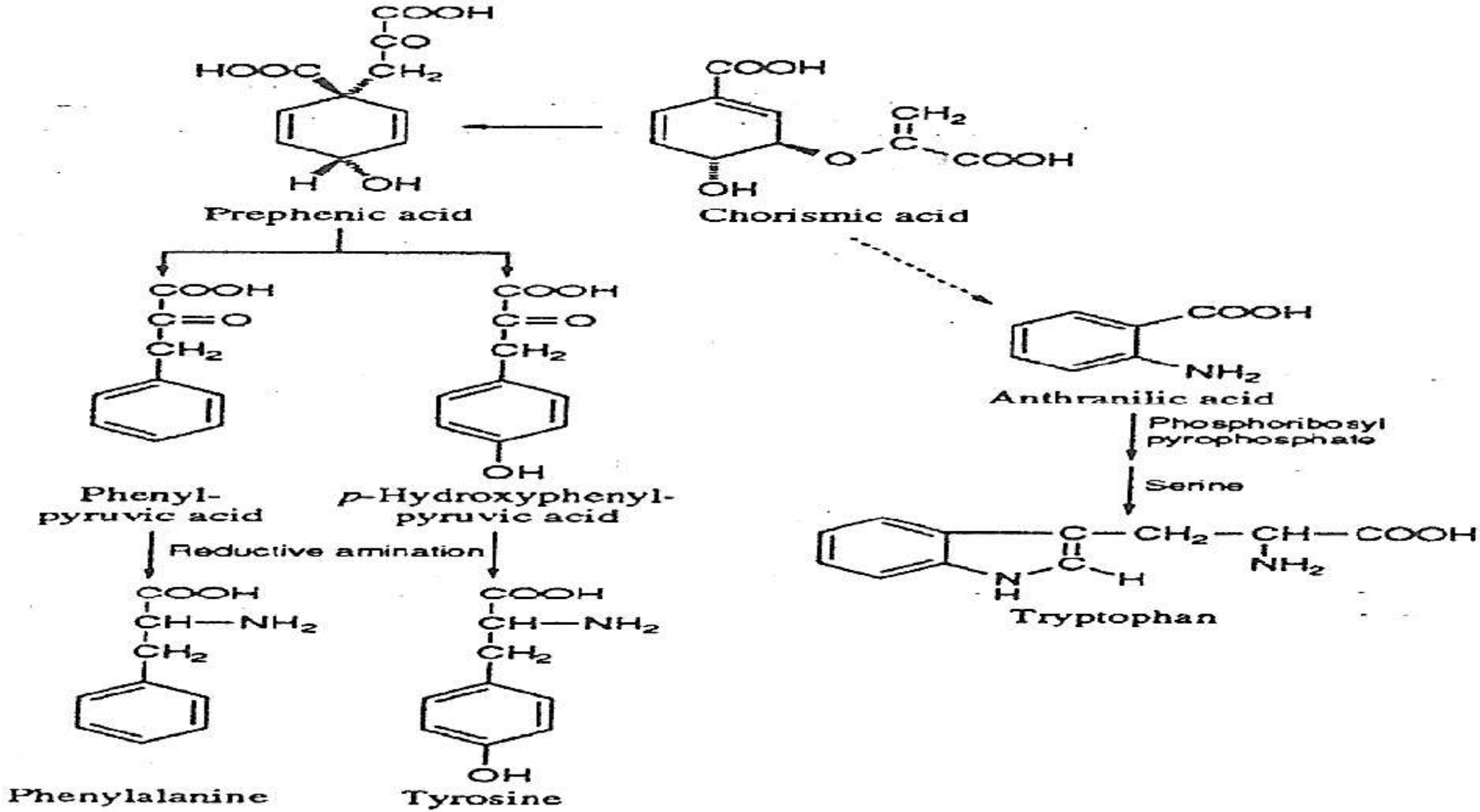
2- Active compounds derived from acetate-mevalonic acid pathway (Non-aromatic compounds

3- mixed pathway derived from shikimate and mevalonate pathways

Shikimic acid pathway

- The shikimic acid pathway is a key intermediate from carbohydrate for the biosynthesis of C6-C3 units (phenyl propane derivative).
- Besides serving as a precursor for the biosynthesis of amino acids, it also an intermediate in the production of tannins, flavones, coumarins and vanillin.
- The shikimic acid pathway is present in plants, fungi and bacteria but is not found in animals, so animals have no way to synthesis the three aromatic amino acids (phenyl alanine, tyrosine and tryptophan) which are therefore essential nutrients in animal diet.
- Shikimic acid pathway converts simple carbohydrate precursor derived from glycolysis and pentose phosphate pathway to the aromatic amino acids as shown in the following figure:


Phosphoenolpyruvic acid
+
Erythrose-4-phosphate
2-Keto-3-deoxy-7-phospho-D-glucoheptonic acid
3-Dehydroquinic acid
3-Dehydroshikimic acid
Shikimic acid
Shikimic acid-3-phosphate
$-H_2O$
Chorismic acid
Prephenic acid


Prephenic acid
Chorismic acid
Anthranilic acid
Phosphoribosyl pyrophosphate
Serine
Tryptophan
Phenyl-pyruvic acid
p-Hydroxyphenyl-pyruvic acid
Reductive amination
Phenylalanine
Tyrosine

- Shikimic acid through a series of phosphorylated intermediates yield chorismic acid which is an important branch-point intermediate.
- One branch leads to anthranilic acid then to tryptophan.
- The other leads to prephenic acid which is the last non aromatic compound in the sequence.
- **Prephenic acid can be aromtized in 2 ways.**
- The first proceeds by dehydration and simultaneous decarboxylation to yield phenyl pyruvic acid, the direct precursor of phenylalanine.
- The second occurs by dehydrogenation & decarboxylation to give p-hydroxy phenyl pyruvic acid , the precursor of tyrosine.

Biosynthesis of aliphatic compounds

Acetate-Mevalonic acid pathway

The Mevalonate Pathway to Isopentenyl Diphosphate

Begins with conversion of acetate to acetyl CoA

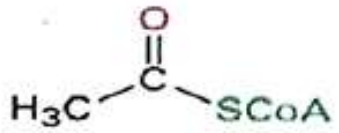
Claisen condensation yields acetoacetyl CoA

Second Claisen condensation reaction with third molecule of acetyl CoA yields six-carbon compound 3-hydroxy-3-methylglutaryl CoA

3-Hydroxy-3-methylglutaryl CoA is reduced to mevalonate

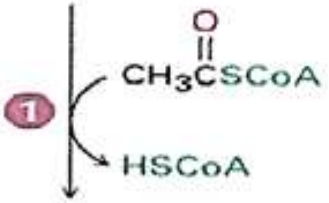
Phosphorylation with loss of CO_2 and phosphate ion completes synthesis

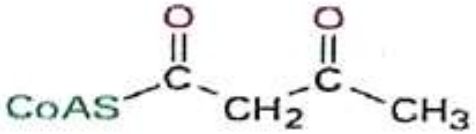
Biosynthesis of isoprenoid compounds(Acetate-Mevalonate pathway)



Acetyl CoA

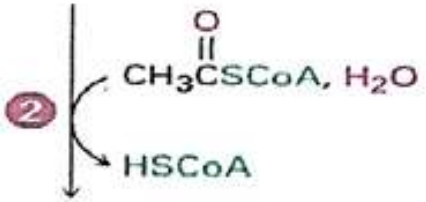
1. Claisen condensation of two molecules of acetyl CoA gives acetoacetyl CoA.

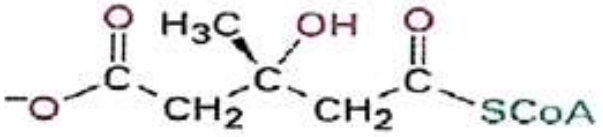




Acetoacetyl CoA

2. Aldol-like condensation of acetoacetyl CoA with a third molecule of acetyl CoA, followed by hydrolysis, gives (3*S*)-3-hydroxy-3-methylglutaryl CoA.

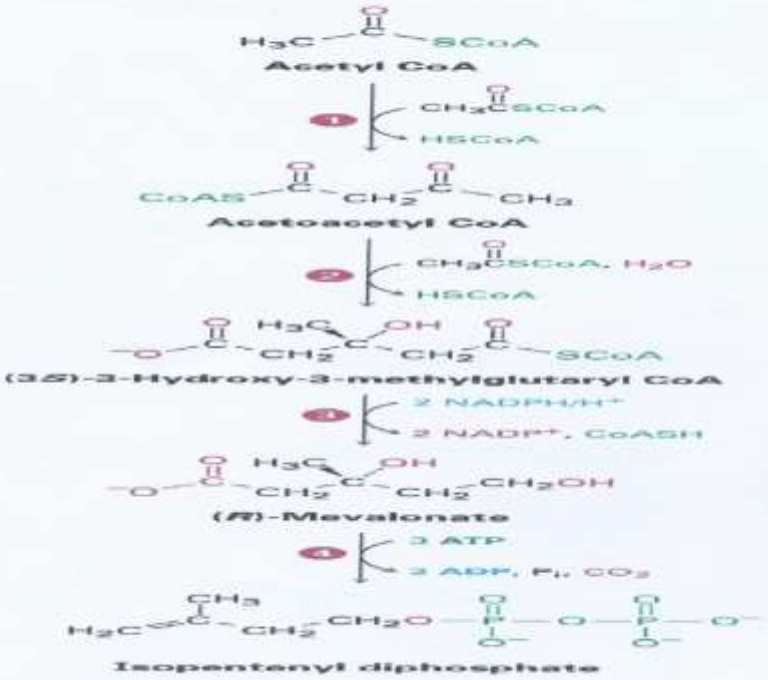




(3*S*)-3-Hydroxy-3-methylglutaryl CoA

Biosynthesis of isoprenoid compounds(Acetate-Mevalonate pathway)

1. Claisen condensation of two molecules of acetyl CoA gives acetoacetyl CoA.
2. Aldol-like condensation of acetoacetyl CoA with a third molecule of acetyl CoA, followed by hydrolysis, gives (3*S*)-3-hydroxy-3-methylglutaryl CoA.
3. Reduction of the thioester group by 2 equivalents of NADPH gives (*R*)-mevalonate, a dihydroxy acid.
4. Phosphorylation of the tertiary hydroxyl and diphosphorylation of the primary hydroxyl, followed by decarboxylation and simultaneous expulsion of phosphate, gives isopentenyl diphosphate, the precursor of terpenoids.



First step in mevalonate biosynthesis is a Claisen condensation to yield acetoacetyl CoA ,Catalyzed by acetoacetyl-CoA acetyltransferase (Acetyl group is first bound to enzyme by nucleophilic acyl substitution reaction with cysteine –SH group).

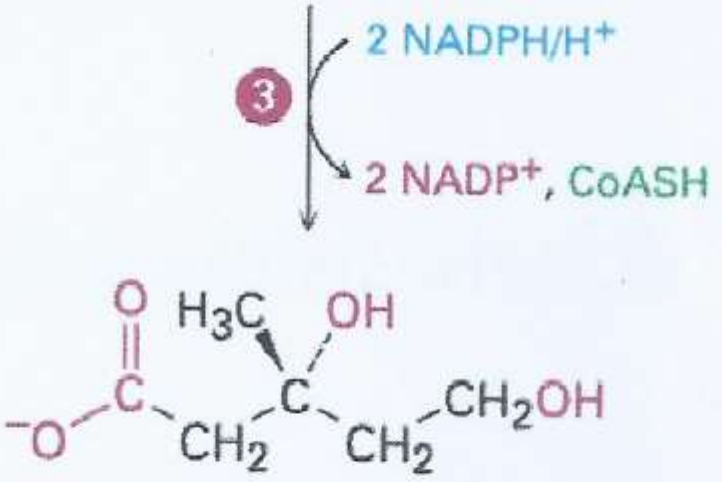
Acetoacetyl CoA undergoes an aldol-like addition of an acetyl CoA enolate ion,Reaction catalyzed by 3-hydroxy-3-methylglutaryl-CoA synthase , occurs by initial binding of substrate to cysteine –SH group followed by enolate addition and hydrolysis.

Reduction of HMG-CoA to give (*R*)-mevalonate is catalyzed by 3-hydroxy-3-methylglutaryl-CoA reductase ,Requires 2 equivalents of NADPH, reaction occurs in two steps and proceeds through an aldehyde intermediate.

Three additional reactions convert mevalonate to isopentenyl diphosphate:

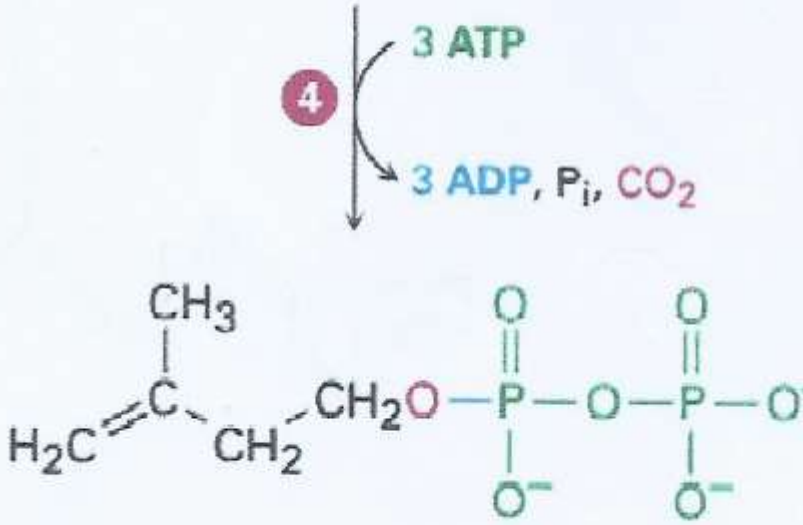
(3*S*)-3-Hydroxy-3-methylglutaryl CoA

3 Reduction of the thioester group by 2 equivalents of NADPH gives (*R*)-mevalonate, a dihydroxy acid.



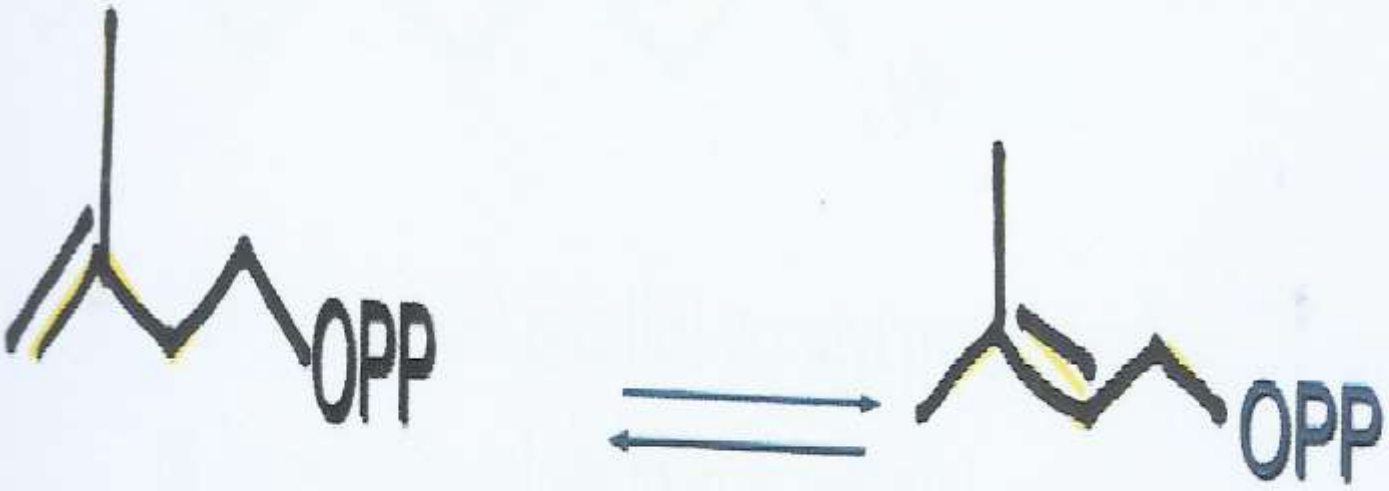
(*R*)-Mevalonate

4 Phosphorylation of the tertiary hydroxyl and diphosphorylation of the primary hydroxyl, followed by decarboxylation and simultaneous expulsion of phosphate, gives isopentenyl diphosphate, the precursor of terpenoids.



Isopentenyl diphosphate

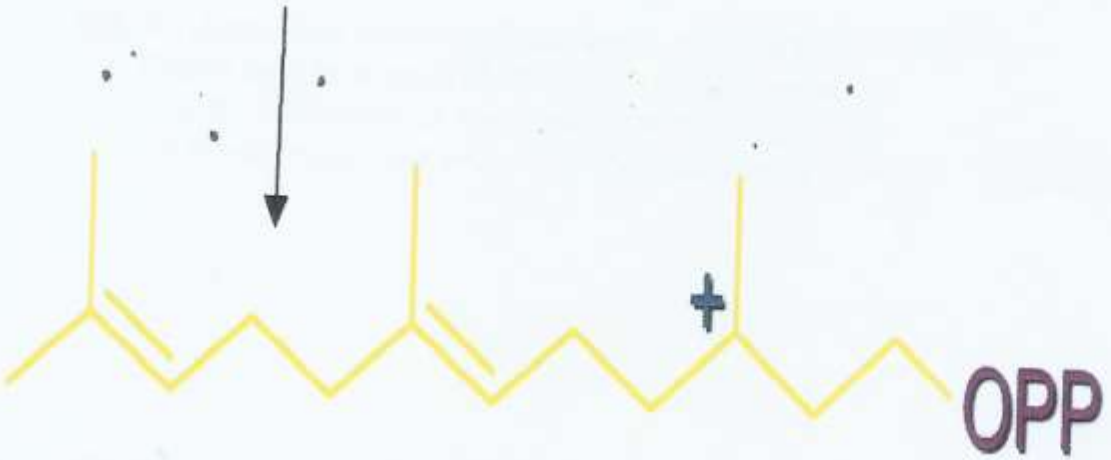
Isopentenyl pyrophosphate is interconvertible with 2-methylallyl pyrophosphate.



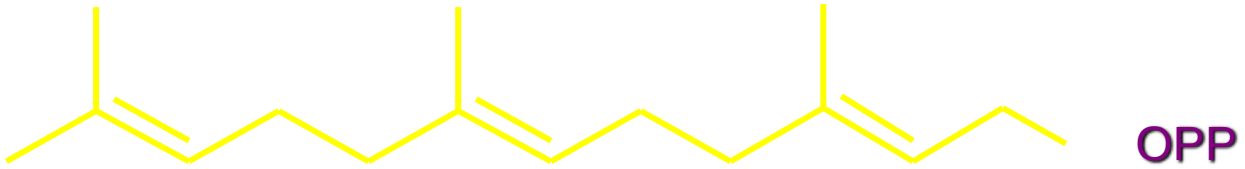
Dimethylallyl pyrophosphate has a leaving group (pyrophosphate) at an allylic carbon; it is reactive toward nucleophilic substitution at this position.

Geranyl pyrophosphate with one molecules of isopentenyl pyrophosphate in the same manner mention previously will give (15 C) atom compound called farnesy pyrophosphate.

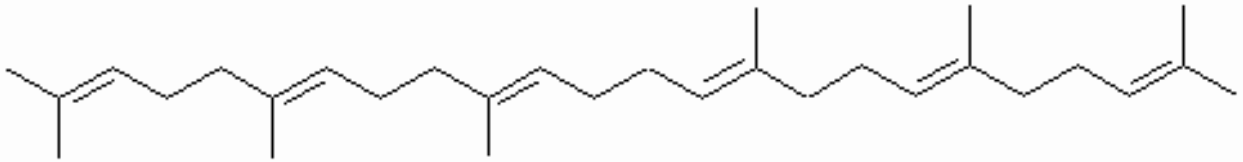
Geranyl pyrophosphate



From 10 Carbons to 15

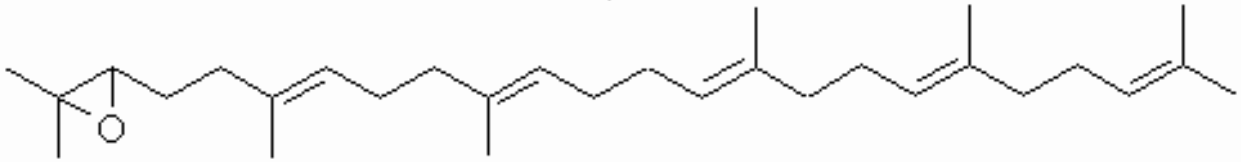


- This compound is called farnesyl pyrophosphate (15C) two F.pp with NADPH will give squalene which direct precursor for steroidal nucleus

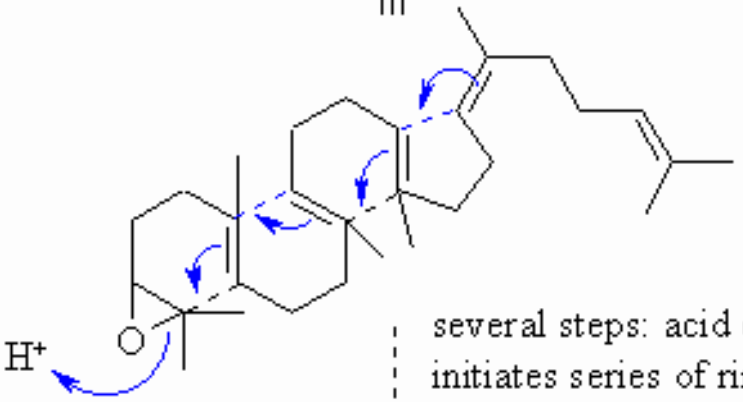


squalene (a terpene)

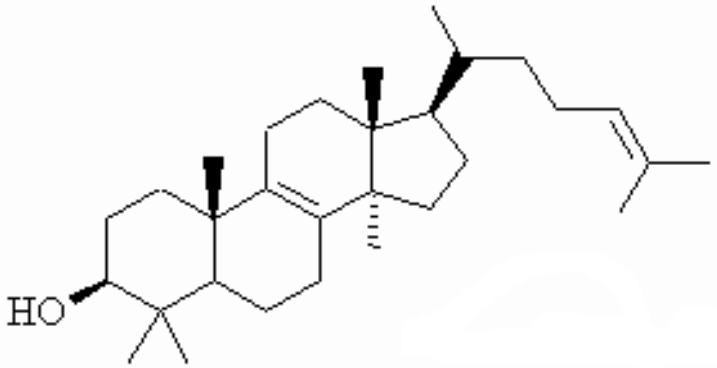
enzymatic oxidation



redrawn folded



several steps: acid catalysed opening of the epoxide initiates series of ring closures using the π electrons, then 2 hydride shifts and a methyl shift, and proton loss give steroid



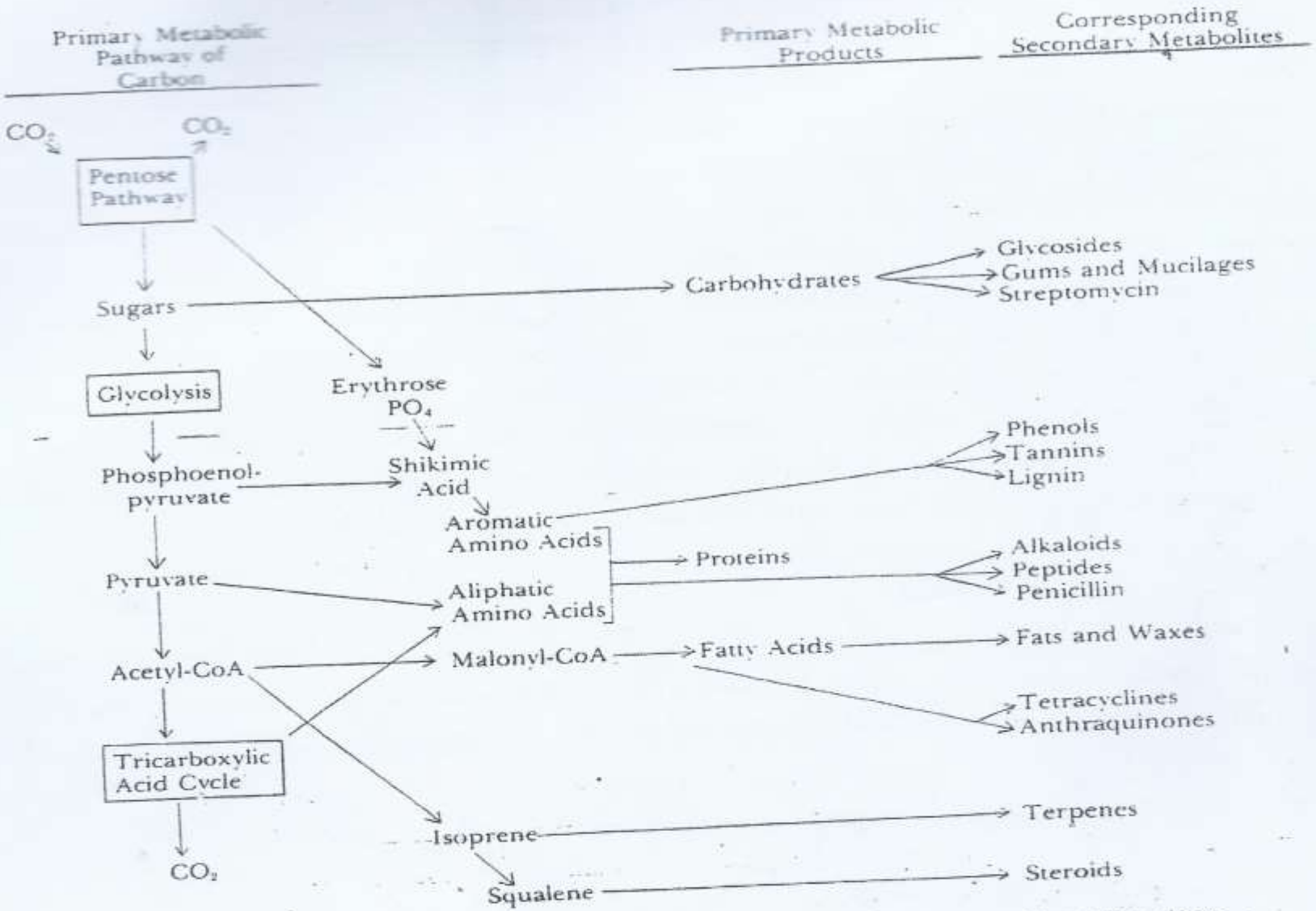


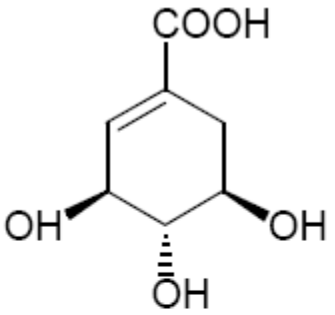
Fig. [redacted]. Interrelationships of biosynthetic pathways leading to secondary constituents in plants.

Biosynthesis of aromatic compounds

Shikimic acid pathway

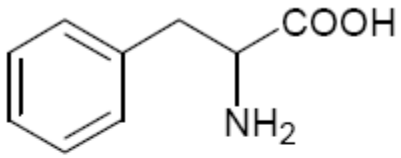
Phenylpropanoids

Shikimic Acid

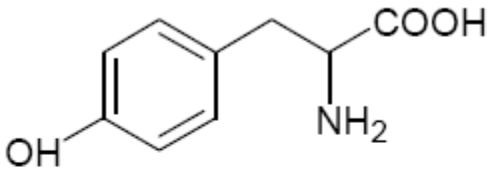


The shikimic acid pathway gives rise to a large number of aromatic compounds

eg. phenylalanine



tyrosine



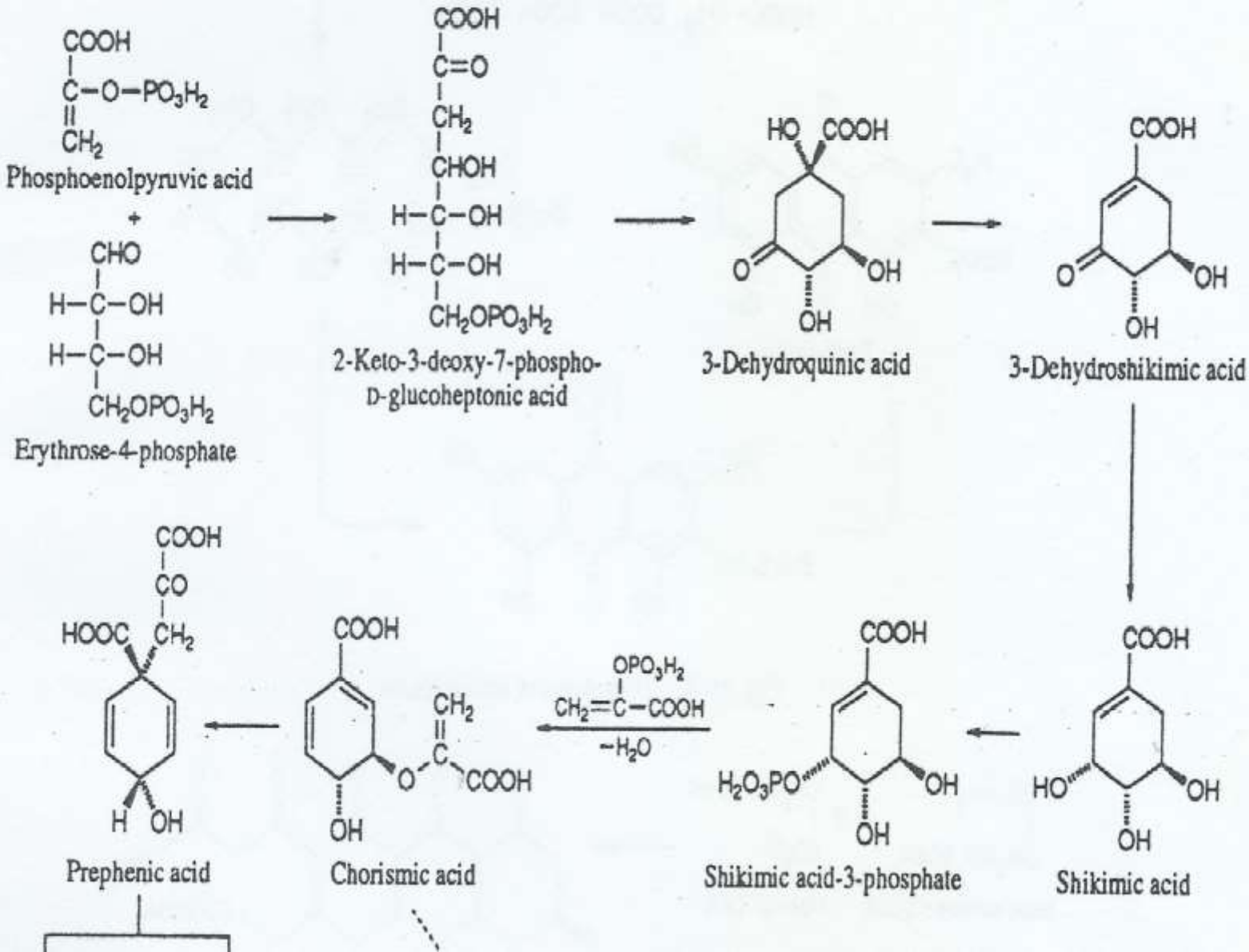
The path gives the aromatic substitution patterns *para*-hydroxy, *ortho*-dihydroxy, or 1,2,3 trihydroxy-

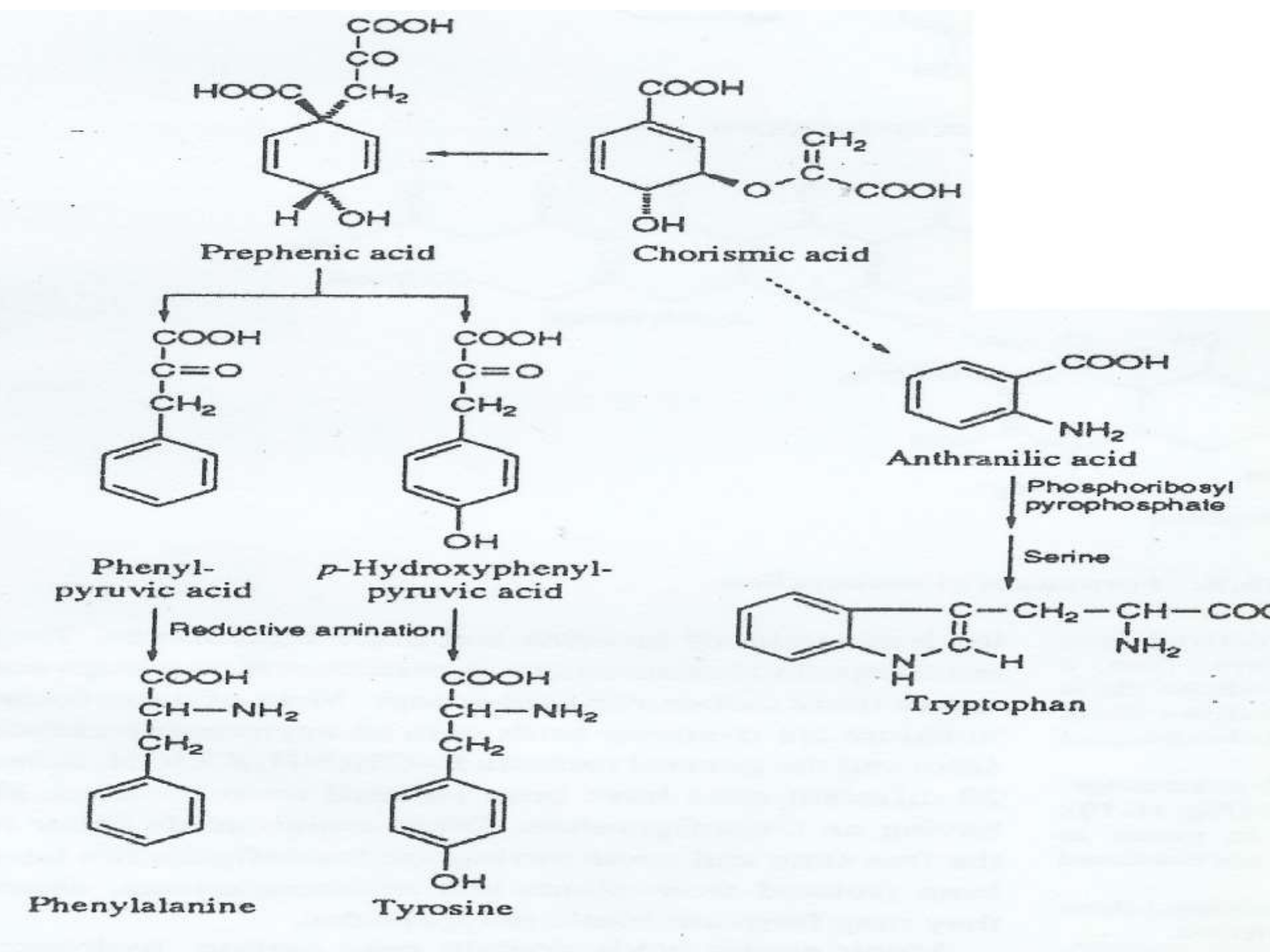
cf. *meta* substitution in polyphenols from acetate

Shikimic acid through a series of phosphorylated intermediates yield chorismic acid which is an important branch-point intermediate. One branch leads to anthranilic acid then to tryptophan. The other leads to prephenic acid which is the last non aromatic compound in the sequence.

Prephenic acid can be aromtized in 2 ways. The first proceeds by dehydration and simultaneous decarboxylation to yield phenyl pyruvic acid, the direct precursor of phenylalanine. The second occurs by dehydrogenation & decarboxylation to give p-hydroxy phenyl pyruvic acid , the precursor of tyrosine.

Biosynthesis of aromatic by shikimic acid




Prephenic acid
Chorismic acid
Anthranilic acid
Phosphoribosyl pyrophosphate
Serine
Tryptophan
Phenyl-pyruvic acid
p-Hydroxyphenyl-pyruvic acid
Reductive amination
Phenylalanine
Tyrosine

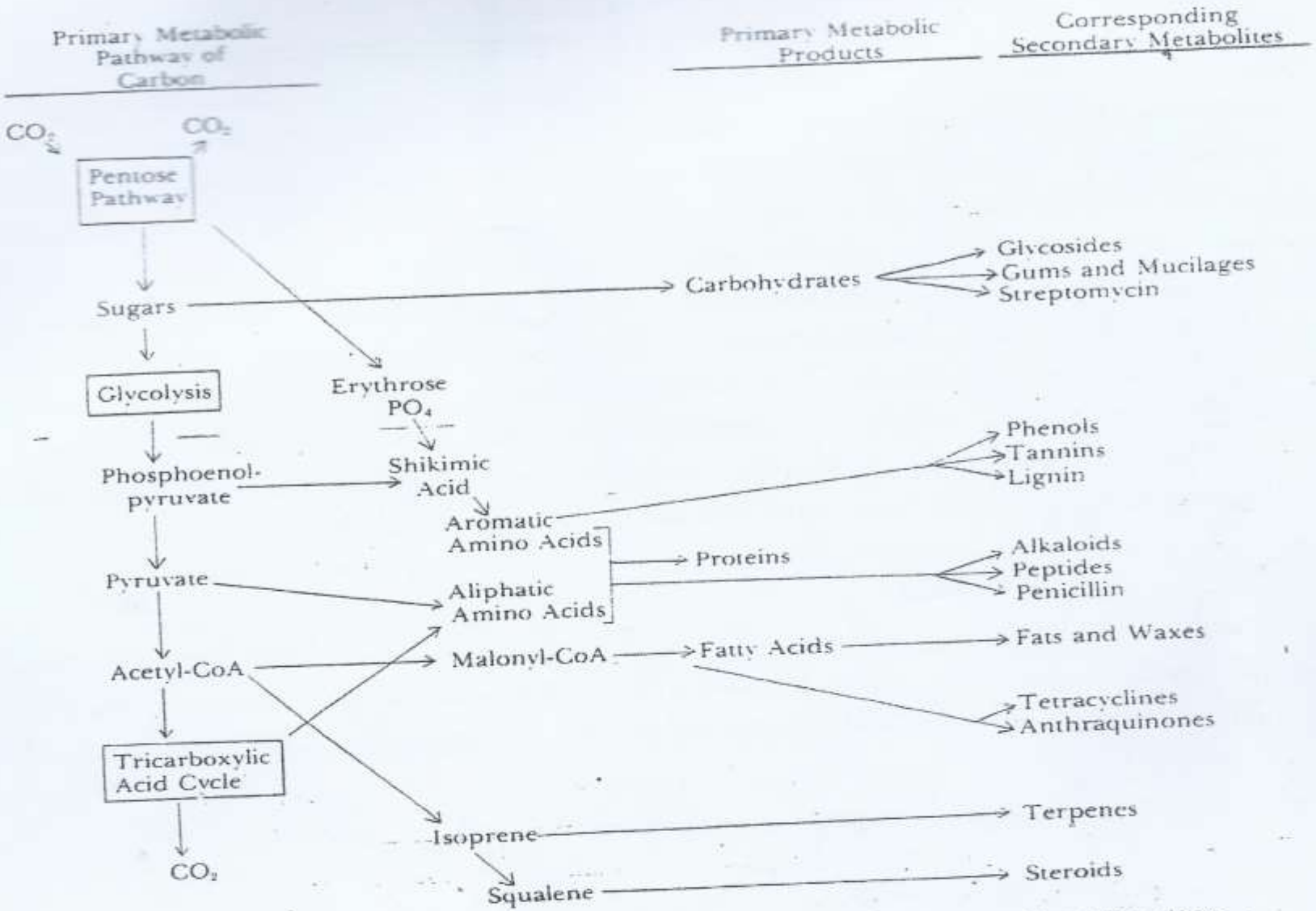
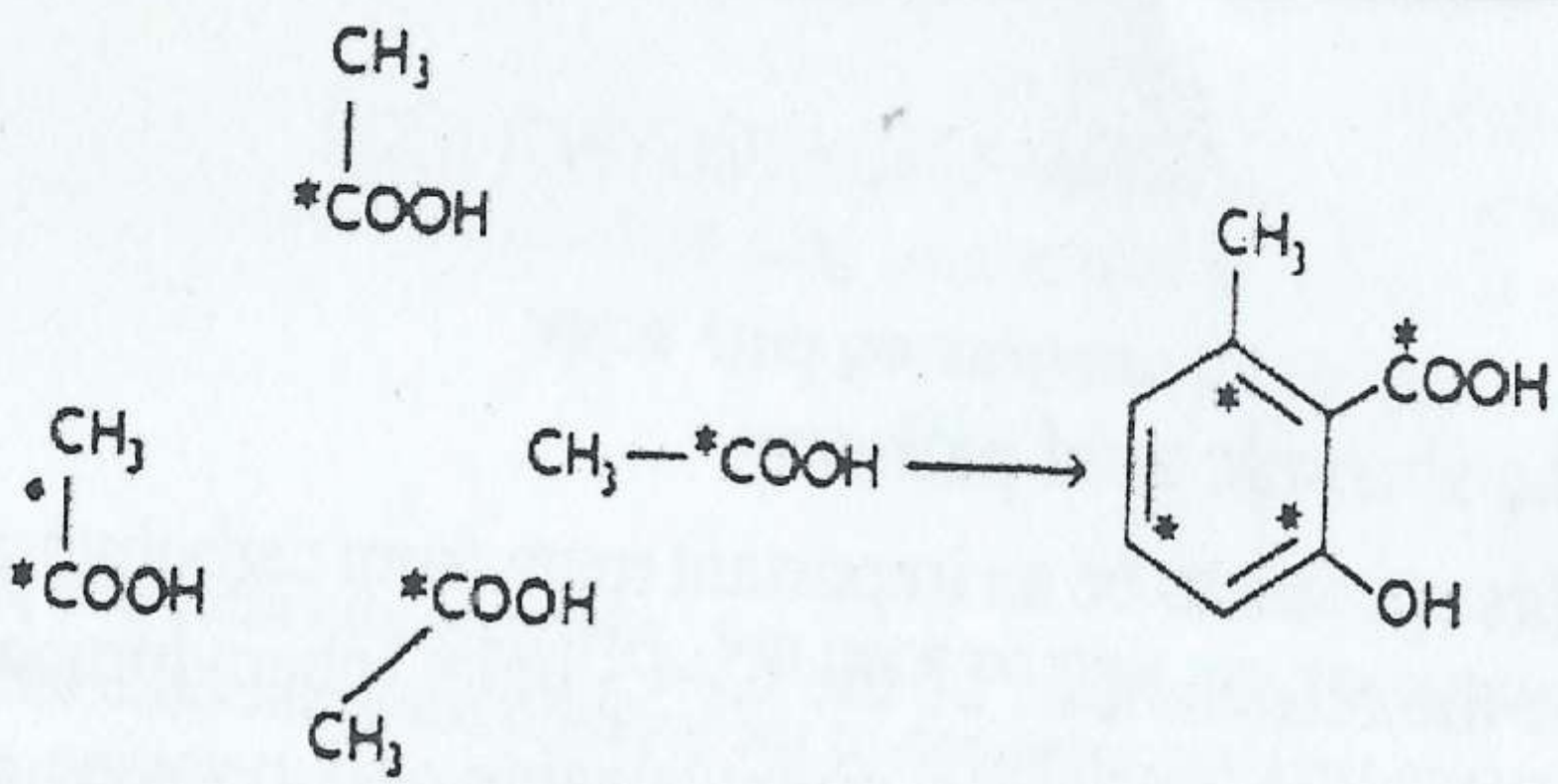


Fig. [redacted]. Interrelationships of biosynthetic pathways leading to secondary constituents in plants.

Acetate hypothesis

4- acetate groups when linked together they gives rise to the formation of 6-methyl salicylic acid. This was found when using labeled carbon in certain Penicillium species.

Acetate occupies a central position in relation to the general metabolism of plants. Acetate condensation occurs in many possible routes which give rise to variety of aromatic compounds. Acetic acid is the starting unit in the biosynthesis of a wide variety of straight chain and aromatic natural compounds. Acetate hypothesis: building block of acetate biosynthesis is linear poly acetic chain $CH_3CO-(CH_2\_CO)_n-CH_2\_COOH$ formed by repeated head to tail condensation of acetate units.


CH3
*COOH
CH3
*COOH
CH3—*COOH
CH3
*COOH
OH
*COOH
CH3

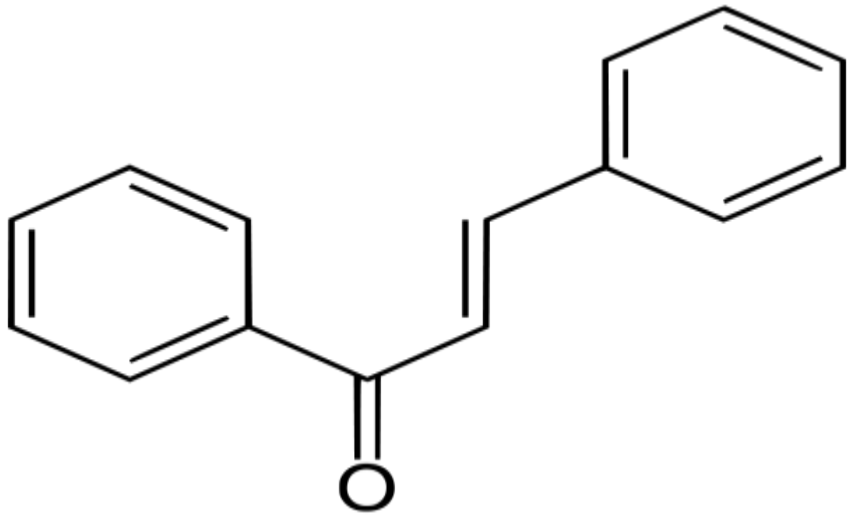
Flavonoids(or) **bioflavonoids**

Dr:Thukaa Zuhair abdul-jalil

Lec. 3

Flavonoids (or bioflavonoids)

(From the Latin word *flavus* meaning yellow, their color in nature) is a class of plant secondary metabolites. Flavonoids are polyphenolic compounds, which constitute one of the most characteristic classes of compounds in higher plants. The flavonoids have aroused considerable interest recently because of their potential beneficial effects on human health. They have been reported to have antitumor and antioxidant activities. They are aromatic secondary plant metabolites, basic structure consist of 15C atom and built up on a C6-C3-C6



Two benzene rings which are joined together with a short three carbon chain, the 3C bridge between the two phenyl groups is commonly cyclized with oxygen.

They are glycoside compound consist of 2 parts (aglycone) which is responsible for pharmacological activity or therapeutic effect and (glycone) part sugar part which have no pharmacological activity but it increase solubility and absorption of aglycone through human body.

Flavonoids are found in most plant material. The most important dietary sources are fruits, tea and soybean. Green and black tea contains about 25% flavonoids; other important sources of flavonoids are apple (quercetin), citrus fruits (rutin and hesperidin).

Flavonoids are powerful antioxidant and their activity is related to their chemical structures, they are belong to the class of plant phenolic, those substance derived from shikimate and phenyl propanoid metabolism are:

The major classes of plant phenols:

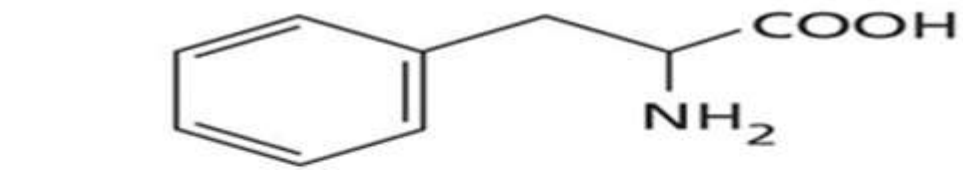
Basic skeleton	Class	Example
C6	Simple phenol	Catechol
C6-C1	Phenol acid	Salicylic acid
C6-C3	OH-cinnamic acid	Ferulic acid
C6-C3-C6	Flavonoids	

Function of flavonoids in plant:

1. Flavonoids the widest group of natural products, contribute the color of the plants. They have varied functions in plant tissues for the healthy growth and proliferation of the plants.
2. Flavonoids in plants are implied in the pigment characteristics, in plant growth and development.
3. Flavonoids have a function in screening the plants from ultraviolet radiation.

Biosynthesis of Flavonoids

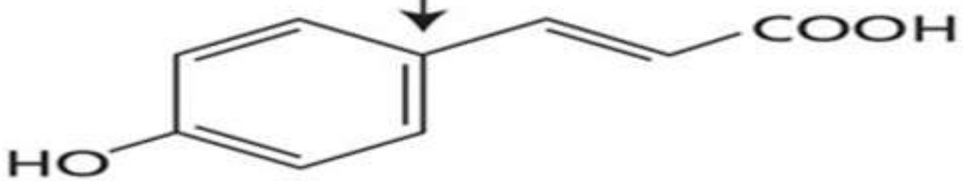
Flavonoids are synthesized by the phenyl-propanoid metabolic pathway (shikimic acid pathway) in which the amino acid phenylalanine first undergo deamination to give cinnamic acid or called coumaric acid which is then hydroxylated at the (para) position to produce (4-hydroxycoumaryl or cinnamyl-CoA) or called *p*-hydroxy coumaryl or cinnamyl CoA which is then combined with three acetate molecules to yield the true backbone of flavonoids, a group of compounds called chalcone, which contain two phenyl rings. Conjugate ring-closure of chalcone results in the familiar form of flavonoids



Phenylalanine

NH_3 ← Phenylalanine ammonia lyase (deamination)

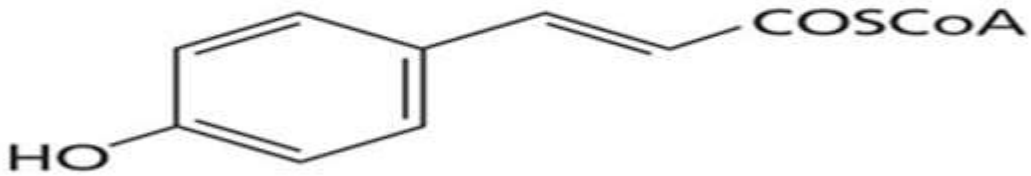
Cinnamic acid



hydroxylation at para

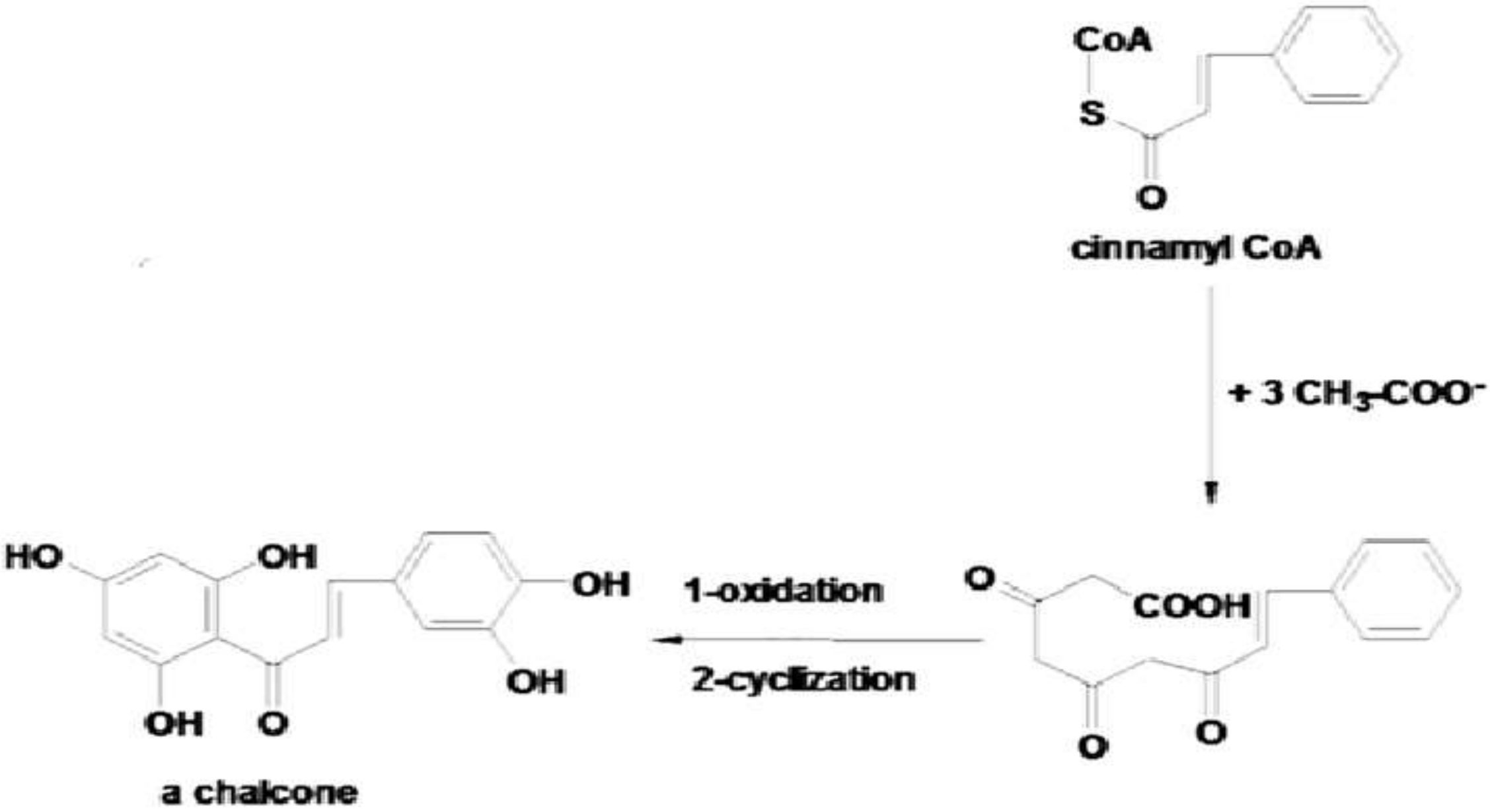
***p*-Coumaric acid**

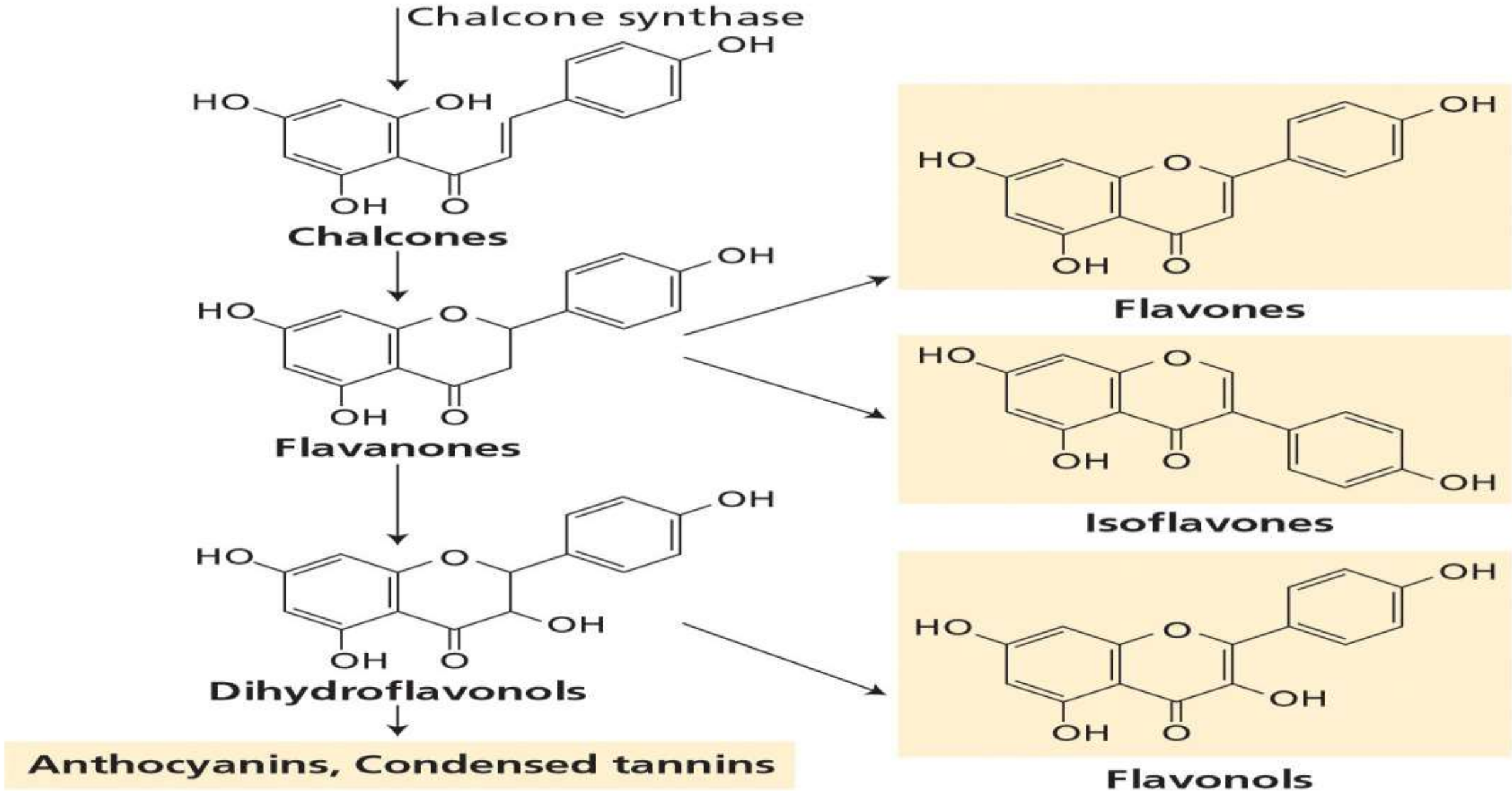
CoA-SH → activation by CoASH



***p*-Coumaroyl-CoA**

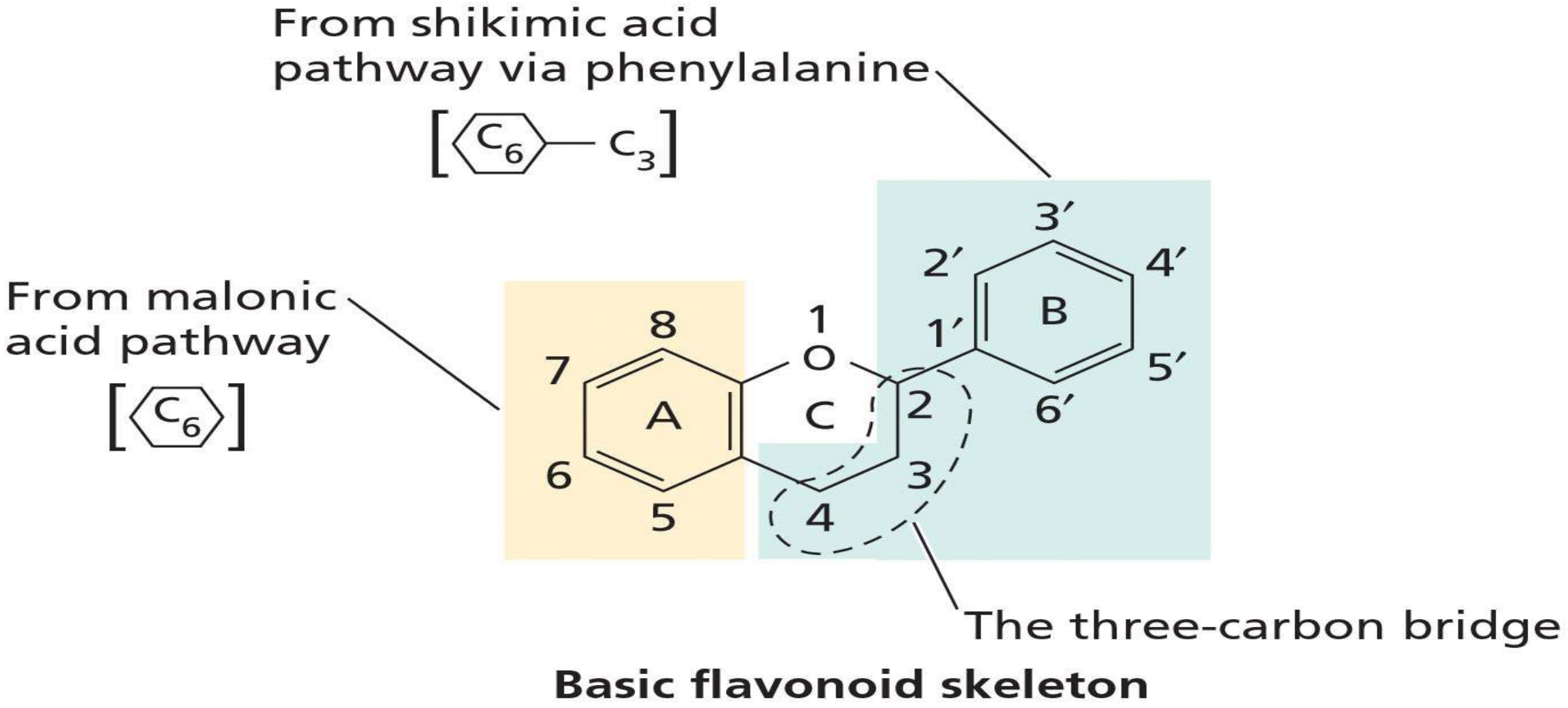
3 Acetate molecules →


CoA
S
O
cinnamyl CoA
+ 3 CH3-COO-
COOH
O
O
O
1-oxidation
2-cyclization
HO
OH
OH
OH
O
a chalcone



PLANT PHYSIOLOGY, Third Edition, Figure 13.10 (Part 2) © 2002 Sinauer Associates, Inc.

Flavonoids are therefore of mixed biosynthesis, consisting of units derived from both shikimate and acetate pathways.



Basic flavonoid skeleton

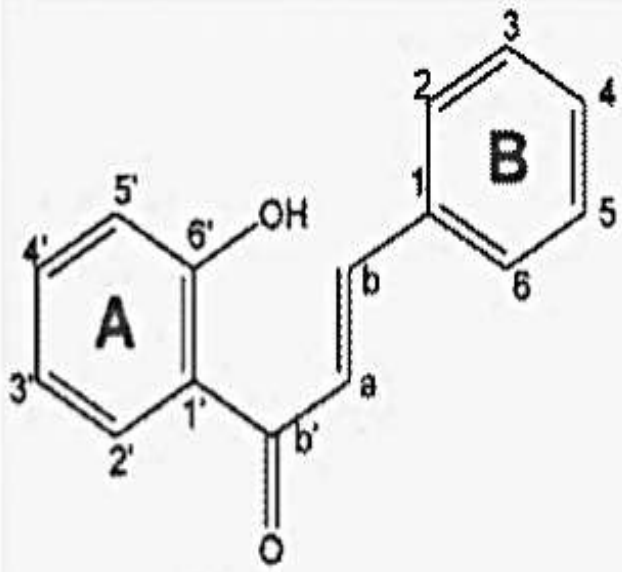
PLANT PHYSIOLOGY, Third Edition, Figure 13.12 © 2002 Sinauer Associates, Inc.

Chemical classification of flavonoids:

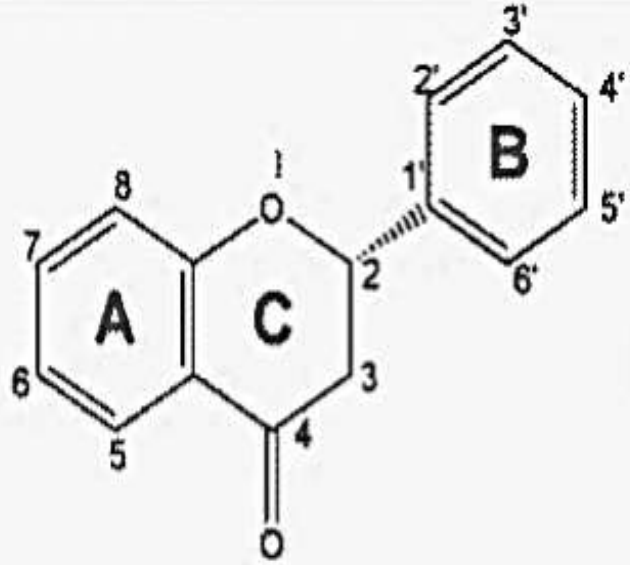
Several classes are differentiated according to

1. the degree of un saturation,
2. degree of oxidation of the three carbon segment
3. based on the number and nature of substituent groups attached to the rings.

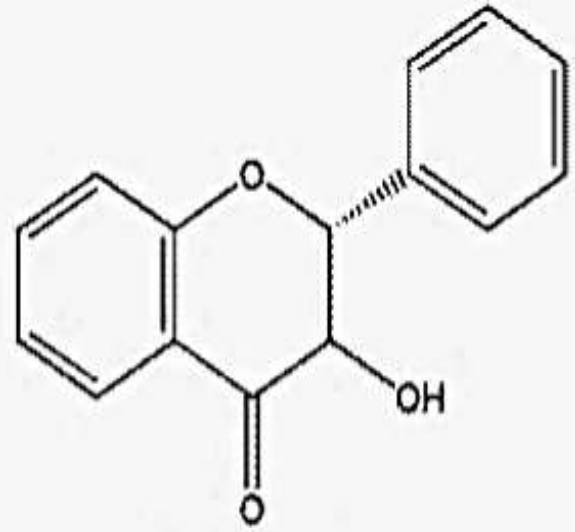
So we have different sub-groups of Flavonoid.



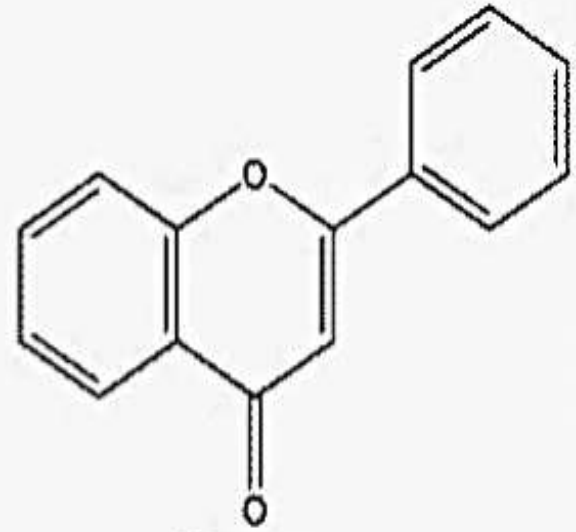
Chalcone



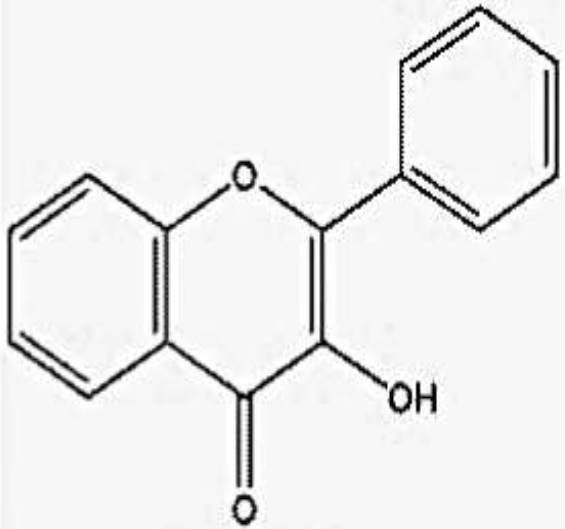
Flavanone



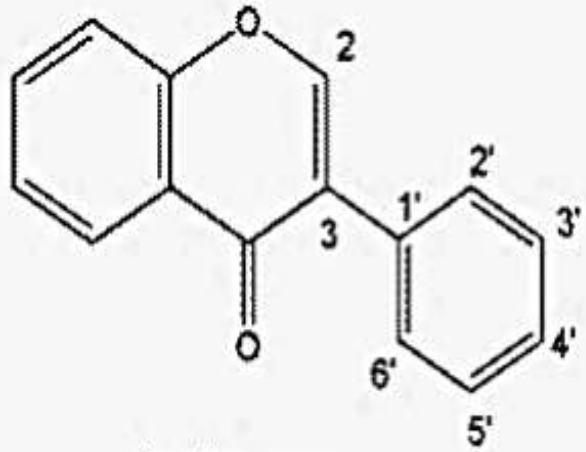
Flavanonol



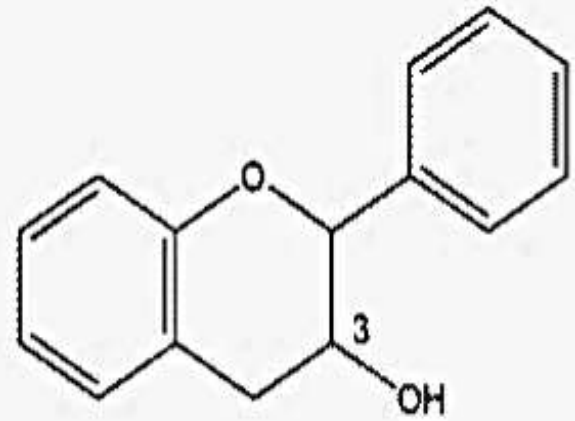
Flavone



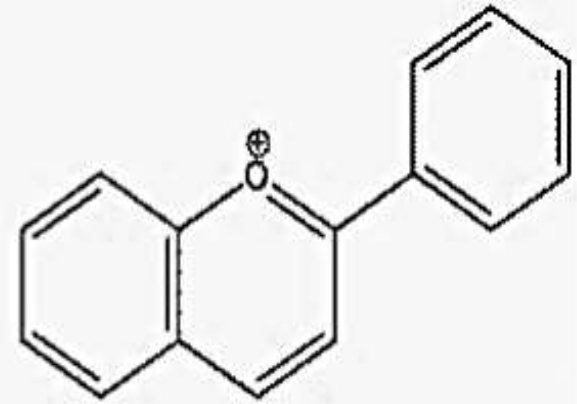
Flavonol



Isoflavone



Flavan-3-ol



Anthocyanidins

Any of the OH- group can be glycosylated but certain position favors glycosylation: **7**-hydroxyl in flavones and isoflavones. **3** and **7**-OH in flavonol. **3** and **5** hydroxyl in flavan. Glucose is the most commonly encountered sugar with galactose, rhamnse and fructose.

Glycosylation has a profound effect on the flavonoids rendering it more water soluble, permitting storage of flavonoids in the cell vacuole where they are commonly found. Glycosylation may also occur by direct linkage of the sugar to the benzene nucleus by C-C bond.

(FLAVONOIDS)
Pharmacological action

Dr:Thukaa Zuhair abdul-jalil

Lec. 4

Antioxidant activity(free radicals scavenging)

Body cells and tissues are continuously threatened by the damage caused by free radicals and reactive oxygen species, which are produced during normal oxygen metabolism or are induced by exogenous damage , Flavonoids can prevent injury caused by free radicals in various ways**. One way is the direct scavenging** of free radicals. Flavonoids are oxidized by radicals, resulting in a more stable, less-reactive radical. In other words, flavonoids stabilize the reactive oxygen species by reacting with the reactive compound of the radical. Because of the high reactivity of the hydroxyl group of the flavonoids, radicals are made inactive, according to the following equation :-

Flavonoid(OH) +R• ➡ flavonoid(O•) + RH

where R• is a free radical and O• is an oxygen free radical

Indirect action: flavonoids also interfere with inducible nitric-oxide synthase activity . Nitric oxide is produced by several different types of cells, including endothelial cells and macrophages. the much higher concentrations of nitric oxide produced by inducible nitric-oxide synthase in macrophages can result in oxidative damage. Nitric oxide reacts with free radicals, thereby producing the highly damaging peroxynitrite. When flavonoids are used as antioxidants, free radicals are scavenged and therefore can no longer react with nitric oxide, resulting in less damage also nitric itself can directly scavenged by flavonoids .

Characteristics of flavonoid structure for most effective radical-scavenging activity:

1. The catechol (O-dihydroxy) group in the ring A confers great scavenging ability.

2. A pyrogallol (trihydroxy) group in ring B of a catechol, as in myricetin, produces even higher activity.

3. The C2-C3 double bond of the C ring appears to increase scavenger activity because it confers stability to the phenoxy radical produced.

4. The 4-oxo (keto double bond at position 4 of the C ring), especially in association with the C2-C3 double bond, increases scavenger activity by delocalizing electrons from Bring.

5.The 3-OH group on the C ring generates an extremely active scavenger; in fact, the combination of C2-C3 double bond and 4-oxo group appears to be the best combination on the top of the catechol group

6.The 5-OH and 7-OH groups may also add scavenging potential in certain cases**.**

Anti-inflammatory effects :

Cyclooxygenase and lipoxygenase play an important role as inflammatory mediators. They are involved in the release of arachidonic acid, which is a starting point for a general inflammatory response. Selected phenolic compounds were shown to inhibit both the cyclooxygenase and 5-lipoxygenase pathways. This inhibition reduces the release of arachidonic acid thus diminishing the formation of these inflammatory metabolites.

Another anti inflammatory feature is the ability of flavonoids to inhibit eicosanoid biosynthesis Eicosanoids, such as prostaglandins, are involved in various immunologic responses and are the end products of the cyclooxygenase and lipoxygenase pathways. **Another** anti inflammatory property of flavonoids is their suggested ability to inhibit neutrophil degranulation. This is a direct way to diminish the release of arachidonic acid by neutrophils and other immune cells.

Antitumor effects

The antitumor activity of flavonoids is still a point of discussion. Antioxidant systems are frequently inadequate, and damage from reactive oxygen species is proposed to be involved in carcinogenesis . Reactive oxygen species can damage DNA, and division of cells with unrepaired or mis-repaired damage leads to mutations. If these changes appear in critical genes, such as oncogenes or tumor suppressor genes, initiation or progression may result. Reactive oxygen species can interfere directly with cell signaling and growth. The cellular damage caused by reactive oxygen species can induce mitosis, increasing the risk that damaged DNA. Flavonoids, as antioxidants, can inhibit carcinogenesis by inhibiting cell proliferation **(potent growth inhibitory effects on several malignant tumor cell)** by inhibiting several biochemical events associated with cellular growth example : **Quercetin** impeded aerobic glycolysis in tumor cell ,**Kaempferol** inhibit DNA, RNA and protein synthesis in the tumor cell. **Other flavonoids** may inhibit both cytosolic & membranal Tyrosine Kinase ezn which play very important role in the signal transduction pathway that regulates cell proliferation.

Hepatoprotective effect :

Silymarin, Quercetin & Rutin possess a powerful antioxidant activity which help to prevent free radical oxidative damage to cells also help in the treatment & prevention of alcohol and chemical-induced hepatotoxicity by **increase Glutathione in the liver,** Glutathione responsible for detoxifying a wide range of drugs & chemicals which cause liver damage **also increased protein synthesis** in the liver this action has important therapeutic implications in the repair of damaged hepatocytes and restoration of normal functions of liver.

Effect on blood vessels

Rutin and Hesperidin have been called **vitamin P or Permeability factors** they have been used in the treatment of various conditions characterized by capillary bleeding & increased capillary fragility.

When **reactive oxygen species** are in the presence of iron, lipid peroxidation results. Specific flavonoids are known to chelate iron , thereby removing a causal factor for the development of free radicals**.** **Quercetin** in particular is known for its iron-chelating and iron-stabilizing properties so provide direct inhibition of lipid peroxidation flavonoids may have preventive action against atherosclerosis.

Flavonoid drugs

Dr:Thukaa Zuhair abdul-jalil

Lec.5

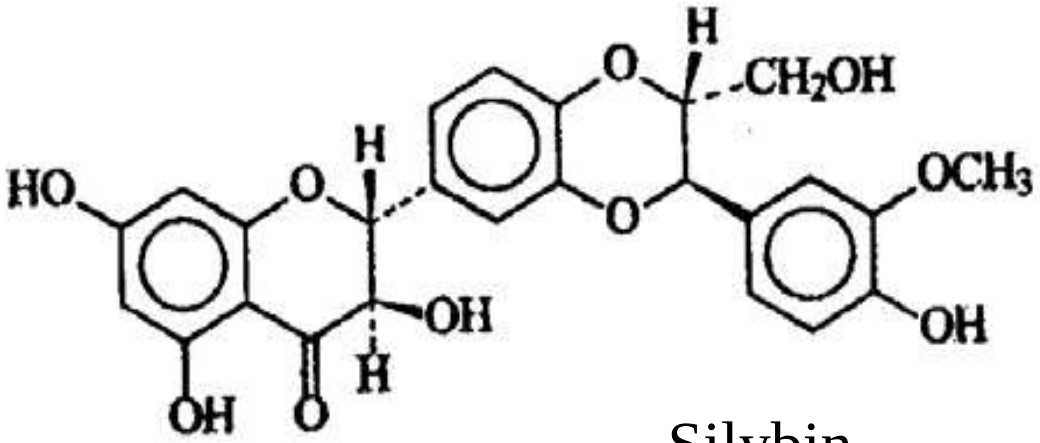
Drugs:

Silymarin

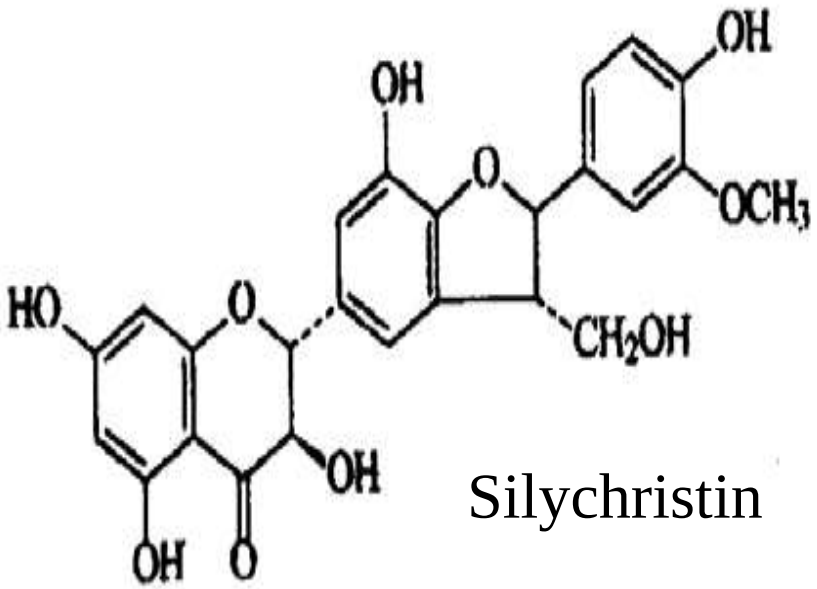
is a flavonoids mixture of silybin, silychristin and silydianin, which is obtained from seeds of Milk thistle *Silybum marianumn (L). Family Asteraceae* chemical formula: (C25H22O10) شوك الحليب

USES

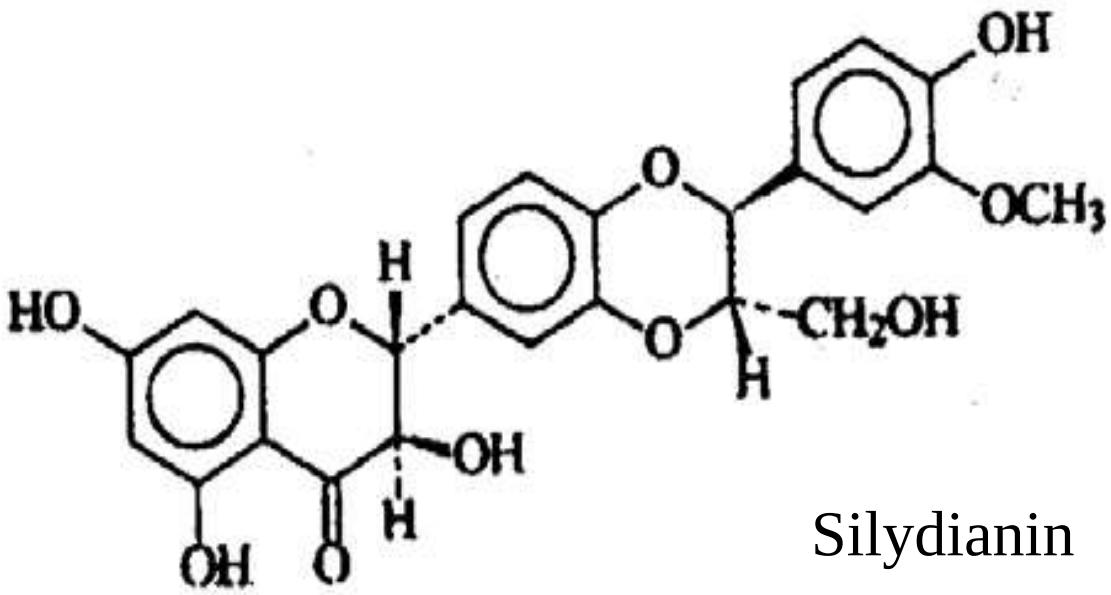
1. Lowering cholesterol levels.
2. Reduces cell damage caused by radiation and chemotherapy treatments.
3. Reducing insulin resistance in people with type 2 diabetes who also have cirrhosis.
4. Reducing the growth of cancer cells in breast, cervical, and prostate cancers.
5. Alzheimer's disease prevention or treatment.



Silybin



Silychristin

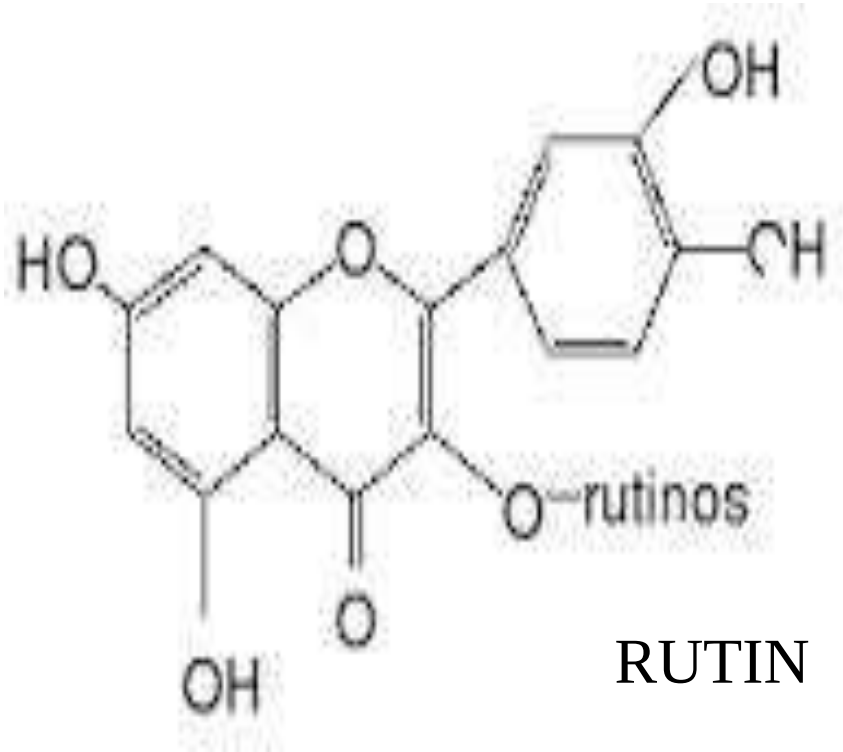


Silydianin

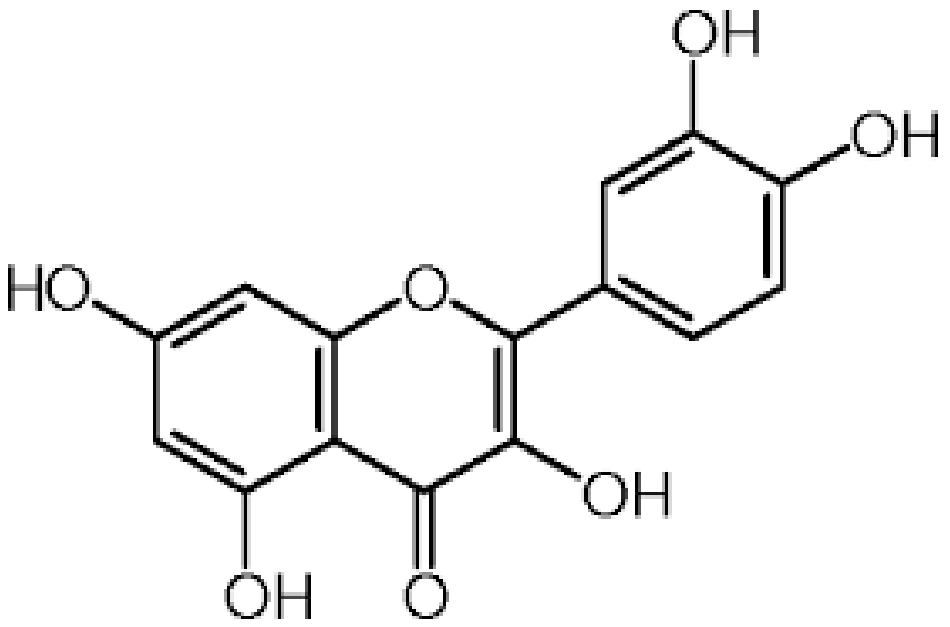
Quercetin

is a tetraoxyflavonol, is a plant-derived flavonoid. It can be found in nature not only alone(as an aglycone), but also as a glycosides, the non-sugar compound remaining after replacement of the glycosylic group from a glycoside by a hydrogen atom. Quercitrin and rutin are two examples of glycosides containing quercetin as an aglycone.

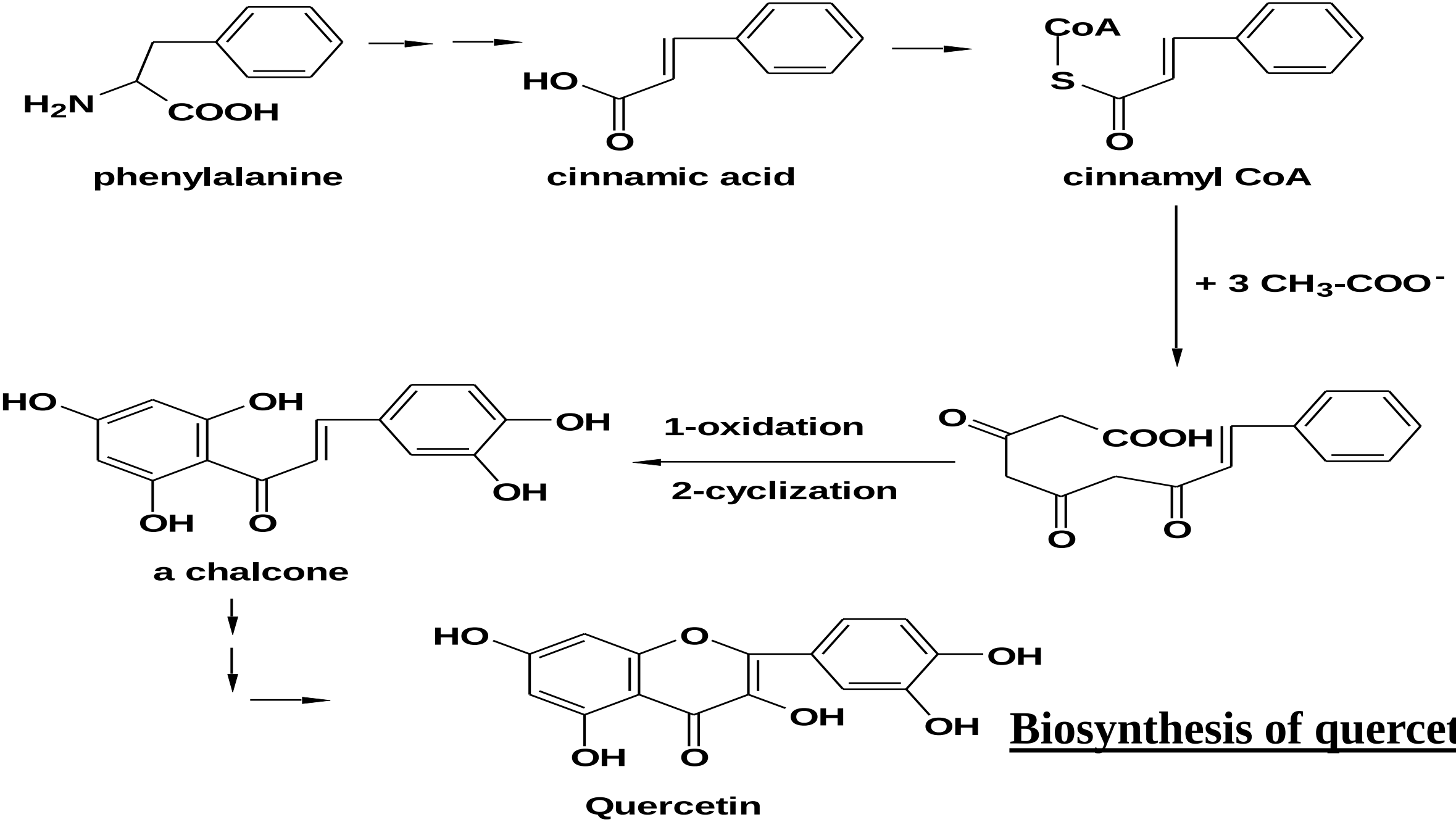
USES: Quercetin has powerful antioxidant role in the cell. This function helps to reactivate tocopherol (i.e. vitamin E), work off superoxide ions, which are reactive oxygen species (ROS). ROS can be accumulated in the skin when it is exposed in an excessive manner, in terms of time or intensity, to sunrays. Also, quercetin blocks the production of nitric oxide (NO) (Inhibition of inducible nitric oxide synthase and cyclooxygenase-2 during inflammation.



RUTIN



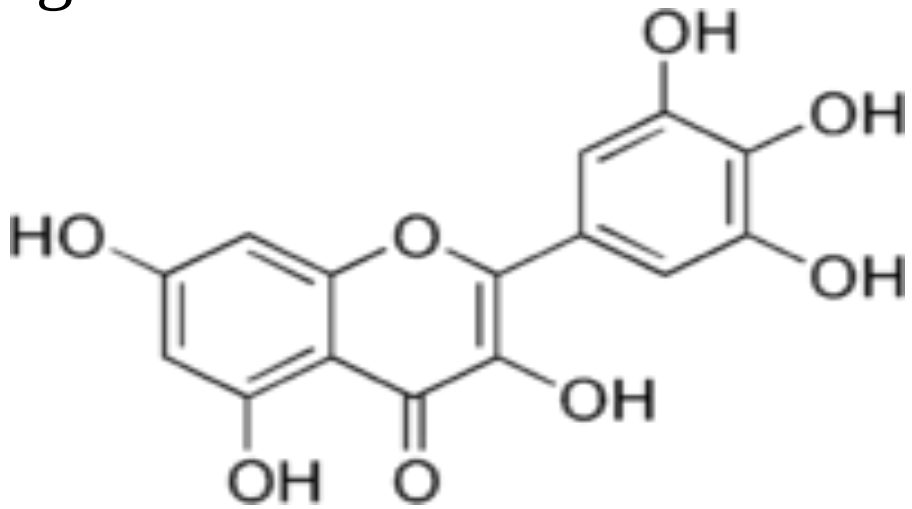
QUERCETIN


H2N
COOH
phenylalanine
HO
O
cinnamic acid
CoA
S
O
cinnamyl CoA
+ 3 CH3-COO-
O
COOH
O
O
1-oxidation
2-cyclization
HO
OH
OH
OH
O
a chalcone
HO
O
OH
OH
OH
O
Quercetin
Biosynthesis of quercetin

Myricetin

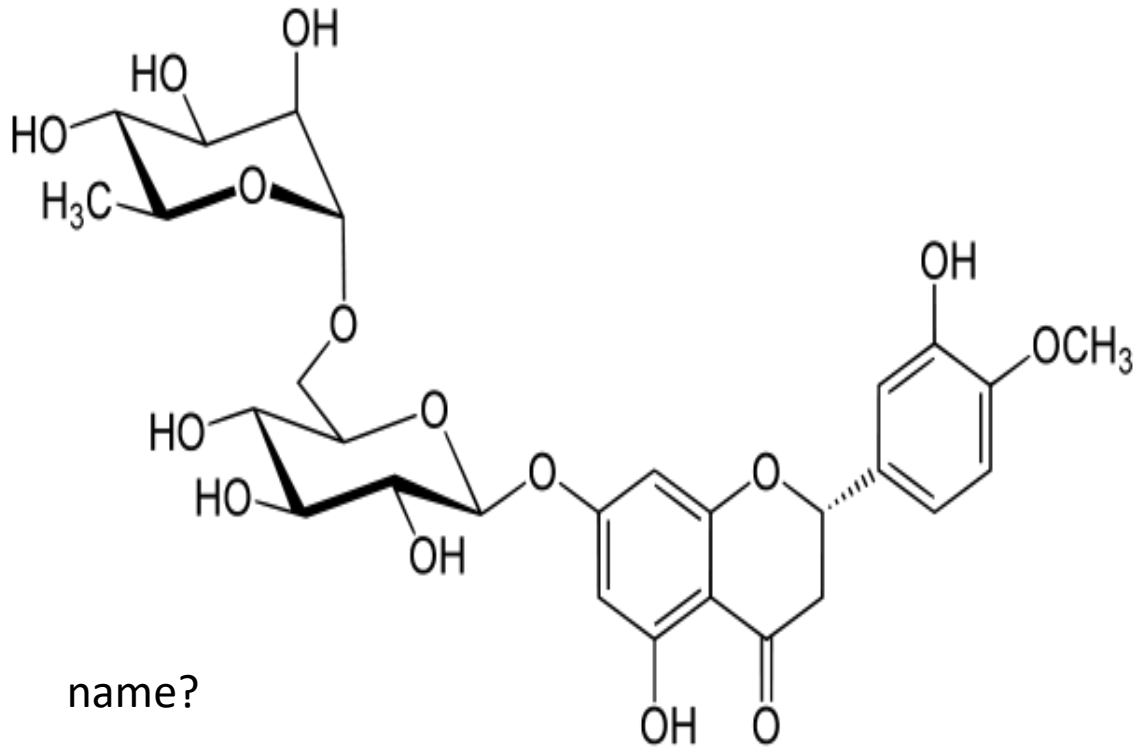
is a flavonoid, which means it is a natural polyphenolic compound with antioxidant properties. It is commonly derived from vegetables, fruits, nuts, berries, tea.

USES : Myricetin is very effective in protecting cells from carcinogenic mutation. Myricetin provided protection against most type of tumors by different mechanisms like free radical scavenger action.

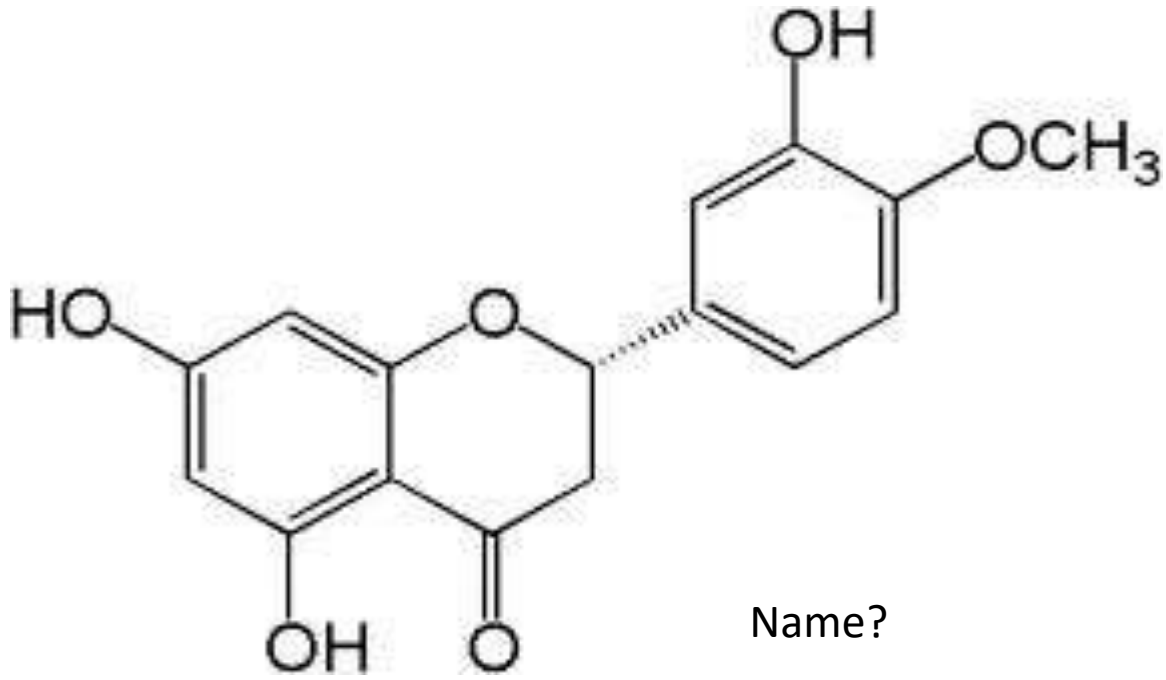


Hesperidin (glycoside) & Its aglycone (hesperetin)

Found in high concentration in fruit of citrus trees.



name?



Name?

Volatile Oils

Dr:Thukaa Zuhair abdul-jalil

Lec:6

Volatile Oils

Are the odorous principles found in various plant parts , because they evaporate when exposed to air at ordinary temperatures, they are called volatile oils ,ethereal oil or essential oils. The last term applied because vol. oils represent the(essence).or odoriferous constituents of the plants.vol. oils are colorless as rule, particularly when they are fresh but on long standing they may be oxidize and resinify thus darkening in color. To prevent this darkening they should be stored in a cool, dry place in tightly stoppered amber glass container.

Distribution:

Essential oils occur virtually only in higher plants, there are 17,500 aromatic species.

Myrtaceae, Lauraceae, Rutaceae, Lamiaceae, Astraceae, Apiaceae. Cupressaceae, Poaceae, Zingiberaceae, and Piperaceae.

Volatile oils may formed directly by the protoplasm by decomposition of the resingenous layer of the cell wall, or by the hydrolysis of certain glycosides. frequently associated with other substances like gums, resins.

Several point of differentiation exit between volatile oils and fixed oils:

Volatile oils:

- not glyceryl esters of fatty acids

-do not leaves permanent grease spot in paper

-not saponified with alkali

– not become rancid but on exposure to air and light becomes oxidized and resinify

Function of Essential oils:

The biological function of essential oils remains obscure

Allelopathic, particularly germination inhibitors

Protection against predators (insect and fungi)

Attraction of pollinating species

Therapeutic action:

Oil of eucalyptus: Bronchitis and Mucolytic.

Oil of lemon: flavouring

Oil of turpentine: starting materials for the synthesis of other compounds

Those oils with a high phenol content, e.g. clove and thyme have antiseptic properties. Carminatives, antispasmodic activity are much used in popular medicine as those of *Rosmarinus officinalis, Mentha piperita, Matricaria chamomilla, Foeniculum vulgare, Carum carvi and Citrus aurantium*.

Volatile oils are stated to interfere with respiration and electron transport in a variety of bacteria, hence accounting for their use in food preservation and in cosmetic preparations.

Physical properties of Essential Oils

They possess **characteristic odors**, they are characterized by **high refractive index** ,most of them are **optically active** and their **specific rotation** is often a valuable diagnostic property also vol. oils are **immiscible** with water but soluble in ether , alcohol and most organic solvents.

Chemistry of Volatile Oils:

*Volatile oils vary widely in the chemical composition almost any type of organic compound may be found in vol. oils (hydrocarbon, alcohols ,ketones, aldehydes---------- other).

*V.Oils generally consist of **Eleoptenes** which is hydrocarbon portion of the oil which is liquid and **Stearoptene** which is oxygenated compounds derived from hydrocarbons & it is Solid.

*The odor and taste is mainly determined by the oxygenated constituents which is immiscible in water but more soluble in alcohol.

*Many of them are terpenoids in origin with some containing aromatic derivatives.

Methods of obtaining Volatile Oils

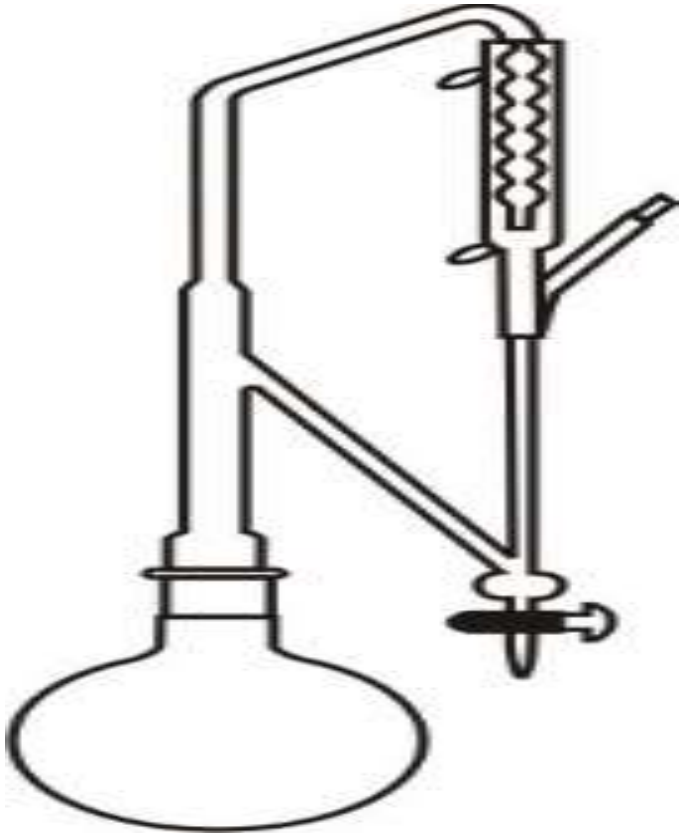
Volatile oils are usually obtained by following different methods, depending upon the conditions of the plant material.

1- Distillation:

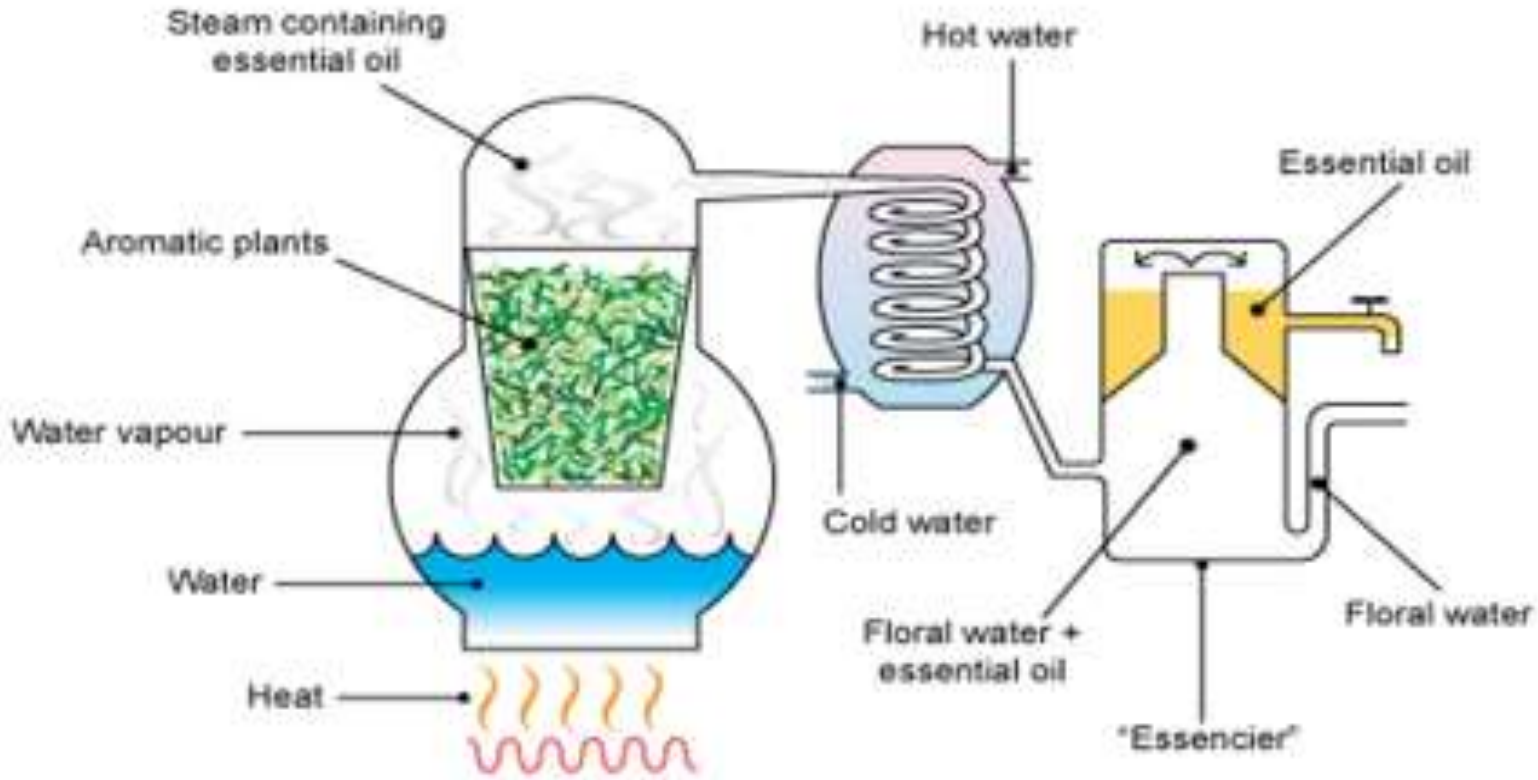
A- Water distillation : applied to plant material that is dried and not subject to injury by boiling

B- Water steam distillation : applied to plant material that is dried or fresh that may be injured by boiling

C- Steam distillation : is employed for fresh plant.



Clavenger apparatus method of distillation

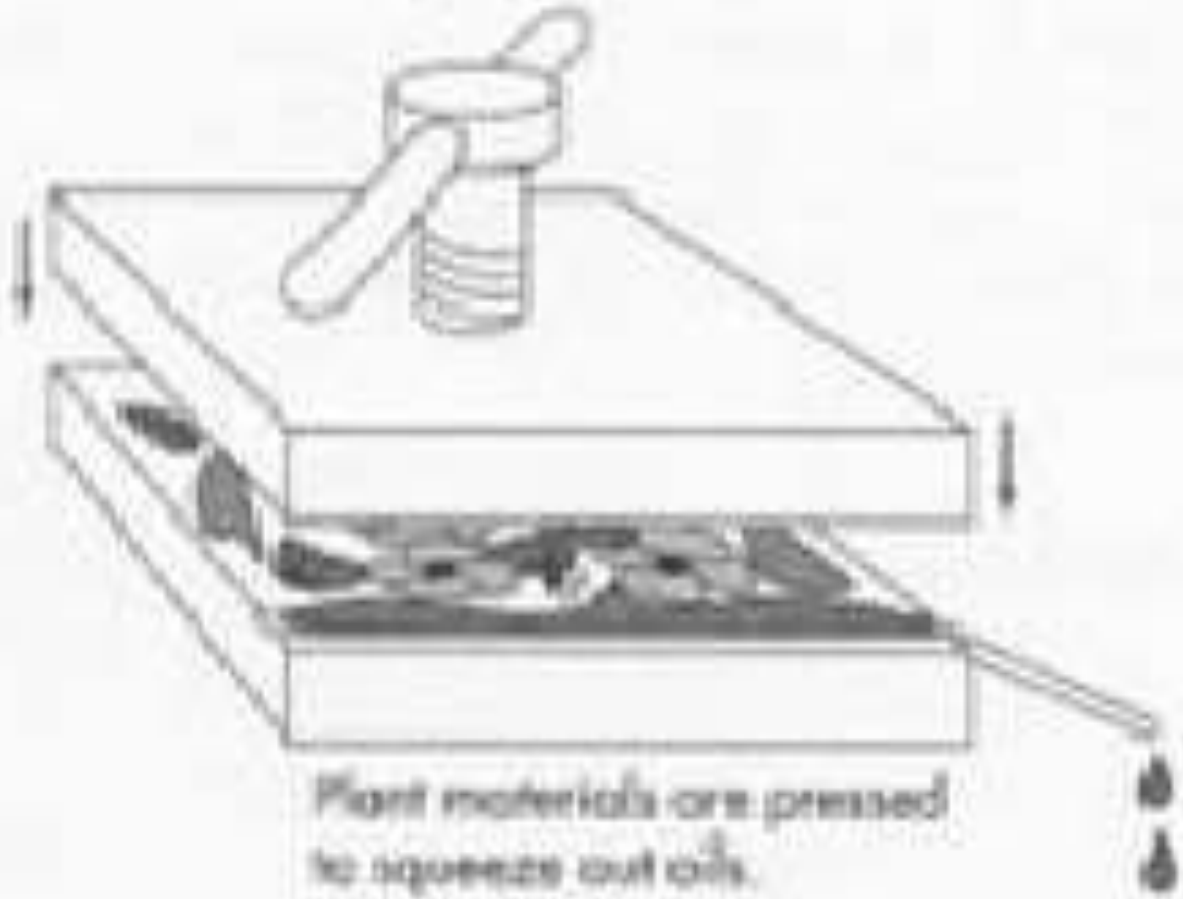


Steam distillation

2. Expression method:

Mostly the citrus oil is obtained by this method. This is a mechanical method in which fruits are rolled over a trough lined with sharp projections just long enough to penetrate the oil glands present in the fruits. The droplets are collected in trough and finally separated. This method is used avoid the decomposition of volatile oils, which will necessarily take place by any other distillation method.

Expression



Plant materials are pressed to squeeze out oils.

3. Enzymatic Hydrolysis:

Glycosidic volatile oils like bitter almond, mustard oil is obtained by enzymatic hydrolysis of glycosides. In bitter almond seeds amygdalin is acted upon by enzyme emulsin resulting in a mixture of constituents from which the volatile oil may be distilled with steam. In black mustard seeds the glycoside, sinigrin is hydrolyzed by the enzyme myrosin with the product of volatile mustard oil.

4. Enfleurage:

This method is especially used for those volatile oils, which are present in such a part which is very small and also liable to decomposition on distillation. In this case odourless and bland fixed oil or fat is spread in a thin layer on glass plates. The part of plant from which V.O has to be extracted say for example flower petal is placed in the fat or fixed oil for some time until its fragrance is removed as the oil or fat will absorb it. Then the petal is removed from the fixed oil or fat and is subjected to extraction with alcohol.

5. Extraction by Solvent:

This is very costly method and is mostly used in perfume industry. The parts containing volatile oil are extracted directly by one of the organic solvents and they are then separated.

Evaluation

- preliminary examination: odor and taste
  - taste, if diluted with a sugar solution in ethanol as prescribed by BP)
- Physical measurements: optical rotation, relative density, refractive index
- to determine individual proportions of components - Gas Chromatography
- volatile oil content in crude drugs - determined by distillation (clavenger method)

Classification of volatile oils

Dr:Thukaa Zuhair abdul-jalil

Classification of volatile oils:

Either according to the **biosynthetic pathways** or according to **the basic structure**.

according to the **biosynthetic pathways**: volatile oils are divided into 2 classes based on their biosynthetic origin:

1. Terpenoid derivatives - acetate - mevalonic acid pathway

2. Aromatic compounds - shikimmic acid - phenyl propanoid pathway

Classification according to the basic structure

1. H.C Volatile Oils
2. Alcohols V.Oils
3. Aldehydes V. Oils
4. Ketones V. Oils
5. Phenols V. oils
6. Phenolic ether V. Oils
7. Oxide V. Oils
8. Esters V. oils

Biosynthesis of Terpenes

Terpenes :- they are defined as natural products whose structure may be divided in to isoprene units (C5H8) , these units arise from acetate by mevalonic acid and are branched – chain, 5- carbon units containing two unsaturated bonds, they are linked in a head to tail fashion to form:

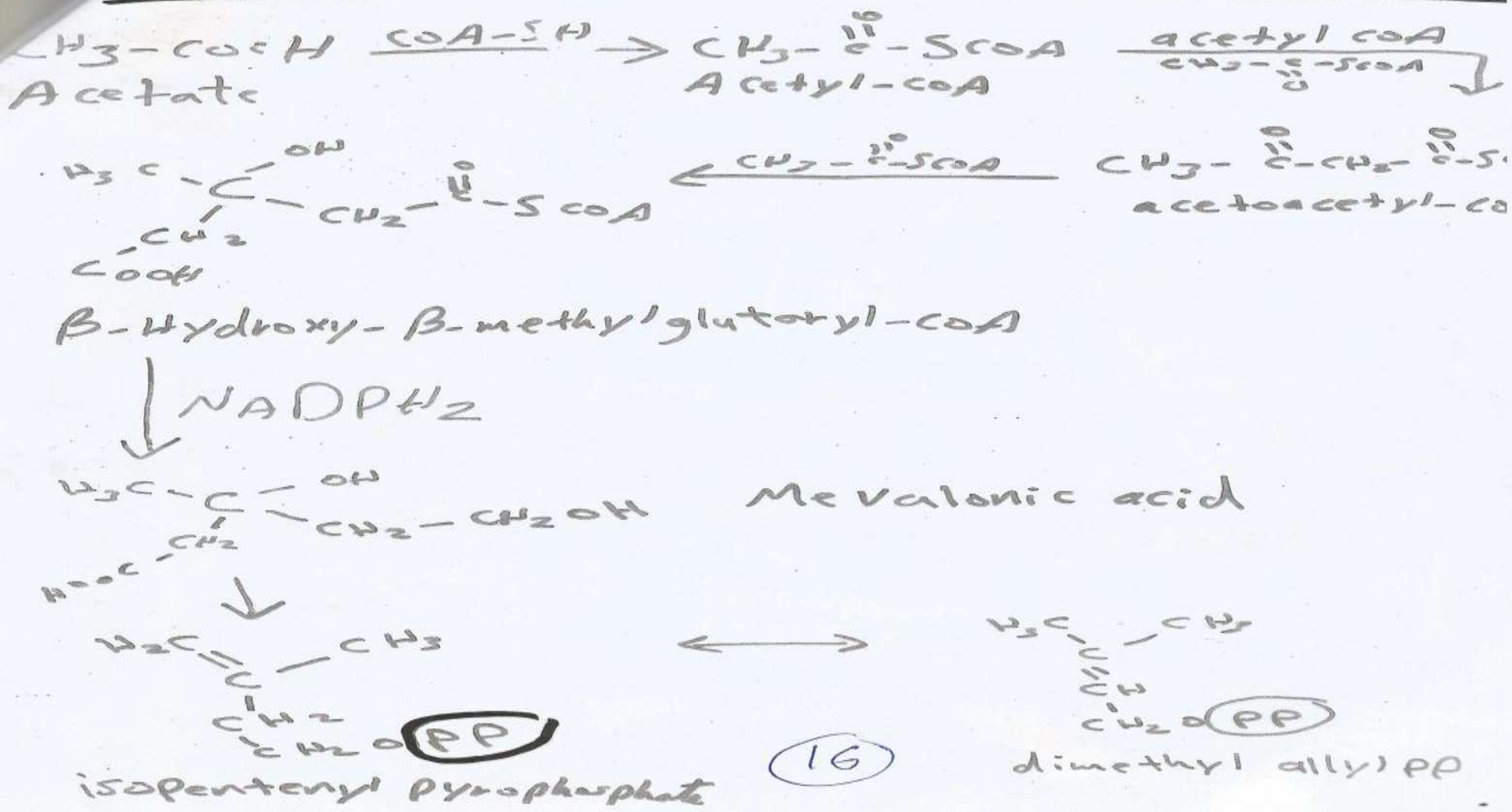
1. Monoterpene (two isoprene units) C10H16

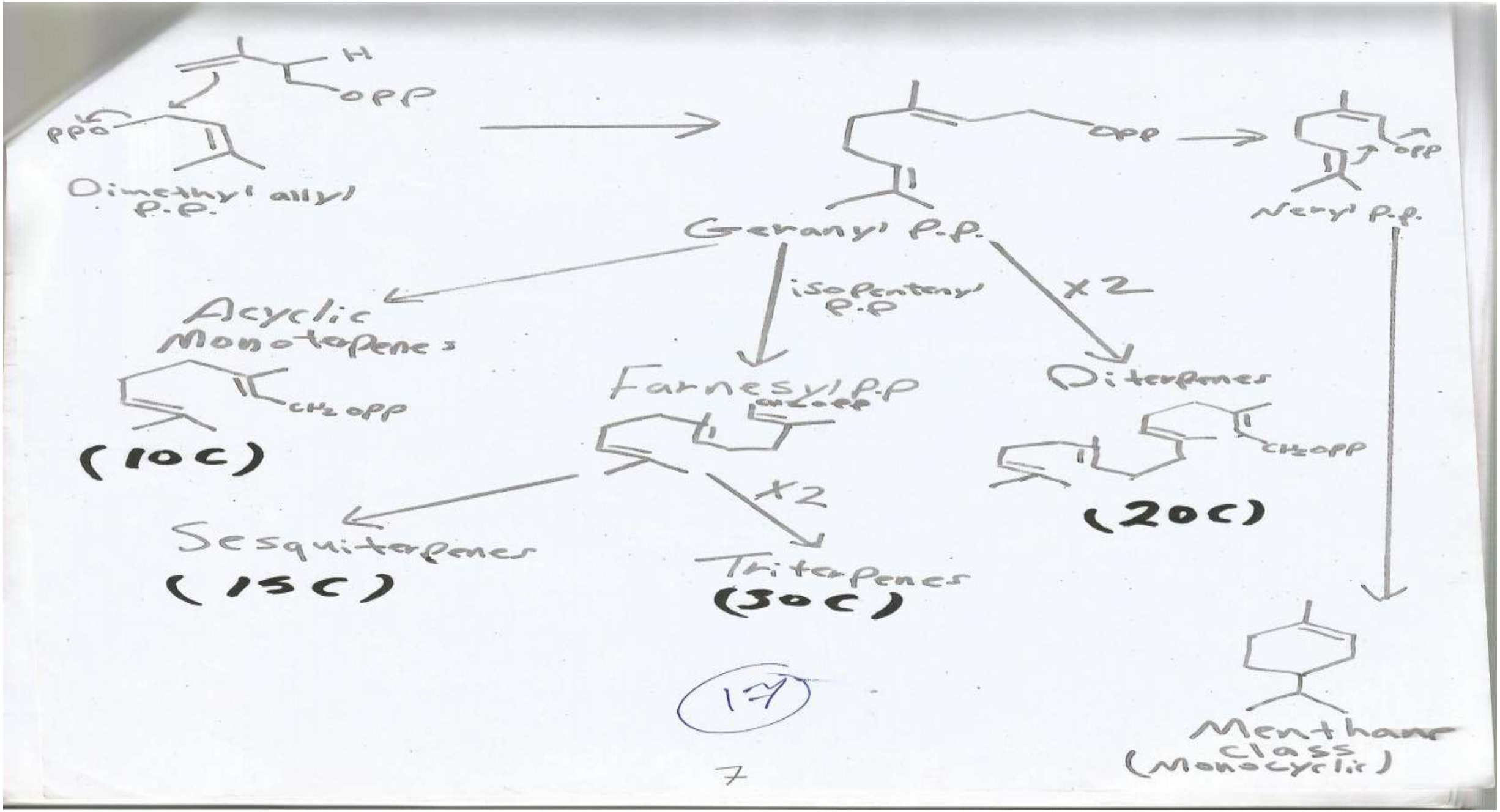
2.Sesquiterpenes (three isoprene units) C15H24

3. Diterpenes (four isoprene units) C20H32

4.Triterpenes (six isoprene units) C30H48

Biosynthesis Pathway of Terpene




H
OPP
OPP
Dimethyl allyl P.P.
Geranyl P.P.
OPP
OPP
Neryl P.P.
Acyclic Monoterpenes
CH2OPP
(10C)
isopentenyl P.P
X2
Farnesyl P.P
OPP
X2
Diterpenes
CH2OPP
(20C)
Sesquiterpenes
(15C)
Triterpenes
(30C)
Menthane Class (Monocyclic)

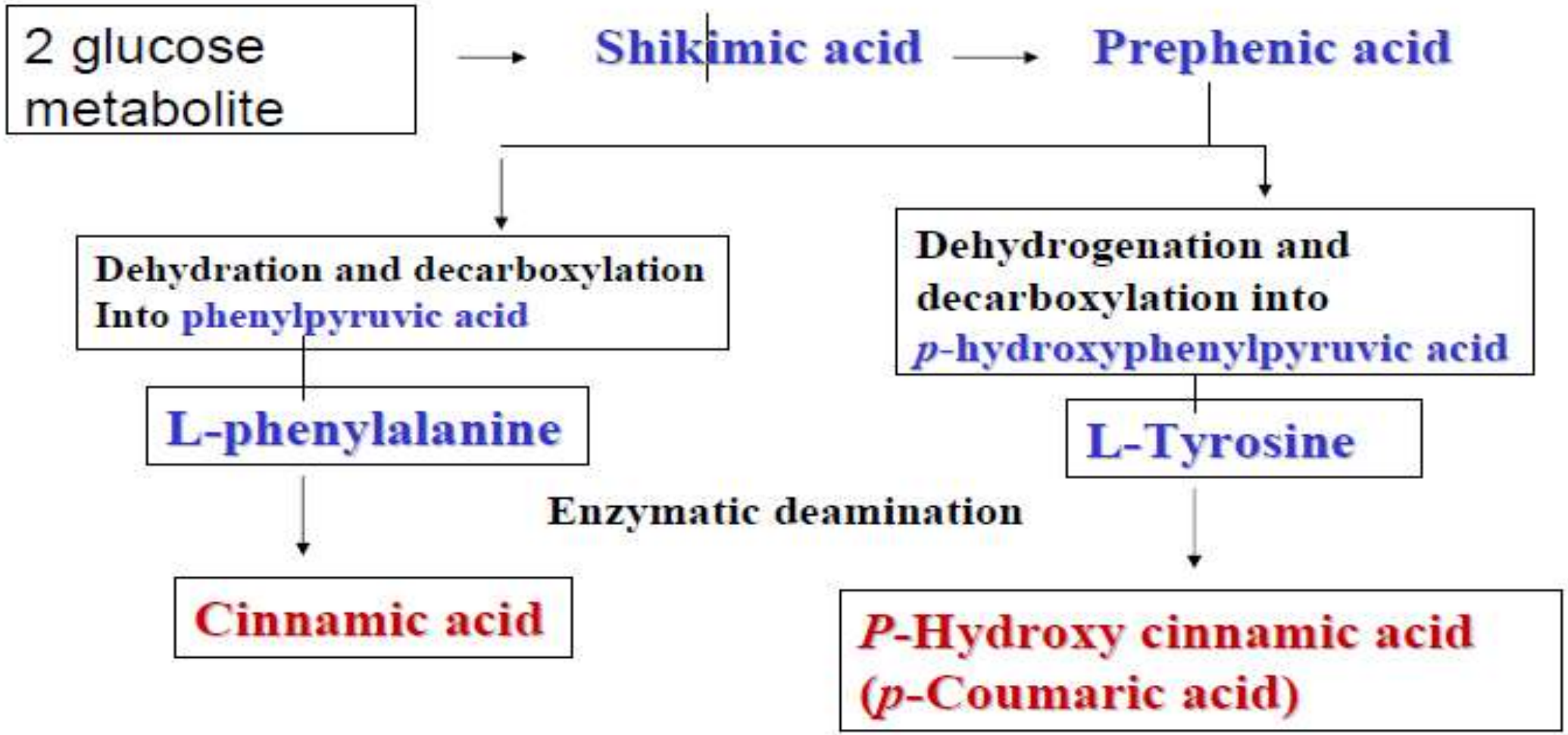
17

Terpene Classification

•Class Name Carbon Number	No. of Isoprene Units & Molecular Formula
• Hemiterpene 5	1 (C5 H8)
• Monoterpene 10	2 (C10 H16)
• Sesquiterpene 15	3 (C15 H24)
• Diterpene 20	4 (C20 H32)
• Triterpene 30	6 (C30 H48)

Biosynthesis of phenylpropanoids

Shikimic acid pathway

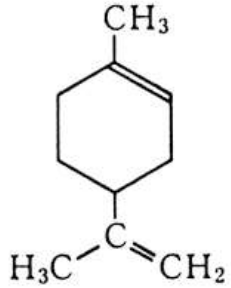


Hydrocarbons volatile oils:

Monocyclic
Dicyclic
Acyclic
Sesquiterpene

Lemon Peel

Synonym: limon
Origin: yellow outer rind of the fresh ripe fruit of *Citrus limon*(Rutaceae)
constituents :terpene (limonene), aldehyde volatile oil,
Coumarins, flavonoids rutin, hesperidin
Use: flavor, stimulant, stomachic, perfume



ALCOHOLIC VOLATILE OILS

Acyclic Alcohols

Monocyclic alcohols

Bicyclic alcohols

Sesquiterpene alcohols

Peppermint oil

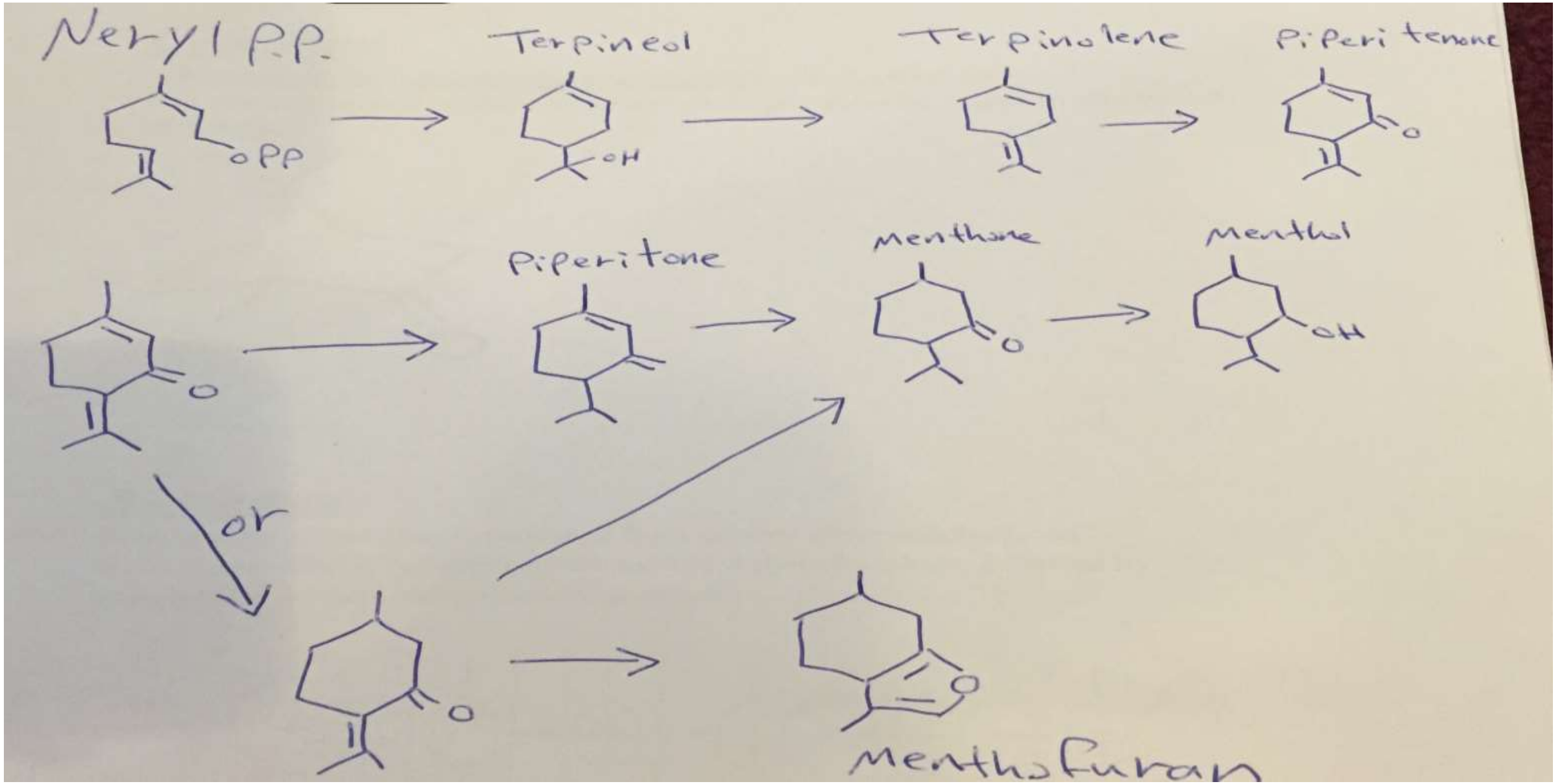
Origin: dried leaves of *Mentha piperita* (Labiatae)
Constituents: menthol, pinene, limonene, resin & tannin
Use: Pharmaceutical aid (flavor), carminative, stimulant, counterirritant, antibacterial, antiviral, antispasmodic, antiflatulence

Adverse:

gallstones, obstructed bile ducts, gall bladder inflammation, severe liver damage

Menthol

used as topical antipruritic in burns and sunburn preparations and in joint pain , counterirritant, antiseptic, stimulant Internally, depressant effect to the heart



Biosynthesis pathway of menthol

Key step in the biosynthesis of menthol appears to be the dehydration of Terpineol to Terpinolene.

NADPH2 is an essential Co-factor in these reduction reaction.

Menthol may be levo (-) Menthol (from natural or synthetic) or racemic (±) Menthol produced synthetically.

Other classes of volatile oil

Dr:Thukaa Zuhair abdul-jalil

Ketone volatile oils

Either:

1.Monocyclic Terpene ketone

2. Di or Bicyclic Ketone

3. Non Terpenic Ketone

The most important drugs of this category are:

Camphor, Spearmint, Caraway

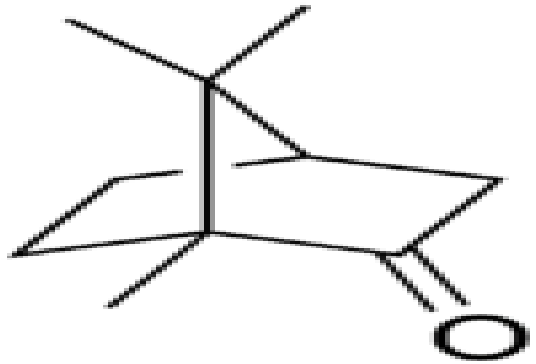
Camphor

Origin: obtained *from Cinnamomum camphora* (F. Lauraceae)

Constituents : Camphor

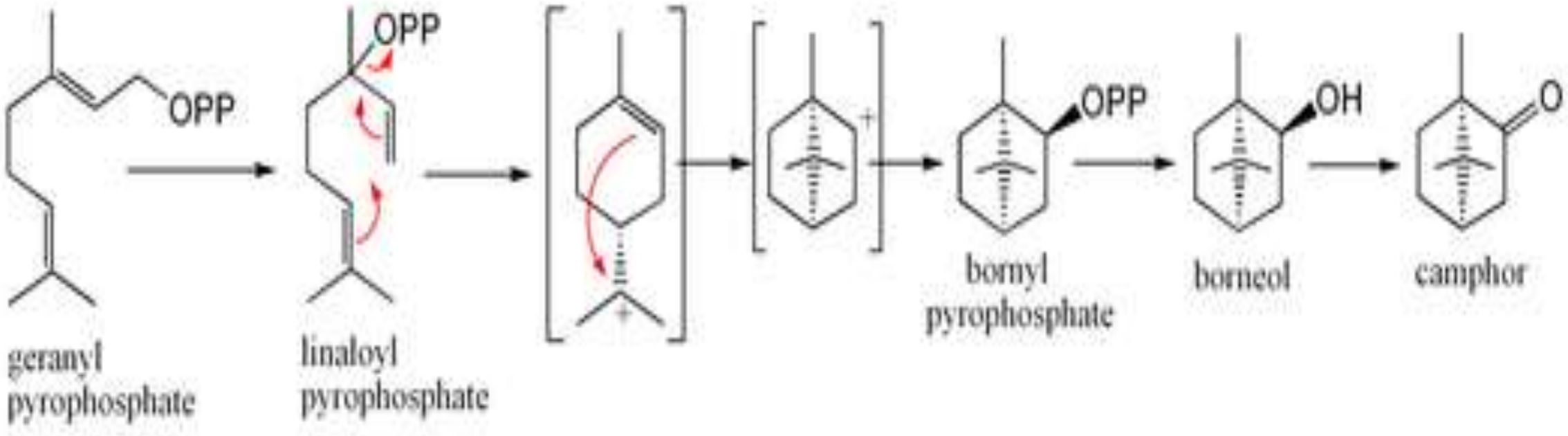
Natural camphor occurs as crystalline product in clefts in the wood of plant.

Use: *Camphor is readily absorbed through the skin and produces a feeling of cooling similar to that of menthol, and acts as slight local anesthetic and antimicrobial substance, anti-itch .*



Biosynthesis

In biosynthesis, camphor is produced from geranyl pyrophosphate, via cyclisation of linaloyl pyrophosphate to bornyl pyrophosphate, followed by hydrolysis to borneol and oxidation to camphor



Aldehydes volatile oils

Acyclic

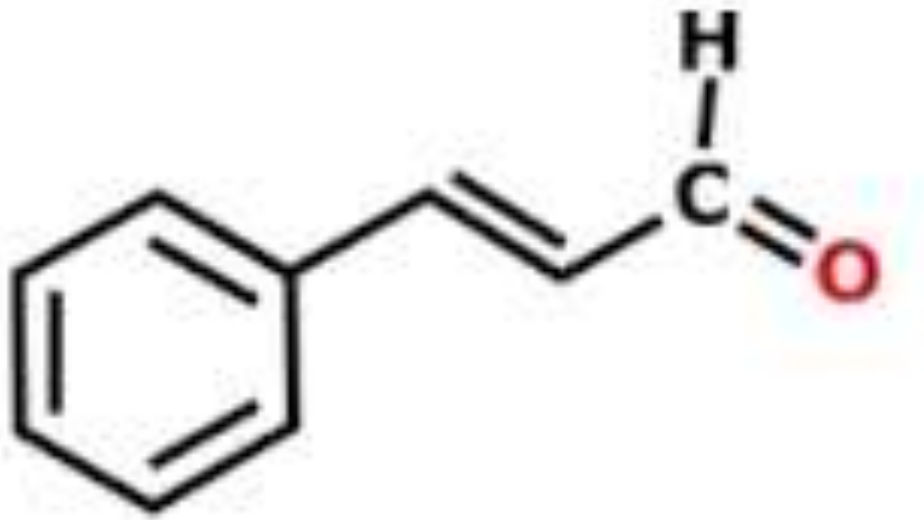
Cyclic

Aldehyde V. Oils are calming to the nervous system. They are best known to relieve stress and promote relaxation.

Cinnamon

Origin :Dried bark of Cinnamomum lureirii (F. Lauraceae)

Constituents :Cinnamon oil contain cinnamaldehyde as a Major compound



Health Benefits of Cinnamon

AnaMariaSerrano.Com

- Reduces blood sugar levels
- Treats bad breath
- Diuretic
- Anti-inflammatory
- Increases blood circulation
- Reduces muscle and join pain and soreness
- Boosts brain activity

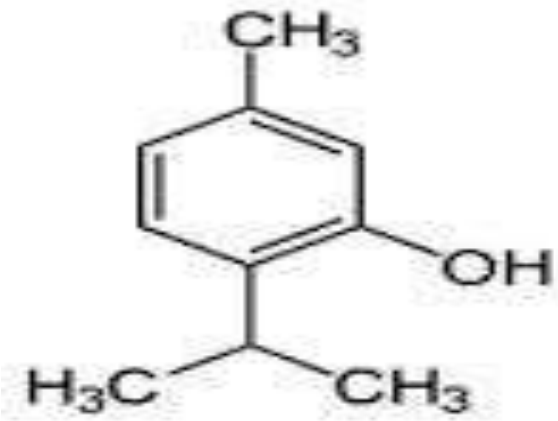
Phenolic volatile oils

Thyme

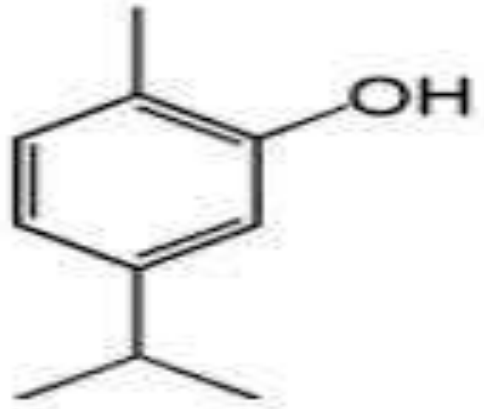
Origin: dried leaves and flowering tops of *Thymus vulgaris* (Labiatae)

Constituents: thymol, carvacrol,

Use: Thymol oil is a powerful antibacterial and antiseptic agent ,thymol was effective against a wide range of bacteria including Echericchia coli, Pseudomonas aeruginosa ,staphylococcus aureus and bacillus



Thymol



Carvacrol

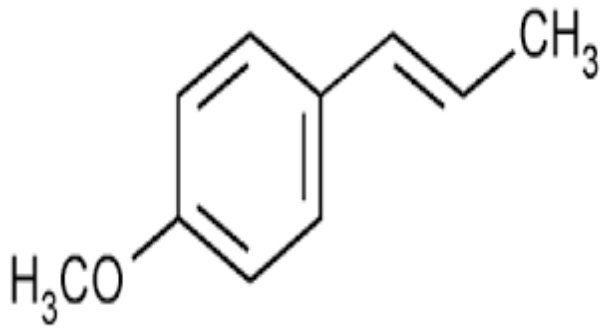
Phenolic ether V. Oils

Anise

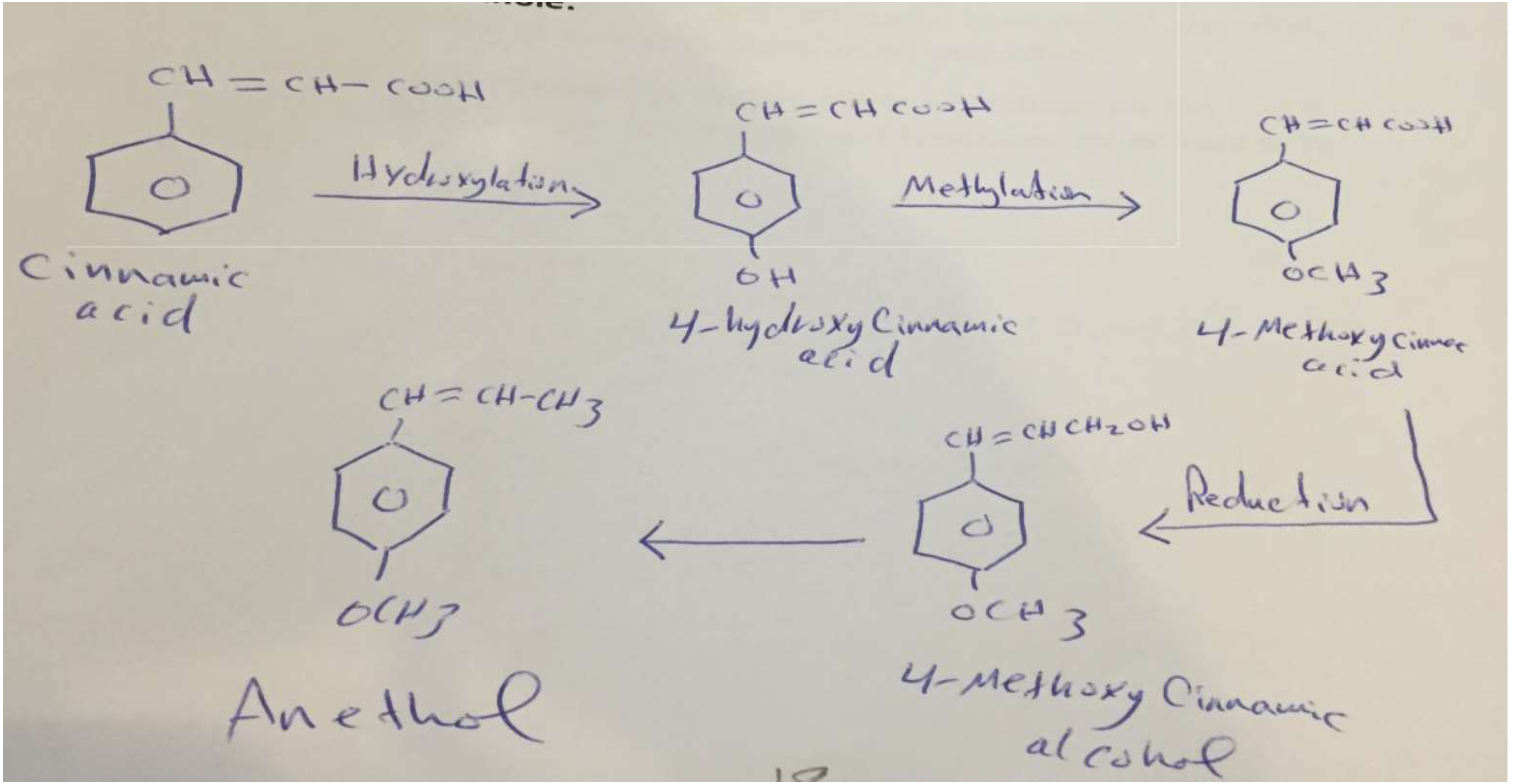
Origin: dried ripe fruits of *Pimpinella anisum* (Apiaceae)

Constituents: volatile oil contains anethole, methyl chavicol, Pinene, Linalool and anisaldehyde

Use: flavor, aromatic stimulant, carminative



Biosynthesis of anethole:



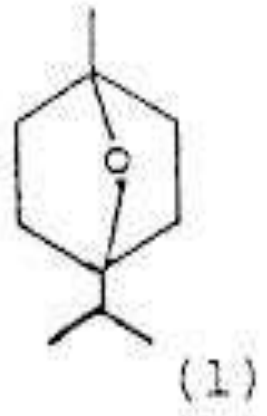
Oxide Volatile oils

Eucalyptus

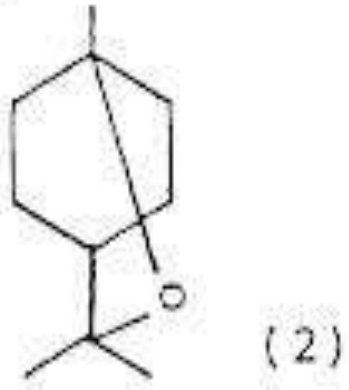
Origin: the dried leaf of *Eucalyptus globulus* (Myrtaceae)

Constituents: volatile oil (1,4-Cineole & 1,8-Cineole) ,resins and tannic acid

Use: alleviate symptoms of nasopharyngeal infections, treat coughs and decongestant.
internally : expectorant.
externally : treat sore muscles and rheumatism.



1,4-cineol



1,8-cineol